AudioDigest

ANESTHESIOLOGY Board Review

3rd EDITION

Written Summaries

Wolters Kluwer

Lecture ANBR19O1O1

Principles of Pharmacology of Local Anesthetics

Mark Dershwitz, MD

The goal of this program is to improve the awareness of current practice in the basic principles of pharmacokinetics and pharmacodynamics of drugs, the role of an individual's genetic makeup in influencing response to medications, and the principles of pharmacology in the treatment of various medical conditions. After hearing and assimilating this program, the clinician will be better able to:

1. *Review the basic principles of pharmacokinetics and pharmacodynamics of drugs.*
2. *Interpret the role of an individual's genetic makeup in influencing response to medications.*
3. *Apply the principles of pharmacology in the treatment of various medical conditions.*

Lecture ANBR19O1O2

Inhaled Anesthetic Agents

Igor O. Zhukov, MD

The goal of this program is to improve the awareness of the history of inhaled anesthetics as well as improve the understanding of current practice involving the use of inhaled anesthetics. After hearing and assimilating this program, the clinician will be better able to:

1. *Discuss the history of inhaled anesthetics.*
2. *Describe the mechanisms of action of modern inhaled anesthetics.*
3. *Identify the comparative differences in pharmacokinetics and pharmacodynamics of modern inhaled anesthetics.*
4. *Explain occupational safety in the use of inhaled anesthetics.*

Lecture ANBR19O1O3

Clinical Pharmacology of Nonopioid Intravenous Anesthetic Drugs

Matthew Whalin, MD

The goal of this program is to improve the awareness of the clinical pharmacology and current anesthesia practice involving the use of nonopioid intravenous (IV) anesthetic drugs, including the mechanism of action, pharmacokinetics, metabolism, potential adverse effects, and possible clinical applications. After hearing and assimilating this program, the clinician will be better able to:

1. *Explain the mechanism of action of nonopioid IV anesthetic drugs.*
2. *Discuss the pharmacokinetics of nonopioid IV anesthetic drugs.*
3. *Describe the metabolism of nonopioid IV anesthetic drugs.*
4. *List the potential adverse effects associated with nonopioid IV anesthetic drugs.*
5. *Explain some of the possible clinical applications for nonopioid IV anesthetic drugs.*

Lecture ANBR19O1O4

Local Anesthetics

Mark Dershwitz, MD

The goal of this program is to improve the clinician's knowledge of the mechanisms of actions of local anesthetics and their potential adverse effects, as well as their use in clinical practice. After hearing and assimilating this program, the clinician will be better able to:

1. *Describe the mechanisms of actions of the most commonly used local anesthetics.*
2. *Identify the potential adverse reactions of the most commonly used local anesthetics.*
3. *Discuss some of the common procedures in which blocks and other common local anesthetic administrations are used.*

Lecture ANBR19O1O5

Pharmacology of Neuromuscular Blocking Drugs and Reversal Agents

Kristopher M. Schroeder, MD

The goal of this program is to improve the awareness of current practice for appropriate use of succinylcholine, nondepolarizing neuromuscular blocking agents, and patterns for evaluating neuromuscular blockade. After hearing and assimilating this program, the clinician will be better able to:

1. *Outline appropriate administration of succinylcholine and associated adverse events.*
2. *Articulate clinical factors that may alter expected effects of nondepolarizing neuromuscular blocking agents.*
3. *Discuss the decision process for choosing a reversal agent.*
4. *Identify advantages and disadvantages of the four basic stimulation patterns.*

Lecture ANBR19O1O6

Clinical Pharmacology of Local Analgesic Drugs

Anita Gupta, MD

The objective of this program is to improve knowledge of the pharmacology of local anesthetics and increase awareness of adverse effects associated with local anesthetics. After completing this program, the clinician will be better able to:

1. *Identify the primary mechanism responsible for the effects of local anesthetics (LA).*
2. *Describe physical and chemical distinctions which are used to classify LAs, and determine their pharmacodynamic and pharmacokinetic properties.*
3. *Monitor patients receiving LAs for possible adverse drug reactions at the cytotoxic, local, neurological, and cardiovascular level.*
4. *Determine whether patients can safely receive LA formulations containing vasoconstrictors such as epinephrine, or may be at high risk for associated complications.*

Lecture ANBR19O1O7

Cardiovascular Drugs

Shamsuddin Akhtar

The goal of this program is to improve the understanding of the importance and essential role of cardiovascular drugs and overall hemodynamic management of patients in the perioperative period. After hearing and assimilating this program, the clinician will be better able to:

1. *Discuss the clinical pharmacology of adrenergic drugs and use them properly.*
2. *Discuss the clinical pharmacology of anti-arrhythmic drugs and use them properly.*
3. *Discuss the clinical pharmacology of digoxin and use it properly.*
4. *Discuss the clinical pharmacology of drugs used to manage heart failure and use them properly.*
5. *Discuss the perioperative management of patients who are receiving cardiovascular medications.*

Lecture ANBR19O108

Mathematics, Physics, Statistics, and Computer Applications

David Steward, MD

The goal of this program is to improve physicians' knowledge of the storage and risks of anesthetic gases, including information on basic gas laws, management of electrical and fire-related operating room hazards, and relevant basic statistical terms and tests. After hearing and assimilating this program, the clinician will be better able to:

1. *Explain how anesthetic gases are stored, how to calculate the amount remaining, and the relevance of basic gas laws to anesthesia.*
2. *Identify types of electrical and fire hazards that occur in the operating room, including ways to reduce risk and to manage related emergencies.*
3. *Distinguish important statistical terms and tests, including ways in which they are used in medical studies and to aid in collaborative decision making with patients.*

Lecture ANBR19O19

The Anesthesia Machine and Breathing System

Eugene A. Hessel II, MD

The goal of this program is to improve the awareness of common features of the anesthesia workstation, sources of anesthesia machine failure, and common problems encountered with the use of the anesthesia machine. After hearing and assimilating this program, the clinician will be better able to:

1. *Describe common features of the anesthesia workstation.*
2. *Discuss sources of anesthesia machine failure.*
3. *Identify common problems encountered with the use of the anesthesia machine.*

Lecture ANBR19O110

Anesthesia Ventilators and Their Application

George Williams, MD

The goal of this program is to improve the comprehension of anesthesia ventilators and their uses. Upon completion of this program, the clinician will be better able to:

1. *Understand ventilator physics and physiology.*
2. *Explain the differences between ICU ventilators and anesthesia ventilators.*
3. *Discuss ventilator modes and their applications in lung disease.*

Lecture ANBR19O111

Airway Management

William Rosenblatt, MD

The goal of this program is facilitate implementation of airway management algorithms specified in the American Society of Anesthesiologists (ASA)'s Difficult Airway Guidelines. Upon completion of this program, the anesthesiologist will be better able to:

1. *Determine which pathway from the ASA's guidelines to follow, in context of a patient's presentation and history.*
2. *Describe the function of different forms of equipment used in airway management (including facemasks, supraglottic devices, laryngoscopy devices, and tracheal tubes).*
3. *Explain the procedure of intubation to patients, in order to improve their preparedness.*
4. *Recognize the advantages and disadvantages of video laryngoscopy.*
5. *Employ a flexible intubation scopes to secure more complicated or obstructed airways.*
6. *Discuss the challenges associated with awake intubation, including nerve innervation of the airway, analgesia, sedation, and time management.*
7. *Identify emergency situations wherein use of a scalpel technique can facilitate a life-saving surgical airway.*
8. *Prevent post-surgical complications associated with emergence and extubation.*

Lecture ANBR19O112

Anesthesia Standards and Procedures

Angela Selzer, MD

The goal of this program is to improve the awareness of current practice guidelines for preanesthetic evaluation and preparation in patients including completing a review of systems, evaluating risk stratification and performing preoperative testing, and managing specific patient populations. After hearing and assimilating this program, the clinician will be better able to:

1. *Apply current guidelines of preanesthesia evaluation, including performing a complete a review of systems.*
2. *Evaluate patient risk stratification based on various scoring methods.*
3. *Understand when to perform preoperative testing and which tests are needed.*
4. *Discuss specific patient populations and considerations for preoperative management.*

Lecture ANBR19O113

Monitoring During Anesthesia: Part 1

Jesse Ehrenfeld, MD, MPH

The goal of this program is to improve the practitioner's compliance with guidelines establishing standards for patient monitoring and improve their understanding of the limitations associated with various monitoring methods and devices. After implementing the program, the clinician will be better able to:

1. *Discuss the mechanics and limitations of cardiac function monitoring.*
2. *Describe how pulse oximetry devices measure oxygen saturation, and circumstances in which they may produce inaccurate readings.*
3. *Compare invasive and noninvasive techniques for monitoring blood pressure monitoring, as well as the advantages and disadvantages of each method.*
4. *Identify the ideal sites and technologies for obtaining accurate temperature readings from a patient.*

Lecture ANBR19O114

Monitoring During Anesthesia: Part 2

Jesse Ehrenfeld, MD, MPH

The goal of this program is to improve knowledge and understanding of standard procedures for monitoring patients during anesthesia and how they are performed. Upon completion of this program, the clinician will be able to:

1. *Review various approaches for monitoring patients during anesthesia.*
2. *Describe indications, and contraindications, and techniques for insertion for various monitoring approaches.*
3. *Discuss the principles guiding the monitoring approaches and the available devices/equipment for measurement.*

Lecture ANBR19O115

Control of Body Temperature

Daniel Sessler, MD

The goal of this program is to improve the awareness of current practice for managing thermoregulatory control during general and neuraxial anesthesia, preventing hypothermia, and maintaining normothermia. After hearing and assimilating this program, the clinician will be better able to:

1. *Explain regulation of body temperature during general anesthesia.*
2. *Identify thermoregulatory problems during neuraxial anesthesia.*
3. *Describe complications associated with hypothermia in unwarmed surgical patients.*
4. *List methods for reducing heat loss in surgical patients.*

Lecture ANBR19O116

Respiratory Physiology and Pulmonary Function

Peter D. Slinger, MD

The goal of this program is to improve the awareness of current practice for recognition and management of hypoxemia, hypercarbia, and inspiratory stridor. After hearing and assimilating this program, the clinician will be better able to:

1. *Discuss appropriate treatment methods for intraoperative and postoperative hypoxemia.*
2. *Identify potential causes of increasing hypercarbia.*
3. *List causes and treatment of inspiratory stridor.*

Lecture ANBR19O117

Cardiovascular Physiology

June Chan, MB, BS

The goal of this program is to increase understanding of cardiac physiology and blood flow. After reading, the clinician should be able to:

1. *Describe the steps of ventricular systole and diastole in terms of mechanical and electrical processes.*
2. *Relate the concepts of preload, afterload, and contractility to cardiac output.*
3. *Identify the major factors contributing to oxygen consumption.*
4. *Explain the concept of autoregulation and how it pertains to regional organ flow.*

Lecture ANBR19O118

Renal Function, Fluid and Electrolyte Balance, and Intraoperative Fluid Therapy

Eric B. Kistler, MD, PhD

The goal of this program is to provide an overview of renal function and fluid and electrolyte balance; and to improve knowledge of intraoperative IV fluid administration. After hearing and assimilating this program, the clinician will be better able to:

1. *Describe the basic anatomy and function of the kidney.*
2. *Discuss the mechanism and site of action of loop diuretics, thiazide diuretics, and angiotensin II antagonists.*
3. *Calculate and interpret the fluid deficit for intraoperative IV fluid use and apply it in practice.,*
4. *Outline appropriate intraoperative IV fluid choice, volume, and rate, depending on specific patient variables.*
5. *Explain the differences between, and list examples of, crystalloid and colloid IV fluids.*
6. *Summarize the meaning of "the third space" and its impact on intraoperative IV fluid administration.*

Lecture ANBR19O119

Hematology and Blood Component Therapy

Robert Wegner, MD

The goal of this program is to improve the awareness of current practice for the administration of packed red blood cells on patient outcomes, use of classic and newer anticoagulants, and management of thrombocytopenia. After hearing and assimilating this program, the clinician will be better able to:

1. *Discuss the implications of administration of packed red blood cells on patient outcomes.*
2. *Identify the laboratory measures of coagulation, mechanisms of action, and reversal methods of classic and newer anticoagulants.*
3. *Explain the epidemiology, mechanism, and management of thrombocytopenia.*

Lecture ANBR19O120

The Central and Peripheral Nervous System

Kyle Marshall, MD

The goal of this program is to improve the comprehension of central and peripheral nervous system anatomy and function. Upon completion of this program, the clinician will be better able to:

1. *Describe the anatomy of the central nervous system.*
2. *Identify and diagnose symptoms of central nervous system conditions.*
3. *Discuss conditions that affect the central nervous system, anesthetic challenges, and how to treat them.*

Lecture ANBR19O121

Lower-extremity Regional Analgesia

Arthur Atchabahian, MD, PhD

The goal of this program is to improve the awareness of current practice for lower-limb regional anesthesia including the use of the quadratus lumborum block for hip surgery, suprainguinal fascia iliaca compartment block, regional anesthesia after a hip fracture and before surgery, lateral femoral cutaneous nerve block, adductor canal block, and IPACK block and ultrasound-guided local infiltration analgesia for knee surgery. After hearing and assimilating this program, the clinician will be better able to:

1. *Explain the use of the quadratus lumborum block for hip surgery.*
2. *Describe the suprainguinal fascia iliaca compartment block and compare it with the regular infrainguinal fascia iliaca compartment block.*
3. *Discuss regional anesthesia after a hip fracture and before surgery.*
4. *Describe the lateral femoral cutaneous nerve block and its usefulness in clinical practice.*
5. *Detail the adductor canal block and compare with the femoral triangle block.*
6. *Explain the IPACK block and ultrasound-guided local infiltration analgesia for knee surgery.*

Lecture ANBR19O122

Physiology of the Endocrine Systems

Robert Peterfreund, MD, PhD

The goal of this program is to improve the comprehension of endocrine diseases that may affect anesthesia. Upon completion of this program, the clinician will be better able to:

1. *Describe the anatomy and physiology of the thyroid, parathyroid, pituitary, and adrenal glands.*
2. *Discuss typical presentations for common endocrine disorders.*
3. *Explain and implement different management strategies before, during, and after anesthesia for common endocrine disorders.*

Lecture ANBR19O123

Physiology and Pharmacology of the Autonomic Nervous System

Arthur Wallace, MD

The goal of this program is to provide an overview of the anatomy and physiology of the autonomic nervous system (ANS) and the pharmacology and physiology of agents that affect the ANS., as well as risks and benefits of blocking the ANS in the perioperative period After hearing and assimilating this program, the clinician will be better able to:

1. *Summarize the function of the sympathetic and parasympathetic nervous systems and the differences between them.*
2. *List the receptors and neurotransmitters found in the sympathetic and parasympathetic nervous systems, and the similarities and differences between them.*
3. *Describe the action and list examples of agonists and antagonists for each type of receptor found in the parasympathetic and sympathetic nervous systems.*
4. *Explain the mechanism of action of the phosphodiesterase inhibitors.*
5. *Discuss the benefits of beta blockers in the preoperative and intraoperative periods.*

Lecture ANBR19O124

Risks, Benefits, and Selection of Inotropes

Arthur Wallace, MD

The goal of this program is to improve the awareness of current practice for the use of various inotropes available for cardiovascular management and their risks and benefits, as well as strategies for choosing an inotrope in patient management. After hearing and assimilating this program, the clinician will be better able to:

1. *Review the various inotropes available for cardiovascular management.*
2. *Explain the risks and benefits associated with inotrope use.*
3. *Discuss the strategies used to choose an inotrope in patient management.*

Lecture ANBR19O125

Pain Mechanisms and Pathways, Management of Chronic Pain

Vikram B. Patel, MD

The goal of this program is to improve the comprehension of pain physiology, disorders of pain, and pharmacodynamics of opioids. Upon completion of this program, the clinician will be better able to:

1. *Evaluate the signs and symptoms of neuropathic pain and complex regional pain disorder.*
2. *Understand management strategies for these disorders.*
3. *Discuss types and categories of opioids.*
4. *Explain basic opioid pharmacodynamics.*

Lecture ANBR19O126

Postoperative Care and Management of Complications

Jesse Ehrenfeld, MD

The goal of this program is to improve the awareness of standards for postoperative care and management of postoperative complications. After hearing and assimilating this program, the clinician will be better able to:

1. *List the standards for postoperative care.*
2. *Explain criteria for discharging patients from the PACU.*
3. *Identify postoperative respiratory and hemodynamic complications.*
4. *Discuss recommendations for managing postoperative nausea and vomiting.*

Lecture ANBR19O127

Monitored Anesthesia Care and Sedation

Tae W. Kim, MD

The goal of this program is to improve the awareness of monitored anesthesia care (MAC) and sedation, and to identify adverse outcomes. Upon completion of this program, participants will be able to:

1. *Formulate a comprehensive plan for MAC.*
2. *Differentiate the different levels of sedation and their anesthetic management*
3. *Identify challenges for providing sedation services in remote locations*
4. *Evaluate the role of nonanesthesiologists in providing sedation services*

Lecture ANBR19O128

Ethics, Patient Safety, and Medicolegal Issues

Barbara Jericho, MD

The goal of this program is to improve the comprehension of ethics, patient safety, and medical legal issues as they pertain to the anesthesiologist. Upon completion of this program, the clinician will be better able to:

1. *Explain principles of ethics.*
2. *Comprehend the concepts of informed consent.*
3. *Evaluate procedures that can affect patient safety.*
4. *Discuss medical errors, adverse events, and malpractice.*

Lecture ANBR19O129

Essentials of Neuroanesthesia: Part 1

Ehab Farag, MD

The goal of this program is to improve the knowledge of physicians regarding the anatomy and physiology of the brain as they relate to neuroanesthesia, factors affecting cerebral blood flow and intracranial pressure, and neuroprotective options. After hearing and assimilating this program, the clinician will be better able to:

1. *Explain the structure and function of the cerebral vascular system as it relates to neuroanthesthesia and the risk of ischemia.*
2. *Describe how different factors affect cerebral blood flow and intracranial pressure, including the maintenance of autoregulation and methods of measuring and monitoring intracranial pressure.*
3. *Explain how neuronal injury occurs and what approaches may help to reduce injury.*

Lecture ANBR19O130

Essentials of Neuroanesthesia: Part 2

Ehab Farag, MD

The goal of this program is to improve physicians' knowledge of temperature management and the use of hypothermia as a neuroprotective, considerations for neuroanesthesia maintenance and monitoring, and the use of different positions during cranial and spinal surgery. After hearing and assimilating this program, the clinician will be better able to:

1. *Explain current knowledge regarding the use of hypothermia as a neuroprotective agent and requirements to use it safely.*
2. *Describe approaches to maintain anesthesia and the types of monitoring needed, as well as considerations for fluid management and upper airway management.*
3. *Explain the procedures, advantages, complications, and appropriate use of different patient positions that can be used during neuroanesthesia.*

Lecture ANBR19O131

Essentials of Neuroanesthesia: Part 3

Ehab Farag, MD

The goal of this program is to improve the knowledge of physicians of essentials of neuroanesthesia, focusing on monitoring techniques, specific conditions such as subarachnoid hemorrhage, and specific techniques such as those used in deep brain stimulation interventional neuroradiology. After hearing and assimilating this program, the clinician will be better able to:

1. *Explain how bispectral index monitors, transcranial Doppler, jugular venous oximetry, and near infrared spectroscopy can be useful with respect to neuroanesthesia.*
2. *Discuss characteristics and management of varied tumors associated with the sella, cerebral aneurysm, subarachnoid hemorrhage, arteriovenous malformation, and diabetes insipidus, including information on potential complications associated with each.*
3. *Explain recommendations for the use of transsphenoidal surgery, awake craniotomy, deep brain stimulation, interventional neuroradiology, and intracranial endoscopic procedures, including details of procedures and potential complications.*

Lecture ANBR19O132

Neurological Trauma

Arne Budde, DO

The goal of this program is to improve the awareness of current practice for the anesthetic management of patients with traumatic brain injury. After hearing and assimilating this program, the clinician will be better able to:

1. *Identify the different types of traumatic brain injury.*
2. *Describe the Glasgow Coma Scale, brain herniation, and its sites and symptoms.*
3. *Summarize the Brain Trauma Foundation guidelines for traumatic brain injury.*
4. *Discuss airway management in patients with traumatic brain injury.*

Lecture ANBR19O133

Acute and Chronic Respiratory Problems

Donald E. Crabtree, DO

The goal of this program is to improve the awareness of patterns of lung disease and related anesthetic considerations. After listening, the clinician will be better able to:

1. *Define the pathophysiology of obstructive vs restrictive lung diseases.*
2. *Classify the effects, outcomes, and complications of lung disease in general vs regional anesthesia.*
3. *Discuss complications of mechanical ventilation.*
4. *Compare and contrast ventilator strategies for ARDS management.*

Lecture ANBR19O134

Asthma, Allergy, and Anesthesia

Thomas A. Moore II, MD

The goal of this program is to improve the awareness of current practice for diagnosis and management of asthma, allergy, and their implications for anesthesia. After hearing and assimilating this program, the clinician will be better able to:

1. *Discuss perioperative management of the adult patient with asthma.*
2. *List optimal anesthesia drugs and techniques to minimize risk of bronchospasm.*
3. *Explain the pharmacology of bronchodilators.*
4. *Identify allergies responsible for perioperative anaphylaxis.*

Lecture ANBR19O135

Anesthesia for Thoracic and Thoracoscopic Surgery

Peter Slinger, MD

The goal of this program is to improve the understanding of the assessment and management of patients undergoing anesthesia for thoracic and thoracoscopic surgery. After hearing and assimilating this program, the clinician will be better able to:

1. *Discuss the needed preoperative assessment for a patient undergoing anesthesia for thoracic surgery.*
2. *Outline the options and considerations for lung isolation, particularly in the patient with a difficult airway.*
3. *Identify strategies for managing 1-lung ventilation.*

Lecture ANBR19O136

Important Aspects of Critical Care

Edward Bittner, MD

The goal of this program is to provide an overview of important aspects of critical care, including the management of respiratory failure, chest trauma, acute pulmonary edema, cardiovascular support of the critically ill patient, septic shock, and prevention of nosocomial infections. After hearing and assimilating this program, the clinician will be better able to:

1. *Recognize ventilated patients who are suitable candidates for a spontaneous breathing trial (SBT) and discuss possible reasons for success or failure of the SBT.*
2. *Summarize the overall management of chest trauma.*
3. *List the possible causes of pulmonary edema.*
4. *Describe the signs, symptoms, and management of hypertensive emergency.*
5. *Explain the role of vasopressors in the treatment of shock.*
6. *Acknowledge the importance of effective hand hygiene to prevent nosocomial infections caused by MRSA and VRE.*

Lecture ANBR19O137

Heart Diseases and Anesthesia: Part I

Jochen Steppan, MD

The goal of this program is to improve awareness of the pathophysiology of heart disease and implications for the anesthesiologist. After hearing this program, the clinician will be able to:

1. *Discuss ischemic heart disease, its ramifications for the perioperative period, and how it affects perioperative management.*
2. *Discuss valvular heart disease, its classifications, echocardiographic findings, and how physiologic changes impact management of patients undergoing non-cardiac surgery.*
3. *Discuss infective endocarditis.*

Lecture ANBR19O138

Heart Diseases and Anesthesia: Part 2

Jochen Steppan, MD

The goal of this program is to improve the comprehension of heart disease and the challenges facing the anesthesiologist when dealing with conditions of the heart. Upon completion of this program, the clinician will be better able to:

1. *Understand multiple cardiac diseases encountered by anesthesiologists and implications for perioperative management.*
2. *Identify and diagnose symptoms of cardiac disease and how to differentiate and treat them.*
3. *Discuss the complications when dealing with cardiac disease when communicating with other primary care providers.*

Lecture ANBR19O139

Cardiac Anesthesiology: Part 1

Arthur Wallace, MD, PhD

The goal of this program is to improve the comprehension of the cardiac anesthesiologist's roles as they pertain to the cardiac patient and the cardiac anesthetic procedure being performed. Upon completion of this program, the clinician will be better able to:

1. *Understand requirements of cardiac anesthesiologists.*
2. *Explain common procedures performed by cardiac anesthesiologists.*
3. *Evaluate cardiac surgery patients preoperatively.*
4. *Discuss types of equipment needed for cardiac anesthesia.*

Lecture ANBR19O140

Cardiac Anesthesiology: Part 2

Arthur Wallace, MD

The goal of this program is to improve the comprehension of the cardiac anesthesiologist's roles as they pertain to the cardiac patient and the cardiac surgical procedure being performed. Upon completion of this program, the clinician will be better able to:

1. *Understand requirements of cardiac anesthesiologists inside and outside the operating room.*
2. *Explain common procedures performed during cardiac surgery that will affect anesthesia.*
3. *Discuss hemodynamics associated with cardiac surgery.*
4. *List types of equipment needed for cardiac anesthesia procedures.*

Lecture ANBR19O141

Anesthesia for Vascular Surgery

Arthur Wallace, MD

The goal of this program is to improve the comprehension of anesthesiology needs for vascular surgery with regard to both the patient and the procedure. Upon completion of this program, the clinician will be better able to:

1. *Understand perioperative evaluation and preparation of the patient for vascular surgery.*
2. *Explain different types of vascular surgeries and their anesthetic requirements.*
3. *Evaluate and discuss common patient issues during vascular surgery (eg, hypotension) and how to address them.*

Lecture ANBR19O142

Anesthesia for Abdominal and General Surgery

Kristopher M. Schroeder, MD

The goal of this program is to improve the comprehension of challenges facing the anesthesiologist when dealing with abdominal surgery, laparoscopic procedures, and hepatic failure. After hearing and assimilating this program, the clinician will be better able to:

1. *Discuss anesthetic management of emergent and elective abdominal procedures (open and laparoscopic) as well as anesthesia for patients with hepatic dysfunction.*
2. *Identify and diagnose symptoms of hepatic failure and how to differentiate and treat them.*
3. *Explain the complications of abdominal surgery when communicating with other primary care providers.*
4. *Assess patients for aspiration risk and adjust procedures to minimize risk.*

Lecture ANBR19O143

Anesthesa for the Obese Patient

Jerry Ingrande, MD, MS

The objective of this program is to improve current knowledge of the pathophysiology and anesthetic management of the obese patient. After implementing the program, the clinician will be better able to:

1. *Discuss organ-system pathophysiology commonly found in the obese patient.*
2. *Discuss and implement pharmacological management of the obese patient in the perioperative and postoperative periods, considering their physiologic and anthropometric characteristics.*
3. *Discuss and implement appropriate regional block anesthetic practice in the obese patient.*
4. *Identify the perioperative and postoperative effects of bariatric surgery in the obese patient.*

Lecture ANBR19O144

The Renal System and Anesthesia for Urologic Surgery

Mark Stafford-Smith, MD

The goal of this program is to increase the understanding of the pathophysiology of renal disease, considerations for specific urologic surgeries, and perioperative management of patients with chronic kidney disease and end-stage renal disease. After hearing and assimilating this program, the clinician will be better able to:

1. *Describe the physiology and pathophysiology of renal disease, particularly as it pertains to anesthetic practice.*
2. *Explain the anesthetic considerations and perioperative complications related to specific surgical procedures involving the genitourinary tract.*
3. *Discuss the perioperative management of patients with chronic kidney disease and end-stage renal disease.*

Lecture ANBR19O145

Hematologic Diseases and Anesthesia

Aryeh Shander, MD

The goal of this program is to improve the awareness and current management of hematologic disorders in anesthesiology practice. After hearing this program, the clinician will be better able to:

1. *Discuss the evaluation and treatment of anemia in the preoperative period.*
2. *Discuss and manage hemoglobinopathies (sickle cell disease and thalassemia) during the perioperative period.*
3. *Identify and implement effective interventions for reversal of anticoagulants during the perioperative period.*
4. *Identify strategies to manage blood cell and blood factor deficiencies during the perioperative period.*

Lecture ANBR19O146

Endocrine Diseases and Anesthesia: Part 1

Bobbie Jean Sweitzer, MD

The objective of this program is to improve current practice in diagnosis and anesthetic management of the major diseases of the endocrine system and pheochromocytomas. After listening and implementing the program, the clinician will be better able to:

1. *Describe the physiology of the pituitary, thyroid, parathyroid, and adrenal gland.*
2. *Identify the physiologic effects of the major diseases of the pituitary, thyroid, parathyroid, and adrenal gland.*
3. *Summarize the treatment and anesthetic considerations of the major diseases of the pituitary, thyroid, parathyroid, and adrenal gland.*
4. *Explain the pathogenesis and anesthetic considerations of pheochromocytomas.*

Lecture ANBR19O147

Endocrine Diseases and Anesthesia: Part 2

Bobbi Jean Sweitzer, MD

The goal of this program is to understand endocrine diseases such as diabetes and carcinoid syndrome and their implications on anesthesia during surgery. Upon completion of this program, the anesthesiologist will be better able to:

1. *Describe the different forms of diabetes and their diagnosis and complications.*
2. *Explain implications of diabetes on surgery and glucose management during surgery, including complications such as hypoglycemia, diabetic ketoacidosis, nonketotic hyperosmolar state, and gestational diabetes.*
3. *Discuss anesthetic techniques for patients with diabetes, including pancreatic transplantation, and in emergency surgery of diabetic patients.*
4. *Outline the diagnosis and treatment of carcinoid syndrome and its implications for anesthetic management of patients.*

Lecture ANBR19O148

Anesthesia and Adult Neuromuscular Disease

Sergio Bergese, MD

The goal of this program is to improve the awareness of current practice related to anesthetic considerations for patients with multiple sclerosis, the risks of anesthesia for patients with various motor neuron diseases, the types of peripheral neuropathy and how these disease states complicate anesthesia administration, how myasthenia gravis, Lambert-Eaton syndrome, and other disorders of neuromuscular transmission affect anesthetic approach, and special considerations for perioperative management of patients with postpolio syndrome. After hearing and assimilating this program, the clinician will be better able to:

1. *Discuss the anesthetic considerations for patients with multiple sclerosis.*
2. *Describe the risks of anesthesia for patients with various motor neuron diseases.*
3. *Identify the types of peripheral neuropathy and how these disease states complicate anesthesia administration.*
4. *Describe how myasthenia gravis, Lambert-Eaton syndrome, and other disorders of neuromuscular transmission affect anesthetic approach.*
5. *Identify special considerations for perioperative management of patients with postpolio syndrome.*

Lecture ANBR19O149

Acute and Chronic Pain and Its Management

Shaheen Lakhan, MD, PhD, MeD, MS, FAAN

The goal of this program is to improve the awareness of current practice related to the types and mechanisms of pain, including clinical considerations for acute and chronic pain management. After hearing and assimilating this program, the clinician will be better able to:

1. *Describe the states of acute and chronic pain.*
2. *Discuss the gate control theory of pain.*
3. *Identify common pain scales for assessing patient pain.*
4. *Describe the different types of pain management.*

Lecture ANBR19O150

Basic Considerations for Pediatric Anesthesia

Jerrold Lerman, MD

The goal of this program is to improve the comprehension of pediatric physiology, drug metabolism, and anesthesia requirements. Upon completion of this program, the clinician will be better able to:

1. *Understand pediatric physiology, especially of the cardiac and respiratory systems.*
2. *Explain pediatric metabolism of common anesthetic drugs.*
3. *Evaluate the signs and symptoms of certain drug toxicities in pediatric patients.*
4. *Discuss types of equipment needed for pediatric anesthesia.*

Lecture ANBR19O151

Neonatal Surgical Emergencies

Jerrold Lerman, MD

The goal of this program is to improve awareness of the different types of neonatal surgical emergencies and the anesthetic management of these emergencies. After implementing the program, the clinician will be better able to:

1. *Identify 8 congenital anomalies that may present in newborns during surgery.*
2. *Discuss the recommended anesthetic procedure for each congenital anomaly in newborns.*
3. *Identify the recommended anesthetic drugs for newborns who present with a congenital anomaly.*
4. *Discuss the levels and management of dehydration in newborns.*

Lecture ANBR19O152

Pediatric Outpatient Anesthesia

Raafat S. Hannallah, MD

The goal of this program is to improve the understanding of pediatric outpatient anesthesia and knowledge of what patients are candidates for outpatient procedures. Upon completion of this program, the clinician will be better able to:

1. *Describe patients at risk for ambulatory surgery.*
2. *Discuss types of anesthesia and analgesia best used in an outpatient surgical setting.*
3. *Explain criteria for discharge and ways to improve patient comfort before and after discharge.*

Lecture ANBR19O153

Anesthesia Considerations in Pediatric Subspecialty Surgery

Jerrold Lerman, MD

The goal of this program is to improve the awareness of current practice related to the various pediatric surgical procedures and the associated risks/complications in children, anesthesia considerations for various pediatric surgeries and postoperative management, and guidelines for pediatric sedation. After hearing and assimilating this program, the clinician will be able to:

1. *Review the various pediatric surgical procedures and the associated risks/complications in children.*
2. *Discuss anesthesia considerations for various pediatric surgeries and postoperative management.*
3. *Describe guidelines for pediatric sedation.*

Lecture ANBR19O154

Pediatric Anesthesia Challenges

Raafat Hannallah, MD

The goal of this program is to improve the understanding of the anatomy, physiology, and clinical conditions related to the pediatric airway and the management of children scheduled for imaging studies in the non–operating room environment. After hearing and assimilating this program, the clinician will be better able to:

1. *Discuss considerations for pediatric airway management, including management and prevention of laryngospasm.*
2. *Evaluate the pediatric difficult airway and understand techniques for managing the pediatric difficult airway.*
3. *Describe management of airway obstruction caused by foreign body aspiration or infectious processes.*
4. *Identify considerations for providing anesthesia in non-operating room locations, including MRI and CT scans.*

Lecture ANBR19O155

Anesthesia for Pediatric Neuromuscular Diseases

Jerrold Lerman, MD

The goal of this program is to improve the understanding of pediatric neuromuscular disease and anesthetic management. After hearing and assimilating this program, the clinician will be better able to:

1. *Identify the major types of muscular dystrophies.*
2. *Identify types of channelopathies and myopathies.*
3. *Discuss considerations for anesthetic management of patients with cerebral palsy.*
4. *Describe the treatment of malignant hyperthermia.*

Lecture ANBR19O156

Anesthesia for Orthopedic Surgery

Gary Scott, MD

The goal of this program is to improve knowledge of anesthesia for orthopedic surgery in adults and children. The main focus is understanding of concomitant diseases, regional anesthesia, related anesthetic considerations and management of spinal fusions. Upon completion of this program the anesthesiologist will be better able to:

1. *Understand significant concomitant diseases in adults and children that can have an impact on the anesthetic management and outcome of orthopedic surgery.*
2. *Explain regional anesthesia procedures in shoulder and upper arm surgery, as well as surgery of lower extremity and postoperative pain management.*
3. *Discuss the use of tourniquets, understand and manage fat embolus syndrome, venous thromboembolism, and the use of methyl methacrylate and its association with the implantation syndrome.*
4. *Describe the management and complications of scoliosis surgery, spinal cord injury and anterior spinal fusion surgery.*

Lecture ANBR19O157

Anesthesia for Obstetrics: Part 1

David Gambling, MD, BS

The goal of this program is to improve understanding of obstetric anesthesia. Upon completion of this program, the clinician will be better able to:

1. *Describe physiological effects of pregnancy on anesthesia.*
2. *Discuss types of anesthesia for obstetrics.*
3. *Explain utero-placental physiology and transplacental transfer.*
4. *Discuss anesthetic management for emergent or non-emergent patients.*

Lecture ANBR19O158

Anesthesia for Obstetrics: Part 2

David Gambling, MD, BS

The goal of this program is to improve the delivery of anesthesia in cases of obstetric hemorrhage and to increase awareness of conditions complicating pregnancy. After reading, the clinician should be able to:

1. *Discuss common conditions leading to obstetric hemorrhage in terms of anesthetic treatment.*
2. *Identify the forms of hypertensive disorders of pregnancy and their treatment.*
3. *Discuss considerations for administration of anesthesia in pregnant patients suffering from obesity.*
4. *Describe the impact of heart disease on the treatment of pregnant patients.*

Lecture ANBR19O159

Neonatal Resuscitation and PALS

David Steward, MD

The goal of this program is to improve the awareness of current practice of current recommended standards for neonatal resuscitation and cardiopulmonary resuscitation in pediatric patients. After hearing and assimilating this program, the clinician will be better able to:

1. *Review current recommended standards for neonatal resuscitation.*
2. *Discuss current practices for the administration of cardiopulmonary resuscitation in pediatric patients.*
3. *Identify the targets of postresuscitation care.*

Lecture ANBR19O160

Anesthesiology for Ophthalmologic Procedures

Tina Tran, MD

The goal of this program is to improve awareness of anesthetic techniques during eye procedures and the management of anesthesia during eye procedures. After implementing the program, the clinician will be better able to:

1. *Identify causes of an increase or a decrease in the intraocular pressure of a patient during surgery and discuss how to manage these changes with anesthetics.*
2. *Discuss the pathophysiology and anesthetic management of the oculocardiac reflex.*
3. *Identify the anesthetic techniques used in strabismus and glaucoma procedures.*
4. *Describe the methods and procedures of regional anesthesia in ocular surgeries.*
5. *Identify the common ocular emergencies during anesthesia and discuss methods of prevention.*

Lecture ANBR19O161

Anesthesia for Adult ENT Procedures

Sarah Hartlage, DO

The objective of this program is to improve awareness of the anesthetic procedures and unique challenges of otolaryngologic surgery. After implementing the program, the clinician will be better able to:

1. *Discuss the key components in assessing a patient for otolaryngologic surgery.*
2. *Discuss the most commonly used anesthetic blocks in otolaryngologic surgery.*
3. *Describe the advantages and disadvantages of the main tubes used in otolaryngologic surgery.*
4. *Identify the anesthetic procedures used in FESS, facial flap, and head and neck trauma surgery.*
5. *Identify the main postoperative risks of otolaryngologic surgery and prevention of these risks.*

Lecture ANBR19O162

Anesthesia for Trauma and Burns

Donald E. Crabtree, DO

The goal of this program is to improve the understanding of trauma and burns and the related anesthetic considerations. After listening, the clinician will be better able to:

1. *Recognize the correct management of trauma patients in the pre-hospital and immediate hospital setting.*
2. *Discuss recognition and management of hemorrhagic shock.*
3. *Discuss anesthesia management for thoracoabdominal trauma.*
4. *Formulate a plan for the treatment of the burn patient.*

Lecture ANBR190163

Anesthesia for Geriatric Patients

Aman Upadhyay, MD

The goal of this program is to improve the awareness of current practice for anesthesia management of geriatric patients. After hearing and assimilating this program, the clinician will be better able to:

1. *Describe the physiologic implications of aging by organ system along with the implications of chronic diseases in those organ systems.*
2. *Discuss the pharmacologic consequences of advanced age.*
3. *Summarize the current practice guidelines for anesthesia management during common geriatric procedures.*
4. *Review best practices for postoperative pain management, postoperative delirium prevention and management, and postoperative cognitive dysfunction.*

Lecture ANBR190164

How to Pass the Oral and Applied Examinations

David Steward, MD

The goal of this program is to improve the comprehension of the preparation and testing process for the initial board exams. Upon completion of this program, the clinician will be better able to:

1. *Prepare for the initial board exams.*
2. *Understand the testing process and what is expected to secure good marks.*
3. *How to efficiently prepare for the board exams.*

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ANESTHESIOLOGY
Board Review

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Principles of Pharmacology of Local Anesthetics

Mark Dershwitz, MD, *Professor of Anesthesiology, Biochemistry & Molecular Pharmacology, University of Massachusetts School of Medicine, Worcester, MA*

Basics of Pharmacokinetics

Pharmacokinetics: study of time course of drug's journey throughout body; described as what body does to drug, in contrast to pharmacodynamics (described as what drug does to body); *3 main aspects* — absorption, distribution, and elimination

- Absorption: process by which drug crosses biologic membranes to gain access to the circulation; not concern with intravenous (IV) drug administration; however, for oral administration, subcutaneous or intramuscular injection, inhalation, topical administration and other less common ways to administer drugs, drug needs to be absorbed before it can act; chemical nature of drug (*eg*, relative water and lipid solubilities, chemical size) significantly affect absorption, as drug needs to cross biological membranes to be absorbed
- Mechanisms of absorption: *4 mechanisms* — diffusion through lipid membrane, diffusion through aqueous pores in membrane, carrier-mediated transport that may be passive down concentration gradient or energy-dependent active process against concentration gradient, or pinocytosis
  - Diffusion through membranes and carrier-mediated transport: most relevant mechanisms for administered medications; diffusion through membrane usually requires drug to have significant lipid solubility; for drugs whose ionic state depends on pH, acid-base milieu on either side of membrane significantly affects rate and direction of diffusion; for carrier-mediated transport, affinity of drug to carrier molecule affects its transport; many molecules exist in both ionized and unionized forms depending on pH of environment(*ie*, weak acids or weak bases); ionization of drug affects its lipid solubility; at lower pH values, weak acid (*eg*, aspirin) will be protonated, uncharged and more lipid soluble; as pH increases, lesser fraction of the molecules will be protonated and greater fraction will be ionized and more water soluble; opposite occurs with weak base (*eg*, midazolam); at higher pH, most midazolam molecules uncharged and lipid soluble; at lower pH, most midazolam molecules charged, therefore less lipid soluble and more water soluble
- Distribution: describes how drug leaves circulation and enters various other compartments throughout body; like absorption, when drug distributes, must cross biologic membranes, and its chemical nature significantly affects how rapidly and to which tissues it preferentially distributes; described in part by parameter, volume of distribution
- Elimination: consists of both metabolism of drug and its excretion from the body; described in part by parameter, clearance
- Drug concentration: drug concentration usually measured in blood or plasma; effect-site concentration, concentration of drug at site of action; however, in majority of cases, theoretical prediction rather than actual assayed concentration; often poor relationship between concentration in circulation and the concentration at effect site; disparity most pronounced with lipid-soluble drugs used in anesthesia
- Bioavailability: fraction of administered dose of drug that reaches circulation; IV administration of drug has 100% bioavailability; drug may have a bioavailability of <100% because either not absorbed or some of it metabolized prior to reaching circulation
- Volume of distribution: volume in which dose of drug appears to be distributed; calculated by dividing amount of drug in body by concentration in blood; if drug distributes primarily to tissues outside of circulation, blood concentration low and volume of distribution high; if drug distributed exclusively to nonvascular compartments, blood concentration would be 0 and volume of distribution would be infinity; in contrast, drug that distributes exclusively into blood would have volume of distribution equal to patient's blood volume (~5 L)
- Clearance: overall removal of drug from body; 2 most important contributors, metabolism of drug and excretion of drug in urine and feces; for some drugs, exhalation, loss in sweat, or loss in breast milk may also significantly contribute to clearance; *3 important types of clearance* — first order clearance, capacity limited, flow dependent
  - First-order clearance: most common; rate of drug removal proportional to drug concentration; most drugs used clinically fall into this category, at least at therapeutic doses; because first-order clearance proportional to drug concentration, steady-state plasma concentration (*ie*, once desired plasma concentration reached, it can be maintained by regular, repeated dosing) can be achieved; since clearance constant for first-order drugs, constant fraction of drug removed per unit time; drug concentration drops by 50% after each half-life, regardless of concentration; drug concentration drops by 50% after 1 half-life, by 75% after 2 half-lives, by 87.5% after 3 half-lives, by 93.75% after 4 half-lives, by 96.875% after 5 half-lives; drug essentially eliminated after 4 to 5 half-lives

Capacity-limited clearance (zero-order clearance): rate of elimination not proportional to drug concentration; only few drugs in clinical use (*eg*, aspirin, alcohol) fall into this category; capacity-limited clearance results when capacity of elimination pathway exceeded; therefore, most drugs (even those that show first-order clearance in therapeutic doses) start to demonstrate capacity-limited clearance when given at high doses; steady-state concentration cannot be achieved because independent of drug concentration; plasma concentration continues to increase if new dose given before previous dose cleared; capacity-limited clearance observed when elimination pathway for specific drug saturated; regardless of drug concentration, organ of elimination capable of removing only fixed amount of the drug; hence, rate of elimination independent of drug concentration

Flow-dependent clearance: high-extraction drugs; rate of elimination depends on rate of blood flow to organ of elimination; drugs displaying flow-dependent almost completely extracted from blood on first pass through organ of elimination; this class includes common drugs like morphine and propranolol; still useful clinically because rarely cleared by single organ but rather cleared by multiple pathways, particularly at higher concentrations; therefore, even when cleared efficiently by 1 organ, therapeutic plasma levels can be achieved if other routes of elimination less efficient; important to be aware of this drug class because their plasma concentrations disproportionately affected by changes in blood flow, as in some disease states

Systemic clearance: sum of drug clearance by all pathways in body; exact elimination pathway being used cannot be determined from plasma concentration; primary pathways include metabolism in liver and excretion in urine and bile; other pathways include exhalation, sweating, *etc*, but these generally minor

Protein binding: many drugs bind to plasma protein (*eg*, albumin and alpha-1 acid glycoprotein); protein-bound drug molecule that inactive and not available to bind to its receptor or to distribute to other tissues; not filtered or secreted by kidney, not dialyzable; since drugs may compete for same protein-binding sites, one drug may displace another from binding to protein; such displacement another important and common way that drugs may interact with one another; typically highly protein-bound drug that becomes displaced from its binding site may achieve higher-than-expected free concentration in circulation, potentially leading to excessive effect or to adverse effects

Basics of Pharmacodynamics

Pharmacodynamics: effects of drugs and their mechanisms of action; concerned with relationship between concentration of drug at its receptor and magnitude of effect produced; this relationship often called concentration-response relationship or dose-response relationship; *agonist* — drug that binds to its receptor, activating biologic effector and usually mimicking endogenous ligand; at appropriate concentration, full agonist can produce maximum response (efficacy); *partial agonist* — drug that activates biologic effector system but has lower efficacy than full agonist and thus cannot produce maximum effect; *antagonist* — drug that, when bound to its receptor, inhibits effect produced by agonist or endogenous ligand; *inverse agonist* — binds to inactive form of its receptor, inhibiting constitutive activity, much like competitive antagonist

Law of mass action: describes occupancy theory or relationship between drug concentration and magnitude of its effect; states that effect proportional to number of receptors occupied by drug and therefore proportional to concentration of drug; relationship between drug dose and drug effect most commonly depicted by graded log-dose–response curve; in this type of graph, X-axis has drug dose on logarithmic scale, Y-axis displays effect of drug on scale of 0% to 100%; typically sigmoid shape of curve; inflection point of sigmoid called effective dose at 50% (or ED50), *ie*, dose that causes half-maximal response; drug with high potency has lower value for ED50, drug with low potency has higher value for ED50; drug located to left of another drug along X-axis of a graded log-dose–response curve has higher potency because it takes lower dose of drug to produce typical magnitude of effect

Classes of antagonists: *chemical antagonist* — antagonizes action of another drug by chemically binding to and inactivating second drug (*eg*, protamine chemically binds to heparin and inactivates it); *physiologic antagonist* — effects of endogenous or exogenous agonist reversed by physiologic antagonist; antagonist produces physiologic effects opposite to those produced by agonist, typically by activating another receptor (*eg*, muscarinic agonist slows heart rate by muscarinic effect on SA node of heart, while, in contrast, beta-1 adrenoceptor agonist increases heart rate at SA node); *pharmacologic antagonist* — acts at same receptor as agonist (*eg*, naloxone and morphine antagonize each other at opioid receptor); pharmacologic antagonist may be competitive or noncompetitive; competitive antagonism reversible and surmountable; antagonist binds to the active site, preventing agonist binding; if concentration of agonist increases sufficiently, it overcomes binding of competitive antagonist, and agonist be able to produce its effect; noncompetitive or irreversible antagonist not surmountable; may involve covalent binding to the receptor so that even high concentrations of agonists cannot compete and activate receptor (*eg*, phenoxybenzamine, antagonist at alpha adrenoceptors)

Tolerance: when individual develops tolerance to drug, higher dose of drug needed to produce effects, both desirable and undesirable; tolerance that develops rapidly (within hrs) called tachyphylaxis (*eg*, nitroglycerin often causes tachyphylaxis when given by continuous IV infusion); development of tolerance takes days or wks to occur with drugs like opioids; greater degree of tolerance may develop to opioids than to any other class of medications; difference between required dose of opioid for initial management of pain compared with that required after many mos of use or therapy may vary more than 1000-fold; when people misuse opioids, especially those obtained without user's knowledge of purity or identity, accidental overdose may occur because of tolerance; with large doses of street opioids, small increase in potency may lead to excessive effect manifested as apnea and/or death

Drug metabolism: hepatic portal vein formed by veins that drain entire gastrointestinal (GI) tract, except distal part

of the rectum (drained by inferior rectal vein, which carries blood to iliac vein); hepatic portal vein carries blood (containing nutrients and drugs) from GI tract to liver; teleological reason for such system to ensure all compounds that enter body via GI tract presented to liver prior to circulating to rest of body; inherent assumption that all such compounds either nutrients processed by liver or toxins detoxified by liver before entering systemic circulation; medications given by mouth therefore subject to the first-pass effect, metabolized prior to circulating systemically; many oral medications thereby inactivated completely by first transit through liver; *several methods of drug administration bypass first-pass effect* — injections, rectal administration (drug given by suppository inserted to distal rectum), sublingual, transbuccal, and topical administration

Metabolism in liver: much of liver's drug-metabolizing machinery located within smooth endoplasmic reticulum, consists of mixed-function oxidase system; associated enzymes called microsomal enzymes; microsomes do not exist *in vivo*, artifacts of process by which they are prepared; microsomes liposomal vesicles that result when smooth endoplasmic reticula disrupted in process of homogenizing in fractionated liver tissue; microsomal enzymes include group of hemeproteins, cytochrome P450 (CYP450), cytochrome B5, 2 flavoprotein reductases that utilize NADPH and NADH, respectively, group of glucuronyl transferases, and epoxide hydrase; usual (but not universal) result of drug metabolism, rendering drug more polar and therefore more water soluble; increase in water solubility decreases renal tubular absorption of metabolite (process that occurs via passive nonionic diffusion), thus increasing rate of urinary excretion of metabolite; in addition, metabolite may be conjugated (*ie*, covalently bound to small molecule like glucuronic acid or sulfate), further increasing the drug's water solubility, and conjugated metabolite may be actively secreted into urine via transporters in renal tubules; drug metabolites also excreted in bile; increasing water solubility decreases propensity for reabsorption via enterohepatic circulation, thereby increasing fecal elimination of metabolites excreted in bile; drug metabolism reactions may be described in terms of where they occur (*ie*, microsomal vs nonmicrosomal) and whether reactions synthetic or nonsynthetic; *nonsynthetic reactions* — phase 1 reactions; consist of oxidation, reduction, or hydrolysis; *synthetic reactions* — phase 2 reactions; drug or metabolite conjugated to another small molecule; microsomal oxidative reactions catalyzed primarily by CYP450; nonmicrosomal reactions occur in cytoplasm, mitochondria, circulation

Microsomal nonsynthetic reactions: aromatic hydroxylation and aliphatic hydroxylation most common; example of aromatic hydroxylation propranolol, oxidized at its aromatic ring by adding hydroxyl group; alkyl chains connected to nitrogen or oxygen often oxidatively removed by CYP450 (termed N-dealkylation and O-dealkylation, respectively); addition of hydroxyl group to carbon atom adjacent to nitrogen or oxygen atom renders it unstable, leading to spontaneous and nonenzymatic break of carbon-nitrogen or carbon-oxygen bonds, thereby removing alkyl chain from nitrogen or oxygen atom, respectively (*eg*, N-dealkylation of lidocaine); desulfuration, oxidative reaction in which sulfur atom first oxidized to unstable sulfoxide intermediate; spontaneous rearrangement then occurs in which sulfur atom replaced by oxygen atom in molecule (*eg*, metabolism of thiopental to pentobarbital)

Microsomal synthetic reactions: only 1 reaction, *ie*, conjugation to glucuronide; glucuronyl transferases catalyze attachment of glucuronic acid molecule, usually at site of hydroxyl group; hydroxyl group may result from reaction catalyzed by CYP450 or may occur naturally, as in morphine

Nonmicrosomal, nonsynthetic reactions: important reactions include hydrolysis, monoamine oxidation, and alcohol and aldehyde dehydrogenation; esters and amides readily hydrolyzed and broken down into carboxylic acid and either alcohol or amine; ester and amide local anesthetics metabolized by these reactions; oxidation of amines by monoamine oxidase (MAO) important reaction (inhibition of this enzyme associated with clinically important and sometimes quite dangerous drug interaction); 2 distinct forms of MAO; 1 form prevalent in brain, other form prevalent in gut; inhibitors of brain enzyme used to treat depression and Parkinson disease; gut enzyme crucial for detoxifying dietary amines such as tyramine present in high concentrations in such foods as aged cheeses and red wine, pharmacologically active; tyramine potent vasopressor; person taking nonselective MAO inhibitor for depression who consumes foods containing tyramine at risk for suffering hypertensive crisis; initial step in alcohol metabolism catalyzed by alcohol dehydrogenase, yielding acetaldehyde; typically follows zero-order kinetics; acetaldehyde then converted to acetic acid by aldehyde dehydrogenase; aldehyde dehydrogenase may be inhibited deliberately by administration of disulfiram and other medications that have disulfiram-like activity; when aldehyde dehydrogenase inhibited and patient drinks alcohol, acetaldehyde concentration rises to point that patient becomes quite ill, like suffering worst imaginable hangover

Nonmicrosomal synthetic reactions: important reactions include those that transfer acetyl or sulfate group or glutathione; acetyl transferase adds acetyl group to amine; sulfate group may be added to hydroxyl group; hydroxyl group may result from reaction catalyzed by CYP450 or may occur naturally, as in acetaminophen; when taken in usual doses, acetaminophen primarily metabolized by conjugation to corresponding glucuronide or sulfate; as dose of acetaminophen increased, larger fraction of metabolism proceeds via oxidation of nitrogen via CYP450 to form N-hydroxylated metabolite of acetaminophen; this metabolite potentially very toxic and usually rendered harmless by conjugation to glutathione; however, with high doses of acetaminophen, supply of glutathione exhausted and toxic metabolite causes death of liver cells

Drug-interaction mechanisms: 2 common ways in which drugs may interact with each other via drug metabolism pathways; *induction* — process by which drug causes increase in number of enzyme

molecules; all microsomal enzymes subject to induction; barbiturates, prototype inducers for all microsomal enzymes; *process by which one drug increases metabolism of another drug* — important mechanism of drug interactions; some drugs inhibit drug metabolizing enzymes; some important inhibitors of CYP450 include imidazoles (*eg*, cimetidine), antifungal agents (*eg*, ketoconazole and itraconazole), macrolide antibiotics (*eg*, erythromycin and clarithromycin, but not azithromycin), HIV protease inhibitors, and grapefruit juice; other drugs may inhibit MAO or aldehyde dehydrogenase, resulting in other drug interactions

Basics of Pharmacogenetics and Drug Reactions

Pharmacogenetics: of how pharmacokinetics or pharmacodynamics of medications varies among individuals based upon genetic makeup

Glucose-6-phosphate dehydrogenase (G6PD) deficiency: most common pharmacogenetic entity in humans; sex-linked deficiency, most common in people from sub-Saharan Africa or Southern Europe bordering Mediterranean; people with G6PD deficiency suffer hemolysis of red cells when exposed to certain drugs or chemicals that increase rate of hydrogen peroxide generation in red cell; G6PD-deficient people must avoid nitrofurantoin (antibiotic) and primaquine (antimalarial)

Porphyria: pharmacogenetic disease caused by deficiency in heme biosynthetic enzyme; delta-aminolevulinic acid (ALA) synthase rate-limiting enzyme in heme biosynthesis; inducible; *3 types of porphyria from enzyme deficiencies* — acute intermittent porphyria, hereditary coproporphyria, and variegate porphyria; occur because of specific enzyme deficiencies that result in severe illness when inducer of ALA synthase given; upon induction of ALA synthase, ALA accumulates, neurotoxic; medications like barbiturates should be avoided in people with these forms of porphyria

Pseudocholinesterase deficiency: of interest primarily to anesthesiologists; plasma enzyme with no known endogenous substrate; succinylcholine only medication dependent upon it for its metabolism; people deficient in pseudocholinesterase, when given succinylcholine during surgery, will experience prolonged paralysis; ordinarily, drug completely metabolized within few mins; in people with enzyme deficiency, drug eliminated unchanged in urine, with half-life of ~0.5 hr, and will therefore last for few hrs instead of a few mins

Malignant hyperthermia: pharmacogenetic disease that results from abnormality in ryanodine receptor (protein important in excitation-contraction coupling in skeletal muscle); gene has prevalence of ~1 in few thousand in general population; characterized by incomplete penetrance and variable expressivity; when person with abnormal gene given succinylcholine or volatile anesthetic like isoflurane or sevoflurane, intracellular calcium concentration in muscle cells rises dramatically to abnormally high value and muscle fiber contracts but does not relax; this leads to hypermetabolic state characterized by increase in the production of CO_2 and lactic acid, followed by potentially dangerous increase in body temperature; most common early signs include unexplained tachycardia, hypercapnia, and cardiac arrhythmias

Alterations in clearance: disease states may result in alterations in clearance (*eg*, severe liver or kidney disease); *liver* — diseased liver may have lower rates of drug metabolism and may synthesize lesser amounts of plasma proteins that bind drugs; *eg*, rocuronium extensively metabolized by the liver, has longer duration of action in person with severe cirrhosis compared with person with normal liver function; person with severe liver disease may have hypoalbuminemia; drug like propofol, extensively bound to albumin, will have higher fraction of free drug in these patients, who may therefore need lower dose of propofol; *kidney* — glucuronide metabolites normally excreted by kidney; morphine metabolized to both 3- and 6-glucuronides; morphine 6-glucuronide active metabolite; person with compromised renal function who takes morphine chronically and therefore expected to derive significant analgesia from active metabolite may need lower dose of morphine than person with normal renal function

Adverse drug reactions: 3 types

Toxicity: dose-related adverse effect that; will occur commonly if adequate dose given

Idiosyncrasy: also dose related but rare and typically requires genetic predisposition (*eg*, drug-induced hemolysis in a G6PD-deficient person)

Hypersensitivity: allergy; reaction mediated by immune system and most commonly of type 1 or type 4 variety; type 1 reaction results when antigen binds to IgE, thereby releasing factors from mast cell or basophil; type 1 reaction, when severe, also known as anaphylactic reaction, is typically treated with epinephrine; type 4 reaction mediated by lymphocyte; many cases of penicillin allergy (not type 1, or anaphylactic), type 4 and cell mediated; anaphylactoid reaction similar to anaphylactic reaction but not triggered by antigen binding to antibody; certain medications with propensity to cause anaphylactoid reactions cause mast cells or basophils to release their contents, potentially resulting in urticaria, vasodilation leading to hypotension and/or bronchospasm; medications commonly associated with anaphylactoid reactions include morphine, succinylcholine, and atracurium

Other drug reactions: in addition to medications prescribed by physicians, patients may take over-the-counter medications, including nutritional supplements that have minimal oversight by federal government; some of these nutritional supplements may have significant effects in perioperative period; several commonly used nutritional supplements have anticoagulant effects (*eg*, feverfew, garlic, ginkgo, ginseng, danshen, dong quai); may cause increase in perioperative bleeding when taken shortly before surgery; garlic also induces some enzymes of CYP450 and inhibits other isozymes, and may dispose patient to drug interaction; kava has benzodiazepine-like activity and has caused reversible coma in people taking it and later given benzodiazepine; St. John's wort contains compounds that block the reuptake of several neurotransmitters and has caused serotonin syndrome when given in combination with other

medications that block reuptake of serotonin; valerian inhibits metabolism of GABA and potentiates effects of anesthetic medications that modulate GABA, such as volatile anesthetics propofol, benzodiazepines, etomidate, and barbiturates; prudent to stop all over-the-counter nutritional supplements prior to undergoing anesthesia and surgery

Suggested Reading

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Inhaled Anesthetic Agents

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History

Before inhaled anesthetics: several techniques to establish analgesia, if not anesthesia, for rudimentary surgeries; would be inefficacious, dangerous, or barbaric today; performing surgery swiftly with only nerve compression by surgeon or patient, or application of ice or snow to provide analgesia evolved into pharmacologic treatments with various plant extracts, including black nightshade, mandragora, and poppy seeds with or without ethanol

Inhaled anesthetics: era of inhaled anesthetics began with synthesis of diethyl ether; description of process dates back as early as 8th century; in 16th century, Paracelsus, observed and documented anesthetic effect of ether on chickens, but not enough to bring into clinical use; recreational ingestion or inhalation of ether practiced for nearly 3 centuries after Paracelsus's work; nitrous oxide (N_2O) discovered in 1773 by Joseph Priestley, later documented by Humphry Davy, who coined name laughing gas, described euphoric effect; N_2O swept into recreational substance category for >1 century; ether revisited by William Clarke in 1842; first documented use of inhaled anesthetic; also in 1842, Crawford W. Long demonstrated small-tumor resection on patient anesthetized with diethyl ether, captured public's attention; attempts at demonstrating ether's anesthetic capacity followed; in 1846, Massachusetts General Hospital, Sir William Morton anesthetized patient for facial vascular lesion; regarded as beginning of modern anesthetic evolution; other discoveries followed (*eg*, chloroform, between 1831 and 1847, used during Queen Victoria's labor

Flammable anesthetics: era of flammable anesthetics (*eg*, ether, ethyl chloride, cyclopropane) influenced blast chamber–like construction of operating rooms (ORs) and taught lesson in static electricity buildup; discontinued with advent of fluorinated hydrocarbon anesthetics, starting with most recently abandoned halothane; gave way to fluorinated alkene anesthetics

Pharmacology

Mechanisms of action (MOA): many theories on MOA of inhaled anesthetics, still mystery despite >150 years of use in OR; in early 1900s, Meyer and Overton made discovery noting that anesthetic potency directly proportional to lipid solubility; postulated that once certain saturation of neuron cell membrane (lipid bilayer) with anesthetic occurs, causes cessation in signal transmission; exceptions to rule found that certain substances predicted to have anesthetic properties inert, because of difference in size, polarity, or rigidity of molecule; theory became obsolete

Current thought: modern molecular data appeared at end of 20th and into 21st century; *gamma-aminobutyric acid (GABA) and glycine receptors* — common inhaled anesthetics, except N_2O, appear to enhance activity of GABA and glycine receptors; both receptors responsible for inhibitory signaling; GABA in the CNS, possibly reason behind angiolysis, sedation, amnesia, myorelaxation, and anticonvulsant action similar to GABA effects seen with barbiturates, benzodiazepines, and propofol; glycine receptors postulated as cause of inhibitory spinal cord effects of volatile anesthetics; activation of both receptors results in cell hyperpolarization and inhibition of signal transmission; *excitatory glutamate receptors* — inhibition of these receptors, notably N-methyl-D-aspartate (NMDA) receptors seen with halogenated alkene type anesthetics (eg, isoflurane, sevoflurane, desflurane) and with N_2O, xenon, cyclopropane, and other exotic anesthetics; seems to indicate common link where inhaled anesthetic may impart effect; anesthetics and compounds called nonimmobilizers (compounds that produce anesthetic effects without immobility) highlighted importance of acetylcholine receptors, excitatory nicotinic receptors implicated in memory formation and learning; direct interaction with protein structure of ion channel (*eg*, calcium, sodium, potassium) seen with various anesthetics possibly explains effect of negative chronotropic and inotropic effect on heart in addition to anesthetic properties; in contrast, N_2O has no effect on calcium and potassium channels and provides anesthesia with no cardiac depression; no definitive evidence singles out MOA of inhaled anesthetics; cannot explain how inhaled anesthetics function with 1 receptor or ligand mechanism, can only theorize

Potency: more lipid-soluble inhaled anesthetics generally more potent; to quantify and compare various inhaled anesthetics, concept of minimal alveolar concentration (MAC); *MAC* — originally defined as alveolar concentration of agent at 1 atmosphere of ambient pressure required to produce immobility in 50% of patients exposed to noxious stimulus (usually defined as skin incision in humans); analogous to ED_{50} concentration when comparing intravenous (IV) drugs; *MAC values of common anesthetics* — halothane 0.75%, enflurane 1.63%, isoflurane 1.17%, sevoflurane 2.2%, desflurane 6.6%, N_2O 104%, xenon 63%; values obtained without using additional medications commonly supplemented in anesthetic practice (*eg*, anxiolytics, analgesics); if clinician desires only to establish amnesia, value of

0.5 MAC, or half concentration needed for immobility, usually sufficient; since inception of MAC concept, other derivatives, such as MAC_{95}, equivalent to ED_{95}, translates to approximately 1.3 times original MAC value; MAC awake, meaning 50% of subjects open eyes to command exists somewhere between 0.15 MAC and 0.5 MAC, value exhibits significant hysteresis; other variations exist (*eg*, MAC values associated with blocking sympathetic response) not necessary to memorize; seldom rely on inhaled anesthetics alone for sympathetic control; MAC values additive; half of MAC of 1 anesthetic added to half MAC of another produces effect equivalent to 1 MAC of anesthetic; allows clinicians to supplement weaker anesthetic, more favorable side effect profile in some cases; N_2O alone only provides ≤0.07 MAC of anesthesia; usually needs to be accompanied by potent inhalational agent to deepen anesthetic plane without creation of hypoxic mixture, but doing so lowers exposure of patient to volatile anesthetic, possibly advantage on each gas under specific clinical conditions; *factors affecting MAC values*— many factors make patients more resistant to anesthetic, effectively increasing MAC value, and vice versa; age major factor when dosing inhaled anesthetic, MAC values in textbooks derived from population in 40s; chronologically, MAC value highest at age ~1 yr, declines progressively at rate of ~6% per decade; would expect same effect of 2.8% sevoflurane on 1-yr-old as 2.2% on 40-yr-old and 1.7% on 80-yr-old; modern anesthetic machines calculate adjustment of MAC value if patient age entered; *factors that increase MAC, necessitating higher dose for same effect*— increased excitatory neurotransmitter concentrations caused by monoamine oxidase inhibitors (MAOIs), acute amphetamine or cocaine ingestion, administration of ephedrine or levodopa; patients with hypermetabolic states, hyperthermia, hypernatremia, or chronic alcohol abuse also tend to have higher MAC values; redheads reported to have as much as 20% higher MAC values, suggests genetically based modulation of response; another genetic factor reported with sevoflurane with lower MAC values of 1.6 to 1.8 in early Japanese studies, but probably not clinically significant, regarded as controversial; *factors that decrease MAC value, make patients more susceptible to volatile anesthetics*— some factors exploited in OR daily to supplement inhaled anesthesia; advanced age, hypoxia, hypercarbia, and acidemia, as well as decreased excitatory neurotransmitter levels caused by reserpine administration or chronic amphetamine use, administration of alpha-2 agonists (eg, clonidine, dexmedetomidine), hypothermia hyponatremia, administration of lithium, acute ethanol ingestion; opioids, barbiturates, benzodiazepines, and IV local anesthetics lower MAC; obstetric practitioners noted that high progesterone levels as seen in pregnancy can decrease MAC by as much as 25% to 40%, allowing use of nitric oxide, which does not impart uterine contraction during cesarean delivery, with minimal supplementation of other volatile anesthetics; thyroid dysfunction has no significant effect on MAC value

Pharmacokinetics of common anesthetics: several values complement MAC, illustrate how anesthetics behave during induction or emergence, how they accumulate within tissues and their kinetics within vaporizer

Vapor pressure: inversely related to boiling point, value used to derive bypass flow of specific vaporizer or how much fresh gas required for mixing with saturated anesthetic vapor to arrive at appropriate blend selected on dial; vaporizers for agents with similar boiling points and vapor pressures can be used interchangeably without significant loss of calibration (but clinically seldom done); vapor pressures of sevoflurane and now-discontinued enflurane 157 mm Hg and 172 mm Hg, respectively; isoflurane and now-defunct halothane have vapor pressures of 238 mm Hg and 243 mm Hg, respectively; despite that internal workings of vaporizers in each pair similar enough to be interchangeable, accidental or intentional vaporizer cross-filling reason to take vaporizer out of use and have serviced as soon as practical; modern vaporizers employ safeguards to prevent inappropriate filler from engaging wrong anesthetic bottle and fillers unique to respective vaporizer systems; desflurane, with high vapor pressure of 669 mm Hg and low boiling point of 24°C, has its own unique vaporizer that heats up and pressurizes desflurane to ensure uniform output; remaining 2 anesthetics, N_2O and xenon, exist only as gases under normal temperature and pressure conditions; N_2O liquified under modest pressure of 750 psi, stored this way in pressure vessels; partial pressure of anesthetic driving force for anesthetic diffusion from liquid to gas phase in vaporizer, from alveolar air to bloodstream, then to target organ (*ie*, brain and spinal cord in) and nontarget tissue (*eg*, fat, muscle); partial pressure equilibration between alveolar air and brain results in onset of anesthesia; time required to achieve influences rapidity of induction; starting with higher partial pressure of anesthetic produces higher gradient for anesthetic concentration equilibration, speeds up induction; increasing output of vaporizer or minute ventilation both result in this effect, more pronounced with anesthetics that ordinarily have slow induction times

Distribution: conventionally thought that anesthetic gas distributed from alveoli to several compartments within human body, behavior predicted using multicompartment distribution model; *compartments commonly considered*— vessel-rich group comprised of brain, heart, liver and kidneys (10% of body mass, receives 75% of blood flow(; muscle group (50% of body mass, receives 20% of cardiac output); fat compartment (20% of body weight, receives only 6% of cardiac output)

Partition coefficients: partition coefficients of anesthetics between blood and specific tissue or substance describe behavior of inhaled anesthetic within compartments, simply ratio of anesthetic quantity on both sides of blood to tissue interface once partial pressure at equilibrium; *oil-gas partition coefficient*— another term for lipid solubility; predicts MAC value of anesthetic according to Meyer-Overton rule; c*oefficient blood-gas partition coefficient*— describes how anesthetic will equilibrate between alveolar gas and pulmonary capillary blood flow; higher blood-gas partition coefficient, more soluble agent in blood; when anesthetic gas delivered into alveoli through spontaneous or controlled ventilation, taken up by first compartment (blood), diminishing alveolar concentration and slowing induction; more blood-soluble anesthetics have slower induction because blood absorption decreases rate of rise of alveolar

concentration of anesthetic gas, prolonging time to build up necessary partial pressure of anesthetic in alveoli

Solubility coefficients of modern inhaled anesthetic in blood (in ascending order): desflurane 0.42, N_2O 0.46, sevoflurane 0.65, isoflurane 1.46; reasonable to expect inductions with N_2O and desflurane to occur faster under similar conditions because of low blood solubility; as anesthetic delivered to brain and rest of vessel rich compartment from alveolar gas via bloodstream, anesthetic depth increased, vessel-poor groups (muscle and fat) lag behind in saturation with anesthetic gas; in course of steady-state anesthesia when vessel rich group at equilibrium with alveolar air, compartments continue to equilibrate until partial pressure gradient ceases to exist for each separate compartment; not important during short anesthetic cases because no significant accumulation of anesthetic in vessel-poor tissues to prolong emergence from anesthesia when gradient reversed; anesthetics egress from brain through circulation and into alveolar gas to be exhaled

Contact-sensitive half-time: phenomenon that occurs with prolonged exposure to fat- and muscle-soluble anesthetics;, if 2 patients provided same depth of anesthesia for different durations, patient with longer exposure will require longer time to emerge from anesthesia due to saturation of vessel-poor compartments, effectively experiencing longer half-time of agent; *comparative blood-fat solubility (from lowest to highest)* — N_2O 2.3, 10-fold lower than desflurane, 27; isoflurane 45, sevoflurane 48; prolonged anesthesia with sevoflurane and isoflurane results in more significant accumulation of agent, may cause prolonged elimination time; muscle-to-blood solubilities do not vary dramatically, follow same hierarchy, difference from lowest, N_2O, to highest, sevoflurane, only 2.5-fold, solubility in muscle compartment of all agents 10- to 20-fold lower than in fat, decreasing importance of muscle compartment on contact-sensitive half-time

Other factors: effects of ventilation rate, variations in cardiac output, concentration effect and second gas effect; increase in ventilation provides more rapid equilibration between alveolar and inspired concentrations of anesthetic (also known as FA:FI ratio); faster equilibrium due to increased ventilation more pronounced in gases more absorbed by blood (*eg*, isoflurane, sevoflurane); blood carrying anesthetic away from alveoli, diminishing alveolar concentration and slowing rate at which alveolar concentration rises; more blood-soluble anesthetics affected to greater extent by variations in cardiac output, noticeably faster induction in setting of low cardiac output; higher cardiac output means more anesthetic carried away from alveoli, alveolar concentration rises more slowly, causes prolonged time to build up sufficient partial pressure of anesthetic in alveoli; effect more pronounced with blood-soluble anesthetics (*eg*, isoflurane, sevoflurane)

Concentration effect: another concept related to rate of rise of alveolar concentration of anesthetic as influenced by inhaled anesthetic concentration; when constant proportion of anesthetic absorbed by blood, higher inspired anesthetic concentration will yield greater concentration of gas in alveolar air after absorption occurs; N_2O has partition coefficient of 0.47, so from breath of 35% N_2O in O_2 mixture, 11 parts of N_2O will be absorbed and 24 left behind for effective alveolar concentration of 24/89, or 27%; if 70% N_2O in O_2 administered, same proportion, or 22 parts, of N_2O will be absorbed, 48 parts will remain in alveoli, and result on alveolar concentration will be 48/78 parts, or 61.5%; alveolar concentration appears to increase disproportionately with doubled inspired concentration of anesthetic

Second gas effect: tightly related to concentration effect; phenomenon of apparent increase in concentration of volatile anesthetic when accompanied by another gas rapidly taken up from alveolar gas mix; consider 1% mixture of volatile anesthetic with 70% N_2O and O_2 in balance; with rapid absorption of 50% nitric oxide from gas mixture, which would equal 35 parts, and assuming negligible absorption of other gases, new concentration of volatile anesthetic, 1/29 parts O_2 and 35 parts N_2O or 1/65 or 0.015 parts, or 1.5%; if missing volume left over from absorption of 35 parts of N_2O replaced with original fresh gas mixture described above, proportionately adding 0.35 parts potent volatile agent, 24.5 parts N_2O and 10.15 parts O_2, final concentration of potent volatile anesthetic in alveolus still 1.35%, significantly higher than fresh gas delivered to patient; for second gas effect to be clinically significant, gas mixture must contain large fraction of rapidly absorbed gas that creates rise in concentration of potent inhaled anesthetic; aside from N_2O, no other gases included in anesthetic mixture in high-enough concentrations to create second gas effect, as volatile anesthetics have MAC values of ≤6%, absorption does not appreciably disturb balance of alveolar gas; absorption of O_2 from alveolar gas comparatively insignificant to proportion delivered to alveoli during semiopen-circuit anesthetic deliveries that comprise majority of anesthesia practices

N_2O: although N_2O one of most insoluble anesthetics, absorption by absolute volume not insignificant, because of high MAC value, therefore high inspiratory concentration necessary for clinical effect; solubility constant of N_2O (0.46) 30-fold higher than nitrogen's blood-gas partition coefficient (0.015), so theoretical air-space chamber in body of patient exposed to 50% inspired N_2O concentration will rapidly equilibrate to nitrous partial pressure and double in size before nitrogen can equilibrate out; 75% N_2O inhalation will quadruple size of air chamber, as final concentration will have to match 75%; clinically significant in enclosed spaces during middle-ear or retinal surgery, where increase in volume or pressure of air bubble highly undesirable; gastrointestinal (GI) surgery can be impeded by distending of gas-filled bowel; pneumothoraces may expand to potentially double or triple in size as well as air filled cuffs in endotracheal tubes or Swan-Ganz catheters; if patient recovering from N_2O anesthesia and placed on room air before anesthetic has chance to egress sufficiently, equilibration of partial pressure of N_2O between tissues and now room air in alveolus can pose problem; assume a patient still has partial pressure of N_2O equivalent to 30% and breathing spontaneously on room air, egressing N_2O will rapidly equilibrate with alveoli and new composition of alveolar gas will be 21 parts O_2, 79 parts nitrogen, and now 30 parts N_2O; final

O_2 concentration then calculated at 21/130, or 16%; dilutional effect also affects concentration of carbon dioxide, lowering it, potentially decreasing respiratory drive and worsening hypoxia; recommended that all patients recovering from N_2O anesthesia receive 100% O_2 for first 5 mins to 10 mins, when outpouring of N_2O from tissues highest

Pharmacodynamics

Cardiac: all volatile anesthetics except N_2O and xenon produce dose-dependent decrease in blood pressure (BP); older agents like halothane and enflurane had negative inotropy as source of effect, not seen with modern anesthetics like sevoflurane, isoflurane, and desflurane (cause decrease in BP through decrease in systemic vascular resistance); N_2O produces either no change or only slight increase in BP; chronotropy, or heart-rate effects, variable among modern anesthetics; isoflurane and desflurane produce dose-dependent increase in heart rate, especially pronounced with rapidly uptitrated high doses of desflurane; N_2O and sevoflurane not associated with substantial changes in heart rate; myocardial contractility depression, seen with older agents (*eg*, halothane and enflurane), seen to lesser extent with isoflurane, sevoflurane, and desflurane (some argue effect no longer clinically significant); N_2O has slight sympathomimetic activity, increases cardiac contractility; isoflurane known to induce coronary artery vessel dilation, hypothesized to cause redistribution of coronary blood flow away from atherosclerotic areas to areas with normal coronaries (coronary steal syndrome; not validated in clinical practice); N_2O, desflurane, and sevoflurane weaker coronary artery vessel dilators than isoflurane; cardiac dysrhythmias induced with older agents particularly halothane), especially in combination with administration of catecholamines (*eg*, epinephrine); not seen with ether-based anesthetics, less pronounced in pediatric population

Respiratory: all agents, except sevoflurane and N_2O, respiratory irritants, not suitable for inhalational induction; halothane, potent anesthetic and bronchodilator, excellent choice for inhalational induction of reactive airway but no longer in clinical use; sevoflurane next best agent, relaxes smooth muscle as well and has pleasant smell; all inhaled anesthetics cause dose-dependent decrease in tidal volume and increase in respiratory rate; net result, decrease in minute ventilation and increase in $PaCO_2$ if patient allowed to breathe spontaneously; inhaled anesthetics also blunt respiratory response to hypoxia and hypercarbia via central nervous system (CNS) respiratory center depression and alteration of a carotid body response; impairment of response to hypoxia seen at subanesthetic doses as low as 0.1 MAC (factor to consider during postanesthetic care); N_2O increases pulmonary vascular resistance, especially in patients with preexisting pulmonary hypertension; all other inhalational agents may decrease pulmonary vascular resistance and blunt hypoxic pulmonary vasoconstriction reflex, potentially exacerbating shunting through nonventilated alveoli

CNS: all inhalational agents except N_2O exert similar effects on CNS; cerebral metabolic rate decreased in nonlinear fashion and to varying degrees when compared among anesthetics; cerebral blood flow increased in dose-dependent manner, resulting in uncoupling of supply and demand; increased cerebral blood flow thought to be clinically significant with older halothane, but modern anesthetics do so minimally at clinical doses; intracranial pressure (ICP) important in neurosurgical cases, halothane may be worst agent due to strong propensity to increase cerebral blood flow; hypercarbia associated with respiratory depression seen with all anesthetics further exacerbates phenomenon; when increase in ICP must be avoided, hyperventilation preinduction and use of modern inhalational agent warranted, pretreatment with barbiturate may lessen effect; pungency of desflurane and isoflurane may trigger coughing on induction and transient rise of ICP, some may argue sevoflurane better choice for avoidance of ICP spike; *N_2O* — seldom used alone in neurosurgery, weak anesthetic; when supplemented to another volatile agent, appears to cause cerebral vasodilation and increase in cerebral blood flow (but finding controversial); cerebral metabolic rate reports highly variable, with either minimal depression, no change, or increase in metabolic demand; always coadministered with another potent volatile agent, may be confounding variable behind variability of response; rat models of cerebral ischemia with N_2O and isoflurane anesthetic had worse outcomes than isoflurane alone, but translation to humans controversial; concern of expanding pneumocephalus (venous air embolus) in setting of craniotomy in sitting position with N_2O administration adds further argument against application in neurosurgery; benefits of N_2O in neurosurgery not sufficient to warrant attempts at use

Hepatic: dual nature of blood supply to liver affected differently by various anesthetics; hepatic artery flow increased or maintained by modern anesthetics such as isoflurane, sevoflurane and desflurane; portal vein flow decreases to various extents; halothane decreased both arterial and venous flow, implicated in causing hepatitis, both via blood flow reduction as well as immune-mediated effects and metabolic byproducts of halothane degradation; more common reasons for jaundice than halothane hepatitis postanesthesia include viral hepatitis, malperfusion due to hypertension of sepsis, hemolysis, or other drug-induced hepatitides

Renal: dose-dependent decrease in renal blood flow, glomerular filtration rate (GFR), and urine output seen with all potent inhalational anesthetics; older anesthetic methoxyflurane metabolized to high extent in kidney, with resultant release of inorganic fluoride ion, causing occasional high-output renal failure; not seen with newer anesthetics metabolized to lesser extent; sevoflurane has unique interaction with renal system, capable of reacting with CO_2 absorber to form nephrotoxic haloalkene, compound A; production of compound A highest in setting of high sevoflurane concentration with calcium hydroxide and barium hydroxide (Baralyme) instead of soda lime absorber; desiccated absorbers increase CO_2 production in higher CO_2-absorber temperatures; low fresh gas flow decreases CO_2-absorber cooling, lowers dilutional washout of compound A from circle system; sevoflurane package insert recommends <2 MAC-hr of anesthesia at fresh gas flow rates of 1 L/min to 2 L/min, flows <1 L min not recommended

Neuromuscular: all ether-derived potent volatile anesthetics relax skeletal muscle directly and to greater extent than halothane due to direct inhibition of nicotinic acetylcholine receptor, also potentiate action of nondepolarizing

neuromuscular blockers; N_2O does not relax skeletal muscle, may cause rigidity under hyperbaric conditions (effect that would seldom be seen in clinical practice); *malignant hyperthermia (MH)* — more potent inhalational agents appear to have greater ability to trigger MH, an autosomal dominant disorder of ryanodine receptor; all agents listed as unsafe in MH literature; N_2O generally regarded as safe, though minimally potentiates muscle contraction in MH-specific caffeine-induced contraction tests; scattered case reports of N_2O anesthesia triggering MH episode in setting of otherwise nontriggering agent exist, but stress may also be factor; given availability of excellent nontriggering IV anesthetics, use of N_2O may become unnecessary, but no ground to abandon use in MH-susceptible population based on clinical evidence so far; xenon inhalational agent also considered MH safe, can be considered in areas where available for clinical use

Hematologic: all volatile anesthetics degrade in presence of calcium hydroxide and barium hydroxide or soda lime to release CO; effect more pronounced with desiccated absorbers; desflurane releases CO most, followed by isoflurane, then sevoflurane; high CO_2-absorber temperature, calcium hydroxide and barium hydroxide over soda lime, and high anesthetic concentrations enhances CO formation; breakdown process of inhaled anesthetics exothermic reaction, combination of older, desiccated absorber with sevoflurane produces most heat, ≤300°C, and melting parts of circuit; good practice to turn off anesthetic machine at end of case and for prolonged downtime (overnight and weekends); if desiccated absorber situation discovered, replace with new absorber canister; newer CO_2 absorbers have less propensity to break down anesthetics to CO and compound A, exhibit less heat production; effects of N_2O on vitamin B_{12} — another hematologic effect unique to N_2O, oxidation of cobalt 1 to cobalt 2 or cobalt 3 in vitamin B_{12} molecule; irreversible process; prolonged or repetitive exposure can cause symptoms consistent with B_{12} deficiency, even in patients who had normal B_{12} levels; case reports of patients developing megaloblastic anemia due to impairment of DNA synthesis pathway, or even subacute combined spinal cord degeneration due to inhibition and methionine synthase enzyme and demyelination of axons, have been reported both in clinical administration of N_2O and recreational use; when treated early and appropriately with cyanocobalamin (B_{12}), prognosis generally favorable, but making critical diagnosis challenging because of esoteric presentation of disease (anemia, ataxia, incontinence, dizziness, visual disturbances); if B_{12} plasma level <125 pg/mL, clinical suspicion should be elevated and should guide treatment

Environmental Exposure

Exposure and toxicity: given toxicity of N_2O and evidence of detrimental effects of prolonged exposure to potent volatile anesthetic, Occupational Safety and Health Administration (OSHA) limits exposure of health care personnel to anesthetic contamination; when N_2O used as sole inhaled anesthetic, recommended exposure limit 25 ppm, measured as time-weighted average during period of anesthetic administration; also recommended that no worker be exposed to ceiling concentration >2 ppm for any halogenated anesthetic agent over sampling period not to exceed 1 hr; when N_2O and volatile anesthetics used together, maximal exposure 25 ppm and 0.5 ppm, respectively; achievement of goals relies on engineering controls (*eg*, properly functioning anesthetic scavenging system) and appropriate work practices to avoid spillage of agent and gas-mixture leakage from mask airway; testing done on administrative-control level to ensure proper function and compliance; fire risk pronounced with N_2O, a nonflammable gas by itself, but potent oxidizer, on par with molecular O_2, used in high enough concentration enhances chance of OR fire; fortunately, other inhaled anesthetics nonflammable

Xenon

Background: name comes from Greek word *xenos*, meaning foreign, strange, or guest; noble gas with heavy molecule, atomic number 54, atomic weight 131 for its most stable isotope; 4 times denser than air; only exists as gas under normal conditions; found in atmosphere at concentration of 87 ppb; considered trace element; not synthesized but distilled off during processing of raw air to extract O_2 and nitrogen as byproduct; virtually nonreactive with other elements; first use as anesthetic reported by Stuart Cullen, 1951; still far from widespread use

Anesthetic properties: MAC value 60%, blood-gas partition coefficient 0.115 (lowest among all current anesthetics); results in fast induction and emergence; nonflammable, does not support combustion; mechanism of action not entirely known; evidence that xenon inhibits plasma membrane calcium pump, altering excitability; xenon-driven CNS depression results in lower respiratory rate with compensatory increase in tidal volume, at high doses may lead to apnea; diffusion hypoxia mild, as blood gas partition of nitrogen (0.014) and xenon (0.115) more similar to each other rather than to N_2O, so diffusion occurs in more balanced manner; no apparent inhibitory effects on cardiac ion channels such as calcium, sodium, and potassium; causes no significant chronotropic or inotropic effects; does not affect systemic vascular resistance; no sensitization of myocardium to epinephrine; *systemic effects* — in CNS, xenon may increase cerebral blood flow, but magnitude of effect remains to be elucidated; no known liver or kidney toxicities, no hematologic disturbances reported when used at routine anesthetic level; not reported to trigger MH; *advantages and disadvantages* — environmentally friendly; derived from air and any loss in the atmosphere creates no personal hazard or contribution to greenhouse effect or pollution; expensive because of complex nature of extraction from air; thorough denitrogenation preinduction and use of circle system with excellent scavenging and recycling of anesthetic required; measurement of xenon levels generally difficult because diamagnetic, does not absorb infrared radiation; low reactivity precludes use of specific fuel cell or electrode-type device; mass spectrometry only way to detect reliably (expensive)

Suggested Readings

Eckenhoff RG: Promiscuous ligands and attractive cavities: how do the inhaled anesthetics work? *Mol Interv*. 2001;1(5):258-68; **Robinson DH et al:** Historical development of modern anesthesia. *J Invest Surg*. 2012;25(3):141-9; **Sonner JM:** A hypothesis on the origin and evolution of the response to inhaled anesthetics. *Anesth Analg*. 2008;107(3):849-54; **Whalen FX et al:** Inhaled anesthetics: an historical overview. *Best Pract Res Clin Anaesthesiol*. 2005;19(3):323-30.

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Clinical Pharmacology of Nonopioid Intravenous Anesthetic Drugs

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Nonopioid intravenous (IV) anesthetic drugs: backbone of anesthesiology practice; act on variety of molecular targets, most importantly GABA A receptor (ligand-gated ion channel for inhibitory neurotransmitter gamma-aminobutyric acid [GABA]); propofol, etomidate, and benzodiazepines positive allosteric modulators of GABA A receptors; when bound to receptor, indirectly increase influx of chloride ions into cells in response to endogenous ligand GABA

Propofol: potentiates effect of GABA on GABA A, but can also activate receptor directly; versatility and popularity owe great deal to favorable pharmacokinetic profile

Pharmacokinetics and metabolism: bolus of propofol reaches peak effect-site concentration within 90 secs in adults, ~2 mins in children; clinical effect of bolus terminated by redistribution such that concentration at effect site less than half peak value 5 mins after injection; propofol metabolized by conjugation and allows rapid recovery even after prolonged infusions; this property captured by context-sensitive half-time (time required for plasma concentration to decrease by 50% once infusion stopped); here, duration of infusion=context, and propofol context-sensitive half-time remains low and relatively constant even after 10 hrs of infusion

Physiologic effects: in addition to action on brain, propofol has effects on several other organ systems; *respiratory* — blocks airway reflexes and impairs swallowing, which can facilitate endotracheal intubation, but also increases risk of obstruction and aspiration when used for sedation; also decreases respiratory drive and causes bronchodilation; *cardiovascular (CV)* — causes significant vasodilation, which can lead to hypotension; patients with severe hypovolemia may require only 10% to 20% of usual induction dose; *other* — also has antiemetic effect, even at some anesthetic doses

Adverse effects: pain during injection most common side effect, appears to be related to free aqueous concentration; meta-analysis concluded that coadministration with lidocaine and injection into larger veins most effective ways to mitigate this discomfort; most reported drug interactions involve additive effects when propofol given with other respiratory or central nervous system (CNS) depressants; evidence suggests propofol weak inhibitor of liver enzyme CYP3A4, so it can potentially increase levels of 3A4 substrates, such as lidocaine and midazolam; lipid carrier contains soybean oil and egg lecithin, has been source of concern; risk of bacterial growth decreased by addition of antimicrobial agents; discard any unused drug after opening based on label instructions; another concern with formulation, potential for adverse reactions in patients with egg or soy allergies; despite warnings on label, both available evidence and American Academy of Allergy, Asthma and Immunology suggest propofol safe to use in these patients; although perioperative use rarely leads to serious toxicity, prolonged infusion can sometimes cause life-threatening reaction called propofol infusion syndrome, characterized by metabolic acidosis, may lead to rhabdomyolysis and renal failure; long infusions may also lead to hypertriglyceridemia

Clinical uses: induction and maintenance of general anesthesia as well as sedation for patients undergoing procedures or receiving mechanical ventilation in intensive care unit (ICU); procedural sedation may be quite deep and can inadvertently transition to general anesthesia (*eg*, study of patients receiving propofol for colonoscopy revealed 50% had processed EEG consistent with general anesthesia); for maintenance of anesthesia, propofol infusion may be used as adjunct to follow anesthetics or as part of total intravenous anesthesia (TIVA); *potential advantages of propofol-based TIVA over maintenance with inhaled anesthetics* — necessary in patients with history of malignant hyperthermia; from sustainability perspective, environmental impact of TIVA 2 to 4 orders of magnitude smaller than that of volatile technique; TIVA also associated with lower rates of postoperative nausea and vomiting (PONV), so technique of choice for patients who have suffered PONV despite usual prophylaxis; several studies have found decreased postoperative pain with TIVA, though 2016 meta-analysis did not show statistical; retrospective studies have found association between TIVA and either decreased recurrence or improved survival after cancer surgery; large clinical trials under way to test this association

Etomidate: acts at GABA A receptors with higher selectivity and fewer effects on other ion channels than with propofol; like propofol, allosteric modulator at lower doses and direct agonist at higher doses;

Pharmacokinetics and metabolism: bolus of etomidate rivals speed of propofol, with peak effect within 2 mins of injection; however, effect-site concentration declines more slowly after bolus of etomidate; etomidate metabolized in liver by ester hydrolysis; relatively short context-sensitive half-time, but usually not given as infusion because of side-effect concerns

Physiologic effects: binds to enzyme 11-beta-hydroxylase with high affinity, leading to suppression of cortisol synthesis at plasma levels 20 times lower than those required to induce unconsciousness

Adverse effects: *adrenal suppression from bolus of etomidate* — lasts several hrs even though hypnotic effect lasts for only few mins; although effect on cortisol levels well established, impact of adrenal suppression on patient outcomes remains controversial; in perioperative setting, 1 hospital reviewed ~6000 anesthetics before and after propofol shortage in 2010; found no increase in mortality during shortage even though 80% of patients received etomidate; however, propensity-matched analysis of >7000 patients at Cleveland Clinic found etomidate carried 2.5 odds ratio of death compared with propofol; data from critical care arena also conflicting; consider potential long-term harm with perceived short-term benefits; *other* — few side effects besides adrenal suppression; some (*eg*, pain on injection and myoclonus during induction) transient, rarely with serious consequences; increased PONV frequently cited; no absolute contraindications, but should be reserved for cases in which it has clear advantages over induction with other agents

Advantages: favorable hemodynamic profile compared with propofol, though smaller benefit when compared with induction with mixture of propofol and ketamine; in contrast to propofol, little need to alter etomidate doses in animal models of hemorrhagic shock

Clinical uses: widely used for cardiac surgery; use in surgical population may have decreased over time, but recent, propensity-matched analysis of >6000 cardiac patients found no evidence of harm; in terms of effects on ventilation, causes less respiratory depression than methohexital; in brain, suppresses seizures less than propofol and etomidate; can be used for electroconvulsive therapy

Benzodiazepines: when bound to alpha subunit of GABA A receptor, increase chloride conductance in response to endogenous ligand; inability of benzodiazepines to directly open ion channel may contribute to ceiling effect at higher doses; 3 most important members of this class, from most to least potent: lorazepam, midazolam, and diazepam; lorazepam and diazepam must be formulated in glycol solutions, but midazolam water soluble because of ability to rapidly convert between lipophilic and hydrophilic confirmations

Pharmacokinetics and metabolism: pharmacokinetics can be counterintuitive; based on elimination half-lives, midazolam classified as short-acting, lorazepam intermediate-acting, diazepam long-acting; however, when looking at clinical effect lorazepam has slowest onset and longest duration of effect after bolus; diazepam has most rapid time to peak effect and modestly longer duration than midazolam; although rapid onset, peak effect occurs 5 mins to 10 mins after bolus; this delay, which can be exaggerated in elderly, may lead to dose stacking; children without IV access commonly given oral midazolam as premedication; bioavailability of oral route <30%, time to peak effect ~50 mins; benzodiazepines can also be given by intramuscular (IM) injection (primarily as treatment for seizures); in perioperative setting, neither diazepam nor lorazepam given as infusions because of prolonged context-sensitive half-times; midazolam displays more favorable context-sensitive half-times, but markedly inferior to propofol in this respect; in terms of metabolism, both diazepam and midazolam substrates for the liver CYP3A4 enzyme; both drugs have active primary metabolites; midazolam's metabolite rapidly cleared in patients with normal renal function; in contrast, lorazepam undergoes glucuronidation and has no active metabolites; thus lorazepam has fewer drug interactions, less affected by renal dysfunction than midazolam; mitogenic studies suggest alpha-1 subunit of GABA A receptor mediates amnestic, anticonvulsant, and sedative effects of benzodiazepines, while alpha-2 subunit plays role in anxiolysis and muscle relaxation

Physiologic effects: benzodiazepines have apparent antiemetic effect; midazolam most widely studied in perioperative setting; recent meta-analysis noted reduced PONV; in other organ systems, benzodiazepines can cause modest decreases in blood pressure, but overall, maintain cardiac stability; benzodiazepines can affect respiration both through direct effect on ventilatory drive and by decreasing muscle tone in upper airway

Adverse effects: coadministration of opioids may augment these effects; *respiratory* — study found propofol and midazolam induce similar rates of airway obstruction, but last longer after midazolam; *neurologic* — delirium — as potential side effect of benzodiazepines; mixed data from perioperative arena, may be confounded by underlying risk in study populations; in ICU, clearer association between benzodiazepine sedation and adverse neurocognitive outcomes; may be prudent to avoid or minimize benzodiazepine use in patients with higher risk for respiratory or cognitive side effects; *contraindications* — few absolute contraindications for benzodiazepines; acute narrow-angle glaucoma listed as contraindication for many drugs in this class; however, German systematic review found only 1 case report of harm in glaucoma and many studies suggest these drugs safe in these conditions

Advantages: also useful anticonvulsants, first-line agents for status epilepticus; although now somewhat out of favor, still used for sedation in ICU; central muscle relaxation can be useful for muscle spasticity and accompanying pain; benzodiazepines have competitive antagonist, making them rather unique among nonopioid IV anesthetics

Clinical uses: commonly used as premedication or procedural sedation because of anxiolytic and amnestic properties; large randomized control trial of lorazepam in French surgical patients found no impact on patient satisfaction; benzodiazepine premedication can reduce induction drug requirements and serve as useful component of balanced anesthetic technique and PONV prophylaxis; in large doses, can be used as induction agents; usually provide good hemodynamic stability, but kinetics can slow emergence after short cases

Reversal: flumazenil has onset within 3 mins, but rapidly metabolized by liver and duration of effect shorter than most benzodiazepines, so patients must be closely monitored for resedation; since duration of effect 30 mins to 60 mins, if no sedation within 2 hours, unlikely to occur afterward; actually partial agonist, but effect on GABA A usually produces no sedative effects; usually well tolerated but can precipitate

seizures that have been terminated by benzodiazepines; studies suggest it may reverse general anesthesia, but applicability to human patients remains to be seen

Other agents: thiopental no longer available in United States, 2 other IV anesthetics that do not act primarily at GABA A receptor

Ketamine: relative of phencyclidine, which blocks N-methyl-D-aspartate (NMDA) subgroup of ionotropic glutamate receptors; NMDA receptors play excitatory role in nervous system by allowing calcium influx; channel pore of NMDA receptors normally blocked by magnesium, so calcium influx requires both glutamate binding and membrane depolarization; ketamine blocks pore of NMDA receptors and therefore noncompetitive antagonist of glutamate; ketamine also has effects on other receptors (*eg*, alpha-7 nicotinic receptors, HCN receptors)

Pharmacokinetics and metabolism: bolus kinetics of ketamine feature fastest time to peak effect of IV anesthetics discussed here; ketamine bolus not only reaches peak effect more rapidly than propofol bolus, also dissipates more quickly; modeling in adults suggests that 5 mins after bolus, effect-site concentration 50% of peak for propofol, but only 20% of peak for ketamine; recent study in children found slower offsets after ketamine bolus; rapidly metabolized in liver, primarily by CYP3A4; initial metabolite, norketamine, has ~20% of activity of ketamine; after undergoing further metabolism, excreted in urine; context-sensitive half-times of ketamine infusions shorter than those of midazolam, but longer than those of etomidate and propofol; can also be given by IM and intranasal (IN) routes; kinetics of IM ketamine not well studied despite decades of clinical use; recent pediatric study suggests bioavailability after IM injection ~40% and onset takes 5 mins to 10 mins, depending on dose; peak plasma levels occur between 20 mins and 30 mins, depending on child's age and size; IN route has 50% bioavailability in children and plasma levels peaked 20 mins after administration

Physiologic effects: ketamine anesthesia clinically and electroencephalographically distinct from that produced by other drugs; clinically, "dissociative anesthesia" often used because patients may appear awake but disconnected from their surroundings; *neurologic* — on EEG, ketamine produces high-frequency waves in beta and gamma ranges, with relatively little slow-wave activity in alpha range; some processed EEG monitors may erroneously characterize this state as lightly anesthetized; produces both spinal and supraspinal analgesia; also causes nystagmus and increased sympathetic outflow; *CV system* — sympathetic surge plays key role in CV effects; patients with normal catecholamine reserves usually exhibit tachycardia and hypertension in response to ketamine; depression, rather than stimulation, direct effect of ketamine on heart; patients with depleted catecholamine stores may experience CV collapse after ketamine; *respiratory* — maintains ventilation and produces bronchodilation; sometimes used in children with severe bronchoconstriction, but also causes increased salivation and secretions

Adverse effects: in addition to salivation and nystagmus, may produce emergence delirium and other neuropsychiatric side effects; increases intracerebral pressure via increased cerebral blood flow, also increases intraocular pressure; *contraindications* — allergy only absolute contraindication; many relative contraindications for patients who may be harmed by various end-organ effects; extreme hypertension could be harmful for patients with cerebrovascular disease, and along with tachycardia, could increase myocardial oxygen demand in patients with cardiac disease; CV effects may be exaggerated in patients with thyrotoxicosis; increases in intracerebral pressure may be harmful in patients with brain trauma, cerebral mass lesions, or bleeding; similarly, caution needed in patients with glaucoma, ocular trauma, or ocular surgery; patients with history of psychiatric disease may be at increased risk of adverse neuropsychiatric effects

Advantages: some studies found antitolerance effect in patients taking chronic opioids or those receiving prolonged remifentanil infusions; increased interest in opioid-sparing techniques, both for enhanced recovery after surgery and to mitigate opioid crisis, has led to dramatic increase in ketamine use

Clinical uses: traditional clinical applications include induction of anesthesia and procedural sedation; American Society of Regional Anesthesia and Pain Medicine recently published consensus guidelines for use of ketamine infusions for acute and chronic pain; for acute pain, Grade B recommendations that subanesthetic ketamine reasonable for surgeries with moderate to severe postoperative pain or any surgery in opioid-tolerant patients; also Grade C recommendations for consideration in patients with sickle cell pain or sleep apnea; acute-pain dosing recommendations to limit boluses to 0.35 mg/kg and infusions to ≤1 mg/kg/hr; other applications take advantage of ketamine's preservation of respiratory drive and potent analgesia; can be used as adjunct for regional or neuraxial anesthesia and may sometimes serve as rescue agent if blocks become inadequate; can also be useful for awake intubations, but anticholinergics often required to counter hypersalivation (can be avoided by use of dexmedetomidine)

Dexmedetomidine: s-enantiomer of medetomidine (drug used for 30 yrs in veterinary anesthesia); structurally similar to clonidine (alpha agonist), but 7-fold greater selectivity for alpha-2 adrenergic receptors than for alpha-1 receptors; activation of alpha-2 receptors has sedative, analgesic, and sympatholytic effects; because these receptors abundant in locus coeruleus, dexmedetomidine sedation shares some features with non-REM sleep; even deeply sedated patients often arousable and able to follow commands

Pharmacokinetics and metabolism: usefulness of dexmedetomidine limited somewhat by pharmacokinetics; label recommends delivering loading dose of ≤1 mcg/kg over 10 mins; because this dose may be poorly tolerated in patients with tenuous hemodynamics, many clinicians either reduce or omit loading dose in these patients; without loading dose, >5 hrs for infusion to reach 50% of steady-state concentration; by contrast, propofol infusion reaches 50% of steady state within 30 mins; rapid bolus dosing of dexmedetomidine not widely reported in adults, but studied in anesthetized children; pediatric study found

IV boluses ≤1 mcg/kg given in <5 secs well tolerated; can also be given by IM, IN, and buccal routes; IM dexmedetomidine has ~70% of bioavailability of IV dose; doses in range of 2 mcg/kg to 3 mcg/kg have onset of ~15 minutes in children and adults but may not peak until >1 hr after injection; bioavailability of IN dexmedetomidine reported as 84% in children and ranges between 40% and 60% in adults; IN doses of 1 mcg/kg have onset of 45 mins to 60 mins in adults and 20 mins in children; doubling IN dose to 2 mcg/kg speeds onset to 10 mins in children; recent dose-finding study for transthoracic echocardiography used doses of ≤4 mcg/kg; buccal route has ~80% bioavailability; buccal doses of 2.5 mcg/kg effective in adults and children; precise onset for buccal route has not been reported but appears to be within 45 mins; dexmedetomidine metabolized by glucuronidation, hydroxylation, and methylation; virtually no drug excreted unchanged in urine; hydroxylation occurs via CYP2A6, but polymorphisms in this gene do not appear to impact duration of effect; context-sensitive half-times vary significantly by study; *study findings* — original study by Dick and colleagues (1993) found context-sensitive half-time of 25 mins for 1-hr infusion, 205 mins for 3-hr infusion; several subsequent studies estimated longer half-times for short infusions but predicted that context-sensitive half-times would plateau within 2 hrs; 2 studies suggested that context-sensitive half-time would plateau at 80 mins, another predicted plateau value of ~100 mins; regardless of exact values, clinical studies suggest they correspond to prolonged recovery times, particularly when compared with propofol

Physiologic effects: adrenergic mechanism of action leads to CV effects as well as sedation; *CV system* — bradycardia common but well tolerated in most patients; effects on blood pressure variable, may be biphasic; variation likely reflects differential actions at various alpha-2 receptor subtypes in different locations in body; peripheral alpha-2B receptors can lead to initial hypertension, may be followed by hypotension mediated by central alpha-2A receptors; at very high plasma concentrations, vasoconstriction predominates; but at clinically relevant concentrations, hypotension more common; may be seen during infusion or after it has stopped; *respiratory* — same study that examined CV effects of high-dose dexmedetomidine also examined respiratory effects; respiratory rate increased slightly with escalating doses, as did $PaCO_2$ (from 43 mm Hg at baseline to 47 mm Hg at highest plasma concentration studied); studies using MRI suggest airway tone maintained even during deep sedation with dexmedetomidine

Adverse effects: as might be expected from drug that mimics non-REM sleep, patients with obstructive sleep apnea can experience obstruction during dexmedetomidine sedation; however, study reported that dexmedetomidine infusions decrease likelihood of apnea–hypopnea index >15 compared with baseline state; other effects of dexmedetomidine include decreased shivering and salivation; IV or intrathecal dexmedetomidine has been reported to prolong spinal anesthesia; similarly, adding dexmedetomidine to local anesthetics appears to speed onset and prolong duration of peripheral nerve blocks; important to note that perineural administration can still cause sedation and bradycardia; *contraindications* — no absolute contraindications; use caution in patients at higher risk for side effects of bradycardia and hypotension; at-risk groups include diabetics, elderly, and patients with hypovolemia, heart block, and high vagal tone; labeling still lists 24 hrs as maximum duration of infusion, but widely used for longer periods without significant toxicity or withdrawal phenomena

Advantages: has intrinsic analgesic properties; shown to be opioid sparing

Clinical uses: approved indications include sedation for procedures and sedation for mechanically-ventilated patients in ICU; delirium appears less likely in ICU patients sedated with dexmedetomidine vs benzodiazepines; perioperative dexmedetomidine may reduce postoperative delirium; 2018 meta-analysis supports this, but unclear about patients most likely to benefit, as well as optimal doses and duration of infusion; in children, several studies reported decrease in emergence agitation with boluses of dexmedetomidine; can be used for premedication in adults and children, even without IV access; can be used for procedures that require patient cooperation (*eg*, awake craniotomy, awake carotid endarterectomy); preserved respiratory drive and airway patency useful for fiberoptic intubation, as well as for procedures with limited access to patient's airway (eg, pediatric imaging studies and neurointerventional procedures such as thrombectomy for acute stroke); as with ketamine, dexmedetomidine frequently used as part of multimodal approach to analgesia, particularly in patients at high risk for opioid complications

Conclusion: uses of nonopioid IV anesthetics extend beyond induction and maintenance of anesthesia

Suggested Reading

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Local Anesthetics

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Local anesthetics: medications that block nerve conduction; most commonly used to produce numbness in area in which surgery performed; when injected near nerve containing multiple types of nerve fibers (*eg*, both sensory and motor nerve fibers), both numbness and muscle paralysis may be produced

Studies: ≈50 years ago, Toshio Narahashi and coworkers elucidated site of action and molecular nature of active form of local anesthetics; as model system, used giant axon of squid; squeezed out exoplasm, perfused inside and bathed outside of axon with test solutions of local anesthetics, while at same time measuring transmembrane conductance; studied local anesthetic activity of tertiary amines (charged at low pH values and uncharged at high pH values), and quaternary amines (always charged regardless of pH); *findings* — when they used tertiary amine local anesthetic and perfused inside of squid axon at low pH, conduction block resulted, but when they raised pH, conduction block disappeared; in contrast, when they used quaternary amine local anesthetic and perfused inside of squid axon, conduction block resulted regardless of low or high pH; when they bathed outside of squid axon with tertiary local anesthetic at low pH, no conduction block, but at high pH conduction block resulted; when they bathed outside of squid axon with quaternary amine local anesthetic, no conduction block, regardless of high or low pH; *conclusions* — active form of local anesthetic molecule, protonated amine (charged); charged form of local anesthetic molecule blocks conduction from inside axon; local anesthetic molecule traverses axonal membrane in unprotonated, or uncharged, form; very few exceptions to these conclusions have been found in subsequent decades

Mechanism: voltage-gated sodium channel, target for action of local anesthetic molecule; this transmembrane protein consists of 4 subunits surrounding central pore; when nerve membrane depolarizes, each subunit undergoes conformational change that results in opening of central pore; after all 4 subunits have activated, sodium channel opens and sodium current flows; within few msecs after opening, polypeptide chain between 2 subunits moves to occlude central pore and prevent further ion conductance; *blockade* — local anesthetic molecules block sodium channel while in open state; degree of blockade depends on both resting potential of nerve and rapidity of stimulation; resting nerve less sensitive to local anesthetic blockade; higher stimulation frequency and more positive resting membrane potential cause greater degree of block; *onset, offset, and density of nerve block* — result of various types of fibers contained within nerve; when local anesthetic injected near compound nerve containing many fiber types, efferent sympathetic activity first modality to be blocked; first objective sign of block, vasodilation and increased skin temperature; next, loss of sensations of pain and temperature; loss of motor strength and senses of proprioception and light touch slowest in onset of local anesthetic effects; similarly, as local anesthetic effect wears off, it does so in reverse order; motor strength, proprioception, and light touch first to return, followed by sensations of pain and temperature, then sympathetic tone; in general, smaller nonmyelinated nerve fibers more easily blocked than larger myelinated fibers; *differential block* — low concentration of local anesthetic solution may block only sympathetic nerves; slightly higher concentration may also block sensations of pain and temperature; motor blockade usually achieved only with highest concentration of local anesthetic clinically available; wide variety of [inaudible 00:06:58] species have local anesthetic activity; *eg*, phenothiazines for treating major psychiatric illnesses and histamine H1 antagonists for treating allergy both have local anesthetic activity when injected; in all cases, 1 end of molecule contains substituted aromatic ring; other end, with 1 exception, contains substituted amine; ends bridged by either ester or amide linkage

Local anesthetic agents: *ester local anesthetics* — include procaine, tetracaine, proparacaine, and benzocaine; *amide local anesthetics* — include lidocaine, mepivacaine, bupivacaine, and ropivacaine

Procaine: first synthetic local anesthetic, first used >100 years ago; not commonly used today because of slow onset and short duration; in addition, metabolized to para-aminobenzoic acid (PABA), to which many persons allergic; PABA commonly found in many skin lotions and creams, including sunscreens

Lidocaine: most commonly used local anesthetic; fast onset, short duration, and low toxicity; also most versatile local anesthetic; used for local infiltration, nerve blocks, intravenous (IV) regional anesthesia (Bier block), spinal and epidural anesthesia, and topically on mucous membranes; not used on cornea; when injected, duration of action may be prolonged by using solution containing epinephrine, usually at concentration of 1:200,000, or 5 mcg/mL; vasoconstricting effect of epinephrine decreases local blood flow, thereby decreasing absorption of lidocaine; lidocaine metabolized by the hepatic cytochrome P450 system and subsequently by hepatic amidases; tertiary amine first N-dealkylated to secondary amine, then amide linkage hydrolyzed, yielding ethyl glycine and xylidide; most of xylidide

thus formed oxidized by cytochrome P450 to 4-hydroxy, 2,6-dimethylaniline, excreted in urine

Bupivacaine: compared with lidocaine, slower in onset, much longer in duration, much more toxic; toxicity correlated with higher lipid solubility than lidocaine; long duration of action due largely to slow dissociation from binding site in sodium channel; thus, addition of epinephrine to bupivacaine solution usually does not prolong duration; however, epinephrine decreases toxicity by slowing absorption; bupivacaine used for local infiltration, nerve blocks, and spinal and epidural anesthesia

Mepivacaine: similar to lidocaine in fast onset and low toxicity; longer duration than lidocaine, shorter duration than bupivacaine; used for local infiltration, nerve blocks, and epidural anesthesia

Ropivacaine: only local anesthetic formulated containing 1 optical isomer; primary advantage over bupivacaine, lower toxicity when used in nerve and plexus blocks, in which large dose needs to be injected; achieves lower toxicity primarily by excluding more cardiotoxic and neurotoxic isomer from preparation; slightly less lipid soluble than bupivacaine

Tetracaine: ester local anesthetic used almost exclusively for spinal anesthesia; longest duration of any available local anesthetic; most toxic; systemic toxicity from tetracaine rare, since doses required for spinal anesthesia low compared with doses used for epidural anesthesia or nerve or plexus block

Proparacaine: used for topical anesthesia of cornea; compared with other local anesthetics, causes least pitting of cornea; may be used to anesthetize cornea for measurement of intraocular pressure, removal of foreign body, or surgical procedures; should never be given to patient with ocular pain for self-administration because repeated or chronic use damages cornea and masks underlying disease process

Benzocaine: only used topically; unique in lack of amino group at end of molecule opposite aromatic ring and poorly soluble in water; because nucleus of benzocaine aniline or aminobenzene, systemic absorption causes stoichiometric oxidation of hemoglobin to methemoglobin; since benzocaine typically administered topically on mucous membranes, through which it has very efficient absorption (*eg*, mouth or airway), large doses that may be used to facilitate upper endoscopy or bronchoscopy may cause significant methemoglobinemia; other local anesthetics that have free aromatic ring (*eg*, procaine or proparacaine) not used in sufficient doses to cause meaningful degree of methemoglobinemia; in lidocaine metabolite with aromatic amino group 2,6-dimethylaniline, amino group sterically hindered from acting as efficient oxidizer of hemoglobin

Lidocaine and prilocaine in eutectic mixture: commonly used for anesthesia of the skin; eutectic mixture defined as mixture of solids that has melting point lower than those of individual solids; combination of equal weights of lidocaine and prilocaine melts below room temperature and exists as oil; formulated into emulsion with consistency of cream; useful for producing anesthesia of skin, especially in children, before IV cannulation or lumbar puncture, phlebotomy, or removal of superficial lesions; after application, area should be covered by occlusive dressing; typically takes 1 to 2 hrs to achieve maximum anesthesia; although prilocaine reacts with hemoglobin to form methemoglobin, amount of prilocaine absorbed systemically, after typical dose of preparation, results in subclinical degree of methemoglobinemia

Adverse effects: local anesthetics may cause systemic adverse effects; may result from accidental or, with lidocaine, intentional IV injection, or from absorption from site of injection or application; more common with larger doses of local anesthetics or when local anesthetic injected into well-perfused tissues or applied to well-perfused surfaces or mucous membranes; excellent correlation between blood concentration of local anesthetic molecule and magnitude of adverse effects; adverse effects primarily on central nervous system (CNS) and cardiovascular (CV) system; in general, good correlation between propensity for causing adverse effects and local anesthetic's duration of action and lipid solubility *local anesthetics ranked from least toxic to most toxic* — procaine less toxic than lidocaine (approximately same toxicity as mepivacaine); mepivacaine much less toxic than bupivacaine; bupivacaine less toxic than tetracaine

CNS effects: although local anesthetics inhibit nerve conduction, excitation initial effect on CNS; may result from selective effect of local anesthetics upon inhibitory neurons; initial CNS effects include restlessness, tremor, and altered visual perception; as blood concentration increases, seizures may result; local anesthetic–induced seizures most often self-limited and followed by period of CNS depression that may be accompanied by apnea and hypotension

Treatment: administer oxygen by mask and ensure adequate ventilation; prolonged seizure may be treated with IV barbiturate or benzodiazepine; more recently, administration of 20% IV fat emulsion (Intralipid) shown to terminate CNS or cardiovascular (CV) toxicity; current recommended regimen for treating life-threatening local anesthetic reaction to administer bolus of 1.5 mL/kg of 20% IV fat emulsion over 1 min; may be repeated once or twice for persistent CV collapse; then infusion started at 0.25 mL/kg/min (infusion rate may be doubled if blood pressure remains low); infusion usually needs to be continued for ~10 minutes

CV effects: decreased excitability, conduction rate, and force of contraction in heart; bupivacaine most cardiotoxic local anesthetic and much more likely than other local anesthetics to cause ventricular fibrillation; because bupivacaine dissociates so slowly from sodium channel, once severe cardiotoxicity manifests, prolonged period of cardiopulmonary resuscitation often required until normal rhythm restored; as mentioned previously, administration of 20% IV fat emulsion may also shorten duration of bupivacaine cardiotoxicity

Hypersensitivity and allergy: true hypersensitivity or allergy to amide local anesthetics rare; only few well-documented cases in literature; hypersensitivity to ester local anesthetics more common because of high prevalence of sensitivity to PABA in general population; furthermore, multiple-dose vials of local anesthetics contain methylparabens and/or propylparabens as preservatives; these compounds also demonstrate cross-reactance with PABA in many persons; another

common manifestation of so-called local anesthetic allergy consists of effects attributable to epinephrine included in solution as vasoconstrictor; patient may describe sweating and tachycardia following local anesthetic injection (symptoms almost certainly due to epinephrine); when patient who gives history of local anesthetic allergy should be questioned carefully; even with symptoms of true hypersensitivity reaction and local anesthetic amide used, reaction probably caused by preservative in multiple-dose vial

Adverse effects following spinal anesthesia: attributable to the local anesthetic used; c*auda equina syndrome* — characterized by back pain or pain that radiates down leg, often accompanied by bladder or bowel dysfunction; may be transient or permanent; *transient neurologic symptoms (TNS)* — typically, back pain radiating to buttocks or legs; both of these adverse effects much more common when lidocaine used as spinal anesthetic medication, when higher dose or concentration of lidocaine injected, or when lidocaine was administered via spinal catheter (especially microbore catheter)

Types of Local Anesthesia

Local infiltration: process by which local anesthetic solution injected into tissue in area in which numbness desired; since no need to block motor nerves, dilute solutions of local anesthetic used (*eg*, lidocaine 0.5% to 1%, bupivacaine 0.125% to 0.25%); epinephrine often included as vasoconstrictor; with bupivacaine, even though epinephrine does not appreciably increase duration of block, it does decrease peak blood concentration of drug, thereby decreasing likelihood of toxicity; also decreases bleeding at surgical site; epinephrine-containing solutions generally contraindicated in 5 areas of body supplied by end arteries: fingers, toes, ears, nose, and penis; *major advantages* — requires no knowledge of anatomic course of any nerves; usually does not disrupt any physiologic functions; *disadvantages* — impracticality of anesthetizing large areas, difficulty in anesthetizing certain tissues by local infiltration (*eg*, peritoneum), and difficulty in anesthetizing viscera

Peripheral nerve block: local anesthetic solution injected in close proximity to nerve; injection site may be located in one of several ways

1. if course of nerve known to have little variation with respect to another landmark, needle may be inserted with respect to landmark and injection made (*eg*, blockade of median nerve at wrist with respect to palmaris longus tendon)
2. nerve may be intentionally touched with needle to produce paresthesia; important to ensure that intraneural injection, usually extremely painful, not inadvertently performed; femoral nerve at level of inguinal ligament may be located this way, but less common since advent of ultrasound
3. needle may be connected to nerve stimulator and to seek evoked motor activity; practical only for mixed sensory and motor nerves; sciatic nerve may be located by this method
4. needle may be visualized in proximity to nerve or plexus via ultrasound; ultrasound guidance evolving into standard of care for nerve and plexus blocks of upper and lower extremities

Plexus block: similar to peripheral nerve block; in plexus block, brachial or lumbar plexus blocked proximal to point at which various peripheral nerves separate from one another; *eg*, brachial plexus may be blocked by injection just superior to clavicle as it passes over first rib; choice of local anesthetic solution for peripheral nerve or plexus block based upon desired duration and density of block; in general, blockade of plexus or large nerve (*eg*, sciatic nerve), has longer duration of action than blockade of small nerve (*eg*, digital nerve); higher concentration of local anesthetic solution will provide both sensory and motor blockade, while lower concentration of local anesthetic solution may produce numbness without paralysis; lidocaine may provide 1 hrs to 3 hrs of anesthesia, mepivacaine 4 hrs to 6 hrs, bupivacaine 8 hrs to 24 hrs; in addition to epinephrine, other medications may be added to local anesthetic solution for nerve or plexus blocks; clonidine (alpha-2 adrenoceptor agonist) potentiates quality and duration of anesthesia produced by nerve or plexus block; glucocorticoids also used in combination with local anesthetics in nerve and plexus blocks, although data supporting their efficacy weaker than data supporting clonidine use

Spinal anesthetic: consists of injecting local anesthetic solution into cerebrospinal fluid after performing lumbar puncture; since spinal cord ends at L1 in ~90% of people, and at L2 in remaining 10%, spinal anesthetics administered at L2-3, L3-4, L4-5, or L5-S1 interspaces; typically, spinal anesthetic causes temporary and reversible pharmacologic transection of spinal cord; autonomic, sensory, and motor nerves blocked below level of anesthetic solution, even though injection made no higher than L2-3 interspace, possible to achieve blockade of high thoracic nerves to allow intraabdominal surgery under spinal anesthesia; local anesthetic solution may be made hyperbaric (having higher specific gravity than spinal fluid), by addition of glucose; tilting patient in head-down position after spinal injection causes local anesthetic solution to move cephalad and anesthetize higher dermatomes; spinal anesthesia often accompanied by hypotension due to sympathetic blockade; effect may be mitigated by adequate hydration of patient prior to spinal injection and by IV administration of vasoconstrictor (*eg*, phenylephrine); permanent neurologic sequelae, such as paralysis or numbness, rare following spinal anesthesia; duration of spinal anesthesia depends on specific local anesthetic and whether epinephrine added to injection; *eg*, lidocaine produces spinal blockade of ~1 hrs to 1.5 hrs in duration, while spinal with tetracaine plus epinephrine lasts up to ~6 hours

Epidural anesthetic: consists of injection of local anesthetic solution into epidural space; most commonly, epidural injections made through thin catheter threaded into the epidural space; this technique permits anesthetic effect to be continued for long time via repeated bolus injections or continuous infusion of local anesthetic solution; *epidural block* — segmental block, localized to dermatomes above and below site of catheter insertion (*eg*, for thoracic surgery, epidural catheter may be inserted at T7-8 interspace in attempt to provide blockade of T4 through T12 dermatomes); analogous to peripheral nerve block, density of epidural block may be adjusted based upon concentration of local anesthetic solution (*eg*, to provide

analgesia but no numbness or motor blockade in woman in labor, dilute solution of local anesthetic may be infused)

Postoperative analgesia: may be achieved by infusion of dilute local anesthetic solution; usual goal to permit patient to ambulate without motor weakness; in addition to epinephrine, other medications may be added to local anesthetic solution for spinal or epidural anesthesia; opioids (typically morphine, fentanyl, or sufentanil) often included in spinal or epidural injections; potentiate analgesia produced by local anesthetic, used at much lower doses than those given systemically, thereby minimizing opioid-induced ventilatory depression; clonidine potentiates analgesia when included in solution used for neuraxial anesthesia

IV regional/Bier block: method for producing anesthesia of arm or, less commonly, leg

Technique: IV catheter inserted distally into extremity; extremity wrapped tightly distally to proximally with Esmarch bandage to exsanguinate limb; pneumatic tourniquet placed proximally on limb and inflated to pressure approximately twice systolic pressure; dilute (usually 0.5%) solution of lidocaine injected into catheter

Advantages and disadvantages: highly reliable; does not require much expertise to perform; many orthopedic and hand surgeons routinely perform it; limited to procedures with duration of <~1.5 hrs to 2 hrs; since no anesthesia underneath tourniquet, pain from tourniquet usually limits overall duration of block; dissipates rapidly after tourniquet deflated; as long as tourniquet has been inflated for <~15 minutes following lidocaine injection, low risk of systemic toxicity; conversely, tourniquet failure shortly after lidocaine injection likely associated with systemic toxicity

Topical anesthesia: most commonly used to facilitate endoscopic procedures; pharynx, nares, trachea, and esophagus readily anesthetized by topically applied anesthetics; systemic absorption of local anesthetic solution from mucous membranes very efficient; since high concentrations of local anesthetic solutions used topically (*eg*, 4% lidocaine), important to limit total volume of local anesthetic solution used to minimize systemic toxicity; also, topical benzocaine associated with methemoglobinemia

Suggested Reading

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Pharmacology of Neuromuscular Blocking Drugs and Reversal Agents

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Neuromuscular blocking agents: produce immobility and improved intubating and operating conditions; can either mimic or block nerve depolarization; tracheal intubation uncommon before introduction of these agents; inappropriate use may cause residual postoperative muscle weakness and increased intraoperative awareness

Anatomy and physiology of neuromuscular junction: consists of prejunctional, postjunctional, and synaptic cleft; impulses begin in ventral horn of spinal cord or brainstem at cell body of motor neuron; axon of this nerve extends to skeletal muscle that it innervates and divides into several branches; nerve terminal located at terminal portion of each branch, which produces and stores acetylcholine; acetylcholine synthesized from choline and acetyl coenzyme A with aid of choline acetyltransferase; following synthesis, acetylcholine transported into storage vesicles; nerve action potentials result in depolarization of prejunctional neuron, leading to influx of calcium into nerve, stimulating vesicles to release acetylcholine into synaptic cleft; calcium influx continues until membrane potential normalized by outward flux of potassium; prolongation of calcium current can occur with use of potassium channel blockers; conditions that decrease or alter calcium influx can result in muscle weakness; administration of magnesium sulfate can block calcium entry, resulting in muscle weakness; calcium channel blockers should not significantly affect neuromuscular transmission or blockade; synaptic or junctional cleft separates motor nerve ending from skeletal muscle; acetylcholine diffuses across synaptic cleft and binds to postjunctional nicotinic cholinergic receptors in muscle endplate; mature nicotinic acetylcholine receptor consists of 5 distinct subunits (2 alpha, 1 beta, 1 gamma, and 1 epsilon) organized to form central transmembrane channel; simultaneous binding of 2 acetylcholine molecules to alpha subunit induces conformational change that allows inflow of sodium and calcium and outflow of potassium, depolarizing endplate membrane and resulting in muscle contraction; in synaptic cleft, acetylcholine that did not bind with receptor or has been released following binding with receptor rapidly removed by acetylcholinesterase; acetylcholinesterase catalyzes hydrolysis of acetylcholine into acetate and choline; choline taken up by prejunctional nerve terminal and reused as substrate for formation of additional acetylcholine

Depolarizing neuromuscular blocking agents: function by binding to postjunctional acetylcholine receptors and triggering sustained depolarization

Succinylcholine: now only clinically relevant depolarizing agent; chemical structure, 2 acetylcholine molecules linked together; binding stimulates depolarization; occupation of postjunctional receptor causes skeletal muscle to remain depolarized, and response to subsequent stimulation rendered impossible; depolarizing blockade characterized by rapid onset and short duration of action; dose of 1 mg/kg results in reliable muscle paralysis in 60 to 90 secs; doses as high as 2 mg/kg failed to provide ideal intubating conditions in some patients; short duration of action (5-10 mins); *considerations for succinylcholine administration* — surgical procedures requiring endotracheal intubation of short duration, patients presenting with full stomach, or otherwise at risk for aspiration of gastric contents, for surgical procedures needing monitoring of nerve function, or where airway management may be difficult; dose of 4 mg/kg intramuscular (IM) results in acceptable intubating conditions in 4 mins; consider if muscle relaxation required and intravenous (IV) access not established; may be required in children if IV access not established and patient presents with laryngospasm; *fasciculations* — succinylcholine administration results in muscular fasciculations prior to onset of effect; pretreatment with 5% to 10% of typical effective dose of nondepolarizing agent standard to reduce severity of fasciculations; doses of 1.5 to 2 mg/kg should be considered if defasciculating dose used secondary to interactions between nondepolarizing and depolarizing agents; diazepam, lidocaine, fentanyl, calcium, vitamin C, magnesium, and dantrolene may also prevent or decrease muscle fasciculations

Phase I block: depolarizing blockade of neuromuscular junction; characteristics include train-of-four ratio >0.7, no train-of-four fade, sustained tetany in response to tetanic stimulation, no post-tetanic facilitation, and rapid recovery; can be augmented with neostigmine or additional succinylcholine

Phase II block: occurs if postjunctional membrane repolarized but desensitized and unable to respond to subsequent stimulation; usually, 7 to 10 mg/kg or 30 to 60 mins of succinylcholine exposure required before Phase II blockade results; resembles blockade from nondepolarizing agents; characterized by train-of-four ratio <0.4, unsustained response to tetanic stimulation, and presence of post-tetanic facilitation; can be augmented by administration of nondepolarizing agent

or additional succinylcholine, and antagonized by administration of neostigmine

Duration of action: action of succinylcholine rapidly terminated by hydrolysis by plasma cholinesterases (*eg*, butylcholinesterase [pseudocholinesterase]); duration of action significantly prolonged in patients with severe hepatic disease; other conditions known to affect pseudocholinesterase activity include renal disease, malnutrition, pregnancy, malignancy, burns, cardiopulmonary bypass, and leprosy; anticholinesterases may affect ability to hydrolyze succinylcholine and may prolong duration of bolus administration; other drugs known to affect pseudocholinesterase activity include echothiophate eye drops, organophosphate insecticides, cyclophosphamides, neostigmine, physostigmine, edrophonium, oral contraceptives, phenelzine, pancuronium, bambuterol, and metoclopramide; *atypical plasma cholinesterases* — result in impaired ability to hydrolyze both succinylcholine and mivacurium; recognition of this disorder occurs after succinylcholine administration results in dramatic prolongation of neuromuscular blockade; patients may require prolonged mechanical ventilation until adequate strength returns; subsequent evaluation of patient's dibucaine number will demonstrate severity of deficit in plasma cholinesterase activity; normal dibucaine number 70 to 80, associated with duration of succinylcholine neuromuscular block of 5 to 10 mins; dibucaine number 50 to 60 associated with heterozygous cholinesterase deficit and duration of action of succinylcholine ~20 mins; dibucaine numbers 20 to 30 associated with homozygous cholinesterase variant; succinylcholine administration can result in neuromuscular blockade for 60 to 180 mins; failure of block resolution following succinylcholine therapy should result in planned ICU admission; laboratory tests include pseudocholinesterase activity, and dibucaine and fluoride inhibition tests

Potential adverse outcomes: cardiac arrhythmias (eg, sinus bradycardia, junctional rhythm, or sinus arrest) because of muscarinic effects; additional doses within 5 mins of initial administration increase probability of arrhythmias; IV atropine or nondepolarizing neuromuscular blocker pretreatment can reduce likelihood of arrhythmias because of catecholamine release; anaphylaxis should be considered in event of refractory hypotension, bronchospasm, and rash at anesthesia induction; succinylcholine anaphylaxis rare (≤1 in 5000 to 1 in 10,000 cases); *increased potassium levels* — succinylcholine administration known to result in transient increase in plasma potassium levels but may be lethal in certain patients; proliferation of extrajunctional receptors makes succinylcholine unsafe as early as 2 days following spinal cord injury; following denervation injury, administration remains unsafe for at ≥3 to 6 mos; risk of hyperkalemia following administration in burn patients increases over time, peaking 7 to 10 days following injury; patients with acute burn and spinal cord injuries may receive succinylcholine for airway management, but beyond 24 hrs, other neuromuscular blocking agents should be considered; other risk factors include infection, IV drug abuse, myotonia and muscular dystrophies; because of risk of undiagnosed muscular dystrophies, administration of succinylcholine must be carefully considered in children; administration of defasciculating dose of nondepolarizing agents prior to administration of succinylcholine does not affect rise in serum potassium; *other adverse events* — intense fasciculations can result in profound postoperative myalgias; pain occurs in 1.5% to 89% of patients, typically presenting 24 to 48 hrs after administration; pain most intense in muscles of back, abdomen, and neck; higher risk in young patients having minor surgery; defasciculating doses of nondepolarizing neuromuscular blockers or preemptive IV lidocaine administration effective at decreasing incidence; myalgias can typically be managed with patient education and NSAIDs; succinylcholine causes 5 to 15 mm Hg increase in intraocular pressure that lasts for ~5 to 10 min; may result from sustained contraction of extraocular muscles placing pressure on the globe of the eye; in patients having neurologic surgery, consider that succinylcholine may result in increased intracranial pressure; etiology may be increase in pCO_2 associated with fasciculations; trismus, or masseter muscle rigidity, can accompany succinylcholine administration, usually seen in children and young adults; can be severe enough to produce difficulties with mouth opening and intubation; large doses of nondepolarizing neuromuscular blocking agents usually effective; *malignant hyperthermia* — 25% to 29% of patients with history of masseter muscle rigidity found to be susceptible to malignant hyperthermia (MH); patients with masseter muscle rigidity should be monitored for 12 to 24 hrs postoperatively to ensure MH does not develop; contracture or histologic testing may help diagnose MH or other myotonic conditions; family counseling or testing may prevent MH in close relatives; MH most feared complication of succinylcholine administration; in 1990s, FDA issued black box warning against use in children and adolescents; fear was children might have undiagnosed myopathies that would elevate risk of triggering MH or hyperkalemic events; hypermetabolism typical presentation; profound and rapid increases in body temperature; arterial blood gas analysis reveals hypercarbia and combined metabolic and respiratory acidosis; other laboratory tests are also indicative; MH may manifest in operating room or postoperatively; in case of suspected triggering event, Malignant Hyperthermia Association of the United States has 24-hr, toll-free line for assistance; upon recognition of MH, no further succinylcholine should be administered; *management of MH* — discontinue inhaled agents and may use filter; maintain anesthesia with IV agents; obtain dantrolene and additional help; hyperventilate patient with 100% oxygen and set ventilator flow rate high to quickly remove any inhaled agent from patient and anesthesia circuit; administer dantrolene early in IV doses of 2.5 mg/kg and repeat as necessary; insert urinary catheter and arterial line for monitoring; administer bicarbonate as indicated by blood gas analysis; make active attempts to reduce core body temperature to <38°C; rhythm should be monitored carefully; avoid calcium channel blockers; manage hyperkalemia; obtain laboratory tests

Nondepolarizing neuromuscular agents: bind to postsynaptic nicotinic acetylcholine receptors, occupy binding site, and prevent binding of acetylcholine and subsequent depolarization; 2 molecules of acetylcholine required to bind to postsynaptic receptor to open channel, but only 1 molecule needs to bind for effective blockade; typically, large percentage of sites need to be blocked for clinical effect (~75% of receptors require blockade before twitch height altered; 92% of receptors require blockade before stimulation fails to produce muscle contraction in response to electrical stimulation)

Classification by duration of action: short-duration drugs either have short elimination half-life (*eg*, mivacurium) or extensively redistributed (*eg*, rapacuronium); intermediate-duration drugs include atracurium, cisatracurium, vecuronium, and rocuronium; long-duration agents (*eg*, pancuronium) depend heavily on liver or kidney function for metabolism, elimination, and termination of effect

Classification by chemical structure: aminosteroid drugs include pancuronium, vecuronium, rocuronium, and rapacuronium; benzylisoquinoline compounds include atracurium, mivacurium, cisatracurium, and curare

Pancuronium: prototypical long-acting neuromuscular blocking drug; ED95, 70 mcg/kg; standard dose lasts 60 to 90 mins; elimination primarily renal; kidney disease can increase duration of action; mild vagolytic effect; administration results in mild increase in heart rate, blood pressure, and cardiac output; may have sympathomimetic effect or increase release of catecholamines; significant tachycardia possible; exaggerated responses can be seen in patients with preexisting heart disease or taking certain drugs; patients with limited cardiac reserve, significant valvular lesions, or exaggerated hemodynamic response may develop cardiac ischemia

Vecuronium and rocuronium: commonly used aminosteroid, intermediate-duration neuromuscular blocking drugs; *vecuronium* — ED95=50 mcg/kg; standard duration of action 20 to 35 mins; metabolism both hepatic and renal; significant renal impairment may result in prolonged effect; *rocuronium* — ED95=0.3 mg/kg; duration of action 20 to 35 mins; may be administered in large doses to produce rapid intubating conditions; may be useful in patients not candidates for succinylcholine; with standard dose, onset of effect within 2 mins; onset times mimicking those seen with succinylcholine achieved with 1.2 mg/kg; at increased doses, duration of neuromuscular blockade exceeds 1 hr; renal and hepatic metabolism renal and hepatic; significant renal impairment prolongs duration of action

Atracurium and cisatracurium: benzylisoquinoline, intermediate-duration neuromuscular blocking agents; *atracurium* — dosed at 0.2 mg/kg; duration of action 20 to 35 mins; degrades via ester hydrolysis and Hofmann elimination; hepatic and renal impairment do not prolong duration of action; metabolism produces laudanosine; long-term administration or administration to patients with hepatic impairment may result in elevated levels of laudanosine, resulting in CNS excitation; atracurium associated with histamine release and accompanying increases in heart rate and decreases in blood pressure; histamine release is greater with rapid administration and in elevated doses; *cisatracurium* — ED95=50 mcg/kg; duration of action 20 to 35 min; Hofmann elimination responsible for drug degradation; administration not associated with significant histamine release, so does not alter hemodynamics; does not result in laudanosine production; may be used for prolonged administration

Mivacurium: short-acting, benzylisoquinoline neuromuscular blocking agent; ED95=80 mcg/kg; duration of action 12 to 20 min; hydrolyzed by plasma cholinesterases; patients with altered plasma cholinesterase activity may experience prolonged blockade; attempted reversal of profound mivacurium-induced neuromuscular blockade with neostigmine may be associated with prolongation of block effect; may be associated with histamine release; anticipate transient changes in heart rate and blood pressure

Adverse events: cardiovascular system can be affected through vagolytic action or released histamine; histamine release associated with bronchospasm; consider use of histamine-releasing agents carefully in patients with asthma; slow administration and pretreatment with antihistamines may decrease effect; can cause prolonged skeletal muscle weakness after lengthy use, particularly in patients with critical illness; weakness can persist for months; prolonged paralysis should be limited; consider other sedative drugs (*eg*, opioids, benzodiazepines, alpha-2 agonists) as alternative therapies; nondepolarizing agents implicated in perioperative allergic reactions; severe allergic reactions usually IgE mediated; these drugs cause nearly 50% of all anesthesia-related anaphylactic reactions, with relative incidence of 1 in 1000 and 1 in 25,000 anesthetics; may be cross-sensitivity between all neuromuscular blocking drugs because of common structure; consider allergy testing if patient presents with history of allergy to neuromuscular blocking drugs; previous exposure to cosmetics or soaps with antigenic quaternary ammonium group can sensitize patients to subsequent neuromuscular blocker exposure

Clinical factors that alter dosage requirements or duration of action: burn patients may require increased dose; for obese patients, calculate dose based on lean body mass, not current total body weight; patient age can have a large impact; ethnicity can be factor with certain neuromuscular blocking agents

Drug interactions: inhalational agents may potentiate effect of neuromuscular blockade; IV agents have little effect on duration or intensity of neuromuscular blockers; local anesthetics may potentiate both depolarizing and nondepolarizing neuromuscular blockers, but clinical impact not known; aminoglycoside antibiotics (specifically, neomycin and streptomycin) exert inhibitory action at neuromuscular junction and potentiate neuromuscular blockade; effects of aminoglycoside antibiotic most pronounced in setting of aminoglycoside–neuromuscular blocker administration; chronic use of anticonvulsants produces resistance to neuromuscular blocking agents and decreases their duration of action; beta blockers and calcium channel blockers have demonstrated *in vitro* effects on neuromuscular blockade but apparently little effect clinically; ephedrine administration at time of induction shortens time to onset of neuromuscular blockade; esmolol slows onset of blockade; magnesium shortens onset and potentiates

neuromuscular blocking effects; lithium associated with additive and synergistic effect with depolarizing and nondepolarizing neuromuscular blockers, respectively; patients on lithium may demonstrate prolonged recovery from depolarizing neuromuscular blockade

Administration of 2 different neuromuscular blocking drugs: can alter expected neuromuscular blockade; either additive or synergistic effect; *eg*, combination of cisatracurium and rocuronium synergistic, produces more profound neuromuscular blockade than with either of doses administered; in sequential administration of 2 different neuromuscular blocking agents, agent administered second maintains duration of action properties of agent administered first; administration of nondepolarizing agent following succinylcholine may result in deeper blockade, but effect on duration varies; administration of nondepolarizing agent prior to succinylcholine lessens depolarizing blockade, so succinylcholine dose needs to be increased following defasciculating dose of nondepolarizing agent

Antagonists: recovery from effects neuromuscular blocking drugs important to avoid postoperative problems with ventilation and airway protection; many surgical procedures require muscle relaxation until near end of procedure and waiting for metabolism to make patient ready for extubation inefficient, and response to electrostimulation can overestimate true return of muscle strength; consider use of neuromuscular blocking drug antagonists; classic antagonists of neuromuscular blocking agents broadly classified as anticholinesterase drugs; administered to increase amount of available acetylcholine at motor endplate; *factors that influence time for anticholinesterase activity* — level of paralysis, reversal agent used, dose of antagonist, duration properties of blocking agent, concentration of inhaled anesthetic; do not attempt to reverse neuromuscular blockade without evidence of block resolution with anticholinesterase agents

Neostigmine: most commonly administered anticholinesterase agent; typically dose 0.07 mg/kg; 6 to 10 mins may be required for full effect; time to onset of action depends on dose and agent being reversed

Edrophonium: more rapid onset of action; typical dose 0.25 mg to 0.5 mg/kg

Adverse events: significant bradycardia or asystole; to avoid problems with significant bradyarrhythmias, give 0.2 mg glycopyrrolate for every 1 mg of neostigmine; edrophonium has short onset of action, so atropine administered with it to prevent bradycardia; other cholinergic effects include bronchospasm, increased salivation, and increased bowel motility; acetylcholinesterase inhibitors may be associated with increased incidence of postoperative nausea and vomiting; duration of action prolonged in patients with significant renal failure

Drug interactions: drugs that increase intensity of neuromuscular blockade (*eg*, halogenated agents, aminoglycoside antibiotics, magnesium) may decrease effectiveness of acetylcholinesterase inhibitor administration

Sugammadex: approved by FDA in 2015; modified gamma cyclodextrin that binds to and inactivates aminosteroid neuromuscular blocking agents (*eg*, rocuronium, vecuronium) to form complex; full reversal takes ~3 min; dosing based on level of neuromuscular blockade; when second twitch present on train-of-four analysis, 2 mg/kg can be given to reverse neuromuscular blockade; when only post-tetanic twitches present, dose should be increased to 4 mg/kg; when no response to nerve stimulation can be elicited, 16 mg/kg can be given to rapidly reverse neuromuscular blockade; associated with lower incidence of postoperative weakness and lower likelihood of respiratory and cardiovascular adverse effects; adverse effects comparable with anticholinesterase agents; use associated with faster discharge from OR to PACU, and from PACU to surgical unit

Adverse effects: nausea, vomiting, hypotension, headache; counsel patients on steroidal contraceptives to use alternative contraceptive methods for 7 days; large doses associated with increased PT, PTT, and INR; severe bradycardia and cardiac arrest minutes after administration have been reported; hypersensitivity reactions have been reported

Choice of reversal agent: drug availability or cost may significantly affect which agent administered; level of return of neuromuscular function also affects choice; for patients without significant block resolution, sugammadex more appropriate; patients who may not tolerate tachycardia well may benefit from sugammadex because no need for accompanying glycopyrrolate administration; not appropriate choice to reverse muscle relaxation produced by nonaminosteroid agents

Monitoring of neuromuscular blockade: high rates of postoperative residual weakness secondary to neuromuscular blockade; significant safety risk in patients undergoing anesthesia; complications include muscle weakness, anesthetic awareness, respiratory compromise, and airway obstruction; need to monitor neuromuscular function; accomplished through nerve stimulators that deliver electrical stimulus in vicinity of peripheral motor nerve; resulting motor output evaluated to assess depth of and recovery from neuromuscular blockade; stimuli described in terms of current, frequency, and duration

Anatomic sites for monitoring stimulation: adductor pollicis supplied by ulnar nerve, sensitive to neuromuscular blocking agents; typically blocked to greater extent than muscles involved in respiration or laryngeal tone; orbicularis oculi innervated by facial nerve; stimulation causes eyebrow movement; orbicularis oculi recovers from neuromuscular blockade more rapidly than adductor pollicis; posterior tibial nerve can be stimulated for flexion of big toe; decision regarding site of monitoring depends on anatomic availability during procedure

Single twitch: stimuli typically delivered at frequency between 1 and 0.1 Hz; response to initial control twitch noted and amplitude of subsequent twitches compared with control and expressed as percentage; single twitch stimulus should not be repeated more than every 10 secs (evoked response will decrease); decreased response may be misinterpreted as deeper blockade; can be used to monitor deep levels of neuromuscular blockade via post-tetanic count; single twitch cannot be used to

differentiate depolarizing and nondepolarizing block; control needs to be established to evaluate blockade; return to level of control response does not guarantee full recovery

Tetanic stimulation: rapid delivery of electrical stimuli, typically 500 to 200 Hz for 1 to 5 secs; sustained stimulus of 50 Hz for 5 secs most common; painful, should be avoided in conscious patients; tetanic stimulation should not be repeated more than every 2 mins (diminished response will occur); under normal neuromuscular transmission and pure depolarizing block, results in sustained muscle contraction; fade occurs during nondepolarizing block and phase II depolarizing block, visualized as unsustained muscle contraction; following tetanic stimulation during nondepolarizing blockade, increase in twitch response occurs, known as post-tetanic facilitation; post-tetanic facilitation maximal around 3 secs after stimulation, lasts 1 to 2 mins; post-tetanic count (number of single twitch responses following tetanic stimulation) can be used to detect deep neuromuscular blockade; number of twitches inversely related to depth of neuromuscular blockade

Train-of-four stimulation: consists of 4 supramaximal stimuli delivered every 0.5 secs at frequency of 2 Hz; should not be repeated more frequently than every 10 to 12 secs; amplitude of fourth stimulus can be divided by amplitude of first stimulus to provide train-of-four ratio; with progressive deepening of nondepolarizing block, responses to stimuli gradually eliminated, with elimination of fourth twitch, followed by third twitch, then second twitch; when <4 twitches present, train-of-four ratio cannot be determined; train-of-four cannot be used as monitor for deep blockade; train-of-four ratios of 75% associated with visual disturbances, decreased hand-grip strength, inability to sit up, and overall weakness; train-of-four ratio ≥0.9 should be achieved to decrease incidence of residual weakness secondary to neuromuscular blocking agents; at train-of-four ratios <0.9, discoordinated and difficult swallowing, reductions in upper esophageal sphincter function, and aspiration occur; accelerometry required to accurately assess train-of-four; visual or tactile means inaccurate at detecting train-of-four ratios >40%; train-of-four stimulation can differentiate between depolarizing and nondepolarizing blockade; with depolarizing block, equal depression of all 4 twitches and fade absent; *advantages* — stimulation offers less pain compared with tetanic stimulation, increased sensitivity in detecting residual paralysis compared with single twitch stimulus, and no need for control stimulus as in single twitch stimulus; *disadvantage* — ineffective at monitoring deep blockade and near-complete recovery

Double-burst stimulation: 2 short bursts of tetanic stimulation (50 Hz, each separated by 750 msecs); should not be repeated more often than every 12 secs; can detect residual neuromuscular blockade and deep neuromuscular blockade; when neuromuscular blockade present, muscle contraction in response to second stimulation weaker than first; diminished response more easily detected via tactile means; *advantage* — can be used to assess deep block as response to first stimulation; *disadvantage* — more uncomfortable for patient than train-of-four (but less painful than tetanic stimulation); use caution when using both train-of-four and double-burst stimulation; responses can be falsely diminished; ~90 secs required for stabilization of responses if using both techniques

Other assessments of evoked responses: visual and tactile assessments insensitive; can use other methods (*eg*, mechanomyography, electromyography)

Conditions that affect drug administration: some patient conditions have significant effects on neuromuscular blocker drug administration

Myasthenia gravis: autoimmune disease in which antibodies reduce number of nicotinic acetylcholine receptors available at postjunctional membrane; strength decreases with repeated stimulation; patients resistant to succinylcholine effects and require larger doses than expected based on patient size; with nondepolarizing neuromuscular blocking agents, greatly reduced doses and prolonged duration of action; consider techniques that avoid need for neuromuscular blockade; sedative drugs should be minimized because of increased risk of respiratory depression; if neuromuscular blockade required, small, titrated doses of short- or intermediate-duration neuromuscular blockers can be used; train-of-four should be followed closely; acetylcholinesterase inhibitors not expected to function as well in patients on chronic anticholinesterase therapy; do not extubate until full resolution of neuromuscular blockade; make postoperative ventilation plans if evidence of residual paralysis

Myotonia: skeletal muscles remain contracted for abnormally long time following stimulation; repeated stimulus leads to increased strength of muscular contraction; succinylcholine administration can lead to profound/sustained contractures that can complicate ventilation or jaw opening; succinylcholine administration may result in life-threatening hyperkalemia; nondepolarizing agents safe; avoid acetylcholinesterase inhibitors

Muscular dystrophies: diverse group of diseases with varying clinical pictures and patterns of inheritance; question patients regarding achievement of motor milestones; those with significant delays of unknown etiology should be evaluated before procedure or treated as suspected muscular dystrophy patients for emergent surgery; cardiac disease common and can lead to death from cardiomyopathy; concerns for MH-like symptoms or rhabdomyolysis and hyperkalemia paramount in anesthesia planning; adequate cardiac and pulmonary workup essential for proper perioperative planning

Suggested Reading

Hristovska AM et al: The comparative efficacy and safety of sugammadex and neostigmine in reversing neuromuscular blockade in adults. A Cochrane systematic review with meta-analysis and trial sequential analysis. *Anaesthesia*;2018;73(5):631-41; **Luckey-Smith K, High K:** A 20-year-old-trauma patient with suspected malignant hyperthermia following induction with succinylcholine: a case study. *Adv Emerg Nurs J*. 2018;40(3):171-5; **Naguib M et al:** Conceptual and technical insights into the basis of neuromuscular monitoring. *Anaesthesia*; 2017;72(suppl 1):16-37.

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Clinical Pharmacology of Local Analgesic Drugs

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Key concepts in pain management: the ultimate responsibility of every physician is to relieve pain in the best possible way; this requires a discrete understanding of the complexity of pain, and an appreciation of factors determining its expression in the clinical and operative setting; initiation of disease-modifying procedures and implementation of a proper perioperative pharmacologic local anesthetics (LA) requires a clear understanding of how LAs function in urgent and acute surgical settings

Background on LAs: block transmission of impulses in nerve fibers, and reduce or eliminate sensation; used in surgical environments to relieve and urgently address acute pain; *traditional uses* — neural-axial analgesia and anesthesia; peripheral nerve blocks; subcutaneous and tissue infiltration; topical anesthesia; *benefits* — alleviating acute pain; preventing acute pain from developing into long-term chronic pain; mitigating effects of chronic pain

Nociception

Background on nociception: *ie*, pain perception; result of sensory detection, transduction, and neural transmission of noxious events to the central nervous system

Nociceptors: high-threshold primary afferent sensory neurons; *ie*, free nerve endings; located in superficial skin or mucosa, deep soma (*ie*, muscle and bone), and viscera (*ie*, organs); *subtypes* — mechanoreceptors (activated by intense mechanical stimuli); thermal nociceptors (activated by intense heat or cold); chemical nociceptors (directly excite primary afferent sensory neurons, and represent the most important source of stimuli); sensitizing agents — *eg*, prostaglandin E_2; increase the sensitivity of nociceptors to chemical activators

Mechanisms of nociception: protons from low extracellular pH (associated with ischemia and inflammation) activate acid-sensitive ion channels and transient receptor potential ion channels (critically important); high levels of extracellular adenosine triphosphate (ATP), which are associated with cell injury, activate P2X purinoreceptors (a family of ligand-gated channels) P2Y receptors (a family of G protein-coupled receptor)

Bradykinins: associated with tissue damage and inflammation; activate G2 protein-coupled bradykinin B1 and B2 receptors; *B1 receptors* — expressed in response to bacterial lipopolysaccharides and inflammatory cytokines; *B2 receptors* — expressed constitutionally in neurons; promote synthesis of prostaglandin E_2

Sodium channels: activation of peripheral sensory terminals by noxious stimuli leads to intracellular sodium and calcium ion influx, and neuronal depolarization; if the threshold for activation of voltage-sensitive sodium channels is reached, neuronal depolarization leads to AP generation; *voltage-gated sodium channels (VGSC)* — 4 types are expressed uniquely in primary afferent sensory fibers; 2 types respond only to high-threshold peripheral stimuli

Calcium channels: initially, incoming APs in the trigeminal dorsal root complex activate presynaptic voltage-sensitive calcium channels, which in turn leads to synaptic release of glutamate and subsequent AP generation in secondary neurons; afterward, secondary afferent neurons project to the thalamus and synapse with tertiary afferent neurons; these tertiary neurons project to the somatic sensory cortex (responsible for the localization of pain) and limbic system (responsible for the emotional aspects of pain)

Role of sensory fibers: nociceptive information is conducted by myelinated AΔ and non-myelinated C fibers; information carried via AΔ fibers arrives rapidly (as in, *eg*, initial pain which is perceived as sharp, bright, and well-localized but not particularly persistent) and is immediately associated with tissue injury; in contrast, information carried via C fibers arises slowly (as in, *eg*, secondary pain which is perceived as dull throbbing, burning, diffuse and persistent); it is critical to recognize that AΔ and C fibers play a highly important role in the transmission of pain, as well as in how LAs generally function

Mechanisms of Action (MOA) Associated With Local Anesthetics

Regulation of ion channels: homeostatic mechanisms and excitable neuronal cells maintain a chemical gradient between high extracellular sodium and high intracellular potassium concentrations, ensuring the interior of neuronal cells is electronegative (approximately -50 to -90 mV) while the exterior is electropositive; nociceptive signals alter the distribution of these ions and briefly reverse electrical polarity, leading to neuronal membrane depolarization which provides the energy to activate VGSCs; if the threshold for activation of VGSCs is reached, sodium ions flow into the cell and AP is generated; duration of this inward sodium current is limited as the VGSCs close spontaneously behind the passing AP; after activation of the voltage-gated channels, sodium-potassium ATPase pumps sodium out of the cells, and the leak of potassium ions through passive ion channels restores the resting membrane potential; LAs reduce the

amplitude and conduction velocity of APs in a reversible, dose-dependent manner

Biochemistry of VGSCs: site of action for LAs; large membrane proteins which consist of a poor-forming alpha subunit and 1 or 2 beta subunits; receptor sites of LAs are located on the intracellular alpha subunits; consequently, in order to gain access to the receptors, LAs must diffuse across lipophilic neuron membranes at the site of administration; in most cases, this occurs via passive diffusion across biologic membranes

Diffusion of LAs: since LAs are weak bases in an aqueous environment, they exist as a mixture of a protonated or positively-charged ionized molecule and a deprotonated or neutral unionized molecule; the ratio of ionized-to-unionized forms of an LA is predicated on its acid dissociation constant or pKa (*ie*, pH at which an agent is 50% ionized and 50% unionized) and the pH of the agent's milieu (*ie*, the environment at the site of drug administration)

Ion trapping: only unionized molecules of an agent can translocate across biologic membranes; as such, ionized LA molecules will be unable to reach their target receptors or diffuse into the circulation, and thus are trapped at the site of administration; this phenomenon is known as ion trapping; *eg*, when lidocaine (with the pKa of 7.9) is deposited into an infected or inflamed site with a pH <7.9, >50% of its molecules become protonated, and it is thus unable to diffuse across a biologic membrane; however, if sufficient quantities of an LA molecule can interact with the VGSC, AP will be temporarily halted; because differentials in functional blockades are predicted by the degree of myelination around the nerve fibers and the LA's concentration gradient, LAs block different fiber types at different times; *general progression of functional deficits induced by LAs (in sequential order)* — first pain; second pain; temperature; touch; proprioception; motor functions

Summary of MOAs associated with LAs: reversible inhibition of nerve transmission via binding with VGSCs (integral membrane proteins anchored in the nerve plasma membrane); after LAs bind to VGSCs, the nerve plasma membrane is rendered impermeable to sodium (which prevents AP initiation and propagation)

Properties of Local Anesthetics

Chemical classifications of LAs: commonly used LAs have similar structural characteristics, and consist of a lipophilic aromatic ring plus a hydrophilic tertiary amine (which are linked together via a carboxylic ester or amide bond); *commonly used amino ester LAs* — include chloroprocaine, procaine, and tetracaine; *commonly used amino amide LAs* — include lidocaine, bupivacaine, ropivacaine, mepivacaine, levobupivacaine (used outside of United States), and articaine (used primarily in dentistry)

Chemical characteristics of LAs: typically weak bases that exist in solution (in both charged and uncharged forms); all clinically utilized LAs share certain structural features; the presence of an aromatic benzene ring leads to greater lipid solubility; however, lipid solubility declines and aqueous solubility increases when the amine nitrogen (located at the end of the molecule and opposite to the aromatic ring) is protonated; when the amine nitrogen is in a tertiary form, it is uncharged and thus more lipid soluble; molecules with an uncharged (and thus more lipophilic) form of amine nitrogen permeate nerve membranes more readily, whereas molecules with the charged (and thus more water-soluble) form show greater affinity for binding with sodium channels; LAs are supplied by manufacturers in quaternary form as a hydrochloride salt; the proportion of charged versus uncharged molecules (and thus the speed at which they permeate the plasma membrane and produce clinical effects) is determined by the pKa to which the LA is manufactured, by the (in vivo) pH of relevant tissues

Cocaine: one of the first recognized LAs; its addictive properties, toxicity (*ie*, psychological and physical dependence, mood alterations, CNS and cardiac excitation), and intense vasoconstrictive effects preclude contemporary clinical use

Procaine: an analog of cocaine that has a shorter duration of action (relative to cocaine), but shows high rates of allergic side effects; no longer readily available, but occasionally utilized

Lidocaine: the current gold standard for LAs; used in many forms; common agent in anesthesiology due to its ease of use, history of safety, and broad-use applications

Rate of absorption and distribution: modulated by several determinants of passive diffusion (which include molecular weight, pKa, lipid solubility, formulation, concentration gradient, pH, and vascularity of the tissue environment

Distribution of LAs: in plasma, LAs bind to albumin, alpha-1-acid glycoproteins, and erythrocytes; the protein binding capabilities of an LA are the primary determinant of its ability to distribute from the vascular compartment to other body fluids or tissues; this distribution occurs in 3 distinct phases; *phase I* — characterized by rapid fall of plasma concentration as the LA is distributed to well-perfused tissues (*eg*, the brain, liver, heart, kidney, and lungs); *phase II* — associated with a slower decline in plasma levels, as the LA is distributed to less well-perfused tissues (*eg*, skeletal muscles and fat); mirrors the distribution half-life of LAs; the degree of tissue uptake associated with LAs is expressed as a volume of distribution (*eg*, a lower plasma protein binding capacity coupled with greater lipid solubility results in a greater volume of distribution); *phase III* — reflects the decline in plasma concentration due to clearance (including metabolism and excretion), and thus represents its elimination half-life

Elimination half-life of LAs: in general, half-life is primarily determined by an LA's volume of distribution; the metabolism of an amino amide-type LA takes place primarily in the liver via cytochrome-P (CYP)-450 isoenzymes 3A4 and 1A2; with some exceptions, the excretion of metabolites and any unchanged LAs takes place in the kidneys; in general, systemic clearance of LAs occurs after 5 half-lives

Effects of LAs: local anesthesia is a reversible sensory loss in a defined area of the body associated with transient inhibition of a peripheral nerve conduction; use of an LA agent should be followed by complete recovery (*ie*, without evidence of structural or functional nerve damage); an ideal LA agent should provide profound, reversible, and local relief of pain with rapid onset and satisfactory duration of action with minimal adverse effects

Formulations: the current vehicle for LAs is sterile water; some include contain citric acid (an antioxidant) or liposomes; future LAs may incorporate longer-acting delivery mechanisms

Additives: possible functions include extending duration of action, propagating function, and increasing

vasoconstriction (in order to extend the density of the block); *eg*, epinephrine; can cause vascular smooth muscle contraction at the site of LA administration and slow the rate of LA absorption into the stomach circulation; often enhance the duration of LA action

Potency of LAs: the aromatic group comprising the structural domain of LAs is responsible for their lipophilicity; the lipid solubility (*ie*, partition coefficient) of an LA determines its ability to pass through biologic membranes and reach receptor sites; consequently, LAs must be able to partition into, diffuse across, and dissociate from neuronal plasma membranes; as the lipid solubility increases, the partition of a LA through neuronal membranes also increases; LAs with higher partition coefficients must be used in lower doses to achieve the same degree of neuronal blockade achieved by agents with lower lipid solubilities; therefore, the primary determinant of an LA's potency is its partition coefficient; however, this relationship reverses when lipid solubility reaches a certain level, as a highly lipid-soluble LA becomes trapped in the neuronal membrane

Relative potency: reflected by an LA's concentration in an aqueous solution; the structural domain of LAs responsible for their hydrophilicity is the amine group

Onset of action in LAs: an aqueous solution of an LA (*eg*, the quaternary form provided by manufacturers) exists as a mixture of protonated (positively charged) or ionized and deprotonated (neutral) or unionized forms; only the deprotonated or neutral forms of LA molecules can translocate across neuronal membranes; the ratio of protonated-to-deprotonated forms is predicted by the agent's dissociation constant (*ie*, pKa) and the pH of tissue at the site of administration; greater similarity between an LA's pKa and the pH at the site of administration (physiologic pH of 7.4) allows a greater fraction of deprotonated molecules to translocate across neuronal membranes; therefore, the dissociation constant of an LA is the primary determinant of its onset of action; after reaching the neuronal cytoplasm, most of the deprotonated molecules are rapidly converted into their protonated form (which typically bind to VGSCs with higher affinity compared to their deprotonated form)

Duration of action in LAs: LAs with high protein binding capacity bind more tightly to and dissociate more slowly from their associated receptor sites; therefore, the primary determinant of a LA's duration of action is its protein binding capacity; *highly lipophilic LAs* — tend to form tighter bonds with their targeted receptors, due to structural fatty acids associated with receptor sites; *protonated forms of LAs* — tend to dissociate from the receptor site more slowly; *other variables* — dosage administered; vascularity of injection site; presence of a vasoconstrictor in the LA's formulation

Adverse Reactions to Local Anesthetics

Background: non-selective blockade of VGSCs is responsible for most adverse drug reactions (ADR) associated with LAs

Causes of excessive plasma concentrations (in absence of overdose): rapid absorption; intravascular injection; low plasma protein binding; slow clearance; repeated doses

Dose determination: in healthy adults and children, basing the dosage on body weight is critically important; due to high rates of variability in current and future products, it is also critically important to check the manufacturer's recommendations for rules and formulas necessary to calculate appropriate dosages; focus on determining a reasonable approach to calculating the appropriate recommended dosages for your patients

Hypotension: urgent hypotensive events are extremely common, and it is thus highly important for anesthesiologists to remain attentive for these critical circumstances; ensure lipid emulsions are rapidly available, and that relevant protocols are in place (particularly when administering spinal neuraxial or ultrasound-guided blocks using LAs in the intra-operative setting at high doses)

Interactions: ADRs may occur at therapeutic doses of LA due to interactions with other medications, foods, herbal supplements, and diseases which can affect pharmacokinetic or pharmacodynamic processes

Other causes of ADRs: since LAs or their metabolites may be inherently toxic, they may produce cytotoxic reactions; LA-related ADRs may be immune-mediated or idiosyncratic; anesthesiologists must remain vigilant and prepared to address any ADRs that may occur

Medication-specific ADRs: *prilocaine* — may induce methemoglobinemia; *bupivacaine* — known to be cardiotoxic

Local reactions: epithelial and vascular reactions (may be attributed to the dosage-related cytotoxic nature of LAs, or vasopressor-induced); edema; desquamation; ischemic; note that some adverse events can be transient in nature; LA-associated myotoxicity (caused by injection into muscles); vasoconstrictor-associated necrosis; acute pain; trismus (healing with fibrosis may lead to chronic trismus)

Neurologic deficits: may represent LA-induced neurotoxicity related to the total dose of LA administered, the particular LA used, and the technique employed (*eg*, infiltration versus nerve block); however, most cases of neurologic deficit involve direct nerve injury, or nerve injection; signs and symptoms include transient anesthesia or paresthesia (characterized as a sensation of pricking or tingling at the area of where the nerve blocks were conducted); although many patients note that the symptoms resolve after several months, close monitoring on follow-up is recommended

Perioperative precautions: clinicians should always consider the evidence when assessing risks and benefits of administering any block or LA (particularly in the perioperative setting); discuss risks, benefits, alternatives, and all potential options that are available with the team, patients, and families

CNS effects of LAs: *excitatory effects* — may be brief; include lightheadedness, restlessness, nervousness, anxiety, apprehension, and euphoria; neurologic effects — vision deficits; tremors; convulsions; *depressant effects* — include respiratory depression and respiratory arrest; *other CNS effects* — include nausea, vomiting, chills, and miosis

Cardiovascular effects: include signs and symptoms of decreased cardiovascular function, which may be direct effects of LAs (as they can depress cardiac conduction, excitability and contractility); patients may develop decreased cardiac output, hypotension, and progressive cerebral hypoxia (which can lead to seizures); effects may progress to ventricular arrhythmias, atrioventricular (AV) block, and even cardiac arrest

Hypersensitivity reactions: allergic reactions to LAs may manifest as pruritus, erythema, angioedema, wheezing, asthma, and anaphylaxis (rarely)

Ester-type LAs: allergic reactions have been confirmed, and may be attributed to plasma cholinesterase has been confirmed; para-aminobenzoic acid (PABA; a breakdown product of LAs) is highly antigenic and capable of sensitizing lymphocytes or eliciting the formation of immunoglobulin E (IgE) antibodies

Amide-type LAs: true allergy to these agents is extremely rare; patients allergic to ester-type LAs have not shown cross-sensitivity to amide-type LAs; cross-sensitivity among amide-type LAs has not been reported

Sulfites: LAs formulated with the vasoconstrictor metabisulfite may precipitate an allergic reaction; prevalence of sulfite allergy in general populations is unknown; however, sulfite sensitivity is seen more frequently in patients with asthma

Methemoglobinemia: uncommon idiosyncratic reaction most notably associated with prilocaine and topical benzocaine (as their metabolites bind to hemoglobin and interfere with its oxygen carrying capacity); *signs and symptoms* — typically appear 3 to 4 hrs after exposure to large doses; include cyanosis, fatigue, weakness, nausea, sedation, seizures, and coma; *risk factors* — extremely young age; congenital methemoglobinemia; glucose-6-phosphate deficiency

Sympathetic reactions: healthy adults can safely receive ≤0.2 mg of epinephrine (although greater amounts may be used depending upon the dosage of LAs given); inadvertent intravascular injection of an LA containing a vasoconstrictor or a high-dose amount of vasoconstrictor can cause a sympathetic effect

Absolute contraindications for vasoconstrictors: high risk for a cardiovascular event; severe hypertension (*ie*, >180/110 mmHg); severe cardiovascular disease (*eg*, recent myocardial infarction [MI], unstable angina pectoris, decompensated heart failure, severe valvular disease, supraventricular arrhythmia with an uncontrolled ventricular rate, symptomatic ventricular arrhythmias, high-degree AV-block); uncontrolled hyperthyroidism

Sympathetic toxic reaction: high-risk patients who inadvertently receive a vasoconstrictor with an LA may be at high risk for a sympathetic toxic reaction; *symptoms of mild reactions* — restlessness; headache; tremor; dizziness; pallor; *symptoms of severe reactions* — palpitations; tachycardia; chest pain; ventricular fibrillation; cardiac arrest

Role of functional capacity in predicting risk: when obtaining medical history, seek to determine the patient's functional capacity; capacity to perform a spectrum of common daily tasks has been shown to correlate well with maximum oxygen uptake by treadmill testing; in a man who weighs 70 Kg and is 40 yrs of age, oxygen consumption at rest is 3.5 mL/kg/min and requires the functional capacity of 1 metabolic equivalent (MET); cardiac risk is increased in patients unable to meet demands for oxygen equating to 4 METs; hemodynamic effect of a 0.045 mg dose of epinephrine was reported to be less than the hemodynamic effect produced by an ergonomic stress test of 25 watts in young subjects, and 15 watts in older subjects; the workload of ergonomic stress testing at these levels is ~4 METs (approximately equivalent to the workload produced by climbing 2 flights of stairs, walking at 4.8 km/hr, doing light yard work, raking leaves, weeding, painting, or light carpentry work); as such, 0.045 mg of epinephrine can be safely administered to patients who can tolerate these activities noted with minimal or no symptoms (*eg*, diaphoresis, fatigue, shortness of breath, chest pain); 0.045 mg of epinephrine is equivalent to the 1-to-100,000 concentration of epinephrine found in 4.5 mL of any LA formulation; in general, studies provide clear evidence that functional capacity serves as a practical determinant for whether this approximate dose can be safely administered

Pregnancy safety: in 2014, the FDA amended its regulation governing the content and format of labeling for human prescription drugs and biological products; effective June of 2015, all products were requiring to remove the old pregnancy categories A, B, C, D, and X; labeling information about risk to the fetus and recommendations about the use of LAs during pregnancy now found under a new pregnancy subsection specific to package inserts

Breastfeeding: the 2015 FDA amendment also required a subsection regarding lactation on the package insert that addresses related risks to breastfeeding children, and includes recommendations on how to minimize drug exposure when an LA is administered to the mother

Medication interactions: dosages of LAs should be reduced in patients taking CNS depressants, due to additive effects; caution is also recommended when administering LA with a vasoconstrictor in patients taking tricyclic antidepressants, some β_1-adrenergic receptor antagonists, and some general anesthetics (since these agents may cause severe hypertension, cardiac arrhythmias, and cerebrovascular accidents); evidence of interactions with antipsychotic agents and thyroid hormones is less compelling

Epinephrine and pregnancy: epinephrine by may decrease uterine contractions and prolong labor (due to β_1-adrenergic activity), and may decrease uterine blood flow and fetal circulation (due to α_1-adrenergic activity); however, it has been shown that bolus doses containing 0.1 mg of epinephrine did not prolong the duration of labor, and did not adversely affect placental blood flow and fetal circulation; it is of note that researchers considered the addition of epinephrine to LAs beneficial as it reduces dosages of LA required for pain relief

Summary: LAs in anesthesiology have broad applications from the acute to perioperative setting; anesthesiologists play a critical role in the use of LA, and in addressing both acute and chronic pain; pharmacologic properties of LAs vary from agent to agent, and as such it is critically important to understand the role of these products and how they change over time; to compensate for these differences, many manufacturers adjust the concentrations of various LAs such that they produce nearly identical effects; consequently, anesthesiologists should be capable of predicting the doses of LAs required in various clinical situations; there should be a clear understanding of the risks, benefits, and various alternatives of LAs and their different clinical situations; LAs are critically important in anesthesiology, play a future role in the management of pain, and continue to be a critical drug for the pharmacological management of pain in the operative setting

Suggested Reading

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Cardiovascular Drugs

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Types of adrenergic receptors

Alpha-receptors: two types; each type further subdivided into three receptor subtypes

Alpha-1 receptors: particularly important in the cardiovascular system; stimulation causes vasoconstriction

Alpha-2 receptors: predominantly found in neuronal tissue; inhibit neurotransmitter (norepinephrine and acetylcholine) release in brain and autonomic nerve terminals; agonists suppress sympathetic outflow, inhibit smooth muscle contractility, and inhibit insulin release

Beta-receptors:

Beta-1 receptors: mainly in heart; increase heart rate and force of contraction

Beta-2 receptors: cause vasodilation (especially of muscular arteries), smooth muscle relaxation, hepatic glycogenolysis

Beta-3 receptors: activation causes fat breakdown, thermogenesis, and bladder detrusor muscle relaxation

Epinephrine, norepinephrine and isoprenaline: act on alpha and beta-receptors; potency varies; for alpha-receptors, norepinephrine more potent than epinephrine, which is more potent than isoproterenol; for beta-receptors, isoproterenol more potent than epinephrine, which is more potent than norepinephrine

Epinephrine:

Physiologic effects: because of its effects on beta-receptors, epinephrine has more metabolic effects than norepinephrine; affects beta-1 and beta-2 receptors, and alpha-receptors at high doses; at low physiologic infusion rates (for example, 0.01 mcg/kg/min), acts on beta-2 receptors to vasodilate muscular arteries and consequently decrease blood pressure; at high doses (greater than 0.2 mcg/kg/min), it increases peripheral resistance, blood pressure, and heart rate due to positive chronotropic effects

Indications: management of shock, cardiac arrest, anaphylaxis; used to increase duration of local anesthetics through local vasoconstriction; through its effects on beta-1 and beta-2 receptors, it increases frequency of arrhythmias and causes ventricular fibrillation; causes anxiety and tremor; can cause severe hypertension, which can lead to headache, cerebellar hemorrhage, and pulmonary edema; peripheral vasoconstriction causes cold extremities; intravenous use contraindicated in late pregnancy because it stimulates uterine contraction

Norepinephrine: beta-1 and alpha effects, with less beta-2 stimulation; predominately stimulates peripheral alpha-receptors, but has more marked effects than epinephrine; stimulates the beta-receptors in the heart; administered intravenously and titrated to effect; maximal dose is around 0.2 mcg/kg/min; indicated in management of vasodilatory shock; commonly used in conjugation with phosphodiesterase inhibitors, like milrinone, as milrinone can cause significant systemic vasodilation; like epinephrine, norepinephrine should be avoided in late pregnancy, as it can cause uterine contraction, and it may worsen preexisting excess vasoconstriction

Phenylephrine (neo-synephrine): pure alpha selective agonist; causes vasoconstriction and increases vascular resistance in skin, muscles, and renal and mesenteric vascular beds; increases systolic and diastolic blood pressure; increases coronary and cerebral blood flow by increasing diastolic pressure; causes vagally-mediated reflex bradycardia; administered intravenously and titrated to effect; commonly used to manage perioperative hypotension and as a decongestant; adverse effects related to uncontrolled hypertension; inadvertent absorption of large doses during head and neck surgery for vasoconstriction have led to pulmonary edema and cardiac arrest; phenylephrine-induced hypertension should be managed by alpha-1 antagonists (for example, phentolamine) or direct vasodilators

Vasopressin (antidiuretic hormone): endogenous hormone similar to oxytocin; acts on vasopressin V2 receptors to cause water absorption at renal tubule; acts on V1 receptors to cause direct vasoconstriction; increases hepatic glycogenolysis and factor VIII activity, and encourages platelet aggregation and degranulation

Desmopressin (DDAVP): similar to vasopressin, but 12-times more potent in retaining water; used to treat diabetes insipidus; has only 0.4% the vasoconstrictor activity of vasopressin; increases factor VIII activity; used to improve platelet function, especially in mild hemophilia

Felypressin and terlipressin (synthetic vasopressin): long-acting; not available in US

Dopamine: stimulates heart through beta- and alpha-adrenergic receptors; vasodilates splanchnic blood vessels by acting on peripheral dopaminergic receptors; at high doses, causes alpha-receptor stimulation and peripheral vasoconstriction; increases cardiac contractility, stroke volume, and coronary blood flow; little effect on heart rate; effect on blood pressure depends on dose; stimulates carotid bodies to reduce response to hypoxia; affects renal blood flow to increase glomerular filtration rate and urine output

Indications: widely used after cardiac surgery; used to manage cardiogenic shock (equal concentrations of

dopamine and dobutamine may be more advantageous than either drug alone); contraindicated in patients with ventricular arrhythmias, pheochromocytoma, and patients taking MAO inhibitors, as it is metabolized by MAO

Isoproterenol: synthetic beta-receptor agonist; predominantly agonizes beta-1 and beta-2 receptors to produce chronotropic effects; inotropic effect primarily due to effect on beta-1 receptor; lowers peripheral blood vascular resistance in muscular, renal, and mesenteric beds; may decrease diastolic blood pressure and mean arterial pressure; can relax smooth muscles to cause bronchodilation and uterine relaxation; can cause arrhythmias, headaches, anxiety, restlessness, tremor, and flushes; because it stimulates beta-adrenergic receptors, it increases gluconeogenesis; clinically indicated to treat bradycardia caused by heart block, beta-blocker toxicity, and *torsades de pointes* ventricular tachycardia; contraindicated in patients with myocardial ischemia

Cardiac glycosides (digitalis): naturally occurring cardiac glycoside derived from foxglove; used to improve cardiac contractility and reduce cardiac conduction; improves isometric and isotonic contraction of atrial and ventricular muscles; decreases conduction at AV node; inhibits sodium-potassium ATPase, which alters electrolyte balance at the cell membrane to increase intracellular sodium and decrease intracellular potassium; sodium-potassium changes activate the sodium-calcium pump to increase intracellular calcium, which improves contractility; inhibits local neuronal uptake of catecholamines, which may contribute to increased inotropy; can predispose to arrhythmias, especially in the setting of hypokalemia due to its ability to alter membrane potential; selectively used to manage congestive heart failure; may be used to manage refractory atrial fibrillation with or without congestive heart failure; cardiac glycosides have long half-life (~1.5 days); eliminated by kidneys; very low therapeutic index; previously, ideal blood level thought to be 1 to 2 ng/mL; more recent data indicates a lower therapeutic range of 0.5 to 1 ng/mL; contraindicated in patients with Wolff-Parkinson-White syndrome, hypertrophic obstructive cardiomyopathy, diastolic dysfunction, and AV nodal heart block

Phosphodiesterase inhibitors: milrinone inhibits breakdown of cyclic AMP in cardiac and peripheral vascular smooth muscle to augment myocardial contractility and peripheral arterial and venous vasodilation; can substantially increase heart rate and decrease blood pressure; common to use vasoconstrictor (like norepinephrine) in combination with milrinone; indicated in low-output heart failure; because of its vasodilatory properties, may be most useful in patients with acute right heart failure; predisposes to ventricular arrhythmias; contraindicated in patients with acute myocardial infarction, severe aortic stenosis, and hypertrophic obstructive subaortic stenosis

Vasodilators: sodium nitroprusside is a nitric oxide donor; vasodilates arterioles and veins by forming cyclic GMP in vascular tissues; ultra-short-acting agent; particularly useful for increasing left ventricular stroke work in acute severe refractory heart failure caused by mitral or aortic regurgitation; used in severe heart failure complicating acute MI after cardiac surgery and in patients with acute exacerbation of chronic heart failure; indicated in hypertensive emergencies and dissecting aneurysms (especially in conjunction with beta-blockers); due to vasodilating properties, it inhibits hypoxic pulmonary vasoconstriction and increases cerebral blood flow and intracranial pressure; contraindicated in patients with preexisting hypotension, obstructive valvular heart disease (for example aortic, mitral or pulmonic stenosis), and obstructive cardiomyopathy

Toxicity: metabolized as cyanmethemoglobin and free cyanide (1 molecule nitroprusside produces 5 molecules cyanide); cyanide accumulation inhibits oxidative metabolism; presents as increasing lactic acidosis; toxicity avoided by keeping infusion as low as possible and for as short a duration as possible, maintaining high clinical suspicion, monitoring for lactic acidosis, and administering sodium thiosulfate

Nitroglycerin: increases cyclic GMP in vascular smooth muscle; in contrast to sodium nitroprusside, its major effect is on venous system; preferred medication for management of pulmonary edema due to acute myocardial dysfunction; antianginal properties should always be considered in management of acute myocardial ischemia perioperatively; can be used to manage intraoperative hypertension (for example, in pheochromocytoma); increases intracranial pressure due to vasodilation; decreases systemic vascular resistance and systolic, diastolic, venous, and pulmonary artery pressures; decreases myocardial oxygen demand; improves subendocardial blood flow; causes bronchodilation and visceral smooth muscle relaxation in gut and biliary system

Hydralazine: direct-acting vasodilator with unclear mechanism; vasodilates cerebral, coronary and renal arterioles; does not relax venous smooth muscles; causes reflex tachycardia, increased contractility, increased renin secretion, and fluid retention; better tolerated if administered with beta-blockers and diuretics; can worsen myocardial ischemia because of reflex tachycardia; contraindicated in patients with active coronary artery ischemia; chronic use associated with drug-induced lupus; can cause serum sickness, hemolytic anemia, vasculitis, glomerulonephritis; used to manage hypertension in combination therapy for congestive heart failure and pregnancy-induced hypertension

Nesiritide (human recombinant beta natriuretic peptide): natriuretic peptides are secreted in response to atrial and ventricular stretch; cause vasodilation, natriuresis (increased sodium excretion in urine) and increased glomerular filtration rate; in healthy persons, administration causes systemic and pulmonary resistance and left ventricular filling pressures; in patients with congestive heart failure, glomerular filtration rate may increase, decrease, or remain unchanged; intravenous administration has a mean terminal half-life of 18 min; indicated for congestive heart failure with dyspnea; should not replace diuretics or be used in hypotension or cardiogenic shock

Antianginal Drugs: Nitroglycerine, beta-blockers, calcium channel blockers: improve balance of myocardial oxygen supply and demand; increase supply by dilating coronary vasculature and/or decrease demand by reducing cardiac work

Nitrovasodilators: nitroglycerin promotes relaxation of vascular smooth muscle; dilates large blood vessels (greater than 200 μm diameter) more potently than

small vessels; low doses preferentially dilate veins and conduit arteries but do not affect tone of small to medium arterioles that regulate resistance; at low to medium doses, preferential venodilation decreases venous return, which decreases left and right ventricular chamber size and end diastolic pressures; reduce wall stress, thus reducing cardiac oxygen demand; systemic vascular resistance and arterial pressures only mildly decreased so coronary perfusion pressure unaffected; heart rate unchanged or slightly increased secondary to decreased blood pressure; pulmonary vascular resistance and cardiac output slightly reduced; peak plasma concentration within 4 min of sublingual administration; 1 to 3 min half-life; headache is a common side effect that can be severe; patients with autonomic dysfunction and an inability to increase sympathetic outflow, a fall in blood pressure from venodilation may not be fully compensated; in these patients, arterial pressure and coronary perfusion pressure may be significantly reduced and cause life-threatening hypotension and worsening angina; combination of sildenafil or other phosphodiesterase-5 inhibitors with organic nitrate vasodilators can cause extreme hypotension; intravenous nitroglycerin can be used to manage intraoperative myocardial ischemia, as long as blood pressure is maintained; no role for prophylactic use of nitroglycerin in the perioperative period to decrease incidence of perioperative myocardial ischemia

Calcium channel blockers: calcium triggers contraction in smooth muscle and cardiac myocytes; calcium channel blockers inhibit calcium influx into cells; in vascular smooth muscle, causes relaxation in arterial beds and cardiac myocytes and causes negative inotropic effects; all calcium channel blockers exert these two principal actions; ratio and chronotropic effects differ by calcium channel blocker class; exert antianginal effects mainly through peripheral arterial vasodilation and decreased afterload (decreased wall stress); do not work through direct coronary artery dilation; coronary artery dilation plays important role in the management of variant angina

Beta-blockers: only drugs effective in reducing severity and frequency of exertional angina and improving survival in patients who have had a myocardial infarction; recommended as first-line treatment for stable coronary artery disease, unstable angina, and acute coronary syndrome; effectiveness for exertional angina primarily due to decreased myocardial oxygen consumption at rest and during exertion; decreased myocardial oxygen consumption due to negative chronotropic effect, particularly during exercise, and negative inotropic effect and reduction in arterial blood pressure, particularly systolic blood pressure, during exercise; decreased heart rate prolongs time of myocardial perfusion during diastole; increase blood flow towards ischemic regions by increasing coronary collateral resistance and preventing blood shunting from ischemic myocardium during maximal coronary vasodilation; numerous beta-blockers approved for clinical use; beta-1 selective agents without intrinsic sympathomimetic activity used for angina (for example, atenolol, bisoprolol, or metoprolol); patients using beta-blockers should continue to receive them during perioperative period due to risk of withdrawal and rebound tachycardia; prophylactic use to decrease adverse myocardial events in perioperative period is controversial; if used for prophylactic benefit, they should be started at least 7 days prior to elective surgery and titrated up slowly

Angiotensin converting enzyme (ACE) inhibitors and angiotensin blockers: angiotensin II is an important regulator of cardiovascular function; ability to reduce angiotensin II levels or block its effects is important in hypertension and heart failure management

ACE inhibitors: reduce vasomotor tone; reduce salt and fluid retention; cause specific renal vasodilation to enhance sodium and water excretion; decrease preload, afterload, and myocardial work; prevent breakdown of bradykinin, which may cause the side effect of cough; indicated to manage hypertension, congestive heart failure, myocardial infarction, and diabetes nephropathy; large, international, prospective cohort study suggests withholding ACE inhibitors or angiotensin blockers on the day of non-cardiac surgery may reduce the risk of perioperative death, stroke, and myocardial injury in patients who take these medications regularly; thus withholding these medications on the day of surgery is now recommended

Angiotensin II: there are 2 angiotensin II receptor subtypes; role of AT2 receptor unclear, but thought to be antiproliferative at endothelial cell level; AT1 receptor stimulation causes vasoconstriction and aldosterone secretion, which leads to sodium and water retention; angiotensin II receptor antagonists block the AT1 receptor; AT2 inhibitors used as anti-hypertensive agents and have clinical effects similar to ACE inhibitors; their main advantage is the absence of an effect on kinins, so they do not have the side effect of dry cough; other clinical effects of angiotensin II receptor antagonists include reduced sodium and water retention, reduced vasomotor tone, reduced preload, and reduced afterload; reduce blood pressure, especially in the setting of sodium depletion; reduce myocardial work; reduce aldosterone, catecholamine, and atrial natriuretic peptide levels; increase plasma potassium concentration; increase insulin sensitivity

Class I antiarrhythmics: work similarly to local anesthetics; function by slowing sodium entry into cells through fast voltage-gated sodium channels that primarily affect non-nodal areas characterized by fast action potential depolarization; reduce maximum rate of rise of phase zero depolarization; may also reduce rate of phase four sinoatrial node depolarization; these drugs subdivided into 3 classes based on their effect on action potential duration

Class Ia (quinidine and procainamide): increase action potential duration; used to treat supraventricular tachyarrhythmia

Quinidine: many side effects, including diarrhea and nausea; can cause *torsades de pointes*, arrhythmia, and hypotension; need to monitor QRS and QT on EKG and plasma potassium levels; can increase digoxin levels and warfarin potency

Procainamide: effective against a wide variety of supraventricular and ventricular arrhythmias, including ventricular tachycardia; does not prolong QT interval to same extent as quinidine; fewer interactions with muscarinic receptors than quinidine; causes direct sympathetic inhibition, producing vasodilation, so

hypotension is common with intravenous dosing; side effects include fever, rash, and arthralgias; can also cause lupus and agranulocytosis; hypotension, prolongation of QRS and QT widening are common side effects with intravenous administration; heart block may develop or increase; in atrial fibrillation or flutter, the ventricular rate may increase as the atrial rate slows (concomitant blockade advised)

Class Ib (lidocaine and phenytoin): decrease action potential duration; used for ventricular tachyarrhythmias; lidocaine was former standard intravenous agent for suppression of serious ventricular arrhythmias associated with acute myocardial infarction and cardiac surgery; however, its use has decreased significantly since the introduction of intravenous amiodarone

Class Ic (flecainide): used for ventricular tachyarrhythmias; does not affect action potential duration

Adenosine: used for rapid conversion of paroxysmal supraventricular tachycardias to sinus rhythm, including Wolf-Parkinson-White (WPW) syndrome; may also be used to diagnose conduction defects; causes transient slowing of AV nodal conduction; this allows normal sinus nodal discharge to initiate a normal pattern of electrical depolarization throughout the heart, causing normal sinus rhythm to resume before the drug has been eliminated; effect appears to be mediated by increased myocardial potassium influx; its IV injection must be rapid, because it is rapidly metabolized and its half-life is only 8 to 10 s; unlike verapamil, it can be used safely with beta-blockers, but is contraindicated in asthma, sick sinus syndrome, and second and third degree AV heart block

Cardiovascular effects of electrolyte disturbances: excesses or deficiencies of electrolytes, especially potassium, magnesium, phosphorus, and calcium can significantly affect the heart and cardiovascular system

Potassium:

Hypokalemia (defined as <3.5 mmol/L) cardiac cells typically unaffected until serum potassium <3 mmol/L; causes cardiac dysrhythmias (ventricular tachycardia or fibrillation, sinus bradycardia, paroxysmal atrial or junctional tachycardia, atrioventricular block, and premature atrial and ventricular beats); typical electrocardiogram changes are ST segment depression, decreased T wave amplitude, and increased U wave amplitude

Hyperkalemia (>5 mmol/L): common perioperatively, especially in patients with acute kidney injury and oliguria; causes cardiac conduction abnormalities and arrhythmias; can cause cardiac arrest; type of effects and severity not well-correlated to degree of serum potassium elevation; first step in management is to assess EKG; hyperkalemia is classically associated with tall, peaked T waves, and shortened QT intervals; when more severe, PR interval and QRS duration are prolonged, and the P wave may disappear; QRS may widen until it reaches a sinusoid wave pattern

Magnesium: primarily affects cardiovascular system; important effects on calcium channel pumps to regulate transmembrane and intracellular ionic flows; vasodilatory effects on arteriolar vasculature; modulates calcium fluxes to produce smooth muscle cell contraction; exerts calcium antagonist effect on myocytes by inhibiting calcium uptake and reducing cardiac contractility

Hypomagnesemia (<0.75 mmol/L); if severe, PR and QT intervals lengthen and predispose to ventricular arrhythmias, tachycardia, and abnormal T waves; increased arteriolar tone common when extracellular magnesium low because calcium uptake is enhanced, and intracellular calcium concentrations increased

Hypermagnesemia (>0.95 mmol/L): symptoms uncommon until level reaches 2 mmol/L; initial symptoms of nausea, vomiting, flushing, and reduced tendon reflexes; neurologic manifestations precede cardiovascular depression; cardiac effects include bradycardia and hypotension; at higher concentrations (2.5 to 5 mmol/L) prolonged PR interval, QRS complex, and QT intervals may be seen; further elevation leads to complete heart block and cardiac arrest

Calcium: critical role in normal cell function, signaling, and regulating processes like cardiac contractility;

Hypercalcemia: asymptomatic if mild; if severe, can cause neurologic symptoms and decreased renal concentrating ability, which can lead to polyuria, polydipsia, and vasoconstriction; higher levels cause significant electrocardiographic changes including bradycardia, atrioventricular block, and short QT intervals;

Hypocalcemia: can prolong QT interval

Phosphorus (normal serum range, 2.5 to 4.5 mg/dL in adults): most abundant intracellular anion; essential for membrane structure, energy storage, and transport; necessary to produce ATP; reducing available phosphate may compromise any organ system alone or in combination; its critical role in every cell, tissue, and organ explains systemic nature of injury caused by phosphate deficiency

Hypophosphatemia: classified as mild (2 to 2.5 mg/dL), moderate (1 to 2 mg/dL), or severe (less than 1 mg/dL); mild to moderate usually asymptomatic; severe can impair cardiac contractility and lead to generalized signs of myocardial depression; blood pressure and stroke volume improve when serum phosphorus is corrected; hypophosphatemic myocardium has reduced threshold for ventricular arrhythmias; can lead to new-onset arrhythmias

Hyperphosphatemia: most commonly occurs with acute renal failure, tumor lysis, or trauma; results from release of intracellular phosphate into the serum or decreased excretion from the kidney; increased levels cause endothelial dysfunction and flow-mediated vasodilation; chronically, calcification of arteries, increased arterial wall stiffness, and increased pulse pressure can cause cardiomyopathy, arrhythmias, and sudden cardiac death; calcification of cardiac valves and myocardium may also occur in chronic hyperphosphatemia

Perioperative management of chronic-use cardiovascular drugs: what to continue, what to withhold, and when:

Beta-adrenergic antagonists (esmolol, atenolol, metoprolol, and bisoprolol): reduce myocardial oxygen consumption; improve coronary blood flow by prolonging diastolic perfusion period; improve supply/demand ratio; stabilize cellular membranes; improve oxygen dissociation from hemoglobin and inhibit platelet aggregation; suppress perioperative tachycardia; most efficacious in preventing perioperative myocardial ischemia; prophylactic use

of beta-blockers to decrease perioperative myocardial injury has been explored in many trials; Mangano and Poldermans reported beneficial effects on overall survival and cardiovascular morbidity in non-cardiac surgery patients with or without risk for coronary artery disease; subsequent trials have not shown efficacy of high-dose, acutely administered perioperative beta-blockers to reduce overall mortality in patients undergoing non-cardiac surgery; POISE study (largest of these trials)showed better perioperative cardiac outcomes but also a higher mortality rate and rate of stroke in the beta-blocker group as compared to the placebo group; American College of Cardiology and American Heart Association conducted systematic review and found:(1) preoperative use associated with reduction in cardiac events, but few data supported effectiveness of preoperative administration to reduce risk of surgical death; (2) a clear association exists between beta-blocker administration and adverse outcomes such as bradycardia and stroke; currently, the only American Heart Association guidelines Class 1 recommendation for perioperative beta-blocker use is to continue use in patients who are already taking them (Class 1 recommendation; B level of evidence); can be used in patients with elevated risks, especially myocardial ischemia on preoperative testing or in patients with 3 or more Revised Cardiac Risk Index risk factors (Class 2B recommendation; B level of evidence); guidelines differ somewhat between American Heart Association and European Society of Cardiology; they agree that (1) if beta-blockers are used prophylactically in perioperative period, they should be started slowly and titrated over 2 to 7 days prior to elective surgery, and that (2) acute administration of high-dose beta-blockers in high-risk patients undergoing low-risk surgery is not recommended; can be used intraoperatively and postoperatively to manage tachycardia, arrhythmias, and hypertension

Alpha-2 adrenergic drugs (clonidine): decrease sympathetic outflow, blood pressure, and heart rate; despite previous studies suggesting possible beneficial effects of alpha-2 agonists, POISE 2 trial (10,000 patients) did not show any statistically significant benefit of clonidine; clonidine did not reduce 30-day all-cause risk of death or nonfatal MI in patients with or at risk for atherosclerotic heart disease who were undergoing non-cardiac surgery; clonidine did increase rate of nonfatal cardiac arrest and clinically important hypotension; American Heart Association guidelines do not recommend alpha-2 agonists for prevention of cardiac events in patients scheduled to undergo non-cardiac surgery

Nitrovasodilators (nitrates): decrease left ventricular preload by decreasing systemic venous, pulmonary artery bed, and pulmonary vein dilation; decrease left ventricular filling pressure, left ventricular diastolic compressive forces, and left ventricular afterload and improve coronary circulation; reverse or prevent spasm in coronary circulation and improve collateral blood flow; may improve regional subendocardial ischemia; role of nitroglycerin as a prophylactic agent was determined in the past, but no studies within past 10 years examining prophylactic use for prevention of perioperative myocardial ischemia; prior studies were small (less than 50 patients), not blinded, and yielded conflicting results; current guidelines do not recommend prophylactic intravenous nitroglycerin to reduce myocardial ischemia in patients undergoing non-cardiac surgery

Calcium channel blockers (verapamil, diltiazem, nifedipine): reduce myocardial oxygen demand by depressing myocardial contractility; most important effect may be prevention of sympathetically-mediated coronary vasoconstriction; meta-analysis of patients on perioperative calcium channel blockers for non-cardiac surgery (11 studies and 1,000 patients) showed reduced incidence of myocardial ischemia and postoperative supraventricular tachycardia; beneficial effects mostly due to diltiazem; nifedipine use associated with ischemia; another study of 1,000 patients having elective or emergent aortic aneurysm surgery showed that use of nifedipine-type drugs was associated with increased perioperative mortality; use of short-acting calcium channel blockers (nifedipine) should be avoided; American Heart Association makes no recommendations for prophylactic use; routine use of calcium channel blockers to reduce the risk of perioperative cardiovascular complications is not recommended

Angiotensin converting enzyme inhibitors and angiotensin receptor blockers: used for management of hypertension, congestive heart failure, post-myocardial infarction, and diabetic nephropathy; recent ingestion of ACE inhibitors or angiotensin receptor blockers can lead to hypotension in perioperative period; a recent, large, international prospective cohort study suggests that withholding ACE inhibitors or ARBs on the day of non-cardiac surgery may reduce perioperative risk of death, stroke, and myocardial injury in patients who take these medications regularly; it is generally recommended to withhold ACE inhibitors and angiotensin receptor blockers on the day of surgery; these agents should be resumed as soon as possible postoperatively; failure to restart angiotensin receptor blockers within 48 h after surgery is associated with increased 30-day mortality

Digoxin: limited studies in perioperative period; indications are to prevent hospitalization and readmission in patients with reduced left ventricular function and to control ventricular response in atrial fibrillation; one study showed that perioperative use predicts postoperative ischemia, but this is probably because digoxin use is a marker of underlying cardiac disease; subgroup analysis of patients undergoing intrathoracic surgery showed decreased incidence of postoperative supraventricular arrhythmias; current recommendation is to continue digoxin perioperatively; obtaining drug levels preoperatively is not usually required

Suggested Reading

Magoon R et al: Pharmacological update: new drugs in cardiac practice: a critical appraisal. *Ann Card Anaesth* 2017 Jan;20(Supplement):S49-56;
Varelmann DJ et al: Noteworthy literature published in 2017 for cardiothoracic anesthesiologists. *Semin Cardiothorac Vasc Anesth* 2018 Mar;22(1):9-17.

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ANESTHESIOLOGY
Board Review

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Mathematics, Physics, Statistics, and Computer Applications

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Overview: board examination curriculum specifies candidate should have knowledge of physics, electrical and fire hazards, basic mathematics, and statistics

Storage of anesthetic gases: now mostly use pipeline gases, but must also think about cylinders; cylinders store gas under pressure; pressure defined as force per unit area, usually expressed in pounds per square inch (psi); usually measured with a Bourdon tube–type pressure gauge, which contains coiled metal tube that can be slightly deformed by pressure of contained gas; this deformation transmitted and amplified a connecting rod to calibrated rotary gauge

E-type cylinder of O_2: commonly attached to the anesthesia workstation as emergency backup; also commonly used during patient transfer; contains 660 L of O_2 at pressure of 2200 psi when full; O_2 ideal gas, present in gaseous form at all usual temperatures and pressures; when half of supplies in the cylinder exhausted, 330 L of original 660 L will remain at half original pressure (*ie*, 1100 psi); pressure gauge thus reliable indicator of remaining volume of ideal gas in cylinder; if pressure 1100 psi, half original pressure, 330 L of original 660 L remain; if used to administer 3 L/min to patient, will last 110 min; with flow of 3 L/min, full cylinder at 2200 psi would last 220 min (slightly >3.5 hrs); to calculate how many minutes of flow remain from E cylinder at any pressure, multiply pressure times 0.3 and divide by flow rate to be administered in L/min

Other gases: some gases not ideal gases; examples include N_2O and CO_2; form liquids when compressed at room temperature; critical temperature (temperature below which can be liquefied by adequate pressure) above room temperature; cylinders thus contain both gas and liquid when full; when some of gas exhausted, immediately replaced by evaporation of more gas from liquid present in cylinder; thus pressure in cylinder remains constant until all liquid evaporated; pressure in cylinder of N_2O dependent on vapor pressure of N_2O at room temperature (~750 psi); full E cylinder of N_2O contains 1590 L, weighs about 3 kg; amount of N_2O remaining in a cylinder can be measured by weighing the cylinder; once all liquid N_2O has evaporated, pressure in cylinder progressively falls from 750 psi; pressure on dial will now correctly indicate volume of gas remaining; at point at which pressure starts to fall, ~400 L or 25% of original N_2O contents remain; as pressure falls, it will reliably indicate how much of 400 L remains; *eg*, when pressure equals 375 psi (one-half of original), ~200 L of original 400 L, will now remain

Critical pressure: temperature above which it does not become liquid, despite any amount of pressure; ideal gases have critical temperature well below extremes of room temperature; critical temperature of O_2 is –188.6°C; below that temperature, adequate pressure will liquefy O_2; critical pressure for O_2 at –188.6°C is 49.7 atmospheres; critical pressure of gas=pressure required to liquefy that gas at critical temperature

Liquid O_2: commonly used to supply hospital pipeline system; gases supplied from pipeline delivered at ~50 psi; liquid O_2 reservoirs of a hospital should have backup supply from either from second free liquid O_2 reservoir bank of bulk cylinders; construction accidents and other factors may interfere with supplies from primary source; stored in stainless steel containers of similar construction to vacuum flask; kept at –183°C; temperature largely maintained by latent heat of evaporation of liquid; 1 L liquid O_2 yields 860 L O_2 gas; liquid O_2 systems must comply with various guidelines

Flow of gases: in anesthesia machine or workstation, pressure of gas from E cylinder also reduced to approximately psi by reducing valve; reducing valve has 2 chambers, high- and low-pressure chamber; flow of gases from high-pressure chamber into low-pressure chamber regulated by spring-loaded needle valve, controlled by large diaphragm; relative size of large diaphragm to small needle-valve orifice achieves reduction in pressure

Basic Gas Laws (Physics)

Boyle's law: relates pressure and volume of gas at constant temperature; volume of given mass of gas inversely proportional to its pressure if temperature remains constant; $P_1 \times V_1 = P_2 \times V_2$

Charles's law: law of volumes; for ideal gas at constant pressure, volume relates directly to temperature; as temperature increases, so does volume

Gay-Lussac's law: law of pressures; pressure exerted on container by fixed mass and volume of ideal gas directly related to temperature of gas; as temperature rises, so will pressure

Avogadro's law: relates number of molecules in gas to its volume; under same conditions of pressure and temperature, equal volumes of gas contain same number of molecules

Ideal gas law: combines all these laws together and shows relationship of pressure, volume, and temperature of fixed mass of gas; absolute pressure multiplied by volume

equals constant multiplied by temperature and number of gas molecules; *Boltzman constant* — if temperature and pressure remain constant, volume of gas directly proportional to number of molecules of gas present; if temperature and volume remain constant, pressure of gas directly proportional to number of molecules of gas; if number of gas molecules and temperature remain constant, pressure inversely proportional to volume; if temperature changes and number of gas molecules remain constant, either pressure or volume or both will change in direct proportion to temperature

Dalton's law of partial pressures: pressure of mixture of gases equal to sum of partial pressures of gases present; in mixture of gases, pressure exerted by each gas equal to that which it would exert if alone in that container

Henry's law: also related to partial pressures; at constant temperature, the amount of gas dissolved in given volume of liquid related to partial pressure of gas in equilibrium with that liquid

Graham's law: rate of diffusion of gas inversely related to square root of its density; less-dense gases diffuse more rapidly; hydrogen least-dense gas, helium second-least

Compression of gas: if gas compressed, should be increase in temperature; if compression rapid and heat cannot escape, adiabatic compression (principle for diesel engine); such rise in temperature could also occur in cylinder yoke of anesthesia machine when cylinder rapidly opened; if any combustible material (*eg*, grease or lubricants) present, could result in ignition or explosion; essential that no combustible materials come into contact with compressed-gas supply lines

Expansion of gas: when gases expand, cooling effect; may be noted when reducing valve of anesthesia machine feels cold; in past, when not possible to dry anesthetic gases efficiently, water sometimes froze in reducing valve; some earlier anesthesia machines had electric heater coil (or even candle wick) under reducing valve

Implications for storage: compressed gas cylinders may explode if heated by fire; strict regulations on storage of cylinders; must be stored away from flammable materials or sources of ignition, secured in chains or racks, and in well-ventilated area; in UK and some other countries, plug of metal that melts at relatively low temperature incorporated into valve fitting of cylinders; in fire, would melt and allow contents of cylinder to escape; Wood's metal used for this purpose; alloy of bismuth, lead, tin, and cadmium, which melts at low temperature of 70°C; in US, National Fire Protection Agency provides mandatory guidelines for storage of compressed gases

Potential Operating Room (OR) Dangers

Overview: electrical injuries rare in OR, but when they occur, may cause serious injury, even death

Electrical definitions: voltage=electrical potential between 2 points; amperes=amount of current that flows; power, expressed as watts (joules/sec)=product of voltage and amperage; resistance=obstruction to electrical flow when voltage difference

Injuries from electricity: result from amperage that flows and time for which it flows; brief delivery of high voltage (*eg*, from static electricity) causes only brief jolt; 120 V causing current to flow for any time (*eg*, via wet hands) may lead to serious injury, even cardiac arrest

Grounding: casings of electrical equipment normally grounded via ground wire so that if fault occurs and equipment becomes live, stray electrical currents will flow through ground wire rather than through body

In the home: 1 of the 2 active electrical leads also connected to ground; usually termed neutral side; system in home thus has 120 V potential between its 2 wires and also between ungrounded, also called the line or hot side, and ground; has advantages for use in home, as grounded side provides unlimited sink for excessive electric current flow; useful to deal with large power surges or disasters (*eg*, lightning strike); having neutral side less advantageous in OR environment, could possibly introduce dangers

In OR: should be considered wet environment; floor may be conductive and wet, hands may be wet, each enhancing danger from stray electrical currents; therefore, electrical supply to OR, unlike in home, usually not grounded (neither of active wires connected to ground); each of active wires hot, but only in relation to other wire, to prevent any potential leakage currents from completing circuit to ground via patient or staff member and causing injury; ungrounded (floating) electrical supply of OR achieved by use of isolation transformer to removes danger of stray currents completing circuit to ground; integrity of floating ungrounded system must be constantly monitored to detect any accidental grounding, which could reintroduce hazard

Line isolation monitor: integrity of floating ungrounded supply usually constantly monitored by use of line isolation monitor (LIM); continuously measures any leakage current to ground, such as might occur if faulty piece of equipment connected; if so, alarm will sound; the last piece of equipment to be plugged in must then be suspected as source of problem; note that, even though alarm sounding, electricity still being supplied to that faulty equipment until unplugged

Ground fault circuit interrupter (GFCI): alternative method of maintaining isolation of electrical circuits; commonly used in wet areas of home (*eg*, bathroom); if faulty piece of equipment connected and current flows, equipment will switch off electricity supply; considered less desirable in OR, where interrupting power supply may introduce other hazards; LIM usually preferred

Effects on patients: electrical faults in equipment whereby metal casing or connections from apparatus become live may deliver major shock to operator and/or patient; macrocurrent, may cause serious tissue damage, even cardiac arrest; some patients may also be at risk from small currents if delivered into body and bypass normal high resistance of skin (microshocks)

Microshocks: microshocks as little as 10 microamps may cause ventricular fibrillation if delivered directly to heart via indwelling wires or saline-filled catheters; temporary epicardial pacing wires should be handled with great care and insulated against even small currents, (*eg*, from static electricity); saline-filled central venous catheters have also been implicated in delivery of microshocks from faulty infusion pumps; all electrical equipment in OR must be regularly checked for faults

OR Fires

Overview: OR fires serious risk, must be addressed; problem of fires did not go away when use of flammable anesthetic agents stopped; estimated that >100 OR fires occur each year in US; number may be much larger, as no universal mandatory reporting system; fire may result whenever flammable fuel, oxidizing agent, and source of ignition (sometimes called fire triad) are brought together

Flammable items: in OR, the flammable fuel most commonly surgical drapes or gowns, patient's hair or eyebrows, or endotracheal tube; most surgical prep solutions, many ointments and wound dressings flammable; other flammable materials can be involved, including patient's abdominal gas

Oxidizing agent: most commonly O_2; risk directly proportional to concentration of O_2 being used; N_2O slightly weaker oxidizing agent; in mixtures, effects additive to that of O_2

Source of ignition: most commonly electrocautery, laser beam, hot-wire cautery; heat from fiberoptic cable or static electricity spark also implicated in some cases

Common causes of fires: may occur during any surgical procedure; recently, particularly common during monitored anesthesia care for head and neck surgery; common practice to provide supplemental O_2 via loose-fitting mask or nasal cannula; O_2 accumulates beneath surgical drapes; just needs source of source of ignition; O_2 denser than air and will pool in dependent, closed spaces below drapes

Hazards of fires: may cause serious burn injuries; additionally, products of combustion may be harmful, even lethal; CO, ammonia, HCl, even cyanide may be formed; potentially hazardous to OR personnel in addition to patient

Preventive steps: constant attention to prevention of OR fires essential; have well-rehearsed plan to deal with unexpected fire; regular fire drills should be organized for OR team and fire-fighting equipment frequently checked; use minimal, safe O_2 concentrations (Does patient really need additional O_2? What is minimum that can be used?); eliminate accumulation of oxidizers near ignition source; arrange draping appropriately; exercise caution with adding N_2O (preferably, avoid it altogether); use cuffed endotracheal tube or laryngeal mask airway should be used if >30% O_2 required; ban use of ignition sources where oxidizers may inevitably accumulate; ensure skin prep solutions fully dry before any ignition source activated; moisten gauze or sponges should if used in proximity to ignition sources; use nonflammable endotracheal tubes for airway surgery; inflate cuff with saline, colored with indicator dye (*eg*, methylene blue to detect cuff failure; communication between surgeon and anesthesiologist must be maintained; anesthesiologist must warn surgeon when accumulations of oxidizing agents may be present; surgeon must notify anesthesiologist before operating an ignition source

Managing fire: if fire occurs, must be promptly and effectively managed

Airway fire: remove endotracheal tube immediately; discontinue all gas supply from anesthesia workstation; douse airway with sterile saline; when fire eliminated, reintubate patient with new endotracheal tube and resume ventilation; consider bronchoscopy to assess airway damage and remove any debris; examine burned endotracheal tube to determine whether any portion left in airway

Fire elsewhere: if fire does not involve airway, immediately stop flow of all airway gases; maintain ventilation with air and with an bag valve mask (Ambu Bag, etc); remove drapes and all burning materials; douse fire with sterile saline; if fire still not controlled, use CO_2 fire extinguisher; if fire persists, activate fire alarm; turn off all gases to room, evacuate patient, and close OR door; after fire, thoroughly evaluate patient assess for further treatment needs

Fire extinguishers: National Fire Protection Agency standards list 3 types of fire extinguishers; class A used on burning wood, paper, cloth, most plastics; Class B used on flammable liquids and grease; Class C used on electrical equipment; CO_2 fire extinguisher has dual B and C rating; safe to use on liquids or electrical equipment and considered safe to use with fire involving patient; be familiar with locations and types of fire extinguishers OR suite; to operate fire extinguisher mnemonic PASS; P, pull pin; A, aim at base of fire; S, squeeze handle; S, sweep across fire

Statistics

Overview: American Board of Anesthesiology dictate that anesthesiologist have some knowledge of statistics; required to plan studies and to critically read studies reported by others; statistics used to analyze data and interpret results

Definitions: mean value=average value of set of readings; mode=most frequently appearing value; standard deviation of mean=how much each reading differs from mean value; set of data with small standard deviation tightly grouped; if standard deviation large, data widely scattered; range=span of values over which readings occur; median=point midway between highest and the lowest reading; normal curve=bell-shaped curve; many biologic data points in population (*eg*, height and weight) distributed on bell-shaped curve; most observations lie within 1 or 2 standard deviations of mean value; standard error used to determine statistical accuracy, relating standard deviation to sample size and indicating how precise mean of sample population may be to mean of whole population; standard error of mean defines precision of study population mean

Statistical analysis: commonly applied to assess probability that observed results not completely random; to test theory, null hypothesis applied; assumes results entirely random and tests applied to challenge this fact; testing to determine if real difference (*ie*, statistically significant difference between 2 sets of observations)

Power of test: probability of being able to reject null hypothesis when null hypothesis false; power of statistical testing to be used should be determined during planning stage of investigation; statistical power of experiment determined by level of significance to be used, variability of collected data as measured, magnitude of difference required to detect between populations, and size of population samples; power analysis used to determine minimum sample size necessary to be able to detect effect of given magnitude; can also be used to determine minimum effect that would likely be detected in study of given sample size

Type I error: rejecting null hypothesis when true; false-positive suggestion; may suggest that effect of drug has been found when it actually has not

Type II error: failing to reject null hypothesis when in fact untrue; false-negative suggestion; may suggest no effect of drug when actually an effect

Statistical tests: some common statistical tests used

T-test: can be used to establish difference between mean values; will confirm statistical significance of difference between 2 sets of observations (*ie*, unlikely to be just by chance); t-tests may be paired or unpaired;

P value: *P* value derived from t-test represents possibility that null hypothesis correct; remember, null hypothesis was that results purely random; *P* value <0.05 indicates null hypothesis has <5% chance of being correct; indicates results likely not purely random and more probably related to effect

Paired t-test: most appropriately applied to observations on matched pairs of data (*eg*, blood pressure before and after particular drug or intervention); power of paired t-tests to reject null hypothesis higher than power of unpaired t-tests; paired t-tests eliminate differences simply due to individual variation between subjects; observations being compared from same subject

Unpaired t-test: applied when comparing different groups of subjects (eg, *diabetic* vs. *nondiabetic* patients); sample size from 2 groups may or may not be equal; test assumes normal distribution of data and that standard deviations within groups essentially similar; dependence upon these assumptions lowers power of unpaired t-tests

Chi-squared test: applied when whole series of observations across categories to determine if distribution different from that which might occur purely randomly; can be used to study categorical results ≥2 independent groups and determine if significant difference between responses of groups; can only be used with actual numbers, not with percentages or mean values

Regression analysis: method to examine relationships between variables; in its simplest form, linear bivariate analysis, relationship between 2 variables can be examined; one variable may be plotted on x-axis of graph and dependent variable on y-axis; presuming linear relationship between variables, line can be plotted; this line lies at position representing lowest sum of squares of distances between all points and line itself; closer all points are to the line, stronger relationship between variables; correlation coefficient r applied; method used to describe closeness of all points on graph to line, and therefore, closeness of relationship; correlation coefficient approaching 1 indicates very close relationship

Analysis of variance (ANOVA): technique used when necessary to investigate means of >2 groups of data; represents t-test for multiple groups

Confidence interval: provides estimated range of values within which certain parameter of interest may form; determined from set of sample data; conventional to construct confidence intervals to 95% level; large 95% confidence interval indicates low level of precision

Risk ratio: indicates likelihood of given outcome in 1 sample group exposed to specific risk than present in second group not so exposed; risk ratio of 1 indicates no increased risk; risk ratio of 15 indicates that exposed individuals 15 times as likely as others to experience predetermined outcome

Odds ratio: also measure of association between given exposure or intervention and outcome; odds ratio for event calculated by dividing odds of that event in treated or exposed group by odds in control group; may be more prone to overestimate likely incidence of outcomes than does risk ratio, especially when outcome more common in both groups

Number needed to treat: considered to be more useful clinical indicator of likely value of given therapeutic measure; inverse of absolute risk reduction; specifies how many patients must be treated to see benefit in 1 patient; this index may be more readily communicated to patients in discussions about treatment options

Meta-analysis: method used to combine results from several different studies and thus increase statistical power to answer question; may also help reveal bias in individual publications; usefulness of meta-analysis limited by quality of original studies, size of studies, and methods and accuracy of data collection; generally, larger meta-analyses more reliable than those involving only small number of studies; meta-analysis commonly used in systematic reviews such as those conducted by Cochrane Collaboration

Suggested Reading

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ANESTHESIOLOGY
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The Anesthesia Machine and Breathing System

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Anesthesia workstation: preferred term; includes anesthesia machine, breathing circuit, monitoring system; newer workstations more diverse, variable; essential components hidden from view, complex, integrated computer controls; must be fully knowledgeable about workstation; read manuals; use checklist for specific workstation; know components of self-tests for machines; *3 sections of workstation* — anesthesia machine (includes gas supplies, pressure regulators, flowmeters, vaporizers, fresh gas outlet, monitors, alarms, protective devices); breathing circuit (includes circuits, CO_2 absorber, ventilators, tubing, scavenging); monitors (respiratory, cardiovascular, other physiologic variables), alarms

Common features: inlet for hospital pipeline and compressed gases, inlet for compressed gas cylinders; pressure regulators to reduce pipeline, tank pressures to safe levels; fail-safe devices; flowmeters to control amount of delivered gas; vaporizers for adding volatile anesthetic agents to carrier gas; common gas line through which compressed gases mixed with volatile agent enter breathing limb; fresh gas valve with O_2 supply; breathing limb (circle system, O_2 analyzer, gas-sampling lines, barometer to measure inspiratory rate and volume, airway-pressure monitor, mechanical ventilator scavenger system, often humidifiers or heaters, filters)

Additional monitors: required by ASTM for modern anesthesia machines; continuous breathing-system pressure, exhaled tidal volumes, ventilatory CO_2 concentration, anesthetic vapor concentration, inspired O_2 concentration, O_2 supply pressure, prioritized alarm system

Resistance to flow of gases: pressure drop to overcome resistance as gases move through circuit or airway, influenced by flow rate, type of flow; measured in mm Hg per flow rate or cm Hg/L/sec

Types of flow: *laminar flow* — orderly, smooth, particles move in line parallel to wall; flow fastest in center, slower toward walls, pressure drop described by Hagen–Poiseuille law (proportional to length, viscosity, flow rate, inverse to 4th power of radius of tube); *turbulent flow* — disorderly, flow lines not parallel; particles move all directions including sideways and opposite of flow; flow rate equal across diameter of tube, Hagen–Poiseuille law does not apply (pressure drop influenced by gravity, friction, density, length, flow rate, inverse to 5th power of radius); because impact of density, helium has usual velocity but low density, useful in relieving resistance of turbulent flow; turbulent flow generalized (when flow exceeds critical flow rate as defined by high Reynolds number) or localized (at constrictions, curves, bends, valves, irregularities)

Resistance: reflected by flow-volume loops, discrepancy between peak and plateau pressures when using volume-controlled mode of ventilation with 20% inspiratory hold; peak pressure reflects compliance, resistance to flow; plateau pressure reflects compliance only

Sources of resistance: difference between peak and plateau ~2 cm H_2O to 5 cm H_2O; if higher, look for causes of increased resistance in airway circuit or patient; *circuit sources of resistance and turbulent flow* — circle system, breathing circuit's corrugated tubing, usually trivial; heat and humidifier exchange devices, filters, generally minimal but problematic if condensation or if secretions accumulate, should be avoided with spontaneous breathing, especially in children; endotracheal (ET) tube most important site of resistance; increased resistance and turbulent flow, increased work of breathing if patient doing their breathing during spontaneous or assisted ventilation

Level of resistance: no agreement on what level excessive; be aware of how much resistance caused by each component; use components with least resistance

Minimizing circuit resistance: use gas-conducting pathways of minimal length, maximal diameter, without sharp curves or sudden changes; beware of use of filters and heat and moisture exchangers (HMEs)

Gas-flow controlling valves (flowmeters): control gas flow; vertical tubes or electronic devices; glass or plastic tubes mounted vertically, tapered, become wider moving upward; inside tubes, floats (bobbin or ball); specific for each gas, subject to damage, causing leaks, low pressure; employ principle of constant pressure; pressure gradient of gas flow around float balances weight of float; as flow of gas increases, velocity of flow increases, gradient increases, float rises; tube lumen increases velocity of flow, so gradient falls until again it equals weight of float, thus height of bobbin reflects flow rate; if leaks in O_2 flowmeter tube, hypoxic mixture could be delivered to patient, so O_2 flowmeter mounted last

Anesthesia-delivery system: *high-pressure section* — gas cylinders, pipelines to high pressure reduction valves (50-2200 psi); *intermediate section* — between low-pressure reduction valve to flowmeter (~12 psi); *low-pressure section* — beyond flowmeters, in circle system breathing bag (<1 psi, or <50 mm Hg)

Safety systems: alarms for apnea, disconnect, inspired O_2 saturation; activate alarms, set at sensitive threshold, near current settings; sound light, annunciators, messages and sound message, sound alarm; alarms monitor for

low pipeline pressure, low tank pressure, low cylinder pressure, low airway pressure while ventilator in use

Systems protecting against delivery of hypoxic mixtures: O_2 fail-safe, nitrogen-O_2 ratio limiting system, PISS, DISS, inspired O_2 saturation monitor; *O_2 fail-safe* — monitors pressure coming into machine from pipelines or cylinders, turns off all gas flow if pressure <~30 psi; did not prevent dialing in hypoxic mixture by excess N_2O if O_2 available; several O_2-N_2O proportioning systems developed; original Ohmeda system (Link 25) had ratcheted chain-linked interconnection, prevented O_2 delivery <30%, or N_2O delivery >70%; North American Dräger system monitors pressure in 2 gas-flow systems, keeps O_2 ratio ≥30%; Diameter Index Safety System (DISS), special connectors on lines from wall gas outlets to workstation prevent misconnection; Pin Index Safety System (PISS), pins and holes on gas cylinders, yokes on workstation to ensure proper tanks connected to proper locations; machine must have dedicated monitor for inspired O_2 saturation (adequate functioning part of daily preuse check)

O_2 failure: if O_2 cylinders off, O_2 pressure machine lines falls when wall O_2 fails; if O_2 cylinders on, automatically feed O_2 at ~40 psi;, alarms on older machines may not sound until O_2 cylinders empty; after machine checkout, turn off O_2 cylinders; newer workstation should alarm when line pressure falls; line-pressure gauge should inform loss of line pressure; room alarms in operating room (OR) wall should sound when O_2 supply lost; if pipeline O_2 lost, open up O_2 cylinder on workstation, check pressure, calculate O_2 amount left; reduce O_2 use by hand-ventilating with breathing bag, avoids O_2 use to drive bellow-driven ventilators; reduce fresh gas flow, turn off auxiliary O_2-supply flowmeters; call for extra O_2 cylinders; notify hospital authorities

Ventilator disconnect: when ventilation controlled by mechanical ventilator, continuous use of device capable of detecting disconnection, must give audible signal when alarm threshold exceeded; how alarm triggered varies (*eg*, tidal volume, minute ventilation, peak airway pressure, capnography); default limits often set too low

Gases: include O_2, air, N_2O, helium, heliox, CO_2

Gas pressures: source from pipeline or wall (~50 psi) or from cylinders (~700 psi to 2200 psi, depending on gas); pressure in tanks decreased to ~45 psi by reducing valves before joining pipeline gas; if pipeline pressure >45 psi, flow will not come out of cylinders; when pipeline pressure <45 psi, gas flows out of cylinders; pressure then reduced to ~12 psi before going to flowmeters

E-cylinders: color coded; in US, O_2 green, N_2O blue, air yellow; may differ in other countries; pressures, volumes vary with gas; O_2 and air, gases in cylinders, full tanks at ~2200 psi contain ~600 L, volume directly proportional to pressure; N_2O and CO_2, liquids in cylinders, full tanks at ~750 psi contain ~1600 L; when gas in liquid form, pressure does not show how much gas left in cylinder until three-quarters empty

O_2 flush valve: fills ventilation system, receives O_2 from pipeline or cylinders after initial pressure reduction valve, pressure at ~50 psi (~2500 mm Hg); flushed O_2 bypasses vaporizer, potentially exposing to high pressures (modern circle systems limit to ~50 cm H_2O to 70 cm H_2O); pressing flush valve dilutes concentration of anesthetic vapor; if flush valve sticks in open position, can cause barotrauma; if partially open, can dilute anesthetic agent, contribute to awareness

Leaks: occur in high-pressure circuit, low-pressure circuit, circle, connection to patient, ET tube, lungs; detected by capnograph, failure of bellows or breathing bag to refill, need to increasingly tighten adjustable pressure threshold device, loss of exhaled volume, odor of anesthetic gases in room

Circuits: various types with multiple classification systems, conflicting definitions (*eg*, open, semiopen, semiclosed, closed); include circle systems, Mapleson circuits, self-inflating nonrebreathing bags (*eg*, bag valve mask [Ambu device])

Circle system: most commonly used system; 3 valves (inspiratory, expiratory, pop-off valve), CO_2 absorber, reservoir bag; can provide none or total rebreathing of expired gas, excluding CO_2; operated in semiopen, semiclosed, or closed nonbreathing mode; arrangement of components important for optimal functioning

Flow: fresh gas inflow occurs just before inhalation 1-way check valve, to inspiratory corrugated limb tubing, to Y-piece, to patient; expiratory corrugated limb tubing through exhalation 1-way valve, through tubing to CO_2-absorbing canister, back to start

Ventilator switch: teed into tubing between exhalation check valve and CO_2-absorbing canister, bag-ventilator selector switch, connects flow to ventilator or breathing reservoir bag and accompanying adjustable pressure-release, or APL, valve

Dead space: despite size and length, due to 1-way check valves, only dead space in circle system, Y-piece and extensions to patient

Rebreathing: CO_2 rebreathing prevented by CO_2 canister; on other hand, rebreathing of other expired gases depend on fresh gas flow; when fresh gas flow=minute ventilation, almost no rebreathing of expired gas, so CO_2 absorber may be unnecessary; as fresh gas flow drops, amount of rebreathing rises; minimal fresh gas flow applies only enough O_2 and agent to match O_2 consumption and agent uptake; requires ~250 mL O_2/min in 70-kg adult

Low-flow or closed systems: low flow=fresh gas flow 0.5 L/min to 2 L/min; closed system=fresh gas flow only balances uptake (~300 mL/min); *advantages* — conserves heat, H_2O, agent, decreases pollution, economic; *disadvantages* — slow concentration changes of agents and gases to patient, changes in fresh gas flow may change delivered tidal volume, may be discrepancy between concentration dialed on vaporizer and inspired concentration of agents

Changes in fresh gas flow: affect time it takes for changes in dialed O_2 concentration by flowmeters and of agents by vaporizer; time estimated from time constant (time to achieve 63% equilibrium); takes ~3 time constants to achieve near equilibrium; time constant=volume÷fresh gas flow rate; typical volume of circle system ~5 L, if fresh gas flow=5 L/min, then time constant=5÷5, or ~1 min, so it takes ~3 mins to 4 mins for equilibrium; if fresh gas flow=0.5 L/min, then time constant=5÷0.5, or 10 min, so it takes >30 mins to reach equilibrium; to change concentration, need to temporarily raise fresh gas flows until equilibrium reached, then go back to low flows

Vaporizer-to-patient concentration: low gas flow increases discrepancy between concentration of agent out of vaporizer and inspired concentration to patient; when fresh gas flow ≥ minute ventilation, some inspired gas comes from exhaled gas from patient, has less agent because of removal by lungs; if minute ventilation=5 L/min and fresh gas flow=0.5 L/min, then >90% inspired gas from exhaled gas, only 10% from fresh gas flow, so discrepancy between that dialed and what patient receives; when fresh gas flow=minute ventilation, almost no discrepancy between inspired concentration to patient and that dialed on vaporizer

Noncircle systems: Mapleson described and classified noncircle systems as Class A through F, depending on components and arrangements; some had reservoir bags and/or valves; some expired gas goes out to atmosphere, some goes back into inspiratory limb; amount of rebreathing dependent partly on fresh gas flow and other characteristics; require relatively high fresh gas flows to prevent CO_2 rebreathing; most systems replaced by circle system, but Bain circuit and Jackson-Rees circuit (both modifications of Mapleson D system) sometimes used

Rebreathing and dead space: inhalation of previously expired gas; may include CO_2; influenced by circuit type, component function, fresh gas flow, dead space (mechanical in breathing circuit, physiologic in patient)

Rebreathing: causes retention of heat, moisture, but decrease in O_2, anesthetic agent, possible increase in CO_2; important to prevent CO_2 rebreathing; in circle system, accomplished by CO_2 absorber, proper functioning of 1-way check valves; in other circuits (*eg*, Mapleson), highly dependent on fresh gas flow

Causes of rebreathing in circle system: incompetent inspiratory or expiratory valves and failed CO_2 absorber; evaluated or recognized mainly by capnograph with elevation of baseline CO_2 (normally <1-2 cm H_2O, or mm Hg), sloping of inspiratory curve

CO_2 absorbents: original and traditional agents, *eg*, soda lime, SodaSorb; barium hydroxide lime (Baralyme) largely removed from US market; newer agents have less or no strong bases (*eg*, calcium hydroxide lime [Amsorb, Amsorb Plus], lithium hydroxide [Litholyme]); consist of granules of absorbing material; granule size compromise between absorbency and resistance; smaller size increases both absorbency and resistance; usual mesh size ~4 to 8 spaces per linear inch; exhaustion of CO_2 absorbers indicated by pH-sensitive dyes; soda lime uses ethylene blue, changes from white to purple, but after time color may revert to white, capacity lost; others turn purple, remain permanent; best precaution, change canisters regularly, monitor inspired CO_2 levels

Absorbent problems: CO_2 absorbents can cause toxicity of volatile agents (*eg*, compound A with sevoflurane, production of CO with desflurane); heat, fire can occur when sevoflurane becomes dry with use of Baralyme, produces inflammable products (*eg*, formaldehyde), these have been largely eliminated by avoiding drying, eliminating use of Baralyme; sevoflurane can result in production of compound A, may be renal toxin; production of compound A worse with fresh absorbent, dry absorbent, soda lime, high sevoflurane concentrations, low fresh gas flows, higher absorbent temperature; US Food and Drug Administration (FDA) limits fresh gas flow with sevoflurane to >1 L/min during first 2 MAC-hrs, >2 L/min thereafter; absorbents can also produce CO, worse with desflurane, modest with isoflurane, very little with halothane or sevoflurane; aggravated by dry absorbent, increased absorbent temperature, high desflurane concentrations, low fresh gas flows, small patients

Anesthesia Patient Safety Foundation: recommends absorbents that do not degrade significantly when exposed to volatile agents; avoid desiccation by regularly changing absorbent and avoiding O_2 flow through absorbent at end of day

Modern absorbents: newer agents with less or without strong base widely adopted and recommended because do not produce strong alkaline; *advantages* — do not produce CO or compound A, fires less likely; *disadvantages* — 50% less absorbent, more expensive

Vaporizers: volatile anesthetic agents liquid at room temperature; at equilibrium, some vapor in atmosphere above liquid (amount dependent on vapor pressure, in turn dependent on agent, temperature); concentration expressed as percent or mL/dL, calculated as vapor pressure÷total barometric pressure; vapor pressure of isoflurane at 20°C ~240 mm Hg, thus concentration above liquid isoflurane at sea level ~31%; sevoflurane vapor pressure ~160 mm Hg, concentration 21%; desflurane vapor pressure ~660 mm Hg, concentration 87%

Types of vaporizers: *conventional variable bypass vaporizer* — isoflurane, sevoflurane; *dual-gas blender* — desflurane; *Datex-Ohmeda Aladin cassette* — all 3 agents; *Maquet series injector* — not commonly used in United States; *traditional Tec vaporizers* — sevoflurane and isoflurane; variable-bypass, flow-over-wick temperature-compensated, agent-specific, out-of-system vaporizers; based on temperature, desired concentration; fresh gas flow entering these vaporizers divided, some gas goes through vaporizing chamber where exposed to vapor above liquid, producing concentration described; concentrated vapor then passed back to join fresh gas flow to produce desired concentration; desflurane has very high vapor pressure and relatively low potency, cannot be used with contemporary variable-bypass vaporizers; led to specialized vaporizer that contains separate circuits for fresh gas flow and desflurane vapor

Desflurane vaporizer: pure desflurane generated in separate vaporizing chamber or sump, then heated to constant 39°C to produce vapor of pure desflurane at vapor pressure ~1300 mm Hg; based on amount of fresh gas flow through unit and desflurane concentration dial setting; appropriate amount of pure desflurane vapor added to fresh gas flow to produce desired concentration; desflurane vaporizers have special alarms for low volume, tilt, power failure, abnormal output; automatic shutoff if low desflurane level, vaporizer tilts, power failure, or if failure of pressure controlling devices inside vaporizer; alarm should sound when turned off

Datex-Ohmeda Aladin cassette vaporizer: plug-in cassette; contains vaporized liquid; agent-specific vapor changers for halothane, enflurane, isoflurane, sevoflurane, desflurane; variable control knob on outlet

from vapor chamber into bypass chamber, controlled by computer; flowmeter measures fresh gas flow and flow out of vapor chamber, adjusts flows to produce desired vapor concentration; computer system receives information from anesthesia machine regarding flow of gases, amount of fresh gas flow, type of agent in vapor chamber, temperature and pressure in vapor chamber, desired concentration of anesthetic on dial; based on data, computer adjusts valves in chamber to assure proper mixture goes to patient

Maquet system: injector available for halothane, isoflurane, enflurane, but uncommon in US

Hazards with vaporizers: misfilling with wrong agent, tipping, overfilling, underfilling, leaks

Factors influencing vaporizer output: temperature, but modern vaporizers temperature compensated; extreme fresh gas flows, output linear, range of 0.25 L/min to 10 L/min; presence of N_2O in carrier, at low flow, desflurane output from vaporizer reduced by ~20% in presence of N_2O; tilting, tipping, filling with wrong agent; putting agent with higher vapor pressure in vaporizer designed for agent with lower vapor pressure gives false-high concentration (*eg*, if isoflurane [vapor pressure 250 mm Hg] into sevoflurane vaporizer designed for vapor pressure 75 mm Hg, produces excessive concentration of agent); altitude can affect function of desflurane vaporizers; output constant fraction or percent for given dial setting; if dial set at 6%, at high altitude it puts out same concentration (6%), however, because partial pressure lower, MAC equivalent also lower; in contrast, other Tec vaporizers put out constant partial pressure for given dial setting, therefore at altitude, these put out same partial pressure and same MAC equivalent, but fraction, concentration elevated at higher altitudes since partial pressure relative to barometric pressure higher (*eg*, at 1.2 setting, it produces 9 mm Hg vapor pressure, but now 1.5%)

Factors influencing inspired volume: discrepancies occur between inspired volume delivered to patient vs that delivered by ventilator, breathing bag, that reported by volume monitor; differences in inspired O_2 concentration or anesthetic agent vs that delivered from common gas outlet

Factors influencing tidal volume delivered to patient: in older ventilators, influenced by changing fresh gas flows; modern ventilators designed to compensate for change in fresh gas flow; however, volume delivered can be affected by wasted ventilation due to gas compression, compression or distension of breathing system, or leaks; generally, compression effects small, but leaks may be significant

Tidal volume discrepancies: detected by volume-measuring device inserted between T-piece and ET tube; also assessed by volume-measuring devices on expiratory limb; reflect changes due to fresh gas flow changes from leaks, but do not detect defects caused by, gas compression; can also observe chest wall movement, breath sounds and monitor blood gases, end-tidal CO_2

Gas-concentration discrepancies: caused by rebreathing, air dilution, leaks, uptake of agent by breathing-system components; already discussed discrepancies in time for dialed concentrations to equilibrate with circuit; fresh gas flow also affects gas concentration delivered to patient; actual concentration delivered to patient influenced by fresh gas flow; when fresh gas flow greater than minute ventilation, concentration delivered to patient same as concentration delivered to circuit once equilibrium achieved; however, as fresh gas flow decreased to ≥ minute ventilation, some inspired gas to patient will be expired gas; amount=difference between fresh gas flow and minute ventilation; if minute ventilation=5 L/min and fresh gas flow=1 L/min, 80% of gas delivered, expired gas; because of uptake of volatile agent and O_2, volatile agent and O_2 going to patient ≥ that delivered from fresh gas flow going to circuit

Humidity: amount of H_2O vapor in gas; expressed as absolute humidity (*ie*, mass of H_2O per volume, expressed in mg/L) or relative humidity (*ie*, amount vs capacity when fully saturated at given temperature, expressed as %); saturated=maximum H_2O gas can hold; varies with temperature; at 20°C, gas can hold ~19 mg/L (20 mm Hg H_2O) and at 37° C, ~44 mg/L (47 mm Hg)

Humidifying: gases supplied dry at room temperature; by time delivered to alveoli, fully saturated with H_2O and warmed to body temperature with H_2O and heat delivered by respiratory tract; nose principal HME in body; when air gets to trachea, ~31°C and ~89% saturated; ET tube or supraglottic airway bypasses nasal humidifier

Impact of dry gas during anesthesia: uncertain, probably greater in pediatrics, long procedures, patients at increased risk of pulmonary complications; *potential adverse effects* — damage to respiratory tract, heat loss (minor), fluid loss (minor), and ET tube absorption; effects of dry inhaled gases may include damage to respiratory tract with thickened secretions, decreased ciliary function, impaired surfactant activity, increased mucosal susceptibility to injury, bronchoconstriction, atelectasis, coughing; recommended minimum humidity 2 mg/L to 44 mg/L

How to increase humidity: CO_2 absorbent, breathing of exhaled gases, low fresh gas flow, moisturizing tubes and reservoir bags, use of coaxial circuits (*eg*, Bain circuit), HMEs ("artificial noses," passive or regenerative humidifiers), humidifiers

Humidifiers: cheap, easy, simple, effective; also effective bacterial and viral filters, and avoid overheating or excessive humidification; heated humidifiers no longer commonly used during anesthesia; partly because of associated complications (infection, disconnection, leaks in breathing circuit, overheating, overhumidification, increased volume and compliance in circuit)

Circle system: amount of humidity gradually increases with time, then stabilizes; sources of humidity from exhaled gases if fresh gas flow reduced, absorbent, H_2O during CO_2 neutralization; after ~6 mins at fresh gas flow 0.5 L/min to 2 L/min, humidity ~20 mg% to 25 mg%; higher with decreased fresh gas flow, increased ventilation, wet tubing

Scavenging: advocated because of unproven concerns that chronic exposure to low concentrations of inhaled anesthetic agents hazardous to OR personnel; *National Institute for Occupational Safety and Health (NIOSH) recommendations for minimal environmental concentrations of volatile agents* — 2 ppm for isolated halogenated agents, 25 ppm for N_2O, 0.5 ppm for

halogenated agents when used with N_2O, and 50 ppm for N_2O when used alone in dental facilities; *American Society of Anesthesiologist (ASA) recommendations* — waste anesthetic gases should be scavenged; use appropriate work practices to minimize exposure; educate personnel working in areas where waste anesthetic gases may be present regarding possible hazards and management; insufficient evidence to recommend routine monitoring or for routine medical surveillance

Sources of gases that need scavenging: anesthetic machine on circuit, pressure-release valve, ventilator, gas-sampling device, ventilator drive, leaks, and if fresh gas flow and agents not turned off at end of case; other sites include masks, noncuffed ET tubes, and while filling vaporizer; *several types of scavenging systems* — active or passive, closed or open; all should have positive and negative pop-off valves; scavenging facilitated by use of low fresh gas flow and changing air in room ≥15×/hr

Hazards of scavenging: positive or negative pressure inside scavenger system may interfere with scavenging, delivery of ventilation to patient, failure to connect between machine and disposal system

Workstation preuse checks: O_2 analyzer calibration, low-pressure circuit check leak test, circle system test; testing for leaks in low-pressure system depends on whether check valve proximal to common gas outlet; checklist on many machines; use negative-pressure test with suction bulb; if no checklist, use positive-pressure leak test

Universal negative-pressure leak test: first verify machine master switch and flow valves off; attach suction bulb to common fresh gas outlet, squeeze bulb repeatedly until fully collapsed, and then verify bulb stays collapsed for ≥10 secs; then open 1 vaporizer at time and repeat steps, finally remove suction bulb and reconnect fresh gas hose to fresh gas outlet; be aware when leak test automatically performed by machine; necessary to repeat leak test self-test with each vaporizer dial turned to "on" position to detect internal vaporizer leaks; if flowmeter included to O_2 supply, must be turned off or will appear as leak

Circle system test: includes positive-pressure test and flow test; *positive-pressure test* — set all gas flows to 0 or minimum, close pop-off valve, occlude Y-piece, then pressurize system to ~30 cm H_2O; ensure pressure remains fixed for ≥10 secs, then open pop-off valve and ensure pressure decreases to 0; *flow test* — inhale and exhale through Y-piece or mask and observe that valves open and close proximally; then selectively close end of expiratory and inspiratory limbs separately to ensure not able inhale or exhale, respectively, to ensure competency of valves; can also test with ventilator in circuit connected to breathing bag

Other checks: ensure adequate O_2 supply in E-cylinders and functioning emergency backup (*eg*, Ambu bag, jet ventilator, extra O_2 supply, tubing)

Checklist remarks: checklists often do not emphasize tank pressure must read 0 before turning on to check pressure and do not recommend checking inspiratory and expiratory valves separately; 1993 FDA anesthesia apparatus checklist recommendations outdated; ASA Committee on Equipment and Facilities issued preanesthesia checklist procedure

Example Scenarios

Case 1: 1.5 hrs into case with patient on ventilator, receiving tidal volume 600 mL at 10 L/min, fresh gas flow 2 L/min; low O_2 pressure alarm sounds; pipeline pressure 0; O_2 flowmeter indicates no flow; you immediately turn on O_2 cylinder, pressure reads 2000 psi, O_2 flow resumes with 95% inspired O_2

Question 1: How long can you run anesthetic in this manner? Answer: ~80 min; fresh gas flow 2 L/min; O_2 flow (driving ventilator) using ≥6 L/min to maintain minute ventilation, thus utilizing ~8 L/min, full E-cylinder contains ~660 L, then should last ~84 mins

Question 2: What should you do to extend this time? Answer: First, turn off ventilator if using O_2 to drive it (true on some machines; others piston driven, run off electricity); second, reduce fresh gas flow

Case 2: After your case has settled down, you reduce N_2O and O_2 flows from 2 L/min to 0.5 L/min; inspired O_2 concentration gradually falls to <50%

Question 1: What might explain this fall? Answer: Uptake of N_2O has gradually decreased while O_2 constant; at these relatively low flow rates, concentration of N_2O in circuit will gradually rise and O_2 will gradually fall; *other causes of low FiO_2* — loss of O_2 and pressure or flow from pipeline due to central line failure, local obstruction or disconnect, wrong gas going into O_2 pipeline, misconnection of pipelines to anesthesia machine, wrong gas in O_2 cylinder or wrong attachment; failure of O_2-N_2O proportional system, adding second non-O_2 gas (*eg*, air, helium, CO_2), break in flowmeters, air entrapment from negative pressure, leak in bellows, error in monitoring of inspired O_2 concentration; if raise O_2 flow back to 10 L/min, and yet inspired concentration continues to fall

Question 2: When concentration falls below 90%, what action to take? Answer: If time permits, go through differentials and correct identified causes; if all else fails or out of time, ventilate with self-inflating valve with air, or attach to separate O_2 source other than another O_2 tank from anesthesia machine, if suspect wrong gas attached to anesthesia machine or wrong gas coming out of pipelines

Case 3: During case, circulating nurse in room who happens to be pregnant complains that she smells anesthetic agent around machine

Question 1: How to troubleshoot? Answer: See above sources vaporizer leak, spilled anesthetic liquid or open canister or open vaporizer filter cap, leak in vaporizer, failure with scavenger system or leak elsewhere in circuit or end-tidal ET tube

Case 4: During laparoscopy, end-tidal CO_2 progressively rises >50 mm Hg

Question 1: What is differential diagnosis? Answer: Could be from increased CO_2 production, hyperthermia, hypermetabolism, or absorption of unusual amounts of CO_2 from abdomen; rebreathing due to malfunction of CO_2 absorber or bypass around CO_2 absorber; incompetent inspiratory or expiratory valves; leak in inspiratory limb or addition of CO_2 into fresh gas flow; lower-than-needed alveolar ventilation because of increased dead space or low minute ventilation

Case 5: During case, low minute-ventilation volume alarm sounds

Question 1: What activates alarm? Answer: Already reviewed these issues; limits need to be adjusted for each patient and each case

Question 2: What is included in differential diagnosis and how to troubleshoot problem? Answer: Look at capnograph; if patient ventilated, check if ventilator bellows emptying and filling properly; check ability to drive gas into patient; check if ventilator on or ventilator failure; outflow resistance from high airway pressure; inadequate volume in circuit from loss of gas supply into anesthesia machine or circuit; getting gas back from patient; disconnect; leaking cuff; air leak from lung; nasogastric tube inserted in trachea; suction applied to bronchoscope; leak in system; problem not found, ventilate with self-inflating breathing bag

Case 6: During different case, high airway-pressure alarm sounds

Question 1: What are implications? Answer: High airway pressure may indicate high pressure in lungs, resulting in barotrauma and/or reduced cardiac output; may also indicate obstruction of flow from ventilator to patient, could lead to hypoventilation

Question 2: How to troubleshoot? Answer: Differential diagnoses include obstruction of gas flow to patient, reduced lung compliance, increased resistance to gas flow in circuit, reversed PEEP valve, kinked corrugated tubing, cuff overinflating end of ET tune, kinked or plugged ET tube, endobronchial intubation or foreign body or secretions in airway, gas building up in circuits, failure of ventilator-release valve, excessive pressure or vacuum in scavenger, adjustable relief valve will not open or fails, gas building up in lung, air trapping from ball-valve phenomenon, PEEP or inadequate expiratory time

Question 3: What are some causes of low end-tidal CO_2? Answer: Excessive ventilation, error in ventilator settings, hypothermia, deep anesthesia, low cardiac output, pulmonary embolism, error in monitoring system (*eg*, miscalibration, loose connection)

Case 7: Question 1: What happens if electrical supply into machine is lost? Answer: Modern anesthesia machines should have battery output (~30 min); battery backup powers ventilator controls, alarms, and integral monitors of machine; battery does not power external appliances connected to auxiliary power outlet on anesthesia machine (*eg*, major monitor, airway multigas monitor, cardiac output monitor)

Question 2: What to do about total electrical power failure to OR? Answer: Loss of all monitors, loss of all lighting, loss of all electrical monitoring equipment besides anesthesia machine, includes some suction, cell savers, electrocautery, defibrillator, microscope and if on cardiopulmonary bypass, heart-lung machine; think about and be prepared for managing total loss of electrical power

Case 8: After weekend, start case in same-day surgery center using desflurane; after intubation, notice pulse-oximeter saturation gradually falls from 100% to 94%; peripheral venous blood gas, O_2 190 mm Hg

Question 1: What might be going on? Answer: Causes of low pulse-oximeter reading include low FiO_2, hypoventilation, pulmonary dysfunction, monitor error, carboxyhemoglobinemia, methemoglobin, blue dye in bloodstream; peripheral venous gas showing PO_2 of 190 mm Hg excludes low PO_2 as cause; likely possibility carboxyhemoglobin; read as ~90% oxyhemoglobin and 10% deoxyhemoglobin; if high enough, causes modest reduction in pulse-oximeter reading, should be considered in differential diagnosis of low pulse-oximeter reading; diagnosis confirmed through multi-wavelength O_2 saturation analysis in laboratory; ask for carboxyhemoglobin saturation measurement; carboxyhemoglobinemia not detected by conventional blood-gas analyzers, which estimate saturation from PaO_2 (normal); CO generated by CO_2 absorber when exposed to inhalation agents, especially desflurane through dry CO_2 absorber, if fresh gas flow left on for long periods of time (*eg*, over weekend), especially if rebreathing bag absent or pop-off valve left open (flow of greatest resistance from fresh gas flow backwards, through CO_2 absorber, into environment); CO_2 absorber becomes dry and at risk of developing hyper-CO next day (Monday morning syndrome)

Suggested Reading

Dorsch JA, Dorsch SE: *Understanding Anesthesia Equipment*. 5th ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2008; **Ehrenwerth J et al, eds:** *Anesthesia Equipment:* Principles and Applications. 2nd ed. Philadelphia, PA: Elsevier Saunders; 2013; 7th ed. Philadelphia, PA: Churchill Livingstone/Elsevier; 2010; **Rutort KT, Eisenkraft JB:** The anesthesia workstation and delivery systems for inhaled anesthetics. In: Barash PG, eds. *Clinical Anesthesia*. 8th ed. Appendix-Chapter 25; Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2017:644-705; **Rose G, Mclarney JT:** *Anesthesia Equipment Simplified*. 1st ed. Edition; New York, NY: McGraw-Hill; 2014; **Sandberg W et al:** *MGH Textbook of Anesthesia Equipment*. 1st ed. Philadelphia, PA: Elsevier Saunders; 2010.

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Anesthesia Ventilators and Their Application

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Patient status: must make intraoperative anesthetic management of ventilator relevant to pre- and postoperative disease of individual patient; consistent with perioperative care model endorsed by American Society of Anesthesiologists (ASA); develop clinical plan using information taken from ventilator modes, understanding specific differences between intensive care unit (ICU) and anesthesia ventilators, physics associated with underlying way ventilators work; be able to develop clinical plan for patients that require unconventional modes of ventilation; as for underlying disease in patients, most on ventilator because needed for intraoperative management of respiratory status, to facilitate general anesthesia

Acute respiratory distress syndrome (ARDS): common issue dealt with in ventilator management; causes include blast injury, severe pneumonia, transfusion-associated acute lung injury, inflammatory disease secondary to inhalational injuries

Pulmonary edema: common pathology seen in operating room (OR); neurogenic pulmonary edema (*eg*, patient with severe subarachnoid hemorrhage), in OR for aneurysm coiling, developed neurogenic pulmonary edema because of acute increases in aortic-induced cardiac afterload (this type of pulmonary edema has rapid onset); classic causes of pulmonary edema include chronic hospitalization with ventilator, volume overloaded; pulmonary contusions, which can look like ARDS, commonly seen in traumas from motor vehicle accidents, motorcycle accidents, falls

Emphysema: physiology and understanding for administration of care differs from that characteristically seen for most patients, because of differences in pressure and physiology and approach necessary

Criteria for extubation: classic criteria mirror image of criteria for intubation (*ie*, indications for when patient needs to be mechanically ventilated); *eg*, if arterial partial pressure of O_2 (PaO_2) to fraction of inspired O_2 (FiO_2) ratio <150, ventilator needed, if >150 (common threshold), could extubate; *respiratory minute volume (minute ventilation)* — direct marker to indicate patient CO_2 level; 10 L/min threshold for patient to maintain when extubated, <10 L/min indicative of requiring intubation; *negative inspiratory force* — at least more negative than −20 cm H_2O to −25 cm H_2O; *classic measures* — respiratory rate <30 breaths/min; tidal volume 4 mL/kg to 6 mL/kg; rapid shallow breathing index, ratio of rate to volume (*ie*, rate divided by volume in liters), <85 L to 105 L consistent with >95% of patients for extubation

Anesthesia ventilator and ICU ventilator: purpose of anesthesia ventilator to administer drug while simultaneously facilitating mechanical ventilation; goal of ICU ventilator to facilitate mechanical ventilation, thus simpler machine; fundamental issues, drug conservation and power supply configuration; until recently (past 10 yrs), many anesthesia ventilators bellows based, driven by gas, ICU ventilators used pistons; circuitry can be much simpler, allow for more complex modes on ICU ventilator, whereas anesthesia ventilator requires methods for preserving sevoflurane, CO_2 rebreathing, drug conservation, so cannot facilitate complex modes of ventilation; respiratory therapy in most hospitals available to attend anesthesiologist in OR when complex ventilation needed; most ICU ventilators have portable power supplies

Types of Ventilation

Assist-control (AC) ventilation: essentially set ventilator to minimum rate; often used in ICU; if patient takes additional breaths beyond minimum, get programmed full breath to receive whenever breath triggered; *eg*, if patient at 500 mL with rate of 10 breaths/min and breathes <10 breaths/min, patient gets 500 mL at rate of 10; if patient breathes 12 breaths/min, gets 500 mL at rate of 12; no matter how patient breathes, automatically get full breath

Volume-control ventilation (VCV): in OR, most similar method to AC ventilating by volume control; patient set to receive 10 breaths/min at volume of 500 mL regardless of whether patient breathes; patient automatically gets same volume regardless of effort

Continuous positive airway pressure (CPAP) and positive end-expiratory pressure (PEEP) ventilation: CPAP not synonymous with PEEP; *PEEP* — unique because positive end-expiratory pressure what should be experienced by lung at end of expiration; lungs would not normally perceive additional pressure throughout entire respiratory cycle; respiratory cycle has varying pressures depending on phase (*ie*, whether patient inspiring or expiring); *CPAP* — same amount of pressure exerted on airways at all phases of cycle; *eg*, if patient inhaling, and CPAP set at +5 cm H_2O, will also receive +5 cm H_2O on exhale; keeps airways open throughout all phases of ventilation

Bidirectional positive airway pressure (BiPAP): modification of CPAP; at patient inhale, can set to have additional 5 cm H_2O pressure, and at exhale, can remove 5 cm H_2O; results in PEEP value on exhale; way for understanding patient's inspiratory vs expiratory phase

Pressure-support ventilation: different from CPAP, not synonymous; similar to BiPAP; BiPAP pressure-support ventilation (PSV) without endotracheal (ET) tube

Pressure-regulated volume control: set patient to volume control with regulated pressure, set peak pressures that ventilator can administer and therefore adjust waveforms so ventilator can facilitate patient's receiving full volume while not exceeding set pressures; essentially, volume control with alarm, safety setting

Synchronized intermittent mechanical ventilation (SIMV): essentially combination of assist-control and pressure-support ventilation; patient must reach threshold mandatory number of breaths; if patient not taking enough breaths, ventilator will help achieve threshold number; anything beyond threshold, PSV

Physics of ventilation: positive-pressure ventilation (PPV) fundamentally different from negative pressure-ventilation; if administering PPV, ventilation being given by force, externally, and that force transmitted from trachea through distal airways in sequentially degrading fashion; not necessarily physiologic; *eg*, when taking "normal" breath, chest expands, opening alveoli, allowing them to suction in atmospheric gas, all in organized fashion; cannot mimic this from external circuit; thus, lack of physiologic participation of patient with ventilator has consequences; in most patients, not substantial issue; patients with lung injury show signs of cellular and immune-mediated injury to lungs

Mechanical wall stress: studies have shown that increasing mechanical wall stress (*ie*, giving PPV) leads to secretion of tumor necrosis factor (TNF)-alpha, triggers contractions of cytoskeleton, disrupts adherent junctions, thereby increasing edema formation; thus, giving more pressure, from physics standpoint, because trying to transduce that external pressure to distal airways results in turbulent, not laminar, flow; recall Reynolds number; *ventilator-induced lung injury* — patient has worsening lung disease because of PPV administration; PPV can actually worsen patient's underlying disease

Neuromuscular blockade: *utilization of neuromuscular blocking agents and postoperative pulmonary complications* — study on outcomes between patients receiving neuromuscular blocker but not reversal agent and patients who received both neuromuscular blocker neuromuscular reversal agent; those receiving no reversal agent had statistically significant increase in respiratory complications; not giving reversal not definitively linked with 30-day mortality but study does suggest association (retrospective study); another study looking at dose-dependent associations between neuromuscular blocking agents and postoperative respiratory complications; higher doses of neuromuscular blocking agents showed association with increased respiratory complications; when using neuromuscular blockade, important to administer reversal agent

Individualized PEEP: study looked at utilizing unique method of fixing or setting PEEP by using impedance device; 40 patients who had laparoscopic abdominal procedure, randomized to either receive institutional PEEP at 4 cm H_2O or receive method of assessing and administering PEEP based on electrical impedance tomography (which assesses degree of electrical resistance across chest, commonly used in respiratory monitoring, also in cardiac monitoring); impedance-guided assessment of administration of PEEP led to high intraoperative oxygenation while still preserving hemodynamics; individualized PEEP can be useful in preventing atelectasis; PEEP end-expiratory phase in respiratory cycle, prevents derecruitment of lungs; this prevents rerecruitment (*ie*, reopening of lung pathways repeatedly) and avoids ongoing recurrent injury

Inverse ratio ventilation: inverse of normal administration; *eg*, normally set ventilator to 1:2 ratio of ventilation, meaning one-third of respiratory cycle inspiration, two-thirds expiration; with inverse ratio ventilation, invert, thus, two-thirds of respiratory cycle inspiration, one-third expiration; commonly performed in OR (*eg*, "bagging" patient to improve saturation, try to miss recruitment breaths)

Airway pressure release ventilation (APRV): inverse ratio ventilation can be modified to allow for spontaneous breaths by patient (can be experienced comfortably) and long inspiratory time; sometimes known as bilevel ventilation; commonly used for ARDS treatment; well tolerated; considered by some as "last-ditch" emergency mode, but lecturer states best administered when patients not in maximum duress; *eg*, no need to wait until FiO_2 100%, can start at 60%; for lung transplant patients or average patients, reasonable to administer APRV at high FiO_2 and wean directly down to PSV (*ie*, no need to step down from APRV to SIMV to PSV); can go straight from APRV to PSV because patient breathing spontaneously during inspiratory cycle of APRV, can reduce PEEP pressures gradually while continuing to allow spontaneous breaths on top of inspiratory cycle, resulting in PSV with generous amount of PEEP; *use in ARDS* — in terms of utilization in early ARDS, studies have not necessarily shown definite benefits in mortality, but have demonstrated improved hospital release times and lower ventilator utilization, because APRV prolonged recruitment maneuver; allows for reduced inflammatory cascade (production of TNF-alpha, interleukin [IL]-6, IL-12); also of note, not recommended for patients with emphysema, especially if concurrent COPD, because requires increased expiratory time; "breath stacking" can occur, may result in pneumothorax or blebs

Nitric oxide (NO): dose usually ≤40 ppm; NO combines with hemoglobin, metabolizes to methemoglobin and nitrate; thus, methemoglobinemia concern with NO administration; however, administration of 80 ppm for 8 hrs results in 5% methemoglobinemia; thus, at lower doses for shorter periods, methemoglobinemia lesser issue; NO administration can be helpful for oxygenation; reasonable to use in OR as long as mindful of potential methemoglobinemia

Physiology and precision: important to minimize inflammatory cascade associated with mechanical ventilation; if overcompensate and give too little volume, can cause atelectasis (*ie*, not ventilating effectively so lungs collapse); can reexpand lung to move past atelectasis, but this restarts inflammatory cascade; attempting high PEEP to compensate can result in overdistention, which leads to lung injury, so not only inflammatory mediator issue but also barotrauma, potential pneumothorax

Oscillator: another mode of ventilation; not commonly used, except possibly in pediatrics; takes advantage of hysteresis curve (which starts from atelectasis at recruitment phase to overdistention, then back down to atelectasis, counterclockwise circle); to avoid overdistention and atelectasis, targets single pressure, such; not ventilation in traditional sense; no technical passive expiratory phase,

more of an active expiratory phase; no technical inspiration or full-volume phase; not giving breaths, but mixing gas from bias flow (inspiratory limb) to gas outflow, mixing this gas with everything in trachea; some hyperoxygenated gas in trachea will mix with gas in left mainstem bronchus, upper bronchial passages, *etc*; various mechanisms to explain this, including turbulence (not laminar flow); can directly ventilate some alveoli closer to trachea; *pendelluft effect* — atelectatic parts of lung exposed to more oscillator pressures and more expanded and aerated alveoli not necessarily exposed to higher pressures; end up preferentially recruiting alveoli at farther distances with gas mixing part; near alveoli, have laminar flow as well and radial mixing of gas; allows for an efficient exchange of gas distally, even though it appears more turbulent proximally; can have collateral ventilation between alveoli; allows for avoidance of injury in pathologically affected alveoli while facilitating ventilation in organized fashion more distally (even though mixing gas more proximally); avoids concern with various mean pressures, because mean pressures fixed; important to note, increased frequency does not lead to increased ventilation on oscillator (inverse relationship), oscillator ventilation function of area under curve; mechanical ventilation opposite of relationship to frequency than expected; also of note, ET tube cuff needs to be deflated to allow for secretions and prevent barotrauma; *anesthetic considerations* — can administer anesthetics to patients who have oscillators, but must be total intravenous-based anesthesia (TIVA), otherwise, unreliable administration of gas; limitation, few know how to operate oscillator; not definitively shown to improve outcomes in patients with ARDS

Volume-diffuse respiration (VDR) devices: hybridization of inspiration-to-expiration ratio of ventilation and oscillator; has higher pressure and lower pressure to help maximize secretion clearance

Prone positioning: reduces mortality in patients with ARDS; study showed reduction in mortality from 33% to 16%; prone position can be useful

Other Issues

Blood loss and posterior lumbar infusion surgery: study compared PCV with VCV, found that PCV decreased intraoperative surgical bleeding; lower peak pressures suspected reason; using pressure-control mode instead of volume-control mode of ventilation, results in lower peaks; VCV has high peak and plateau effect, whereas PCV appears as square; to assess volume administered (area under curve), when looking at pressure-volume waveform, then pressure-control mode of ventilation useful to consistently calculate or predict how much gas can be administered without high peak; remember, ventilators have extra settings to prevent overdistending lung or administering too much or too little volume

Obesity and protective lung ventilation: study assessing obese patients receiving protective lung ventilation during laparoscopic surgery; patients had CPAP of 10 cm H_2O during preoxygenation, induction; in control group, no CPAP used; all patients given same FiO_2 within group; CPAP preserved oxygenation, ventilation/perfusion match during anesthesia

High vs low PEEP: study of high vs low PEEP during general anesthesia for open abdominal surgery; patients allocated to receive high PEEP of 12 cm H_2O or lower pressure of <2 cm H_2O; high PEEP group, recruitment maneuvers; low PEEP group, no recruitment maneuvers; recruitment maneuvers did not protect against postoperative pulmonary complications; intraoperative protective ventilation should include low volume

Suggested Reading

Bronsert MR et al: Intermediate-acting nondepolarizing neuromuscular blocking agents and risk of postoperative 30-day morbidity and mortality, and long-term survival. *Anesth Analg*. 2017;124(5):1476-83; **Güldner A et al:** Intraoperative protective mechanical ventilation for prevention of postoperative pulmonary complications: a comprehensive review of the role of tidal volume, positive end-expiratory pressure, and lung recruitment maneuvers. *Anesthesiology*. 2015;123(3):692-713; **McLean DJ et al:** Dose-dependent association between intermediate-acting neuromuscular-blocking agents and postoperative respiratory complications. *Anesthesiology*. 2015;122(6):1201-13; **Piedalue F et al:** Prone positioning in acute respiratory distress syndrome. *Respir Care Clin N Am*. 2003;9(4):495-509; **Zhou Y et al:** Early application of airway pressure release ventilation may reduce the duration of mechanical ventilation in acute respiratory distress syndrome. *Intensive Care Med*. 2017;43(11):1648-59.

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Airway Management

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American Society of Anesthesiologists (ASA) Difficult Airway Guidelines (2013): graphic algorithm of guidelines divided into 2 boxes; *box A* — awake intubation (difficult airway); *box B* — intubation after induction of general anesthesia (routine patient with easily managed airway)

Pathway for intubation in anesthetized patients: progresses from masked ventilation, to supraglottic airway (SGA) devices, to awakening the patient (anywhere along pathway), to establishing surgical airways; ASA guidelines do not represent a strict pathway, and present variety of choices relevant to difficulty with routine intubation or managing difficult airways; *before entering algorithm* — assess possibility of basic problems with patient cooperation, masked ventilation, SGAs, laryngoscopy, and difficult surgical airway access; actively pursue delivery supplemental oxygen; consider merits and feasibility of awake intubation versus intubation after induction of anesthesia, video laryngoscopy versus direct laryngoscopy, non-invasive techniques versus invasive techniques, maintaining spontaneous ventilation versus rendering patients apneic

Choosing algorithm: most important preoperative decision; based on whether maintaining airway is truly necessary or beneficial, difficulty of laryngoscopy and intubation (depends on patient, clinician's skills, availability of tools, and context), setting (*ie*, operating room [OR; controlled environment] versus emergency department [less-controlled environment]), and availability of skilled help; assessment of any given patient may vary due to subjective perspective of anesthesiologists, and many factors in evaluation (*eg*, video laryngoscopy versus direct laryngoscopy)

Evaluation of patients: *Mallampati score (modified)* — based on visual assessment of oropharyngeal cavity with mouth open and tongue out; class 1 score represents fully visible uvula and palatoglossal arches; with a class 4 score, only the hard palate is visible; *inter-incisor gap* — *ie*, distance between teeth or alveolar ridge; preferably 4 cm; *thyromental distance* — *ie*, distance between thyroid cartilage and tip of mentum; preferably 4-6 cm; range of motion of neck — head should extend ≥30 degrees; *upper lip bite test* — ask patient to translate mandible in order to bite upper lip

Cochrane review (2018): these examinations showed poor sensitivity, but modest specificity in detecting potentially difficult intubation; while intubation may be impossible in patients with inter-incisor gap of 0 cm, patients with widely opening mouths may present other problems (*eg*, large tongue, inability to move neck); study data (Nørskov, 2016) suggests judgment of clinician is superior to tests

Assessing viability of supraglottic ventilation: *risk factors for ventilation via facemask* — >56 yrs of age; body mass index (BMI) >26; facial hair; history of snoring; edentulous; patients with >2 of these factors may be difficult to ventilate (Langeron, 2000); later large study affirmed these risk factors, while suggesting additional issues may be seen in men, patients with high Mallampati score, and patients with history of radiation therapy to head or neck; *risk factors indicating difficulty with SGA* — male gender; >45 years of age; high BMI; short thyromental distance; reduced cervical range of motion

Indications for use of ASA difficult airway algorithm (box A): clinician-determined difficulty with intubation and ventilation; in patients at risk for difficult laryngoscopy and intubation who can be rescued via SGA, aspiration risk is primary consideration (based on assessment for systemic disease, severe diabetes, severe obesity, pregnancy, medications, and time of last food intake); after aspiration risk is ruled out, decision is based on ability to perform emergency front-of-neck access airway (based on degree of adipose tissue over cricothyroid membrane [CTM; evaluated by palpating 1-2 cm below thyroid notch, cricoid cartilage, and cricotracheal membrane]); since literature suggests practitioners have poor accuracy using this manual evaluation, consider ultrasonography to locate CTM before induction of anesthesia (when warranted by severe concerns)

Ensuring Adequate Oxygenation

Pre-oxygenation (before anesthesia): classically provided via clear plastic mask fitted over face with inflatable cuff sealing nose and mouth (transparency important to visualize secretions or vomitus in mask, and misting of breath), and held tightly by operator, straps, or patient (if claustrophobic) for 3 to 5 min to fill functional residual capacity (FRC) with oxygen; critically important in case of failure to ventilate or intubate, as it extends time to solve problems with airway management and/or awake patient

Safe apneic period: depends on many factors aside from adequate pre-oxygenation, including patient's cooperation and physiology (*eg*, increased metabolic rate, shunting which prevents adequate oxygenation of blood, lung disease)

Detecting alveolar exchange: many international guidelines accept no substitute for measurement for end-tidal CO_2; *weak indicators of gas exchange* — misting of facemask or endotracheal tube; chest movements; auscultation of breath sounds; however, only true indicator is detection of CO_2 (preferably in waveform capnography)

Alternative devices for pre-oxygenation: *transnasal humidified rapid-insufflation ventilatory exchange (THRIVE)* — provides high-flow nasal oxygen (40-70 L/min); increases safe apneic period (especially when used to continue oxygenation after induction of anesthesia and during intubation attempts); *nasal-only pre-oxygenation and facemask combination* — *eg*, SuperNO_2VA

After induction of anesthesia: ventilate patient with anesthesia facemask sealed tightly over nose and mouth (use thumb and first finger to push mask toward face, and remaining fingers to pull mandible into mask); monitor continuous waveform CO_2 (to detect adequate oxygenation ventilation) as well as facemask misting, chest movement, and auscultation

Laryngospasm: complicates facemask ventilation; typically occurs due to inadequate levels of anesthesia, but may result from stimulating factor (*eg*, secretion of foreign body in airway); overcome via deepening of anesthetic (possibly with muscle relaxants), application of stable positive airway pressure, or removal of foreign body with suction; *laryngospasm after extubation* — occurs due to irritated larynx and possible secretion in airway; dangerous when patient attempts spontaneous ventilation against closed glottis, as negative pressure in intra-thoracic cavity occurs and can cause pulmonary edema; *safe management* –operate with extremely low threshold for rapid diagnosis of laryngospasm, application of positive pressure, removal of foreign bodies, and possibly re-inducing anesthesia

Other solutions for poor facemask ventilation and obstruction: *oral airways* — require deep anesthesia to negate gag reflex); *nasopharyngeal airway* — require caution due to possible epistasis on placement (lubricating tube and treating nasal cavity with vasoconstricting agent recommended); *muscle relaxants* — early use can relieve obstruction in upper airway and improve facemask or SGA ventilation (as well as later intubation conditions)

SGA ventilation: many practitioners no longer assure viability of mask ventilation during anesthesia before giving neuromuscular blocking agents, due to advent of supraglottic devices (*eg*, laryngeal mask airway [LMA]) and video laryngoscopy; this approach requires careful pre-procedure decision regarding use of endotracheal intubation or SGA to manage patient; SGAs are generally used for shorter procedures (*ie*, <1 hour) in patients not at risk for gastroesophageal reflux and aspiration (however, there is no established limit on duration of use); although not designed to protect patient from aspiration of regurgitated gastric content, controlled studies showed excellent protection similar to endotracheal intubation; second-generation SGAs include a lumen placed above esophagus and exiting into the atmosphere, which is intended to diagnose malplacement (positive pressure ventilation results in air leak up second lumen [*ie*, gastric drain]), but can also be used to pass gastric tube; however, passive regurgitation from stomach will come up second lumen (if placed correctly); speaker recommends use of second-generation SGAs whenever possible; SGAs are effective with positive pressure ventilation and spontaneous ventilation maintenance of anesthesia for short or prolonged cases; many SGAs are adequately sized for endotracheal intubation through lumen of SGA (although most require guidance of flexible scope to achieve endotracheal intubation)

Endotracheal intubation: determinations regarding necessity may be based on physiologic factors (*eg*, risk for regurgitation and aspiration), positioning of patient during procedure, time elements, postsurgical care in intensive care unit (ICU) requiring tracheal intubation

Intubation

Laryngoscopy: *ie*, using device to visualize larynx; direct scope (*ie*, Miller or Macintosh type) allows straight line of sight from operator's eye directly into larynx; *Miller type (straight blade)* — displaces epiglottis and bulk of tongue into thyromental space and laterally; *Macintosh type (curved blade)* — used in vallecular (above epiglottis) to displace tongue into similar area

Sequential steps: focus on visualizing epiglottis rather than larynx; open mouth using fingers of dominant hand on teeth or alveolar ridge to rotate and translate temporomandibular joint (disease on temporomandibular joint may result in trismus and cause difficult); after joint is rotated and translated, achieve 3-4 cm inter-incisor, inter-alveolar ridge gap; place laryngoscope blade over anterior and posterior tongue with non-dominant hand while looking for epiglottis (rudimentary tissue at base of tongue without significant physiologic function); after noting epiglottis at base of tongue, larynx can be located distal to epiglottis; Macintosh blade continues down base of tongue into vallecula (area between base of tongue and epiglottis), until pushing against glosso-epiglottic ligament (which lifts epiglottis and reveals larynx); after epiglottoscopy is achieved, Miller blade is used to lift epiglottis against base of tongue; entire procedure should be easy to achieve 95% to 97% of patients;

Cormack-Lehane (CL) classification: describes view of laryx; *grade 1* — full view of vocal cord apparatus; *grade 2* — only posterior of vocal cords visible; *grade 2b* — only most posterior aspect of larynx (including corniculate and cuneiform cartilages) visible; *grade 3* — only epiglottis visible (no view of larynx); *grade 3b* — epiglottis is immobile; *grade 4* — neither epiglottis nor larynx visible; scores mostly used as communication devices between laryngoscopists

Patients who fit evaluation criteria for easily managed airway but show poor CL grades (3, 3b, or 4): classically described as anterior larynx (problematic term); *study (Ovassapian et al, 2002)* — included 33 patients easy-to-manage airway, whose larynx could not be visualized; nasopharyngoscopy showed lingual tonsil hyperplasia (*ie*, hyperplastic lymphoid tissue at base of tongue); thus, their larynxes were not excessively anterior, but excess tissue at base of tongue pushed against laryngoscope blade to posterior; no data exist on prevalence of lingual tonsil hyperplasia, but it may be represented in 3% to 6% of patients with poor CL grades

Tracheal tube: placed after larynx is visualized (CL grade of 1-2b); prevents obstruction after endotracheal intubation; distal end typically has inflatable cuff to seal airway; proximal end has adapter to connect 2-way standard size Ambu bag or anesthesia circuit; *sizing* — adults receive tracheal tube 7-9 mm internal diameter; in children, use Cole Formula to determine size of tracheal tube at different ages

Tube types: traditional tubes have gentle concavity (originally developed for use of blind passage through nasal cavity into larynx); right angle endotracheal (RAE)

tubes — manufactured to facilitate nasal intubation; proximal end of tube aims away from mouth, giving access to surgical field; oral RAE tubes have curvature to allow movement of proximal end away from surgical field after oral intubation; *wire-reinforced flexible tracheal tubes* — highly pliable; tube can be fixated to around surgical field; *laser tubes* — necessary when Bovie or laser device is used in airway (which may present risk of airway fire due to combination of fuel [tracheal tube], oxygen or nitrous oxide [serves as oxidizer and thus promotes fire] and heat source [laser or Bovie cautery]; as such, these procedures require lower oxygen levels and laser or heat resistant tubes available; *microlaryngeal tubes* — typically long with small internal diameter; used in upper airway surgery; allow anesthesiologist to move tracheal tube out of field of surgeon; *recommendations for difficult airways* — regardless of the reason for difficulty, smaller tubes are advantageous, as they are easier to fit into obstructed airway (versus large tubes), and are less of a hindrance to surgeons working in the airway

Intubation procedure: after laryngoscopy, tracheal tube is passed directly into larynx (this may require use of stylet [malleable wire device] within tracheal tube to stiffen and shape it, so the laryngoscopist can manipulate it into larynx); distal end of tube enters larynx, and advances until cuff of tube is below vocal cords by ≥2 cm (to ensure the cuff is below larynx and in trachea); tracheal tube cuff is inflated with air (or saline if procedure involves laser); patient is ventilated with positive pressure to detect leaks (if present, leaked require increased inflation of cuff)

Overinflation issues: it is important to prevent overinflation of the cuff (ie, maintaining <15-30 cmH2O) due to the danger of mucosal damage or nerve damage (in extreme cases); while experienced practitioners may recognize overinflation via palpation of the pilot balloon, manometers simplify detection; SGAs with cuffs should not be inflated to >60 cmH2O;

Verifying successful intubation: absolutely requires capnography; in absence of capnography, proceed under assumption that tracheal intubation has not been achieved (this includes patients in cardiac arrest receiving ongoing cardiopulmonary resuscitation [CPR]); with adequate CPR, patients in cardiac arrest should show capnography waveforms resembling those seen with spontaneous cardiac action; simple indicators (misting, chest movement, lack of movement over stomach) cannot substitute for verification of expired CO_2 (preferably in waveform capnography); after detection of end-tidal CO_2, auscultation remains helpful in verifying ventilation of both lungs (indicating tube placement beyond carina and ventilation of main stem bronchus)

Video laryngoscopy: in normal populations, 3% to 5% of tracheal intubations via direct laryngoscopy pose difficulties (primarily due to lingual tonsil hyperplasia); the first video laryngoscopes improved CL classifications by 1 to 2 grades; more recent devices include video elements with hyper-angulated configurations, which allow better views around the base of tongue and thus negate issues caused by lingual tonsil hyperplasia (thereby reducing rates of poor CL scores to ~2 in 1,000 patients); multiple studies consistently show video-enabled blades can rescue failed direct laryngoscopy procedures in approximately 94% to 95% of cases; speaker recommends use of video laryngoscopy in all tracheal intubations

Disadvantages: although laryngoscopy itself is easier with video-enabled devices, they complicate delivery of tracheal tube into larynx (due to the fact that the tube must be moved along a curve, rather than a straight line as in direct laryngoscopy); using a rigid stylet shaped to the curve of the video laryngoscope can compensate for this, as the operator can move tracheal tubing around curved end of larynx; *limitations in CL grades* — while direct laryngoscopy seeks to obtain best possible views, practitioners are advised to target lesser views with video laryngoscopy (*ie*, CL grade 2); attempting to achieve a CL grade 1 with a video-enabled blade tends to lift the larynx (resulting in less concordance between axes of pharynx and larynx, and thus complicating delivery of tracheal tubes); this does not occur with lesser views (CL grade 2-2b), as axes of pharynx and larynx are better aligned and thus facilitate intubation

Complications: while direct laryngoscopy can cause injuries to soft tissue, teeth, lips, and gums, video laryngoscopy tends to cause soft tissue injuries to upper airway; this occurs when an operator concentrates eyesight on video screen, and thus cannot see injuries caused by tracheal tube as it first enters mouth (since the injury occurs before the bevel of tube can be seen on screen); to prevent injuries, operators should concentrate on patient's mouth and upper airway as tracheal tube enters, and only turn attention to video screen after distal aspect of tracheal tube can be visualized

Flexible intubation scope (FIS): although sometimes considered obsolete, speaker regards FIS as crucial tool in armamentarium of airway operator; *"multi-plane airways"* — when patients have masses in airways, air can no longer flow in single curve from oral aperture down to larynx; as such, these patients require a device capable of moving along multiple planes (*eg*, FIS)

Operation: lever operated by thumb of operator's non-dominant hand moves objective end of FIS in posterior direction of sagittal plane; tracheal tube is fitted on insertion cord; after insertion, images of airway display on video screen; FIS can be directed through upper airway and around masses until larynx is visualized; after scope advances into upper airway, pre-mounted tracheal advances into airway; entire procedure demands high level of skill

Caveats: handle of scope is held in non-dominant hand of operator, and FIS itself is designed to be held in left hand; this is because movements of handle are gross movements (*eg*, rotation of handle, use of thumb on directional levers); fine movement occurs at objective end of FIS (which is entering the patient), and is thus where the dominant hand should manipulate scope; *relationship between tracheal tube and size of scope* –snug fit between tracheal tube and insertion cord of scope is intended (*eg*, FIS with outer diameter of 3 mm and mounted tracheal tube with internal diameter of 7 mm, resulting in ~0.5 cm gap between scope and tube); this gap is liable to catch on various tissues (*eg*, palatoglossal arches, epiglottis, aryepiglottic folds, vocal cords), and thus prevent movement into larynx; speaker

recommends larger scope (~5 mm) and tracheal tube (~7 mm)

Advantages: unlike direct laryngoscopes and video laryngoscopes, FIS does not create airspace in patient's airway (especially when patient is not awake)

Oral airways: used to create airspace needed for visualization; speaker recommends Ovassapian intubating airway device; when using airways to create airspace and passage for FIS, employ maneuvers such as chin lift and jaw thrust to move epiglottis forward and create visual path for FIS; in recent literature, operators used direct or video laryngoscopes to open airspace while FIS is placed into upper airway

Awake Intubation

Indication for awake intubation: patient with difficult airway plus risk of being difficult to intubate and ventilate; patient difficult to intubate and at risk of gastroesophageal reflux and aspiration; patient difficult to intubate with unsafe apneic period (thus at risk for rapid desaturation); in rare circumstances, otolaryngology or trauma surgeons perform awake tracheostomy; speaker prefers awake tracheal intubation

Procedure: does not require FIS; recent literature supports use of video laryngoscope over FIS (Alhomary, 2018); whether using FIS or video laryngoscope, process depends upon preparation of patient; *preparation* — explain rationale for awake intubation, what patient will experience, and how comfort will be ensured throughout the process; administer desiccant as soon as possible (typically glycopyrrolate 0.2 mg via intramuscular [IM] or intravenous [IV] route) to remove secretions and thus ensure topical anesthetic has greater effect on mucosa of airway; always prepare nasal passage (even when planning for oral intubation), so it may be used as backup if patient has difficulty with oral intubation (due to, *eg*, pronounced gag reflex); after airway dries, begin its analgesic preparation

Innervation of airway: *anterior ethmoidal nerve* — innervates nose in anterior one-third of nasal cavity; *lateral nasopalatine nerves* — innervate posterior two-thirds of nasal cavity, pierce hard palate, and innervate palate; *glossopharyngeal nerve* — innervates mouth and pharynx; has 3 branches which innervate palatine tonsils, posterior one-third of tongue (including vallecula), and anterior surface of epiglottis; *pharyngeal branch of glossopharyngeal nerve* — innervates posterior pharyngeal wall; primary sensory input for gag reflex; *internal branch of superior laryngeal nerve* — innervates underside of epiglottis and vocal cords; branch of vagus nerve; *exterior branch of superior laryngeal nerve* — innervates most muscles of larynx (excluding cricothyroid muscle); *recurrent laryngeal nerve* — innervates cricothyroid muscle; branch of vagus; most common site of injury to nerves of larynx (which can result in unilateral vocal cord paralysis with medialization of the affected side); *bilateral paralysis* — can occur during thyroid surgery; results in medialization of both vocal cords and emergency after extubation; treated via immersion tracheal intubation, and often requires tracheostomy

Analgesia sequence: apply lidocaine (2% or 4% solution) to swabs; insert swabs into nasal cavity, push until swabs hit sphenoid bone, and leave in place for 5 min; prepare new set of swabs with 2% or 4% solution of viscous anesthetic, and apply to palatoglossal arches at junction with tongue (this attempts to anesthetize palatoglossal nerve); take syringe of 200 mg of lidocaine (2% or 4% solution, or 2% viscous formulation), and use plastic piece of angiocatheter to gently apply lidocaine to rear of tongue (while holding tongue out of patient's mouth as to facilitate aspiration)

Nerve blocks: rarely utilized; *superior laryngeal nerve block* — 1 to 2 cc lidocaine solution (2% or 4%) bilaterally injected just above lateral cornu of hyoid bone; take precautions against blood aspiration (due to close proximity of carotid arteries) and air aspiration (indicating needle has passed into pyriform sinuses); *trans-CTM block* — pass needle (typically 25 gauge) through CTM with continuous aspiration; after aspiration of air (with needle sitting in larynx), inject 5 cc of 4% lidocaine solution; since lidocaine is only anesthetic used, total dose of lidocaine is readily calculated to remain below 400 to 500 mg (for average adult); *when using FIS* — spray ≤100 mg lidocaine down working channel of scope while visualizing vocal cords, larynx, and trachea; speaker recommends placing epidural catheter through working channel of flexible scope to apply local anesthetic exactly where desired

Sedation: effective topical anesthetic block during awake laryngoscope or FIS intubation minimizes need for sedation; under these circumstances, speaker recommends 1 to 2 mg midazolam or possibly 50 mcg fentanyl; with high risk of losing airway, it is important for patient to be alert and cooperative; in typical routine induction of anesthesia and tracheal intubation, systemic responses from laryngoscopy and placement of tracheal tube in larynx can be extreme (resulting in, *eg*, hypertension, increased intraocular and intracerebral pressure) and require mitigation via potent opioids (*eg*, fentanyl, remifentanil), intravenous lidocaine, beta-blockers (*eg*, esmolol, metaproterenol, labetalol), or induction agent; in contrast, awake intubation relies on successful topical or needle blocks of airway to prevent extreme reactions (since excessive sedation would compromise airway)

Time management: awake intubation requires more time to ensure patient's safety (relative to sedated intubation); initiate analgesia sequence early (eg, while patient is still in holding area); consider providing early sedation if patient has stable airway; patient should arrive in OR nearly ready for intubation; after intubation, verify correct placement of tracheal tube via measurement of exhaled carbon dioxide and auscultation (to assure tube is not beyond tracheal carina)

Surgical airway: *types of emergency front-of-neck access airways* — percutaneous catheter-over-needle technique; large-bore percutaneous technique (places device of ≥3 mm); scalpel technique; when patient cannot be intubated or oxygenated, scalpel technique (with modifications) is the fastest and most successful of these techniques

Scalpel technique: *methods for locating CTM* — ultrasonography before induction of anesthesia; place finger over thyroid notch, move finger downward 1 to 2 cm until palpating depression; measure 4 fingerbreadths above manubrial notch; examine skin creases across patient's neck while in neutral position, locating the second skin crease which crosses over cricoid cartilage (cricothyroid membrane is just above

that cartilage, and just below the thyroid arch); since literature shows most practitioners only succeed at identifying CTM in 30% of patients (or <30% in women and obese patients), speaker recommends incorporating examination of the membrane in routine evaluation of patients; *emergency procedure* — create vertical incision over skin from thyroid cartilage down to cricoid cartilage; after ensuring incision is long enough (inadequate incisions are common), place finger into wound in order to palpate cricoid cartilage and CTM; if not cricothyroid was not incised during initial incision, incise horizontally through lower one-third of membrane (to avoid more vascular anastomoses in upper portion of membrane); spread membrane open with forceps (or other device); place gum-elastic bougie (or similar device) into wound of CTM (bougie is used to appreciate tracheal rings via movement of its Coudé tip up and down inside trachea); after identification of tracheal rings, advance small tracheal tube (fitting snuggly over bougie) into trachea; remove bougie and retreat tracheal tube until top of cuff attached to tracheal tube is barely visible in CTM incision; inflate cuff, and attach anesthesia circuit or Ambu bag to tracheal tube; confirm tracheal intubation via end-tidal CO_2 measurement; confirm bilateral ventilation via auscultation (or possibly FIS)

Extubation: ASA algorithm for difficult airways concentrates on airway management, induction, and intubation; while ASA guidelines lacks information on end-of-procedure emergence and extubation, contemporary education focuses on this time period; initial airway control occurs in controlled environment of OR, and often in stable patients; after surgery (and removal of tracheal tube, laryngeal mask airway, or SGA), patients are left with manipulated airways, residual medications, and airway reflexes blunted by general anesthesia (with reflexes relating to aspiration particularly affected)

Extubation failure: patients whose condition is compromised by pre-existing conditions (*eg*, history of airway surgery, radiation therapy, morbid obesity, obstructive sleep apnea) may be at high risk of extubation failure; even in OR setting, extubation is unsuccessful in 6 out of every 1000 intubated patients; failure rates may be ≤10% in ICU; as such, it is important to prepare patients for extubation

Recommendations for extubation: ensure patietns are fully awake, with neuromuscular function completely intact; trends favor reversal of neuromuscular block in all patients, and sugammadex provides more reliable reversal of deeper blocks in shorter period of time (compared to neostigmine); assess for healthy oxygenation, tidal volume, and strength; *checking for cuff leaks* — remove gas inflating endotracheal tube cuff; deliver positive airway pressure or ask patient to cough against obstruction while listening for leak; if measurable, 12% leak of tidal volume (*ie*, volume that does not return in exhaled breath) is preferable; while significant leakage never guarantees extubation success, the absence of leaks after reducing volume in cuff warrants caution (as indication patient may fail extubation)

Bridge to re-intubation: important consideration; if airways are difficult to manipulate at beginning of surgery, that difficulty will increase if patients require re-intubation after extubation (due to inherent instability of postsurgical state); *airway exchange catheter (AEC)* — tool for reintubation; consists of elongated tube (often hollow) placed inside tracheal tube at time of extubation; must be placed to length of tracheal tube (*ie*, match graduation numbers or marks so both tubes are exact same length); when placed correctly, the distal end of AEC remains in same position previously occupied by tracheal tube (before extubation); speaker recommends 14 French-sized AEC (due to its small size relative to trachea tubes); well-tolerated by patients (as long as it does not reach carina or into main stem bronchi); may be left in place for ≥30 min, or until patient fully awakens in post-anesthesia care unit or ICU; remove AEC if is breathing without stridor or other disturbance

Suggested Reading

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Anesthesia Standards and Procedures

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Current American Society of Anesthesiologists (ASA) guidelines: a preanesthesia evaluation is a history and physical examination preceding the ordering, requiring, or performance of specific preanesthesia tests; consists of the evaluation of pertinent medical records, a patient interview, and a focused physical examination; minimum components of a focused physical exam are an airway exam and a cardiopulmonary exam; routine preoperative tests do not make an important contribution to the process of perioperative assessment; selective tests may assist in making decisions about the process of perioperative assessment and management

ASA fasting guidelines: apply only to healthy patients undergoing elective procedures and allow anesthesiologists to use clinical judgment to determine alternative fasting times for other patients; minimum fasting times prior to procedures requiring sedation or anesthesia: clear liquids up to 2 hours prior; neonates and infants may ingest breast milk up to 4 hours prior or infant formula up to 6 hours prior; a light meal (toast and clear liquids) may be ingested up to 6 hours prior; fried foods, fatty foods, or meat require minimum of 8 hours of fasting

Preanesthetic preparation: evidence does not support routine administration of anti-emetics, gastric acid blockers, antacids, or gastrointestinal stimulants; patients with increased risk for pulmonary aspiration may benefit from these medications; important principle of guidelines — management of the preanesthetic patient must be specific to the patient and procedure; there is no required routine testing or standard preparation

ASA classification system: patients are designated ASA Class 1-6 and may also be given an "E" qualifier which denotes a patient presenting for an emergency surgery, defined as surgery for which delay would lead to a significant threat to life or body part; ASA 1 patients are healthy, non-smoking patients with no systemic disease and no or minimal alcohol use; ASA 2 patients have mild systemic disease without functional limitations; ASA 3 patients have severe systemic disease with substantive functional limitations; ASA 4 patients have severe systemic disease which is a constant threat to life; ASA 5 patients are not expected to survive without the operation and most of these patients are presenting for emergency surgery and considered ASA 5E; ASA 6 patients are patients declared brain dead whose organs are being removed for donor purposes

Care of patients presenting with an active Do Not Resuscitate (DNR) or other order that limits treatment — may present an ethical dilemma for the anesthesiologist, surgeon, or proceduralist; see ASA guideline of 2001 (revised 2013); an individualized decision on the maintenance or suspension of a patient directive must be made which follows the patient's wishes, through an informed discussion between the anesthesiologist and patient or designated surrogate; three alternatives to continuing a full DNR during a procedure requiring anesthetic care are offered: first, full suspension of the DNR until the patient is recovered from the anesthetic; second, patient permission for a limited attempt at resuscitation — specific procedures are agreed between the anesthesiologist and the patient, with the anesthesiologist informing the patient which procedures are essential and which may be refused (patients may elect to refuse specific non-essential interventions); third, the patient may elect to give the anesthesiologist and surgeon the right to use clinical judgment; aligning with a patient's right to self-determination requires a detailed and honest discussion; decisions made should be communicated with all involved in the patient's care and documented in patient's chart

ASA and American College of Obstetricians and Gynecologists committee opinion on non-obstetric surgery during pregnancy: no currently used anesthetic agents have been shown to have any teratogenic effects in humans when using standard concentrations at any gestational age; a pregnant woman should never be denied indicated surgery regardless of trimester; following the decision to proceed with an indicated surgery, each patient should have an obstetrical consultation to assess maternal and fetal health prior to surgery; a collaborative approach is necessary to develop a plan with optimal safety for fetus and mother; elective surgery should be postponed until after delivery; indicated non-urgent surgery should be performed in the second trimester when possible; at a minimum, check pre- and post-op fetal heart rates; intraoperative fetal heart-rate monitoring may be considered in presence of a viable fetus, maternal surgery allowing for fetal monitoring and interpretation, interruption of surgery feasible if necessary, hospital with neonatal care available, and availability of obstetrician who can perform cesarean delivery; otherwise, fetal monitoring is not recommended unless it would inform intraoperative management, such as oxygenation or positioning

Preanesthesia evaluation: the basic components of a preanesthesia evaluation are a physical exam, focused history, review of systems, and review of relevant data

Physical exam: the basic preoperative exam should include vital signs, including heart rate, blood pressure, respiratory rate, and oxygen saturation, a BMI calculation (or height and weight), an airway evaluation, and a cardiopulmonary exam; more specific examination findings may be sought based on the patient's medical history and review of systems; no absolute value should result in case cancellation or delay; however, hypertension with signs of acute organ damage is considered hypertensive emergency requiring immediate treatment; patients presenting with a diastolic pressure above 110 are considered in hypertensive urgency and elective surgery may be delayed or canceled; less evidence supports delaying cases in isolated systolic hypertension; clinical judgment may allow for surgery in chronically hypertensive patient with systolic pressure >180 without evidence of end-organ damage and diastolic pressure <110; if a cause of the hypertension is identified, pre-medication with an anxiolytic or administration of an antihypertensive may be warranted; practitioners should be cautious, as treating elevated systolic pressure may result in a dangerously low diastolic pressure, compromising organ perfusion in chronically hypertensive patients; oxygen saturation and the need for supplementary oxygen are components of pulmonary risk assessment; deviations from baseline status should be investigated and may indicate an exacerbation of underlying pulmonary disease or a new pulmonary infection, either of which may necessitate treatment and postponement of surgery; weight and BMI are important components of ASA physical status classification and obstructive sleep apnea (OSA) risk assessment and are associated with difficult mask ventilation; self-reported weights have been found to be reasonably accurate in adult patients; an accurate preanesthesia weight is more important in the pediatric population, for whom dosing of medication is primarily weight-based; a thorough preoperative airway evaluation identifies patients who are at increased risk of difficult mask ventilation, and/or difficult intubation; failure to manage difficult airways appropriately remains a leading cause of anesthesia-related deaths and anoxic brain injuries
  - Indicators of potential difficult mask ventilation and intubation: airway pathology, Mallampati Class 3 or 4, and limited jaw protrusion; other indicators of difficult mask ventilation use mnemonic OBESE: Obesity, Bearded, Elderly, Snoring, and Edentulous; difficult intubations are associated with mouth opening less than 3 cm, prominent upper incisors, thyromental distance less than 6 cm, and neck extension limitation; prior anesthetic records should be evaluated

Preoperative history: goals are to identify the patient's chronic medical problems, assess if medical problems are well-controlled, document medications taken, and determine baseline functional status; assessing functional status gives an idea as to whether patient has the cardiopulmonary capacity to withstand the stress of surgery and anesthesia, assists in cardiovascular risk assessment, and guides preoperative testing; Metabolic Equivalents of Tasks (METs) are the most commonly used descriptors of functional status; 1 MET is defined as the amount of oxygen used while resting; in general, 3.5 mL of oxygen are consumed per kilogram of body weight per minute at rest; MET standard (first published 1993, updated 2000) includes MET equivalents of 605 activities; useful question is "What is the most strenuous activity you can do without symptoms?" patients able to achieve 4 or more METs of activity without symptoms rarely need additional cardiopulmonary workup; those who are symptomatic or with unknown functional tolerance may require further testing; less-utilized methods of assessing functional status are the Six Minute Walk Test and Cardiopulmonary Exercise Testing

Review of systems: perform for all patients presenting for anesthesia; identify problems with anesthesia, such as severe nausea or vomiting, unanticipated admission following outpatient surgery, difficult airway, prolonged intubation, or personal or family history of malignant hyperthermia; ask about recent illnesses, hospitalizations, or emergency room visits; ask patients being treated for any chronic medical problems if there have been any recent changes in therapy or exacerbations of symptoms; specific, simple review of systems questions are key; for cardiac problems, ask about a history of heart attack, heart surgery, chest pain, arrhythmia, or syncope; pulmonary review of systems should include pneumonia, shortness of breath with activity, asthma, and COPD; neurologic screening for a history of stroke or TIA, dementia, aneurysm, seizure disorder, numbness, or weakness; bleeding issues, such as anemia, prolonged bleeding after surgery or injury, a history of blood clot or pulmonary emboli, prior blood transfusions, or a refusal of blood transfusion; additional questions include the presence of gastroesophageal reflux disease, unintentional weight loss, difficulty performing activities of daily living, recent history of falls, chronic pain, or difficulty lying flat

Preoperative risk stratification: all patients should be assessed for their postoperative nausea and vomiting (PONV) and OSA risk factors; a frailty index in elderly patients can help identify patients at increased risk for perioperative complications; cardiac and pulmonary risk stratification can help determine if patient requires further testing and/or optimization prior to surgery; the most commonly used assessment for PONV is the Apfel Simplified Risk Score (ranging from 0 to 4 points); each of the following contribute one point: female gender, history of PONV or motion sickness, nonsmoking status, and the probable need for postoperative opioids; a patient with a score of 4 has an 80% risk of PONV; modifications of the anesthetic should be made to reduce the risk of PONV in high-risk patients (scores of 3 or 4); these could include avoidance of general anesthesia or the use of total intravenous anesthetic, use of prophylactic medications from three different classes, and minimization of opioids; ASA has guidelines for anesthesia in patients with OSA; anesthesiologist should review sleep studies and prior anesthetic records of such patients to identify successful airway management; home CPAP or BiPAP settings should be recorded; may be necessary to contact patient's respiratory company, as many patients don't know their settings; patients should bring their mask with them the day of their anesthetic so that it can be used postoperatively if necessary; patients with OSA may require longer periods of postoperative observation; patients who have documented hypoxic

episodes in the recovery room may require admission to the hospital, continuation of oxygen, or initiation of CPAP and may not be acceptable candidates for surgery in an outpatient facility; if possibility of OSA is suspected, evaluation should occur before surgery to establish a perioperative management plan; may be started on CPAP preoperatively; the STOP-BANG criteria are most often used to identify patients at high risk for OSA; STOP includes: Snoring, Tired during the day, Observed apneas, and Pressure (hypertension); BANG includes: BMI above 35, Age above 50, Neck circumference greater than 43 cm, and Gender (male); patients are considered high-risk if they answer yes to 2 or more STOP questions and yes to any of the B, N, or G questions in the BANG screening; a total of 5 or more of any of the STOP-BANG questions would also make them high-risk; frailty predisposes a patient to physical and cognitive impairment and is associated with increased disability and death even without stress of anesthesia; frail patients have increased risk of postoperative morbidity, mortality, and readmission; the Fried Frailty Scale gives patients a score of 0 to 5; contributors to the score are: weakness, slowness, exhaustion, a low activity level, and an unintentional weight loss of 10 or more pounds over the last year; a score of 0 to 1 is considered non-frail, 2 to 3 intermediately frail, and 4 to 5 frail; may be possible to improve outcomes by alleviating frailty with nutritional assessment and intervention, physical strength and endurance training, and increased activity, but research evidence is lacking

Cardiac and pulmonary risk assessment: "The Revised Cardiac Risk Assessment" (RCRA) is the most widely used risk scoring system but has limitations; only measured cardiac death, nonfatal myocardial infarction (MI), nonfatal cardiac arrest, complete heart block, and cardiogenic pulmonary edema; only adverse events occurring within 5 days postoperatively were included; small cohort was studied; formulated before many modern techniques came into use; its six elements include: high risk surgery, insulin-dependent diabetes, coronary artery disease, congestive heart failure, cerebral vascular disease, and chronic kidney disease (creatinine >2); the risk of major cardiac complications correlates with number of RCRA risk factors identified; according to 2014 American College of Cardiology/ American Heart Association (ACC/AHA) guidelines, RCRA score can be used to guide preoperative cardiac testing for noncardiac surgery; patients with 0 to 1 risk factor are considered low-risk, and further cardiac testing is not indicated, 2 or more risk factors are considered elevated-risk, and these patients may proceed without further testing if they can achieve a functional capacity of 4 or more METs without symptoms; patients with elevated risk and poor or unknown functional capacity may proceed with pharmacologic stress testing if such testing would impact decision-making or perioperative care; note that high-risk surgery, a risk factor in this scheme, originally included intraperitoneal surgery; this was before minimally invasive techniques were used for such surgeries; 2 other risk scoring systems have been developed by surgical groups; the Gupta Score uses 5 predictors associated with increased risk of myocardial infarction or cardiac arrest; predictors include type of surgery, dependent functional status, age, elevated creatinine, and ASA physical status; scoring requires the input of numerical values into an online calculator; scores were more predictive of MI and cardiac arrest than the RCRA score; the American College of Surgeons National Surgical Quality Improvement Program's Surgical Risk Calculator (ACS SRC) is the most comprehensive and widely validated; it incorporates over 1500 surgical Current Procedural Terminology (CPT) codes and 19 patient factors; it calculates predicted length of hospital stay and the patient's individual risk for 10 complications, compared to the average risk of these complications for all patients with the same surgery; it is more useful than either RCRA or Gupta scale and is easy for patients to understand but is cumbersome to perform

Postoperative pulmonary complications (PPC): occur more frequently than cardiac complications and are associated with increased mortality, morbidity, hospital length of stay, ICU admissions, and rehospitalization; PPCs include complications of respiratory infection, respiratory failure, pleural effusion, pneumothorax, severe exacerbation of existing disease, and atelectasis; there are a number of tools which evaluate risk of PPCs; Gupta developed 2 risk scoring tools, one for respiratory failure and one for pneumonia; the Assess Respiratory Risk in Surgical Patients in Catalonia (ARIS-CAT) Index is the only tool which estimates the risk for any PPC and has 7 variables, each with a unique number of points that calculate a total score from 0 to 123-0 to 25 confers a low risk of PPCs (1.6%), 26-44 is intermediate, and greater than 45 is high-risk (42.1% risk of PPCs); factors are age, preoperative oxygen saturation, surgical site, planned duration of surgery, emergency surgery, anemia, and history of respiratory infection in the last month; identifying patients at a high risk for PPCs may result in case postponement until patient conditions are optimized or relocation of surgery from ambulatory to inpatient setting

Preoperative testing: preoperative tests should not be ordered routinely but be chosen based on the patient's clinical situation and the nature of the surgery; results obtained within 6 months are generally acceptable, barring changes in medication or health status; for stable patients undergoing low-risk noninvasive procedures, no additional testing is necessary; for patients with poorly controlled, newly diagnosed, or unstable conditions, testing may be indicated even for minimally invasive surgery

Hemoglobin: consider based on the likelihood of significant intraoperative blood loss or in patients with a diagnosis of anemia, recent chemotherapy, malnutrition, liver disease, chronic kidney disease, bleeding disorders, or who are on anticoagulants

Electrolytes: consider with diabetes, renal disease with an elevated creatinine (>1.5), malnutrition, lupus, liver disease, alcohol abuse, hypertension requiring antihypertensive medications, recent chemotherapy, and use of diuretics, digoxin, or steroids; although generally lab results obtained within 6 months are acceptable, patients on dialysis should have post-dialysis labs within 24 hours of surgery; if use of contrast dye is expected, consider a baseline creatinine

- Glycosylated hemoglobin: consider for all patients with diabetes; an elevated preoperative hemoglobin A1C level is associated with an increased risk of poorly controlled perioperative glucose levels, cardiovascular events, and postoperative infections; screening for diabetes with a hemoglobin A1c may be considered in preoperative patients who meet criteria for screening; all patients over 45 and overweight patients under 45 with at least 1 diabetic risk factor should be tested; note that there is no consensus on what A1c level constitutes poorly controlled diabetes
- Coagulation studies: indicated only with a diagnosed bleeding disorder, liver disease, malnutrition, or anticoagulant use; a thorough history is more predictive of clinical bleeding than an abnormal PT or PTT; patients who have temporarily discontinued warfarin (Coumadin) prior to surgery typically have a PT/INR drawn the morning of surgery
- Type and screen: if there is a high likelihood of significant intraoperative bleeding, a preoperative type and screen should be drawn; the decision to proceed with a type and cross on the morning of surgery should be made given the likelihood of transfusion and the speed at which blood may be crossed
- Preoperative urinalysis: consider with symptoms of dysuria and for surgeries such as transurethral resection of the prostate or other urologic procedures where breakdown of the mucosal barrier of the bladder may be expected, as this can lead to a high rate of post-procedural bacteremia (only symptomatic patients should be tested); for most patients there is no relation between asymptomatic bactiuria and surgical infections
- Pregnancy testing: there is insufficient evidence to inform patients on whether surgery or anesthesia causes harmful effects in early pregnancy; pregnancy testing should be offered to female patients of childbearing age if testing would alter patient management
- Chest radiographs: unnecessary unless a history and physical exam suggest underlying pulmonary disease
- Pulmonary function testing: usually only indicated in the workup of patient presenting for lung resection to determine if they are surgical candidates
- Electrocardiograms: acceptable if obtained within the prior 6 months if no recent change in medications or symptoms; per ACC/AHA guidelines, asymptomatic patients undergoing low-risk surgical procedures should not have a routine 12-lead ECG; there is no patient age at which an ECG should routinely be ordered; for moderate to high-risk surgery a resting 12-lead ECG is reasonable in patients with coronary heart disease, significant structural heart disease, peripheral vascular disease, arrhythmia, or cerebral vascular disease and may be considered in asymptomatic patients; only patients having low-risk surgery with a history of recent or chronic cocaine or amphetamine abuse or who are on methadone will have 12-lead ECG
- Echocardiograms: evaluate concerning physical exam findings or further evaluate diagnosed disease; echocardiogram indicated for patients with history or suspicion of valve disease, ventricular dysfunction, pulmonary hypertension, or cardiomyopathy; studies within a year should be sufficient unless there has been a change in symptoms; presence of wall motion abnormalities provides strong support for a diagnosis of ischemic heart disease and further workup may be necessary
- Exercise stress testing: detects ischemia at the patient's maximally achieved heart rate; many patients are not able to achieve a heart rate high enough for the test to be adequately sensitive
- Pharmacologic stress testing: often the preoperative test of choice for patients with an elevated cardiac risk presenting for an intermediate to high-risk surgery with an unknown or low functional tolerance; recommended only if a positive test would change management
- Other non-invasive tests: may include myocardial perfusion imaging, cardiac positron emission tomography, cardiac magnetic resonance imaging, and computed tomography/coronary angiography; when non-invasive testing reveals reversible ischemia, patient should be medically managed for coronary artery disease; when deciding to proceed with angiography and revascularization, consider the severity of disease, urgency of surgery, and ability to perform the surgery on dual anti-platelet agents; consult cardiologist

Special considerations and medications for specific patient populations: a brief introduction to common situations

- Elderly patients: screen for depression and a history of falls; evaluate nutritional status; refer to dietician if BMI less than 18.5, albumin less than 3, or unintentional weight loss; frailty assessment can help better determine risk
- Impaired cognition or capacity: may not be able to sign consents and are at an increased risk for postoperative cognitive dysfunction; avoid benzodiazepine use in elderly; dementia medications can lead to the prolongation of neuromuscular blockade; rivastigmine and galantamine can be held for 2 days, with normal return of acetyl-cholinesterase function; donepezil must be held for weeks prior to surgery; such prolonged interruption may be considered for high-risk surgeries, but usually this medication is continued
- Parkinson's disease: if presenting for deep-brain stimulators, may be asked by surgeon to withhold these medications; for all other surgeries, Parkinson's medications are continued up to and including day of surgery
- Monoamine oxidase inhibitors (MAOIs): increased risk of serotonin syndrome; tramadol, meperidine, and methylene blue should be avoided; ephedrine can lead to hypertensive crisis
- End-stage renal disease: concomitant coronary disease is common, and special attention should be paid to the cardiac risk assessment; consult nephrologist and obtain recent office evaluation; timing of hemodialysis needs to be coordinated to optimize volume status and electrolytes; a post-dialysis set of electrolytes is obtained within 24 hours of surgery; patients are often anemic and preoperative hemoglobin may be recommended; continuation of all medications is generally recommended, although angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB)s are often held on the morning of surgery for patients presenting for moderate- and high-risk surgery, this is an area of controversy; withholding these medications leads to a significant increase in perioperative hypertension, while continuing

them leads to increased episodes of hypotension intraoperatively, which can be more difficult to treat; patients undergoing high-risk surgery are usually told to hold these medications on day of surgery; patients undergoing low-risk surgery or patients with poorly controlled hypertension or heart failure may benefit from continuation of ACE inhibitor or ARB; other antihypertensives should be continued; discontinuation of clonidine can result in severe rebound hypertension; diuretics are often held the morning of surgery but should continue in the setting of heart failure or chronic kidney disease; also continue cardiac medications such as antiarrhythmics and statins

Atrial fibrillation: a common diagnosis; patients should be adequately rate-controlled and are at an increased risk of thromboembolic stroke; placing a patient on anticoagulation is dependent upon individual risk of stroke balanced with the risk of bleeding; usually, anticoagulation is interrupted for surgery; calculation of the CHA_2DS_2-VASc (Congestive heart failure, Hypertension, Age (2 points for >75), Diabetes, Stroke/transient ischemic attack (2 points)-Vascular disease, Age, Sex Category (female))score can help determine if bridging with heparin or low-molecular weight heparin is necessary; if a patient has an implanted cardiac device, find the indication for implantation, date of implantation, manufacturer, and model number, and any battery changes; the most recent interrogation report should be obtained and should be no more than 6 months old if the device is a defibrillator; pacemakers should be interrogated within 12 months; more frequent interrogation indicated at end of the device's battery life; if surgery is above the umbilicus and electrocautery will be used, the need for reprogramming or use of a magnet should be determined to avoid interference

Heart failure: patients should continue medications; a recent ECG and echocardiogram should be obtained and repeated if there have been any changes in functional status since patient last tested; preoperative basic metabolic panel (BMP) and chest X-ray may be considered; consultation with patient's cardiologist advisable to determine if the patient is optimized and compliant with prescribed therapy

Acute coronary syndrome (ACS): patients with history of ACS should not proceed with elective surgery for at least 60 days following an MI (ACC/AHA guidelines); patients with stents placed should continue dual antiplatelet therapy for at least 30 days if bare-metal and 6 to 12 months if drug-eluting (12 months recommended for ACS); patients with stents should continue at least 81 milligrams of aspirin for life; most surgeries can and should proceed on low-dose aspirin; obtain an ECG and echo following MI or stent placement; medically manage with antihypertensives, beta blockers, and statins when indicated

Valvular disease: patients with moderate to severe valvular disease should have an echocardiogram within 1 year of elective surgery, sooner if symptomatic; patients with symptomatic severe valvular disease should be evaluated by a cardiologist and a cardiothoracic surgeon to determine if valve replacement is indicated; asymptomatic severe aortic stenosis may require further stress testing or angiography

Pulmonary hypertension: patients have an elevated risk of perioperative mortality; World Health Organization (WHO) Class 3 or 4 patients have a perioperative mortality nearing 40% and elective surgery is rarely acceptable; consultation with a patient's treating pulmonologist or cardiologist should be sought; clarify etiology and severity of disease, time course of illness, and current or former treatments; the most recent ECG and echocardiogram should be evaluated and repeated, if necessary; the estimated right ventricular systolic pressure (RVSP) should be interpreted in the context of the patient's systemic pressure; elevated RVSP in hypotensive patient more worrisome than presence of normal or elevated systemic pressure; the presence and degree of RV dysfunction, and/or dilation should be noted; a right heart catheterization report should be evaluated and usually includes a vasodilator challenge; arrangements to have nitric oxide available may be made for patients deemed responsive on right heart catheterization; patients should continue all of their pulmonary hypertension medications preoperatively; interruption of an antiplatelet agent or anticoagulant is complex decision weighing the concerns of the surgeon and the anesthesiologist and the patient's underlying physiology

Recent thromboembolism or pulmonary embolism: delay non-urgent surgery for at least 3 months; if surgery is urgent and anticoagulation interruption is necessary, a plan for bridging and/or placement of an inferior vena cava (IVC) filter should be in place; patients with stents should continue at least 81 mg of aspirin; duration of interruption of antiplatelet agents should take into consideration the bleeding risk of the surgery and the anesthetic plan

Diabetes: patients should be assessed for the presence of neuropathy, gastroparesis, cardiovascular disease, peripheral vascular disease, and kidney disease; testing includes hemoglobin A1c and may include a basic metabolic panel and hemoglobin; patients with an insulin pump or insulin patch should consult their endocrinologist and are commonly told to reduce basal rate to 50% of usual on the morning of surgery; when patients are fasting for anesthesia, hypoglycemic agents should be modified to reduce the risk of effects including hypoglycemia; sodium-glucose cotransporter 2 (SGL2) inhibitors or gliflozins are associated with ketoacidosis and should be held for 2 days; other oral agents can be held for 24 hours; the weekly, subcutaneous glucagon-like peptide 1 (GLP-1) agonists need not be held but are not generally given the morning of surgery; patients taking long-acting insulin in the evening are recommended to take 80% of their usual dose the night prior to surgery; if patients take this medication in the morning they should take 50% of their usual dose on the morning of surgery; patients on insulin should check their blood glucose at home prior to arriving to the hospital and treat hypoglycemia with clear juice or Gatorade; only recommend the administration of short-acting insulin at half the usual correction dose when the blood glucose is above 200; patients who have treated either a glucose below 80 or above 200 should recheck their glucose after treatment, within the hour

Chronic pulmonary disease: surgery should be postponed if recent exacerbation, infection, or hospitalization

Pneumonia: surgery should be postponed for at least 1 month following exacerbation or pneumonia; consult pulmonologist in order to determine if patient is an acceptable candidate for surgery; most recent chest X-ray and pulmonary function tests should be evaluated; consider repeating them; patients should continue medications perioperatively

Malignant hyperthermia: identify patients with a family or personal history of malignant hyperthermia; schedule these patients as first case, as safe preparation of the room is time-consuming and results in case delays when performed later in the day; the presence of a malignant hyperthermia cart and adequate dantrolene should be readily available; list volatile anesthetics and succinylcholine as allergies in patient's chart

Volatiles and succinylcholine: avoid in patients with muscular dystrophy, King-Denborough syndrome, multiminicore disease, central core disease, and hypokalemic or hyperkalemic periodic paralysis

History of anaphylaxis under anesthesia: allergist should test for allergic reactions to medications prior to scheduled procedure; at a minimum, the triggering anesthetic record should be obtained and interpreted and those classes of medications avoided; antibiotics, neuromuscular blocking drugs, and latex are the most common offenders along with chlorhexidine gluconate (ChloraPrep) and iodine; recommend pre-medication with steroids, H1 and H2 blockers before induction

Smokers: counsel to quit; smoking interferes with wound and bone healing; smokers who quit smoking prior to surgery are more likely to stay long-term non-smokers than those who quit at other times; smoking cessation 6 or more weeks prior to surgery is ideal; shorter cessation may lead to more reactive airways in patients receiving general anesthesia, but this is not associated with long-term morbidity; smoking cessation should always be encouraged

Alcohol or substance abuse disorders: all patients can be screened with simple screening questions

- Alcohol abuse: an accurate assessment of daily intake is important to identify patients at risk of withdrawal during hospitalization; patients should be assessed for malnutrition, neurologic deficits, ascites, and cardiac disease; preoperative hemoglobin, albumin, liver function tests, glucose, electrolytes, and prothrombin time may be indicated; an ECG should be obtained and chest x-ray if findings are significant on examination
- Abuse of other substances: places the patient at an increased risk under anesthetic and also for a withdrawal syndrome; cocaine or methamphetamines can result in arrhythmia or MI during an anesthetic; a screening ECG in patients with recent use may be indicated; heroin and opioid abusers are at risk for severe postoperative pain; kratom, an unregulated herbal medication that acts on opiate receptors can have same effect; former addicts on buprenorphine are at a high risk for severe postoperative pain; recommend patients on high-dose buprenorphine to titrate to a dose of 8 milligrams a day preoperatively to allow some opiate receptors to be unoccupied; these patients will require high-dose narcotics and a multimodal analgesic for pain control; consultation with pain specialist is advised

Chronic pain: patients are at increased risk for severe post-operative pain and unanticipated admission; if able to decrease their total daily opioid consumption, postoperative pain is better able to be controlled than those who do not decrease their opioid consumption; chronic patients on high-dose buprenorphine should also reduce dosage for 3 days prior to surgery whenever possible

Patients on psychotropic agents: should not interrupt therapy without consultation with prescriber; risk of relapse often supersedes the potential risk of interactions with perioperative medications; anesthesiologists should modify their medications in order to avoid interactions; patients on serotonin-specific reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and MAOIs have increased risk for serotonin syndrome — avoid methylene blue, tramadol, and meperidine; patients taking TCAs have increased risk of confusion with scopolamine and atropine and arrhythmias when given epinephrine and norepinephrine; if patients on MAOIs given ephedrine can lead to hypertensive crisis; lithium and valproate can lead to chronic renal and thyroid impairment; careful history should be taken and lab testing considered; antipsychotics can increase sedation, are associated with neuroleptic malignant syndrome, and can lead to hypotension and QTc prolongation; continue anxiolytics as discontinuation associated with withdrawal syndrome; stimulants can increase risk of arrhythmias and anesthetic requirements and should be held the morning of anesthesia; hold 24 hours for long-acting formulations

Herbal supplements: can lead to interactions with anesthesia or an increased bleeding risk; recommend patients to hold all of these medications for 7 days; depending on half-life, shorter cessation periods may be acceptable; relevant supplements include ephedra, fish oil, garlic, gingko, ginseng, kava, ma-huang, and St. John's wort; patients on long-term valerian should taper over 2 weeks to avoid withdrawal syndrome

Suggested Reading

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Monitoring During Anesthesia: Part 1

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Overview of patient and equipment monitoring: critical component of anesthesia care during surgical and nonsurgical procedures; allow for titrating of anesthetics during cases, understanding of physiologic changes in patient's condition, and interventions which ensure patients remain safe, comfortable, and free from harm; *American Society of Anesthesiologists (ASA)* — establishes standards for patient monitoring during anesthesia; initial set of standards adopted in October 1986 have been continuously revised and updated (with most recent amendments made in 2010)

Monitoring devices: "standard ASA monitors" refers to basic physiologic monitors which include pulse oximetry, electrocardiography (ECG), noninvasive blood pressure (BP) device monitoring, and temperature monitoring (when clinically significant changes in body temperature are expected); additionally, quantitative monitoring of volume of expired gas is strongly recommended by ASA

Continual vs continuous monitoring: ASA standards define continual monitoring as measurements repeated regularly and frequently in steady and rapid succession; it is important to differentiate this from continuous monitoring, wherein monitoring is prolonged without interruption (as in, *eg*, an electrocardiography [EKG] monitor); note that neither of these forms of monitoring can supplant the role of a clinician during anesthesia, who maintains constant vigilance over the patient; monitoring devices cannot replace clinical observation; clinical monitoring should include observation of patient, palpation, inspection, and auscultation to determine state of patient

Cardiac Function Monitoring

Overview of ECG: should be monitored continuously during surgical procedures and anesthesia; represents a reliable way to understand a patient's heart rate, rhythm, and cardiac conduction system

ECG systems: standard 12-lead ECG (used in other hospital settings) is impractical in operating room (OR), where 5-lead ECG monitoring is typically utilized; 5-lead monitoring is preferable to 3-lead as it allows the display of 2 channels simultaneously, and provides improved sensitivity for detection of cardiac ischemia during surgical case; *5-electrode ECG* — allows monitoring of 7 leads (1, 2, 3, augmented Vector Right [aVR], augmented Vector Left [aVL], augmented Vector Foot [aVF], plus a single precordial lead); a particular precordial lead can be selected by placing the precordial electrode in any position from V1 to V6; most physiologic monitoring systems display multiple leads simultaneously, and most practitioners typically choose to display leads 2 and V5; *3-lead ECG monitoring* — limited form of ECG used to monitor heart rate and detect P waves or ventricular fibrillation (VFib); insufficient for understanding if patient is having more complex conduction system abnormality or arrhythmia (due to lack of a true V1 lead)

Ischemia detection: requires monitoring of >1 lead; if ischemia is suspected based on 5-lead monitoring, printout of an ECG trace can help provide confirmation (and is possible with most systems in hospitals today); this printout is helpful as it contains a grid that allows for detailed analysis of cardiac rhythm; in high-risk patients, it is recommended to obtain a baseline EKG strip before induction of anesthesia (in order to compare their baseline rhythm to rhythms detected during a surgical case)

Detecting ischemic changes via ECG: lead 2 is typically used for rhythm detection, since P waves are most obvious and upright in lead 2; *ST-segment analysis* — important because most intraoperative ischemia is manifested by ST depression, which is most obvious in lead 5

Important sources of ECG artifacts during anesthesia: electrodes coming out of contact with skin (particularly if patient is moved, skin is inadequately prepared, and cleansing solution, irrigant, or blood gets underneath the lead); EKG baseline can move due to changes in body position or patient movement (caused by, eg, shivering or respiration); ECG tracing may be lost during use of electrosurgery (this type of interference can typically be minimized by placing grounding pad of electrosurgical unit on patient's leg [if appropriate]); electrical interference from other devices in the operating room can also impact EKG traces (this can be minimized by plugging devices into outlets farther away from monintors, or using separate electrical circuit)

Pulse Oximetry

Overview of pulse oximetry (PO): quantitative method of understanding a patient's level of oxygenation during surgical procedures; recommended for every patient undergoing anesthesia; in cases where it is not possible to attach a PO monitor to an uncooperative patient, attach the monitor as soon as they lose consciousness; most clinically available POs display plethysmography (*ie*, "pleth"

waveforms), which is extremely helpful for verifying placement of probes and obtaining an adequate signal

Utility of PO data: the waveforms generated by plethysmography provide additional clinical information beyond values related to oxygenation (*eg*, changes in perfusion index); this potentially includes changes in the patient's fluid responsiveness, which can be indicated by changes in pulse volume on pleth tracing

Important note about PO and respiration: respiratory variation in typically not visible in POs, and represents a late indicator of massive hypovolemia

Mechanics of PO: advent of PO revolutionized monitoring of patients during anesthesia by providing continuous measurements of arterial hemoglobin oxygenation levels; this is possible because oxygenated and deoxygenated hemoglobin absorb light differently at most wavelengths (including 660 nm and 960 nm wavelengths examined by most PO devices today); use of the Beer-Lambert law allows POs to calculate the concentration of each species of light from the absorption of light at those wavelengths; the ratio of absorption is processed by the PO device to give a percentage of hemoglobin saturated by oxygen (*ie*, fractional saturation); most sensors have ≥2 light emitting diodes (LED; at 960 nm and 660 nm wavelengths) inside their light detector; this sensor can be applied to the finger, toe, earlobe, or tongue (and possibly to the nose or forehead with some special probes)

Interpreting PO readings: in healthy adults, normal arterial oxygen saturation (*ie*, SpO2) values range from 96% to 99%; an SpO2 of >88% may be acceptable in patients with lung disease; PO devices report SpO2 values via audible pitches, which allow clinicians to know a patient's relative level of oxygenation without viewing a monitor; monitors also typically sound alarms when saturations fall below user-specified levels

Limitations of PO: relatively late reporter of inadequate gas exchange (since most modern PO devices impose ~10 sec delay between physiologic changes and SpO2 value displayed on its monitor); oxyhemoglobin dissociation curve can also shift, and thus change the patient's partial pressure of arterial oxygen (PaO2) without changing their SpO2

Factors affecting reliability: use of methylene blue, indocyanine green, indigo carmine, and isosulfan blue injections during surgical procedures (transiently cause falsely low SpO2 readings); low perfusion (due to, *eg*, inflation of a proximal BP cuff, cardiac arrest, increased systemic vascular resistance); severe anemia (*ie*, hematocrit of <25%) decreases SpO2 readings and their reliability, while SpO2 readings are almost entirely unreliable in a patient with a hematocrit of <10%

Complications of PO: although rare, LEDs in the PO's sensor can cause burns, pressure sores, or pressure necrosis; always examine the PO sensor relatively frequently during surgical cases, and as device is removed after procedure

Hemoglobinopathies: presence of carboxyhemoglobin can falsely raise SpO2 readings, while methemoglobin can falsely lower SpO2; this results from carboxyhemoglobin's resemblance to oxyhemoglobin at 660 nm wavelengths (which thus raises the apparent percentage of total oxygenated hemoglobin); by extension, methemoglobin resembles deoxyhemoglobin at 660 nm wavelengths (thereby lowering the apparent fraction of deoxygenated hemoglobin); *carbon monoxide (CO)-oximeters* — incorporate sensors that use ≥4 wavelengths of light in order to distinguish varieties of hemoglobin species (and thus more accurately calculate fractional saturation); clinically available for use in OR settings

End-Tidal Carbon Dioxide Monitoring

Overview of end-tidal carbon dioxide ($ETCO_2$) monitoring: method of assessing ventilation via end-tidal measurement of captured carbon dioxide (CO_2) and spirometry; capnography and capnometry are often used as synonyms, since they both involve analysis and reporting of CO_2; *capnography* — includes waveform readings; confirms endotracheal tube intubation, and is diagnostic for certain pathological conditions (in addition to evaluating respiration)

Mechanics of $ETCO_2$ monitoring: measurement of CO_2 is frequently based on its absorption of infrared light (due to its molecular structure); $ETCO_2$ can be continuously measured in real time in order to produce a waveform; CO_2 can be measured at a breathing circuit, or via aspiration of gas samples at the capnography device (*ie*, sidestream capnography)

Plotting expired CO_2 in the OR: *time-based capnography* — plots $ETCO_2$ on y-axis, and time on x-axis; *volume-based capnography* — allow calculation of cardiac output, anatomic dead-space volume, physiologic dead-space fraction, exhaled CO_2 volume, and the patient's metabolic rate (if the volume of CO_2 they produce over time [VCO_2] is known); in contrast to time-based capnography, volume-based capnography plots $ETCO_2$ on y-axis and volume on x-axis; typically, $ETCO_2$ is approximately 2 to 5 millimeters of mercury (mmHg) lower than actual partial pressure of CO_2 ($PaCO_2$), due to dead space in patients and breathing systems; therefore, the ideal range for $ETCO_2$ during general anesthesia is typically 30 to 40 mmHg

Causes of high $ETCO_2$ readings: rapid rise can represent an early sign of malignant hyperthermia (especially if the rapid rise is unresponsive to hyperventilation); general increases in delivery or production may also occur due to fevers, sepsis, seizures, increased metabolic rates, and increased skeletal muscle activity; *iatrogenic causes* — bicarbonate administration; CO_2 infused during laparoscopic surgery; clamp or tourniquet release; *hypoventilation* — associated with chronic obstructive pulmonary disease (COPD), use of neuromuscular paralysis, metabolic alkalosis (if the patient is spontaneously breathing), and some medication side effects; *associated mechanical equipment problems* — exhaustion of device's CO_2 absorbent; ventilator leak; rebreathing; malfunctioning inspiratory or expiratory valve on anesthesia machine

Causes of low $ETCO_2$ readings: decreased CO_2 delivery or production associated with hypothermia, hypometabolism, pulmonary hypoperfusion, low cardiac output or arrest, pulmonary artery embolism, hemorrhage, hypotension, hypovolemia, ventilation/perfusion (*ie*, V/Q) mismatch or shunt, some medication side effects, and periods of hyperventilation; *associated mechanical equipment problems* — ventilator disconnection; esophageal intubation; bronchial intubation; complete airway obstruction or apnea; kinked sample line; leaking endotracheal tube or laryngeal mask airway

Newer anesthesia machines: provide helpful capabilities to continuously monitor inspiratory and expiratory volumes, pressures, and flow; also display pressure-volume loops and flow-volume loops

Endotracheal intubation: $ETCO_2$ is regarded as incredibly valuable for confirming proper endotracheal intubation; however, inadvertent esophageal intubation may result in CO_2 return detected by an $ETCO_2$ (due to swallowed gas), and thus produce readings normally indicative of endotracheal intubation; however, these misleading $ETCO_2$ readings typically diminish to zero after a few breaths if the patient's endotracheal tube is incorrectly placed

Blood Pressure Monitoring

Overview of cardiovascular monitoring: ASA standards indicate BP and heart rate should be measured every ≥5 min during case (or more frequently as indicated); in practice, heart rate is typically measured continuously (via ECG and PO monitors); unless BP is continuously monitored via placement of arterial line, it is typically measured every 3 to 5 min via noninvasive monitoring

Significance of arterial BP: used as surrogate measure of blood flow in organ perfusion; comprised of resistance and flow; blood supply to organ may be low despite adequate BP, due to high resistance; individual organs manifest various degrees of autoregulation, which allows for local changes in resistance to maintain constant blood flow

Systolic and diastolic BPs: measured using variety of different approaches; pressure created by contracting heart corresponds to systolic pressure; pressure during relaxation of heart corresponds to diastolic pressure; *mean arterial BP* — average arterial BP during systole and diastole; can be approximately calculated by multiplying diastolic BP times 2, adding systolic BP to that value, and dividing final number by 3; directly measured, or calculated from systolic and diastolic BP values

Methods of measuring BP: manual; noninvasive; Doppler ultrasonography; arterial measurement of BP

Manual measurement of BP: directly measures systolic and diastolic BP via auscultation of Korotkoff sounds; occlusive cuff contains bladder attached to tube; air is entrained through this tube via inflation bulb until desired pressure is produced; pressure is often measured via manometer; *basic steps* — stethoscope is placed over occluded artery while occlusive cuff is inflated above systolic pressure; the cuff is slowly deflated by 3 to 5 mmHg every second while auscultating for blood flow; the first sound of blood flow corresponds to systolic BP, while the point at which sounds diminish reveals diastolic BP; auscultation via stethoscope detects Korotkoff sounds

Automated noninvasive BP (NIBP): most common method of measuring noninvasive BP during anesthesia; BP cuff is inflated to preset point (often 150 mmHg, or 40 mmHg above previous measurement), and incrementally deflated while transducer senses pressure oscillation in cuff (with accuracy of approximately plus or minus 2%); directly measures mean arterial BP (which correlates to point of maximal oscillation amplitude, and allows estimation of systolic and diastolic pressures via algorithm); more specifically, systolic BP is interpreted as initial detection of rising oscillation, while diastolic BP is interpreted as initial detection of falling oscillation; *benefits* — allows passive participation by clinician in OR; limits interpretative rule of clinician to reading results

Ensuring accurate readings: *selecting appropriate BP cuff* — extremely important; width of cuff's inflatable bladder should be ~40% of upper arm circumference (roughly 12-14 cm in average adult); length of inflatable bladder should be ~80% of upper arm circumference; *manometer recalibration* — must be performed periodically before use; *issues related to cuff size* — overly small cuffs may result in falsely high BP reading, whereas overly large cuffs may result in falsely low BP readings; cuff width should cover two-thirds of upper arm or thigh

Limitations of oscillometric BP monitoring: *motion artifacts* –can result in erroneous values, or prevents devices from giving any value (which delays accurate measurement); *venous congestion, bruising at site of cuff application, and limb ischemia* — can result from frequent BP measurements during rapid or large BP fluctuations; prevented via fast inflation and slow deflation times; *consistency issues* — different manufacturers of NIBP monitors give slightly different recordings of BPs, since nonstandard algorithms are used in estimating NIBP from oscillometric waveform to derive systolic, diastolic, and mean arterial BP values

Measurement of BP via Doppler ultrasonography and direct palpation: ie, use of ultrasound or touch (respectively) in conjunction with inflatable cuff to estimate BP; systolic pressure corresponds to point during cuff deflation at which first pulse is palpated or Korotkoff sounds are heard; therefore, these methods entail placing BP cuff proximal to artery of interest, and inflating cuff until pulse is occluded; afterward, the cuff is gradually deflated until pulse can be appreciated again; palpation can also determine approximate systolic BP, based on whether pulse may be palpated at key points (*eg*, pulse at radial artery signifies systolic BP of ~80 mmHg, femoral artery signifies ~60 mmHg, carotid artery signifies ~50 mmHg); although palpation allows estimation of BP in extreme hypotension, it cannot determine diastolic or mean BP and is limited by issues associated with auscultation methods

Doppler mechanism: ultrasound waves travel through patient's tissue, into flowing blood within artery, and back to probe; movement of blood creates frequency shift, which is transduced by probe and aurally appreciated; change between transmitted and reflected frequency produces audible sound of pulsation; use coupling gel (placed between probe and skin) to minimize air interference

Invasive arterial BP monitoring: gold standard of BP monitoring during anesthesia; most accurate form of BP monitoring; arterial cannulation allows continuous beat-to-beat monitoring of patient's BP during anesthesia; also provides site for obtaining serial lab measurements of oxygenation, ventilation, serum pH, lactate levels, base deficits, electrolyte levels, and hemoglobin

General indications: current or predicted hemodynamic instability; prolonged surgical procedure involving major fluid shifts or significant blood loss; use of vasoactive drugs which require monitoring; need for frequent blood gas measurements; severe obesity; burnt extremities; shock

Cannulation sites: radial or femoral arteries are most commonly used; others options include brachial artery,

axillary artery, and dorsalis pedis artery; while axillary or brachial arterial catheterization is feasible, use of these sites is associated with increased risk of extremity ischemia (due to their necessity as end arteries); choice of artery depends on ability to palpate pulse or locate artery with ultrasonography; *preventing complications* — assessing collateral circulation is prudent when cannulating small arteries (*eg*, radial or dorsalis pedis); however, the Allen test has not shown to be reliability when evaluating collateral circulation in hands; it is therefore important to frequently assess extremities distal to catheter placement both before and after insertion, and to remove catheter immediately with any evidence of ischemia

Contraindications to arterial cannulation: *absolute contraindications* — localized infection at insertion site; preexisting ischemia; nerve damage; Raynaud's phenomenon; traumatic insertion proximal to site of insertion; *relative contraindications* — failure to demonstrate collateral flow in targeted small vessels; presence of arteriovenous fistula in targeted limb; history of surgery disrupting lymphatics of targeted limb (*eg*, axillary lymphadenectomy); if no other arterial sites can be used, these relative contraindications may be outweighed by other considerations relating to the need for invasive arterial BP monitoring

Transducer height: important consideration; *invasive arterial BP monitoring* — height should be level with right atrium; *monitoring cerebral perfusion pressure* — transducer height should be level with tragus of earlobe

Damped tracing: the arterial catheter itself, noncompliant tubing, and 3-way stopcocks can all dampen pressure between the artery and transducer (which provides BP measurement); addressed by reducing any unnecessary length of tubing or extra stopcocks; may also result from air bubble or clot in arterial catheter; however, these occlusions cause characteristic tracing (*ie*, decrease in displayed systolic pressure and falsely narrowed pulse pressure despite accurate mean pressure readings; removal of air or flushing catheter often resolves damping (although in some cases the catheter may require replacement)

Temperature Monitoring

Overview of temperature monitoring: measured intermittently or continuously; external methods of temperature determination are limited in that they do not reflect core patient body temperature (especially in patients exhibiting vasoconstriction); although ASA standards do not require temperature measurement with all anesthetics, it is important to recognize that every anesthetized patient is prone to temperature perturbations

Temperature changes associated with anesthesia: can result from surgical site exposure, cold ORs, long surgical durations, vasodilation, hypothalamic thermoregulatory inhibition [caused by anesthetics], mechanical ventilation, and high gas flows through endotracheal tubes; additionally, evaporation, radiation, convection, and conduction all draw heat away from patients in OR over time

Important considerations: ability to measure temperature is desirable for any procedures which require control of body temperature (*eg*, induced hypothermia and rewarming), or when warming devices are used prophylactically; infants and small children are particularly prone to thermolability, due to their high surface area to volume ratio (and thus typically require temperature measurement more often than adults); *hypothermia* — seen in adults subjected to large evaporative losses or low ambient temperatures (which can occur with exposed body cavity, large volume transfusion of non-warmed fluid, or burn injury)

Indications for temperature monitoring: febrile patients (due to risk for hyperthermia or hypothermia); autonomic dysfunction (since they are unable to autoregulate body temperature); trauma patients (especially those exposed to elements for prolonged durations); ensure that temperature monitoring is always readily available in case of malignant hyperthermia (a rare but always possible pharmacogenetic complication)

Temperature probes: classified as thermistors and thermocouples (both of which are disposable sensors); *thermistor* — semiconductor that undergoes linear and predictable decrease in resistance with increasing temperature (*eg*, nasopharyngeal probe); *thermocouple* — utilizes Seebeck effect to monitor patient; device made of 2 dissimilar metals connected to one another (with one end maintained at constant reference temperature and opposite end exposed to patients); differences in temperatures between these 2 metals cause differences in their potentials, which are mathematically correlated in nonlinear fashion and allow probe to function; *tympanic thermometers* — depend on infrared radiation and thermocoupling; infrared radiation from eardrum is sensed by thermocouples within the thermometer, producing differences in potential (which are correlated in nonlinear way to eardrum temperature)

Measuring from skin: when measuring temperature using color-changing liquid crystal strip on forehead, readings are typically 3 to 4 °F below core body temperature; gradient between skin and core temperature can increase with further cooling of patient; as such, skin-based readings represent relatively poor measurements of temperature and should not be used on patient with facial burns; furthermore, skin temperature measurers are typically slow to display changes in temperature, and can be heavily influenced by environmental factors in OR (*eg*, gust of air from heating or cooling vent)

Measuring at axilla: common site for noninvasive temperature determination; typically 1 °F below body temperature; readings can be taken with nasopharyngeal probe (or similar sensor) placed at axillary artery with arm adducted; site is somewhat prone to measurement error (such as when, eg, probe dislodges)

Measuring at tympanic membrane: temperature measurements near eardrum correlate well with core temperature; requires caution, since it is possible to perforate tympanic membrane with probe

Measuring rectal temperature: changes in rectal temperature readings lag behind core body temperature (this phenomenon is often noted during rewarming after hypothermia, and indicates slower peripheral rewarming); accidental placement of probe into stool further increases this lag time

Measuring nasopharyngeal temperature: monitors temperature of posterior nasopharynx and reflects temperature in brain; measurement performed by measuring distance from external meatus of ear to external nares, and inserting temperature probe to that distance;

may be associated with epistaxis in coagulopathic or pregnant patients, and sometimes leads to skin necrosis (if probe is allowed to press on nares during longer surgical procedure); typically discouraged in patient with head trauma or cerebrospinal fluid rhinorrhea

Esophageal temperature: monitoring reflects core temperature well; probe should be located at lower third of esophagus (behind level of heart); probes are rarely misplaced into airway

Blood and bladder temperature: measurements obtained using thermistor of pulmonary artery catheter

Conclusion: hallmark of anesthesiology is providing patients with pain relief, comfort, and safety during surgical procedures; imparting safety to anesthetized patient requires vigilance, continuous observation, and monitoring of patient; anesthesiologist are responsible for adequate monitoring of oxygenation, respiration, and end-organ perfusion to patients, in order to prevent any adverse harm during surgical procedures

Suggested Reading

Standards for Basic Anesthetic Monitoring. Committee of origin: standards and practice parameters (approved by the ASA House of Delegates on October 21, 1986, last amended on October 20, 2010, and last affirmed on October 28, 2016). https://www.asahq.org/~/media/Sites/ASAHQ/Files/Public/Resources/standards-guidelines/standards-for-basic-anesthetic-monitoring.pdf; **Bartels K, Esper SA, Thiele RH**. Blood pressure monitoring for the anesthesiologist. *Anesth Analg*. 2016;122(6):1866-79; **Francis J**. ECG monitoring leads and special leads. *Indian Pacing Electrophysiol J*. 2016;16(3):92-5; **Shafer SL, Dexter F, Brull SJ**. Deadly heat. *Anesth Analg*. 2014;119(6):1235-7; **Tautz TJ, Urwyler A, Antognini JF**. Case scenario: increased end-tidal carbon dioxide. *Anesthesiology*. 2010;112(2):440-6; **Tusman G, Bohm SH, Suarez-Sipmann F**. Advanced uses of pulse oximetry for monitoring mechanically ventilated patients. *Anesth Analg*. 2017;124(1):62-71.

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Monitoring During Anesthesia: Part 2

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Overview: use of central venous pressure monitoring, pulmonary artery catheters, mixed venous oxygen saturation monitoring, principles of cardiac output monitoring, echocardiography, blood gas and acid-base monitoring, brain function monitors, and evoked responses

Central venous pressure monitoring (CVP): invasive; continuous measurement of right heart pressures, reflects patient's volume status during surgical procedure; central venous catheters provide venous access for rapid infusion of fluids and/or vasoactive drugs; normal CVP during positive pressure ventilation ranges from 6 mm Hg to 12 mm Hg; low CVP with hypotension and tachycardia corresponds to hypovolemic state; persistent hypotension after fluid challenge and higher-than-normal CVP indicates cardiac congestion, which can occur with tension pneumothorax, myocardial ischemia, or cardiac tamponade; collection of blood from the superior vena cava allows central venous blood oxygenation measurements that can be indirect marker of global tissue perfusion and oxygenation

- Indications: assess volume status; CVP can be helpful when adequate access to peripheral IV not possible; when drugs toxic to peripheral veins (*eg*, concentrated vasoactive drugs, hyperalimentation, certain antibiotics); for rapid infusion of fluids through a large cannula as in trauma patient, or if surgery expected to have significant blood loss; aspiration of venous air emboli, such as during sitting craniotomy or other surgery associated with high risk of venous air embolus; if need for frequent blood sampling for laboratory measurements, transvenous cardiac pacing, temporary hemodialysis line; or to introduce pulmonary artery catheter
- CVP placement: common sites include subclavian, internal jugular and femoral veins; external jugular vein used if large enough in given patient; long-arm CVP catheters can be passed from the brachial or cephalic vein into central circulation; portable ultrasound vessel imaging used to visualize vascular device structures to reduce number of cannulation attempts and risk of inadvertent arterial puncture
- Types of catheters: single-lumen catheters, multilumen catheters, and introducer sheaths; multilumen catheter used to administer medications or monitor CVP; introducer sheaths used when larger catheter needed (*eg*, volume administration or insertion of pulmonary artery catheter)
- Complications: immediate complications include failure to successfully place line, bleeding, accidental puncture of artery, arrhythmias, air embolus, injury to thoracic duct, malposition of catheter, or pneumothorax or hemothorax; delayed complications include catheter migration, catheter embolization, venous stasis, infection, venous thrombosis or pulmonary embolus, myocardial perforation, or nerve injury
- CVP waveform: CVP measured at junction of superior vena cava and right atrium; normal CVP waveform has 5 separate components containing 3 peaks (a wave, c wave, v wave) and 2 descents (x descent and y descent); a wave represents end of diastole and occurs with atrial contraction; c wave represents early systole and occurs with tricuspid valve bulging; v wave represents late systole and occurs with systolic filling of atrium; x descent represents midsystole and corresponds to atrial relaxation; y descent represents early diastole and represents early ventricular filling; distinct CVP waveform patterns associated with certain physiologic states include loss of a waves (can occur with atrial fibrillation), cannon a waves (occur with junctional rhythm), regurgitant cv waves (occur with tricuspid regurgitation), prominent a waves (represent tricuspid stenosis or reduced right ventricular compliance)
- Conclusion: CVP monitoring not routinely used to guide intraoperative fluid replacement (relatively inaccurate measure of cardiac preload); central venous catheters provide intravascular access for administration of fluids and medications; catheter also placed to facilitate placement of pulmonary artery catheter

Pulmonary artery catheter (PAC): CVP can be used to approximate pulmonary capillary wedge pressure; PAC provides more accurate estimation of left heart pressures in circumstances such as left ventricular function impairment, significant valvular disease, pulmonary hypertension; PAC also used in severe coronary artery disease, shock, severe lung disease, severe renal disease, need to place temporary pacing wire via PAC, massive trauma, or any other circumstances that require continuous monitoring of pulmonary artery pressure; can be used to obtain blood samples for mixed venous oxygen saturation (can enable evaluation of body's oxygen balance by calculating oxygen consumption and delivery); specialized PACs available to enable continuous mixed venous oxygen monitoring

- Complications: all complications of central venous catheterization apply for placement of PAC; duration of catheterization poses additional risks even with optimally placed catheter; PAC should not be placed

beyond 72 hrs to 96 hrs; several reports of patients with severe anaphylactic reaction to latex in PAC balloon; latex allergy or sensitivity may be contraindication to PAC placement unless non-latex catheter available; no definitive evidence of improved survival with PAC use during anesthetic management; value dependent on attainment of accurate measurements and clinician's ability to appropriately interpret those measurements; clinician should determine whether information provided by catheter justifies risk associated with use; arrhythmias relatively common during PAC placement (~50% of PAC placements, typically when catheter in right ventricle); complete heart block or sustained ventricular tachycardia needs to be treated, but rare

Summary: PAC provides information about pulmonary artery pressures, cardiac output, mixed venous oxygen saturation, cardiac index, systemic vascular resistance, pulmonary vascular resistance, systemic vascular resistance index, pulmonary vascular resistance index, and pulmonary artery wedge pressures

Determination of cardiac output measurement using PAC

Thermodilution: measurement of cardiac output with PAC based on thermodilution; known volume of cold fluid injected into PAC at proximal point and resulting temperature change from cooling measured in bloodstream by thermistor; shape of the curve obtained by plotting temperature change against time provides cardiac output; low cardiac output associated with larger temperature change due to longer delay from time of injection until blood reaches thermistor, allowing more time for cooling effect; calculation of cardiac output using thermodilution depends on accurate representation of volume and temperature of fluid injected, thermodynamic properties of blood and solution injected, and interval of time-temperature curve; both patient and injectate factors significantly affect accuracy of cardiac output measurement via thermodilution, such as tricuspid regurgitation, intracardiac shunt, abnormal respiratory pattern, or dysrhythmia; factors related to injection solution include error in amount of fluid injected (or volume), rate of injection, and temperature of injectate solution

Fick principle: used to estimate cardiac output; states that, under steady state conditions, amount of oxygen consumed per unit time equals the arterial O_2 content minus venous O_2 content, multiplied by blood flow or cardiac output; PAC can measure O_2 consumption, arterial O_2 content, and venous O_2 content allowing cardiac output measurement using Fick principle

Limitations: PAC use for measurement and calculation of any hemodynamic variable based on assumptions that do not hold true under many clinical conditions (*eg*, pulmonary capillary wedge pressure just estimation of left ventricular end-diastolic pressure, and assumes equalization of diastolic pressures in the cardiac chambers when static column of fluid created by inflation of balloon in PAC into wedge position; that relationship does not hold true under certain conditions, such as mitral stenosis or regurgitation, or aortic regurgitation); another assumption, left ventricular end-diastolic pressure same as left ventricular end-diastolic volume, does not hold true in certain clinical conditions (*eg*, if decreased compliance of left ventriculum, as in diastolic dysfunction; increased intrathoracic pressure or ventricular interdependence, such as with right ventricular dilation)

Less-invasive approaches to measure cardiac output: esophageal Doppler, indirect Fick partial rebreathing method, transpulmonary thermodilution, lithium dilution cardiac output, arterial pulse contour analysis, and echocardiography

Esophageal Doppler technique: based on concept that flow in cylinder equal to cross-sectional area of cylinder, multiplied by velocity of fluid flowing through cylinder; placement of thin ultrasound probe into esophagus allows measurement of sound waves transmitted towards descending aorta; frequency of sound waves changes as blood goes through aorta due to Doppler effect; Doppler effect states that frequency of sound waves emitted by moving object (patient's blood) altered proportionately to relative velocity between object and observer (ultrasound probe); since change in frequency, or Doppler shift, proportional to velocity of blood flow, aortic blood flow velocity can be measured and used to estimate stroke volume and to get measure of cardiac output with nomogram

Advantages: relatively noninvasive; provides continuous monitoring of cardiac output once PAC properly placed and patient's variables entered into computer algorithm

Limitations: estimated cardiac output based only on blood flow in descending thoracic aorta, and does not include cardiac output in upper part of body; blood flow measurements may not be accurate if turbulent aortic blood flow, as in tachycardia or aortic stenosis; ultrasound placement in esophagus contraindicated in patients with esophageal disease or severe coagulopathy

Indirect Fick partial rebreathing method: noninvasive cardiac output (NICO) device uses this technique to monitor pulmonary artery blood flow by applying Fick equation to lungs; because blood pumped out of heart (cardiac output) goes through lungs, measurement of pulmonary blood flow can be measurement of cardiac output; NICO uses partial CO_2 rebreathing technique in algorithm to calculate pulmonary blood flow that allows measurement of cardiac output

Advantage: relatively noninvasive, except patient must first be intubated

Limitations: algorithms used to calculate cardiac output make some assumptions that hold true under stable conditions, but probably not under rapidly changing conditions, such as in surgical patient undergoing anesthesia (*eg*, changes in CO_2 production that occur during period of ischemia and reperfusion, as with tourniquet use or clamping of artery, can lead to inaccurate measurements of cardiac output)

Transpulmonary thermodilution: arterial thermodilution from near central artery (in contrast to pulmonary artery) gives measurement of stroke volume and cardiac output; requires central venous catheter and near centrally placed arterial catheter (*eg*, femoral, axillary, or brachial); relatively invasive but less so than placement of PAC

Procedure: cold indicator fluid injected into central venous catheter, and temperature of blood mixed with cold indicator measured at arterial catheter that has thermistor at tip; unlike PAC, transpulmonary thermodilution does not allow measurement of

pulmonary artery pressures or pulmonary capillary wedge pressures, so cannot discriminate between left and right heart function

- Lithium dilution cardiac output (LiDCO): uses lithium dilution instead of thermodilution to measure cardiac output; bolus of lithium indicator solution injected intravenously mixes with patient's blood and resulting lithium concentration-time curve recorded by sensor connected to patient's arterial catheter; analysis of lithium dilution curve enables calculation of cardiac output using nomogram
  - Advantage: central venous catheter not necessary
  - Limitations: sensor outside artery and requires withdrawal of blood sample with each measurement; inaccurate in patients receiving lithium therapy or muscle relaxants
- Arterial pulse contour analysis: during systole, blood pressure increases because of ejection of blood from ventricles; arterial pulse contour analysis based on assumption that systolic part of arterial pressure wave proportional to stroke volume; beat-to-beat analysis of this waveform, or pulse contour, can be used to estimate patient's stroke volume and cardiac output; stroke volume at any given time for given patient influenced by compliance of patient's aorta; pulse contour analysis needs to be calibrated to compensate for effect of aortic compliance on stroke volume and cardiac output; most commercially available devices allow for external calibration by manual injection of indicator solution prior to use
- Echocardiography: transthoracic echocardiography least-invasive way of imaging cardiac structures; involves placement of ultrasound probe over chest; however access to the chest can be fairly limited during many surgical procedures, making it difficult to get adequate image of patient; also challenging in obese or mechanically ventilated patients; transesophageal echocardiography requires placement of ultrasound probe into esophagus or stomach, so more invasive than transthoracic echocardiogram but less invasive than many other monitors for measuring cardiac output; transesophageal echocardiographic measurements of cardiac output correlate well with thermodilution measurements
  - Advantages: transthoracic echocardiogram minimally invasive; low incidence of procedure-related complications; allows observation of frequent changes in cardiac status in real time; fairly accurate detection of hypovolemia, left ventricular dysfunction, and ischemia along with cardiac output

Blood gas and acid-base status monitoring: arterial blood gas test used to measure O_2 tension in the blood, CO_2 tension, acidity or pH, oxyhemoglobin saturation, and bicarbonate in arterial blood; many blood gas analyzers available in hospitals can also measure methemoglobin, carboxyhemoglobin, and hemoglobin levels; growing number of available point-of-care testing devices that measure many of these parameters and others; devices that measure acid-base status and blood gas measurements in humans typically use common analytical principles such as potentiometry, amperometry, and optical methods

- Potentiometry: measurement of electrical potential difference between two electrodes in electrochemical cell; one electrode serves as reference, other electrode ion specific; ion-specific electrode has membrane that attracts ion, creating potential difference; potential difference logarithmically proportional to electrolyte concentration; potentiometry typically used to measure pH, pCO_2, sodium, calcium, chloride, potassium, and magnesium
- Amperometry: measurement of electrical current flow through electrochemical sensor circuit when constant potential applied to electrodes; electrochemical sensor consists of anode and cathode surrounded by selectively permeable membrane that prevents entry of proteins and other oxidants; applying sample to device allows diffusion of substrates and analyte through semiporous membrane, resulting in oxidation-reduction reaction and formation of current under electric potential applied; amplitude of current proportional to substrate level in cell; amperometry typically used to measure PO_2, BUN, glucose, lactate, creatinine, and ketones in blood
- Optical technologies: include optical reflectance, absorbance, fluorescence, and multilength spectrophotometry (used for cooximetry testing); optical reflectance and absorbance measure change in color between absorbed light or reflected light; when analyte oxidized, electrons generated oxidize dye to create color, with intensity proportional to concentration of analyte; device measures reflectance or absorbance of known incident wavelength of light; optical reflectance is typically used to measure glucose, PO_2, pCO_2, and pH
- Sources of error in measurement of blood gas or acid-base status: gas diffusion through arterial blood gas plastic syringe and consumption of O_2 are potential sources of error that can give falsely low PaO_2 measurements, particularly when sample at room temperature for prolonged period; heparin in syringe for arterial blood gas measurement; heparin itself can be acidic and can also dilute the $PaCO_2$, yielding false low $PaCO_2$ reading; air bubbles in syringe that exceed 1% to 2% of blood volume can give false high PaO_2 and false low $PaCO_2$; adherence to good sample care can avoid most problems associated with inaccurate blood gas monitoring

Brain function monitors: intraoperative monitors that can record and process brain electrical activity, convert those waveforms and signals mathematically into continuous measure, typically scaled in commercially available devices from 0 to 100; can monitor spontaneous cortical electrical activity, evoked cortical and subcortical activity, and EMG activity from scalp muscles; typically designed to help reduce incidence of intraoperative awareness (when patient conscious during procedure performed under general anesthesia and has subsequent recall of those events); ideal brain function monitor would inform when patient too lightly anesthetized and has risk of awareness, and when patient unnecessarily deeply anesthetized and at risk of having prolonged recovery or other complications; works similarly across different patients regardless of anesthetic modality and medications being used; no ideal brain function monitor clinically available that meets all these criteria

- Relationship between electroencephalography (EEG) patterns and drug-induced changes in neuronal activity: EEG activity can be correlated with anesthetic depth to some degree; synaptic activity of cortical cells provides voltage change that can be detected by electrodes placed

on scalp; waveform patterns within certain frequency ranges correspond to different neurophysiologic processes; waveform patterns are grouped into frequency bands, most important being delta waves, beta waves, and gamma waves; *delta waves* — slowest frequencies, seen in deep sleep; *beta waves* — present in prefrontal regions of brain, normally seen during alert states, can increase during initial central nervous system depression due to disinhibitory effect; *gamma waves* — role in sensory processing and perception; recent evidence suggests that organized gamma-wave activity may be essential for consciousness and may be interrupted during anesthesia; in patient in sufficiently deep anesthetic state (typically with MAC value ≥1.5), EEG monitoring will demonstrate bilateral pattern of slow and mixed waves; pattern of high-amplitude activity (bursts) upon flat baseline (suppression) called burst suppression; burst-suppression ratio compares percentage duration of suppression and can be calculated with EEG monitor; burst suppression can be seen with brain-injured conditions, such as postischemic state; *2 examples of widely used brain function monitors* — BIS and SedLine; BIS technology based on empirically determined proprietary algorithm first approved by FDA in 1996; current versions of BIS use 4-channel EEG monitoring with 2 channels of information obtained from either side of forehead to allow for hemisphere comparisons; SedLine system uses disposable 5-electrode sensor placed on forehead that allows for 4-channel EEG system to measure patient's state

Limitations: raw EEG signals can be difficult to interpret; ongoing work to create more clinically easy-to-interpret brain function monitors; many factors impact ability of brain function monitor to provide clinically useful information, such as patient age, race, gender, low core body temperature, acid-base imbalance, low blood glucose, or certain drugs (*eg*, ketamine or neuromuscular blocking agent) or lack thereof that allows excess EMG activity to occur; such factors impact raw EEG data processed by brain function monitor and limit ability of signal to be useful or accurate; relatively weak concordance between various devices manufactured by different companies; *controversy around use of brain function monitors*- most recent practice advisory from the American Society of Anesthesiologists (ASA) states that general clinical applicability of these monitors in prevention of intraoperative awareness not established; ASA recommends intraoperative monitoring of depth of anesthesia aimed at minimizing occurrence of awareness should rely on multiple modalities, including checking for clinical signs such as purposeful or reflex movement, conventional monitoring systems, use of electrocardiogram, blood pressure, heart rate, and end-tidal anesthetic analyzer and capnography

Evoked potentials (evoked responses): based on concept that nervous system reacts to somatosensory, motor, and auditory stimuli by generating electrical signals called evoked potentials; somatosensory evoked potentials (SSEPs), motor evoked potentials (MEPs), or brainstem auditory evoked responses (BAERs) can all be monitored during surgery, which puts the brain, spinal cord or certain peripheral nerves at risk for damage or injury (typically from ischemia); common procedures where monitoring evoked potentials may be indicated include spinal fusion deformity surgery such as tethered cord surgery, scoliosis repair, spinal instrumentation or placement of hardware (*eg*, pedicle screws or rods), spinal tumor resection, spinal trauma or fracture repair, spinal vascular surgery, plexus surgery, peripheral nerve surgery, thoracoabdominal aortic aneurysm surgery, epilepsy surgery, brainstem or posterior fossa surgery, aneurysm repair, placement of aortic cross-clamp, carotid endarterectomy, cerebral tumor resection, cortical mapping or regional cortical function, probe localization during stereotactic neurosurgery, or facial nerve monitoring during acoustic neuroma resection; use of evoked potential monitor requires adequate exposure to certain areas of patient, certain equipment, and involvement of qualified person (usually trained technician) to perform monitoring

SSEPs: monitor function of posterior spinal cord sensory tracts and entail placing skin electrodes or needle electrodes over distal portion of peripheral nerve, and delivering stimulation to induce SSEP; common sites of measurement median or ulnar nerve at wrist, along with posterior tibial nerve at ankle, or peroneal nerve near head of fibula; during peripheral nerve stimulation with square wave signal of 0.2 msec to 2 msec, EEG activity measured with recording electrodes on scalp or areas near spinal cord or with cortical surface electrodes during neurosurgery; spontaneous EEG activity within brain typically ranges around 50 mV to 100 mV, while single SSEP significantly lower in amplitude, (typically 1 mV to 2 mV); repeated SSEPs can be delivered to upper- and lower-extremity nerves, and EP waves can be isolated and monitored from rest of EEG pattern through subtraction technique, often on contralateral side away from stimulus; evoked potential waveforms can then be averaged and plotted as voltage against time and contain amplitude, latency, and morphology; SSEPs typically demonstrate 3 positive and 3 negative peaks within waveform; latency simply measure of time between applied stimulus and associated evoked potential; *no set standard or consensus exists on what constitutes clinically significant change in SSEP* — ≥50% decrease in the peak amplitude of positive peaks, or loss of ≥1 of negative peaks, or both, or 10% increase in latency likely indicate damage to peripheral nerve, spinal cord, or false-positive test resulting from anesthesia or hypothermia; SSEPs very sensitive but not particularly specific, so not uncommon to observe false-positive SSEP changes; important to obtain baseline measures before anesthesia and before start of surgery for SSEP monitoring; site of stimulus and change important because can help localize potential damage to more specific area; *many anesthetic agents affect both EEG readings as well as SSEPs* — largest depressant effect seen at level of cortex vs small depressant effect seen at spinal or subcortical levels of brain; tailor anesthetic appropriately to minimize changes to SSEP monitoring; current understanding, all potent inhaled agents prolong SSEP latency and diminish SSEP amplitude in dose-dependent fashion; use of 60% N_2O will decrease SSEP amplitude but will not affect latency, while additive use of N_2O with potent inhalational agent can further decrease SSEP amplitude but will not increase latency more than that seen with use of potent agent alone; intravenous (IV) anesthetic agents typically affect SSEPs less than volatile agents, often

used in patients undergoing SSEP monitoring; IV agents have some impact; etomidate and ketamine typically increase SSEP amplitude while propofol, midazolam, and barbiturates have mild to moderate depressant effect on the SSEP amplitude; opioids have minor effect on SSEP amplitude

MEPs: measured to assess well-being of anterior spinal cord motor tracts, brainstem cranial nerves, and corticospinal tract during surgeries mentioned above; monitored by stimulating (often with multiple techniques in repetition) motor cortex, anterior spinal cord, or peripheral nerves with either electrical or transcranial magnetic signals; stimulating needle electrodes placed on the scalp and recording electrodes put on contracting muscle; muscle or motor nerve evoked potential then produced in response to stimulation; IV anesthetic agents preferred while monitoring MEPs (volatile anesthetics may depress motor neuron and cortical function); neuromuscular blocking drugs also affect MEPs and should be avoided

BAERs: monitored particularly during brainstem surgery, posterior fossa surgery, and surgeries involving the eighth cranial nerve (*eg*, acoustic neuroma removal surgery or facial nerve decompression); BAERs induced by placing earphones on patient and sending repeated clicking sounds to tympanic membrane repeatedly, evoking response through cranial nerve, brainstem, and auditory cortex; brainstem auditory evoked potential waves thus produced can be measured along with EEG activity through electrodes placed on vertex and earlobe; these can be processed and evaluated similarly to SSEPs at level of synapses between eighth cranial nerve through to auditory cortex

Complications: possible skin damage, pressure ischemia and burns at the placement sites with the use of any electrode; MEPS are contraindicated in any patient with retained intracranial metal, skull defect, postictal state, or after any other type of major cerebral insult

Suggested Reading

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Control of Body Temperature

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Body temperature: normally tightly regulated; efferent responses in humans include sweating, vasoconstriction, and shivering, each activated by core temperatures that exceed various thresholds; thresholds for sweating and vasoconstriction vary by only few tenths of degree (near 37°); temperatures >~37° activate sweating; temperatures <~37° activate vasoconstriction; range between sweating and vasoconstriction (interthreshold range) defines normal body temperature (temperatures that do not trigger thermoregulatory defenses); shivering last-resort response; shivering threshold full degree below vasoconstriction threshold (typically ~35.5°)

Thermoregulation during anesthesia: body temperature control changes markedly during anesthesia; true for most anesthetics or combinations of anesthetics, *eg*, volatile anesthetics, propofol, opioid; during anesthesia, interthreshold range increases from 10- to 20-fold because vasoconstriction and shivering thresholds decrease by 1°, 2°, or 3°; sweating threshold remains almost constant during anesthesia; consequently, interthreshold range increases from few tenths of degree to ~2 to ~3 degrees during anesthesia; patients respond to hypothermia, but only if they become cold enough (typically ~34.5 degrees)

Hypothermia: because body temperature not tightly regulated during anesthesia, patients become hypothermic in cool environment; occurs in 3 phases: initial rapid decrease in core temperature, typically lasting ~40 min and 1° to 1.5°; followed by slower, linear decrease in core temperature, typically lasting 2 to 3 hrs; patients who get cold enough have core temperature plateau, which only happens when patients reach ~34.5°; each phase of hypothermia curve has different cause; initial, rapid decrease in core temperature after induction of anesthesia results from internal core-to-peripheral redistribution of body heat; not net exchange of heat with environment, but large flow of heat from core compartment (trunk and head) out into periphery (arms and legs); core temperature decreases and peripheral temperature increases, but no actual change in amount of heat in body or impressive heat loss to periphery; second phase of hypothermia curve results from heat loss to environment exceeding metabolic heat production; radiation, followed by convection, major cause of heat loss; conduction and evaporation usually contribute very little to cooling during anesthesia; core temperature plateau occurs when patients get so cold they trigger thermoregulatory vasoconstriction; vasoconstriction effective, constrains metabolic heat to core, thus preventing core temperature from falling further

Neuraxial anesthesia: 3 thermoregulatory problems; central inhibition of thermoregulatory control results in slight increase in sweating threshold and decrease in vasoconstriction and shivering thresholds, increasing the interthreshold range; similar pattern to that observed during general anesthesia, except lesser magnitude (~0.5° increase in interthreshold range); second problem, peripheral impairment of thermoregulatory defenses; all thermoregulatory defenses neurally mediated; sweating, vasoconstriction, and shivering require intact nerves; during spinal or epidural anesthetic, nerve connections to lower body disrupted, so patients cannot sweat, vasoconstrict, or shiver in periphery; even if patients trying to thermoregulate centrally, decreased ability to do so; third problem, behavioral inhibition; for given type of operation, patients get just as cold during neuraxial anesthesia as with general anesthesia, but don't seem to recognize it (will generally say they feel fine, feel warm, which contributes to overall sense of warmth); however, false signal and patients actually becoming hypothermic; patients having neuraxial anesthesia should have temperature monitoring; should be just as concerned about hypothermia for these patients as during general anesthesia

Temperature monitoring: necessary during general anesthesia lasting >30 min and during neuraxial anesthesia (at least for long and larger cases)

Core temperature monitoring sites: pulmonary artery, distal esophagus, nasopharynx, and tympanic membrane; measured with thermocouple, not infrared device; these 4 sites can be used interchangeably; rarely differ by more than few tenths of a degree, even during warming and cooling on cardiopulmonary bypass; other generally reliable sites include mouth, axilla, and bladder (not core temperature sites, but reasonable approximations during noncardiac surgery); forehead skin temperature, infrared "tympanic" temperature, infrared temporal artery scanners, and rectal temperature not equal to core temperature and don't yield reliable estimates; nasopharyngeal temperature good alternative to esophageal temperature; generally, esophageal temperature most obvious to use during general anesthesia (easy, inexpensive, and highly resistant to artifact); probe needs to be inserted between 10 and 20 cm for highly reliable core temperature reading

Complications of mild hypothermia: not accidental hypothermia, therapeutic hypothermia, or hypothermia levels with procedures such as cardiopulmonary bypass; 1° to 2° of hypothermia, amount of hypothermia that any unwarmed surgical patient will have; hypothermia affects

many different systems; most patients susceptible to ≥1 complication

Coagulopathy: best-documented complication of mild hypothermia; blood loss increases with hypothermia by ~20% per degree of hypothermia; also ~20% increase in risk of transfusion

Wound infections: hypothermia triggers vasoconstriction, which decreases flow of immune cells to wounded tissues, decreases scar formation, and decreases activity of immune cells; surgical-site infections common (~1-3% of all patients, but ~10% of those undergoing colon surgery); patients with surgical-site infection twice as likely to go to ICU and twice as likely to die, and hypothermia makes this worse; concern about forced air interfering with laminar flow; *laminar flow* — designed to prevent surgical-site infections but probably worsens surgical-site infections, as shown in meta-analysis; likely occurs by directing strong stream of air past surgeons and scrub nurses, picking up infective particles and driving them directly into wound; *warm air rising from forced-air warmer* — may interfere with laminar flow and increase risk of infection; study used surgical patients to evaluate infection risk during forced-air warming with laminar flow; investigators put culture plates in and around incision and around patients; patients randomized to forced-air warming or resistive warming; no difference seen in number of colony-forming units of cultures that resulted with or without forced air; clearly indicated that forced air did not interfere with laminar flow;

FDA guidance regarding warming patients: "The FDA has been unable to identify an association between forced air and surgical-site infection. Therefore, the FDA continues to recommend the use of thermoregulating devices, including forced-air thermoregulating systems. Surgical procedures performed without the use of a thermoregulation system may cause adverse health consequences"

Delayed drug metabolism — enzymes sensitive to temperature; *eg*, duration of action of vecuronium doubled with only 2° of hypothermia and exceeds that of pancuronium in normothermic patient; smaller effect for other muscle relaxants , and even smaller effect for propofol, but still ~30%, clinically important; costs more for super–short-acting drugs, but if patients get hypothermic, lose that benefit because drugs not metabolized as quickly; recovery prolonged in hypothermic patients by ~40 min

Discomfort: hypothermia makes patients uncomfortable; they feel cold, and if cold enough, they shiver; patients with 2° of hypothermia take 2 full hrs to recover to the point where they say they feel normal, no longer cold; should keep patients warm, because they dislike being cold; patient comfort important

Maintaining normothermia: covering surgical patients with passive insulators easiest way to reduce heat loss; can use plastic bags, cotton blankets, cloth or paper drapes, special space blankets; each reduces heat loss by ~30%; no clinically important differences among these passive insulators; insulation provided by little bit of trapped, still air under cover, no matter what cover made of; using 3 layers of insulation rather than 1 layer reduces heat loss from ~30% to ~50%; if patient becoming hypothermic with single layer of passive insulation, adding more layers not likely to help; need to use more active system; forced air used in >90% of patients warmed during surgery; effective, easy to use, inexpensive, and safe; other systems good too as long as maintain normothermia; *redistribution hypothermia* — rapid decrease in core temperature that occurs right after induction of anesthesia; hard to treat because large internal flow of heat; can be somewhat prevented by warming patients before induction; warming patients before induction of anesthesia doesn't change core temperature because core temperature still regulated; increases peripheral heat content and peripheral tissue temperature, which reduces or eliminates temperature gradient between core and peripheral tissues; heat, by second law of thermodynamics, can only flow down temperature gradient; if no longer gradient, no flow of heat, no redistribution; prewarming works, but only provides ~0.5° benefit, as shown in meta-analysis; prewarming may be helpful in some contexts but does not replace intraoperative warming

Fluid warming: can't warm patients because can't warm fluids to much warmer than body temperature, so can't transfer heat; can cool patients by administering large volumes of cold fluid; each liter of crystalloid at ambient temperature reduces mean body temperature in a 70-kg patient by ~0.25°; each unit of blood from refrigerator also reduces mean body temperature by ~0.25° because half the volume, but about twice as cold; large amounts of fluid should be warmed; if giving small amounts of fluid, 1 L over 1 to 2 hrs not large volume and not worth warming; amount of heat lost by giving small volumes of fluid not clinically important

Ambient temperature: no effect on core temperature in patients warmed with forced air because forced air produces cocoon of warmth around patient; determines what happens to patient's core temperature; in patients warmed with forced air, can set ambient temperature for comfort of surgeons and rest of OR team; in patients not actively warmed, ambient temperature makes difference, but smaller difference than expected (~1° difference in core temperature at end of 2-hr operation, with 4° reduction in ambient temperature); don't worry much about ambient temperature, because relatively small effect, even in patients not actively warmed; in patients actively warmed, ambient temperature doesn't matter

Suggested Reading

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Respiratory Physiology and Pulmonary Function

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Respiratory physiology: complex and difficult to understand; anesthesiologists need to make quick decisions, mainly by recognizing patterns, diagnosing and treating simultaneously when things change with respect to ventilation in operating room (OR); need to understand fundamentals so if initial treatment not appropriate, can determine logical next step

Patient case 1 — intraoperative hypoxemia: 30-year-old, obese female; smoker; BMI=50; just had anesthetic for minor gynecologic procedure lasting 30 minutes; patient intubated; no problems intraoperatively; surgery finished; muscle relaxant reversed; patient waking up; coughs on endotracheal tube; although O_2 concentration set at 80%, saturation falls to 84%

Possible causes of perioperative hypoxemia: 1. *low alveolar O_2 tension* — not receiving enough O_2; *stop, look, and listen* — **stop** ventilating with ventilator; manually ventilate with bag patient's lung resistance can be felt; **look** at O_2 flow pathway from anesthetic machine to patient to ensure no disconnect; **listen** to patient's chest to ensure ventilating bilaterally; 2. *mixed venous O_2saturation* — uncommon, rare in this context; perhaps pulmonary embolism; assume hemodynamics okay; 3. *venoarterial shunt* — cause of most intraoperative, perioperative hypoxemia; when oxygenated blood returns to lungs, passes through normally ventilated alveoli (normal capillary O_2 blood) and picks up high concentration of O_2; always small amount that goes through unventilated alveoli (called shunt); in normal, healthy person, perhaps 2% to 5% of entire blood flow through lungs; shunt blood mixes with capillary blood, giving arterial O_2 content; calculating shunt complicated — involves 2 major steps; small change in O_2 from capillary blood to arterial blood and large change in O_2 concentration between capillary blood and venous blood; if those 2 fractions put over each other, small step to big step, actually shunt calculation; but normally work with preconceived notions of what patient's shunt should be, and how that shunt will respond as O_2 concentration increased during anesthesia; if shunt small, relationship between arterial O_2 and inspired O_2 concentration fairly linear; it gets more curvilinear as shunt increases, and when shunt gets to ~30%, increasing O_2 concentration does little to increase arterial pO_2

Causes of shunting: this patient has no problem with cardiac output and does not seem to have collapsed lung; relates to lung volumes; we normally breathe starting at functional residual capacity (FRC); FRC=end expiratory lung volume normally in lungs; dynamic volume: balance of spring of chest wall pulling out and spring of lung itself pulling in; we take ~300 mL to 500 mL tidal volume breaths above that; we can take breath up to total lung capacity, maybe 5 L; FRC approximately half of that; as we come down to FRC, can forcibly expire down to residual volume, perhaps just >1 L; FRC changes from minute to minute; *closing capacity* — volume in lung where small distal respiratory bronchi begin to close as we breathe out; when they close, alveolar O_2 tension starts to fall, causing some shunt; more we breathe down below our closing capacity, more it causes shunt; closing capacity changes little in short term, but increases with age, outstripping FRC as we get older; at about ~40 yrs, closing capacity starts to surpass FRC when lying supine, and by 60 yrs, commonly above FRC, even when upright; probably cause of this patient's desaturation; she's coughing, getting down below her FRC, and developing some atelectasis

Treatment: probably don't want to extubate this patient because saturation 84%; no gold standard for acceptable saturation, but concerning when patient's saturation <90%; healthy, young patient will tolerate in 80s for brief time, but should keep patients at >90% if possible; patient's saturation will probably fall even more once we extubate, so return saturation into 90s before extubating; may require deepening patient's anesthetic to control her ventilation; need to raise FRC back up; can do by applying positive end-expiratory pressure (PEEP), which tends to decrease lung elastic recoil and restore relationship between closing capacity and FRC; once patient well oxygenated, can be extubated; if primary treatment does not help, situation becomes more complex

Patient case 2 — hypercarbia: 70-year-old man admitted to emergency department (ED)few hours ago with exacerbation of chronic obstructive pulmonary disease (COPD); on admission, breathing air, blood gas showed pH 7.34, arterial CO_2 55 (elevated), arterial pO_2 45, bicarb 30; hypoxic and hypercarbic; treated with aerosolized salbutamol (albuterol)/ipratropium and put on O_2 50% mask; they called anesthesiologist because becoming increasingly somnolent; repeat blood gas on 50%, pH 7.25, pCO_2 85, PaO_2 130, bicarb 38; ED asking that patient be intubated and anesthesiologist take over ventilation to can manage his CO_2; why did his CO_2 increase when given 50% O_2?; when chronic CO_2 retainers become hypoxic, they get hypoxic drive but once hypoxia relieved by supplemental O_2, ventilation returns to normal but CO_2 continues to go up

Normal respiratory drive: primarily results from arterial CO_2 tension; CO_2 diffuses freely through blood-brain

barrier into cerebrospinal fluid (CSF) around medulla (which contains primary respiratory centers); CO_2 interacts with bicarb to form hydrogen ion; pH in CSF surrounding medulla basic driving factor for respiration; peripheral chemoreceptors in carotid body sense arterial pO_2; backup mechanism; when pO_2 falls below threshold (varies from patient to patient, depending on how accustomed to hypoxia), in most people will swing into effect once PaO_2 falls below 80; in COPD patient who may live with PaO_2 of 70, maybe not until PaO_2 goes below 60; once chemoreceptors swing in, hyperventilation results; backup drive that knocked out when supplemental O_2 given; carriage of CO_2 in blood complicated; CO_2 normally comes from tissues because of aerobic metabolism into venous blood, where it enters red blood cells; it reacts with bicarbonate ion in red blood cells to form hydrogen ion and bicarb in red cell; hydrogen ion and bicarb excreted; CO_2 has passed through red cell and been excreted back into blood as bicarbonate ion; vast majority of CO_2 in body actually contained in bicarb in blood; CO_2 measured in arterial blood sample only dissolved CO_2; also small amount of CO_2 that attached to hemoglobin molecules; venous blood carries more CO_2 than arterial blood; oxygenation tends to decrease affinity of hemoglobin for CO_2 (Haldane effect), which can be very important in CO_2 retainers; in part, Haldane effect contributing to patient's increase in CO_2 when he has received supplemental O_2; alveolar dead space major cause of this patient's increase in CO_2; to understand, imagine lungs of patient with severe COPD; those lungs have regional inequalities of ventilation and perfusion; some poorly ventilated alveoli in which alveolar O_2 tension falls, setting up hypoxic pulmonary vasoconstriction; lung only tissue in body that tends to vasoconstrict when hypoxic; lung vasoconstricts blood and forces it away from poorly ventilated alveoli to well-ventilated alveoli; matching of ventilation and perfusion, which occurs in patients with COPD to keep them alive; we administer supplemental O_2 to avoid hypoxemia because that causes myocardial ischemia, poor wound healing; however, when we treat hypoxemia, we wash out much nitrogen in lung, resulting in high alveolar pO_2 even in poorly ventilated alveoli; this abolishes hypoxic pulmonary vasoconstriction, so blood flow returns to sick areas of lung; shunt has been increased, but giving them supplemental O_2so no longer hypoxemic; but in areas of healthy lung, excess of ventilation to perfusion because perfusion stolen over to sick lung; excess of ventilation to perfusion called increase in dead space; ventilation now not efficient; decreased efficiency of matching of ventilation and perfusion; normal, healthy, people can deal with increase in dead space; patients with severe COPD do not have that reserve, cannot deal with increase in dead space, and arterial CO_2 rises

Causes of increasing hypercarbia: patient could have increased CO_2 production; could be hypermetabolic state or malignant hyperthermia, but unlikely in our patient; could have failure of CO_2 removal (can happen in OR when anesthetic machine has valve malfunction), but unlikely in patient breathing spontaneously with mask; could have COPD exacerbation; can look at respiratory rate, listen to lungs, and look at use of accessory muscles of respiration; if COPD not worse, then cause most likely O_2 therapy that has exacerbated his CO_2; CO_2 benign but O_2 not benign, body does not store it

Oxygen therapy: body has ~4-minute excess supply of O_2; we have lot of CO_2 because quite benign as long as no mass lesion in brain that will swell with vasodilation; problem with CO_2, at levels approaching 100 mm Hg, begins to be anesthetic; could kill a CO_2 retainer with O_2; CO_2 will increase, people lose consciousness, then may be unable to protect their airway; CO_2 not totally benign, stimulates autonomic nervous system, causes tachycardia, vasodilator; respiratory acidosis can make patients unresponsive to vasoconstrictors; alone, hypercarbia usually quite well tolerated; in awake state, never hypercarbic because brainstem pH will not allow

Treatment: turn down O_2-may need 26%, 28%, not 50%; monitor respiration; continue to check arterial CO_2; level of consciousness most important thing to monitor in this patient; these patients must be monitored in recovery room when given supplemental O_2 postoperatively

Patient case 3 — inspiratory stridor: 20-year-old man in recovery room developed inspiratory stridor 20 minutes after general anesthetic for excision of laryngeal polyp; has adequate bilateral air entry; respiratory rate 22; he has 40% O_2 mask; saturation 99%; patients can have inspiratory or expiratory stridor or both; just inspiratory stridor suggests variable airway constriction above level of thoracic inlet; above this level, when we inspire, negative pressure generated and upper airway, upper trachea, glottis, and oropharyngeal airway tend to constrict; expiratory stridor alone below thoracic inlet distal airway obstruction; may be foreign body, tumor, asthma; patient had surgery on glottis, so likely related to his surgery; could be inadequate reversal of muscle relaxant (can check quickly with physical exam, head lift, grip strength, and by looking at chart); convinced he has adequate reversal and really problem in his upper airway, probably related to laryngeal biopsy; normal trachea 15 mm to 20 mm wide in adult; normal adult will develop stridor with exertion when airway narrows to 9 mm; by time airway narrows to 6 mm, patients develop stridor at rest

Cause: probably related to surgery; trauma, injury to vocal cord, hematoma, laryngospasm, or glottic edema

Treatment: similar initial treatment for all these causes; give nebulized racemic epinephrine, if available, to decrease edema; give nebulized racemic lidocaine if laryngospasm; if mechanical (injured vocal cord or hematoma related to surgical procedure), those treatments probably will not help; at least symptomatically, will likely help to give patient mixture of helium and O_2; *stridor* — when laminar flow in airways or in any vessel with liquid, resistance to flow related inversely to radius of tube and directly to viscosity of gas or liquid flowing; turbulence=involuntary noise, stridor (while speaking, creating voluntary turbulence in expired airflow); turbulence in gas flow relates to radius inversely, but all relates to density of gas; little difference in viscosity of gases that commonly used in OR; helium has low density, approximately one-third to one-half of either O_2 or air or mixture of both; can give helium-O_2 mixture — commonly commercially available as 70% helium in 30% O_2; decreases resistance to airflow and may convert turbulent airflow into laminar, quiet gas flow and

symptomatically decrease patient's work of respiration; only symptomatic measure until definitive diagnosis reached; if patient doesn't respond fairly quickly to nebulizers, then probably would perform fiberoptic laryngoscopy to see if structural damage; next step depends on whether or not any structural damage present

Patient case 4 — metabolic acidosis: ED needs management of airway of unconscious 60-year-old burn victim, found in burning house; second-degree burns to upper chest and face; unconscious; blood pressure (BP) 140/90 mm Hg; saturation with pulse oximeter 100%; heart rate 130; breathing ~30 times/minute; initially, secure airway before edema makes it worse; patient intubated without any complication; ventilating bilaterally; blood gas comes back with pH 7.0, arterial CO_2 35, arterial O_2 70, and bicarb 8; patient has metabolic acidosis; found in fire, so probably inhaled CO, causing metabolic acidosis

Causes of metabolic acidosis: when breathed in, CO has high affinity for hemoglobin and forms carboxyhemoglobin; *oxyhemoglobin* saturation curve — normally live on upper part of this curve, operating from arterial O_2 tension, perhaps 90 or 100 torr, down to 70 or 65 torr in venous O_2; family of oxyhemoglobin saturation curves, all with similar S-shape and can be shifted to left or right of normal oxyhemoglobin; physiologists developed term p50 (saturation of normal O_2 at 50%), PaO_2, when O_2 50% saturated; in adult, p50 normally in range of ~26 to 29 mm Hg; fetal hemoglobin left shifted from adult hemoglobin; fetal hemoglobin p50 ~19; O_2 tends to move to left easily and to right with more difficulty; O_2 in pregnant woman moves from her blood into fetus, because fetal hemoglobin has stronger affinity for O_2 than mother's hemoglobin; carboxyhemoglobin totally left shifted; O_2 moves from normal hemoglobin to carboxyhemoglobin, and carboxyhemoglobin has such high affinity for O_2 that extremely reluctant to give it up; circulates but does not release that O_2 to tissues; tissues become hypoxic and switch into anaerobic metabolism, generating lactate, which returns by venous blood; carboxyhemoglobin causes this lactic acidosis because it will not release its O_2; *right shifts* — such things as acidosis, septic patient with acidosis tends to give up oxyhemoglobin more easily; increase in 2,3-DPG, glycolytic product in red cells, tends to make hemoglobin give up its O_2; *left shifts* — things like fetal hemoglobin (or "lousy hemoglobins"), carboxyhemoglobin, methemoglobin; mnemonic device, "L" and "F" in "left," so lousy hemoglobin, fetal globin; "H" (for hydrogen ion) and "G" (for 2,3-DPG) in "right"; bank blood loses its 2,3-DPG after storage; recovered once back into circulation, but immediately after transfusion, red cells tend to not give up O_2 as readily as normal hemoglobin; hydrogen ion causes shifts of oxyhemoglobin curve, Bohr effect; Haldane effect, ability of oxygenated hemoglobin to carry CO_2; to remember difference, think of word "Bohr"; O-H oxyhemoglobin, so Bohr effect=shifts of oxyhemoglobin curve

Diagnosis and treatment: arterial O_2 70, even though ventilated with 100% O_2; seems to have good bilateral air entry, but pulse oximeter reading 100%; with PaO_2 of 70, would expect saturation in low 90s; common clinical pulse oximeters read carboxyhemoglobin as oxygenated hemoglobin; more sophisticated pulse oximeters can tell different between them, but need to get actual carboxyhemoglobin level on blood sample to find out how much of patient's hemoglobin already occupied as carboxyhemoglobin; need to wait to cure metabolic acidosis until CO can be displaced from hemoglobin; high PaO_2 tends to displace it, can get PaO_2 much higher with hyperbaric O_2; if carboxyhemoglobin level >20% and other symptoms present, patient should receive hyperbaric O_2

Patient case 5 — gradient change between arterial and end-tidal CO_2: 60-year-old man received anesthetic for elective repair of abdominal aortic aneurysm; has been very stable case; two-thirds of way through procedure; surgeon has completed vascular graft on descending aorta and about to release cross-clamp; before surgeon releases cross-clamp, heart rate 80, BP 140/70 mm Hg, end-tidal CO_2 35, arterial CO_2 37, pH 7.4, arterial O_2 150, patient ventilated with 40% O_2, bicarb 22; after surgeon releases cross-clamp, heart rate increases to 110, BP falls to 80/40 mm Hg, end-tidal CO_2 falls to 29, pH 7.1, arterial CO_2 47, arterial O_2 140, bicarb down to 13; end-tidal CO_2 has fallen and arterial CO_2 has risen; gradient between arterial and end-tidal CO_2 usually stable during anesthetic

Dead space in lung: may be cause of patient's gradient change; normal healthy patient has only little dead space in lung; regions of lung divided according to matching of ventilation perfusions; zone 1 dead space, alveoli not being perfused; zone 2, large proportion of lung, region with intermittent flow through pulmonary capillaries depending on pressure in alveoli; zone 3, normally largest portion of lung, with unimpeded flow through pulmonary capillaries (pulmonary capillary pressure exceeds alveolar airway pressure); with positive-pressure ventilation, mean alveolar pressure increases, zone 3 decreases, zone 2 increases, and start to get more zone 1; *2 kinds of dead space* — airway and alveolar dead space; airway dead space almost never changes; almost all respiratory dead space in healthy patient, airway dead space; in normal tidal-volume breathing, amounts to about one-third of ventilation; during anesthesia, particularly when capillary pressure falls, zone 1 increases, and alveolar dead space becomes important; *major cause of dead space and fall in end-tidal CO_2 in this patient* — hypoperfusion of pulmonary capillary; as cardiac output falls, perfusion pressure of lung falls, and increases in zone 2 and particularly in zone 1; cause of decrease in end-tidal CO_2 sudden increase in zone 1 because of hypotension and decreased cardiac output; if we have increase in dead space, and if start hypoventilating because of increase in alveolar dead space, arterial CO_2 goes up; arterial CO_2 actually rises fairly slowly, even in context of complete apnea; if patient not ventilated at all, CO_2 will normally rise only ~3 mm Hg/min; in this patient, in space of 1 minute, arterial CO_2 risen by 10; probably more than ventilation; store of CO_2 in body quite large, so pool level rises fairly slowly; small store of O_2, so patient not ventilated or is apneic, arterial PaO_2 falls quickly; when surgeon released clamp, lactic acid generated by poorly perfused limbs has now returned via venous circulation; now reperfused, and lactate has gotten into venous blood; hydrogen ion in that lactate reacting with bicarb in blood, causing formation of CO_2 and water; bicarb has fallen in blood

and CO_2 has risen; we have 2 unusual changes in CO_2 — falling in end-tidal and rapid rise in arterial; combined metabolic and respiratory acidosis in this patient

Treatment: treatment has nothing to do with managing ventilation; to treat this metabolic and respiratory abnormality, restore hemodynamics; give this patient volume, vasopressors; may temporarily treat with IV bicarbonate because vasopressors not very active once pH falls below 7.2, for chemical reasons

Patient case 6 — hypoxemia in recovery room: 40-year-old had anesthetic, few minutes ago, in recovery room with nurse; quite stable, 75 kg, no comorbidity, and just had 2-hour general anesthetic for laparoscopic appendectomy; anesthetic induced with propofol, maintained with sevoflurane, rocuronium as muscle relaxant, and fentanyl as intravenous opioid, 250 mcg at induction, then 50-mcg boluses throughout case; patient reversed with appropriate doses of neostigmine and glycopyrrolate; patient extubated, alert, in OR, with full muscle strength; saturation on arrival in recovery room 96%, with normal hemodynamics; 10 minutes later, saturation has fallen to 84%; other vital signs unremarkable; heart rate 72 and BP 130/70 mm Hg; respiratory rate 7, low; chest clear, patient comfortable and alert

Causes of perioperative hypoxemia: alveolar O_2tension, mixed venous O_2 saturation, or venoarterial shunt; *mixed venous O_2 saturation* — nothing to indicate that patient had pulmonary embolism or gaseous embolism from laparoscopic procedure; nothing to suggest problem with cardiac output that should cause desaturation of venous blood, so very unlikely; *venoarterial shunt* — not being ventilated, FRC should be okay; on auscultation, nothing to suggest atelectasis; can take deep breath, nothing to suggest pneumothorax or collapsed lung; *alveolar O_2 tension* — in normal awake state, people do not tolerate hypoventilation; if we try to hold breath for 60 secs, brainstem overrides and we start to breathe; if we hypoventilate in breathing air, start to desaturate very quickly because alveolar O_2 tension falls; in 75-kg patient, normal ventilation, breathing spontaneously, ~5 L; of that, alveolar ventilation approximately two-thirds, so ~3.5 L; pO_2 in air ~160, and in normal healthy patient, alveolar pO_2 ~110 to 130; pO_2 from air diluted because of CO_2 and water vapor in alveoli; if alveolar ventilation decreases by about one-third just down to 2 L/min from normal alveolar ventilation of 3.5 L/min, alveolar O_2 will fall to 70; because of some obligatory shunt, patient will desaturate; normally, pH of our CSF does not allow us to tolerate acidosis caused by increasing CO_2; opioids and other sedatives affect brainstem and decrease sensitivity of CO_2 drive; one reason this patient hypoventilating, decreased sensitivity because not much surgical pain, and he received moderate amount of fentanyl intraoperatively within last 2 hrs; he may be unusually sensitive to fentanyl; as he desaturates, peripheral chemoreceptors should click in and drive ventilation; but doesn't have ventilatory drive because trace amounts of volatile anesthetics tend to abolish response or decrease it from peripheral chemoreceptors; patient has residual narcotic blunting his medullary drive and residual sevoflurane blunting peripheral chemoreceptor drive; so, very comfortable, not really reacting, but saturation falling to dangerous level

Treatment: supplemental oxygen; if given 40% O_2, his ventilation can fall basically to half of its normal level and without significantly desaturation, because increased alveolar O_2; hypoventilation can cause desaturation, but not in healthy person; it can easily do it to patients in perioperative period; most anesthesiologists routinely give supplemental O_2 for at least first 30 to 60 mins after general anesthetic to cover this period when peripheral chemoreceptor drive may be decreased

Suggested Reading

Habre W, Peták F: Perioperative use of oxygen: variabilities across age. *Br J Anaesth*. 2014;113(suppl 2):ii26-36; **Kulcke A et al:** The accuracy of pulse spectroscopy for detecting hypoxemia and coexisting methemoglobin or carboxyhemoglobin. *Anesth Analg*. 2016;122(6):1856-65; **Scheeren TWL et al:** The oxygen reserve index (ORI): a new tool to monitor oxygen therapy. *J Clin Monit Comput*. 2018;32(3):379-89.

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Cardiovascular Physiology

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Cardiac cycle: encompasses electrical and mechanical events across systole and diastole; best described by Wiggers diagram, used to illustrate cardiac physiology

Ventricular systole: 3 main phases include isovolumetric contraction, rapid ejection, and slow ejection; begins immediately after onset of QRS complex of electrocardiogram (ECG), which represents action potential conduction; leads to near-simultaneous activation of both ventricles, triggering excitation contraction coupling and myocardial contraction; cavity pressure rises inside ventricle until mitral and tricuspid valves close, producing first heart sound and C-wave; when intraventricular pressure overcomes aortic and pulmonary arterial pressures, aortic and pulmonic valves open

- Isovolumetric contraction: occurs when both inflow and outflow valves to ventricle closed; absent in patients with regurgitant valve lesions
- Ventricular ejection: begins with opening of aortic and pulmonic valves; stored energy within ventricles propelled into aorta and pulmonary artery, causing systolic upstroke on arterial pressure trace; maximal ejection occurs in first third of this period; remaining 30% of ventricular volume ejected in latter two-thirds, subdividing ejection into rapid and slow phases; T-wave appears at cusp of rapid and slow ejection, marking beginning of ventricular repolarization; as intraventricular pressure falls below aortic and pulmonary arterial pressure, aortic and pulmonic valves close, causing second heart sound and dicrotic notch; systole ends and diastole begins

Ventricular diastole: 4 phases include isovolumetric relaxation, early filling, diastasis, and atrial contraction

- Isovolumetric relaxation: occurs when ventricular muscle relaxes with both mitral and tricuspid valves, as well as outflow valves, closed; several ATP-consuming processes under way; during ventricular systole, atria slowly fill in preparation for diastole; peak atrial pressure occurs at end of isovolumetric relaxation, just before mitral and tricuspid valves open and corresponds to V-wave; lusitropy describes rate of myocardial relaxation
- Early filling: begins when atrial pressure rises above ventricular pressure and mitral and tricuspid valves open; corresponds to Y-descent as atrial pressure rapidly falls; 80% to 90% of ventricular filling occurs; in patients with rapid filling (*eg*, with athletes' heart physiology or volume overload), can cause third heart sound
- Diastasis (slow filling): as ventricular volume increases, atrial and ventricular pressures approach equality and filling slows; ends with onset of P-wave, signaling atrial contraction
- Atrial contraction: final phase of diastole; actively kicks remaining atrial volume into ventricle and accounts for 10% 15% of ventricular filling; causes A-wave; patients with impaired ventricular function reliant on atrial kick for up to 30% 40% of ventricular filling

Cardiac Output

Definition: product of heart rate and stroke volume; stroke volume in turn influenced by preload, afterload, and contractility

Preload: describes mechanical forces exerted on myocardium in diastole, just prior to contraction; influenced by venous return, atrial function, ventricular compliance, and filling time

- Venous return: affected by volume status, patient position, changes in venous compliance, muscle pump activity, and intrathoracic pressure
- Atrial function: changes such as atrial fibrillation or rhythm disturbances can impair filling through loss of atrial kick or discordant atrial contraction
- Ventricular compliance: affects preload by making heart easier or harder to fill during early phases of diastole
- Heart rate: changes in heart rate change time spent in diastole during each cardiac cycle
- Frank-Starling mechanism: any increase in preload causes a matched increase in stroke volume; can be represented by graph with end-diastolic volume on x-axis and stroke volume on y-axis; typical curve begins with relatively linear relationship between stroke volume and end-diastolic volume; as end-diastolic volume -increases, curve gradually flattens out and turns sharply downward, signifying heart failure; as end-diastolic volume increases, curve represents increasing stroke volume due to increased ventricular contractility; these changes in inotropy intrinsic to heart
- Measurement: when cardiac muscle stretched and held to certain length, then stimulated to contract against constant load; increasing stretch causes increase in force, rate, and amount of contraction
- Contributors to Frank-Starling effect: optimal overlap of actin and myosin at specific sarcomere length; titin, giant elastic protein within sarcomere attached to myosin proteins on one end and Z disc (structure that joins one sarcomere to another) on other; titin functions as both molecular spring that maintains sarcomere length and as stretch receptor; when stretched, titin increases force in velocity and muscle shortening by increasing calcium released from sarcoplasmic reticulum and by sensitizing

sarcomeric contractile proteins to effects of calcium; also called length-dependent activation

Other factors: preload tightly integrated with other determinants of cardiac output; increasing inotropy or decreasing preload steepens curve while doing opposite flattens curve and render it less responsive to increases in volume; increasing preload stretches atria and triggers Bainbridge reflex, which further increases heart rate and increases cardiac output

Afterload: force myocardium must overcome during systole; aortic pressure and systemic vascular resistance major determinants of left ventricular afterload

Law of Laplace: describes relationship between pressure, volume, and wall tension of sphere; myocyte tension, or afterload, proportionate to pressure generated by ventricle and radius (related to the volume of ventricle) and inversely proportional to wall thickness of ventricle; explains concentric hypertrophy as adaptive mechanism to chronic increases in afterload, as increasing wall thickness relieves wall tension; radius, or volume, related to preload (also contributor to afterload); compared with pressure loading, effect of volume on afterload not as significant; small effect of any increase in volume on afterload

Measurement: instead of stretching muscle to set length, set weight applied to muscle sample allowed to shorten while contracting to apply constant load; as load increased, velocity of shortening slows significantly; effect mitigated by both increasing stretch (through Frank-Starling mechanism) and increasing inotropy

Effects of increased afterload: decreases stroke volume; increasing velocity of shortening in systole improves stroke volume for same stroke work, helps with ventricular emptying, makes heart smaller, and moves heart down to more efficient part of Starling curve

Contractility (inotropy): intrinsic ability of myocardium to contract, independent of influence of preload, afterload, or heart rate

Contributing factors: preload increases contractility through Frank-Starling mechanism; *Anrep effect* — increase in inotropy when afterload abruptly increased in ventricle; Bowditch, or Treppe, effect increases inotropy by increasing heart rate

Mechanism: calcium = currency for myocardial contraction; in excitation-contraction coupling, action potentials propagated down T-tubule system, opening L-type dihydropyridine calcium channels to release small amount of calcium into myocyte; with repeated stimulation, enough calcium accumulates to activate ryanodine receptor on sarcoplasmic reticulum, triggering much larger release of calcium that binds troponin; calcium binding to troponin C subunit induces conformational change that allows actin to bind myosin, initiating cross-linking and sarcomere shortening; after shortening, intracellular calcium levels fall due to sarcoendoplasmic reticulum calcium ATPase (SERCA) pump and sodium-calcium exchanger; below certain concentration, calcium disengages from troponin, actin and myosin break apart, and contraction stops

Altering inotropy: calcium influx can be modulated at dihydropyridine calcium channel by sympathetic stimulation; catecholamines increase cyclic AMP (cAMP) and protein kinase A, which then enhances calcium channel function; phosphodiesterase 3 (PDE3) inhibitors such as milrinone enhance this effect by inhibiting breakdown of cAMP; calcium efflux and lusitropy also enhanced by sympathetic stimulation of beta-receptors through inhibiting phospholamban, protein that regulates function of SERCA; calcium levels can respond to many physiologic and pathologic conditions, contributing to hypo- and hypercalcemia

Measurement: pressure-volume loops generating end-systolic elastance curve (end-systolic pressure-volume relationship); myocardial strain using echocardiography; rate of pressure increase during isovolumetric contraction; products of systolic ejection such as stroke volume and ejection fraction

Ejection fraction: ratio of stroke volume and end-diastolic volume; measuring products of systolic ejection phase loading dependent; normal ejection fraction ~65%, with normal range between 52% and 74%; ejection fraction represents 1 point on Frank-Starling curve, with end-diastolic volume on x-axis and stroke volume on y-axis; as inotropy increases, slope on curve increases for same end-diastolic volume; ejection fraction can be measured by cardiac imaging modalities (echocardiography, cardiac MRI, contrast ventriculography, and nuclear scintigraphy)

Cardiac Metabolism and Oxygen Consumption

Metabolism: myocardium can utilize almost any energy substrate; fatty acids, carbohydrates, lactate, amino acids, and ketone bodies can be fed back into oxidative phosphorylation and ATP formation; myocardium has little reserve for anaerobic metabolism because cardiac muscle has limited amount of glycogen stores; myocardium has highest oxygen consumption by weight of all organs in body; in 1 min, myocardium can consume between 8 mL and 70 mL of O_2 per 100 g of tissue, depending on its activity; brain uses only 3 mL of O_2 per 100 grams; heart also has one of highest O_2 extraction ratios of any organ in body, extracting about 60% to 80% of O_2 delivered via coronary arteries

Oxygen consumption: 3 major factors include heart rate, contractility, and ventricular wall tension; external work during rapid ejection phase of systole (which propels blood into aorta) and basal O_2 consumption (which keeps heart beating at rest) secondary contributors; at 25% of total myocardial O_2 consumption, basal O_2 consumption relatively high; O_2 delivery to myocardium contingent on coronary blood flow and O_2 content of arterial blood

Oxygen content: determined by hemoglobin concentration in the blood, arterial O_2 saturation, and O_2-carrying capacity of hemoglobin; O_2-carrying capacity of hemoglobin 1.36 mL of O_2 per g of hemoglobin; contribution from dissolved O_2 (0.3% of partial pressure of arterial O_2) very low at atmospheric pressure and can be ignored

Coronary blood flow: delivered by right and left coronary arteries; blood flow between 2 coronary arteries at rest represents 5% of cardiac output; coronary perfusion pressure driving blood flow into myocardium = difference between aortic root pressure and intraventricular pressure; little to no gradient for left ventricular perfusion during systole because left ventricular systolic pressure generates same aortic root pressure that perfuses it; entirety of left ventricular perfusion only occurs during diastole, when

intraventricular pressures fall below systemic diastolic pressure; left ventricular perfusion = difference between aortic root diastolic pressure and left ventricular end-diastolic pressure; the right ventricle has larger perfusion reserve and receives blood flow throughout cardiac cycle; because right ventricle generates pressures at about one-fifth that of systemic, always gradient for perfusion between aortic root and right ventricular myocardium

Subendocardial arterial plexus: small penetrating intramuscular branches from coronary arteries within myocardium; supplies part of myocardium closest to ventricular cavity where pressure during systole is highest; when left ventricular myocardium contracting, small muscular and subendocardial arteries squeezed shut; blood sitting in small muscular and subendocardial arteries pushed forward into coronary sinus or backward into epicardial arteries; with onset of diastole, these small vessels relax and flow resumes; in patients experiencing high cardiovascular demand, subendocardium vulnerable to ischemic infarction if O_2 supply cannot be met (extreme tachycardia increases metabolic demand but reduces supply by decreasing diastolic time per cycle)

Factors influencing coronary vasomotor tone: myocardial contraction; coronary blood flow autoregulated within range mean arterial pressure of ~60 to 140 mm Hg in healthy individuals; increased local metabolic demand results in production of adenosine to cause vasodilatation; vasodilators, such as nitric oxide, prostacyclin, and bradykinin; vasoconstrictors, such as endothelin, angiotensin. and thromboxane

Local vasomotor control: can increase coronary blood flow 4 to 5 times above resting levels when maximally dilated; capacity to increase flow called coronary flow reserve, compensatory mechanism in patients with coronary artery stenosis; coronary flow reserve exhausted when vessels maximally dilated; beyond this, distal flow becomes entirely pressure dependent, which makes larger parts of myocardium vulnerable to ischemia

Delivery of cardiac output: heart serves 2 systems in parallel (pulmonary and systemic circulation); systemic circulation, panel of parallel circuits that feed organ systems with independent internal resistors; cardiac output, sum of all tissue and organ blood flows together; systemic vascular resistance (SVR) accounts for resistance of flow through all these organ beds together; when cardiac output ejected from heart, it encounters SVR and arterial blood pressure (BP) generated; this relationship described by *Ohm's law* — $V = I \times R$; I = current (cardiac output), R=resistance, and V = voltage (difference between mean arterial pressure and central venous pressure [CVP]); because CVP usually close to 0, can be ignored; cardiac output and SVR independent variables, so mean arterial pressure result of alterations in cardiac output and SVR

SVR: changes in small-vessel diameter major determinant of resistance to flow; cross-sectional areas of all arterioles most significant factor in resistance to flow; Hagen-Poiseuille's law says flow in tube proportionate to fourth power of radius of that tube and inversely proportionate to its length and viscosity; in large artery, vasoconstriction may not significantly change diameter, but in small arteriole, small changes in vascular tone can lead to large changes in vessel caliber; viscosity of blood additional contributor to SVR; increasing viscosity reduces blood flow; red blood cells greatest contributor to; increasing hematocrit dramatically increases viscosity, as do pathologic conditions such as sickle cell anemia and macroglobulinemia

Pressure relationships: BP function of cardiac output and SVR and compliance of arterial system; ejecting stroke volume into aorta causes rise and fall in its pressure, which registers as systolic and diastolic pressures; with compliant aorta, energy from stroke volume ejection absorbed and expended during diastole, where elastic recoil propagates arterial blood to distal organs (Windkessel effect); in patients with noncompliant arteries, pulse pressure increases and Windkessel effect decreases; factors that can alter arterial compliance include age-related arterial sclerosis and changes in smooth muscle tone due to neurohumoral input from sympathetic, parasympathetic, and renin-angiotensin systems

Pulmonary circulation: high-volume, high-compliance system; pulmonary arterial pressure product of cardiac output and pulmonary vascular resistance; lungs only perfused organs receiving 100% of cardiac output from right ventricle; pulmonary vascular resistance lower than systemic; pulmonary arterial pressures lower (about one-fifth that of systemic in healthy adults); pulmonary artery subjected to much lower pressures and ~5 to 6 times more distensible and compliant than aorta; pulmonary vascular compliance spread throughout pulmonary arteries in contrast to systemic arteries, which quickly become stiffer as they leave aorta due to their thicker wall

Pulmonary vascular resistance: small juxta-alveolar vessels and alveolar capillaries sites of greatest resistance; lung volume one determinant of PVR because changes in lung size will either distend or collapse juxta-alveolar vessels and capillaries; as lungs progressively distended, extra-alveolar vessels distend because of radial traction; distension increases their size and reduces their resistance; alveolar capillaries progressively compressed by increasing alveolar pressure, with overall effect of increasing PVR; with decreasing lung volumes and atelectasis, extra-alveolar vessels collapse around lung tissues, also increasing PVR; graphical representation with lung volume on x-axis and PVR on y-axis shows U-shaped curve, with high PVRs at extremes and the lowest PVR in middle, near functional residual capacity

Other determinants of PVR: endothelial mediators, alveolar oxygen and carbon dioxide, neurohumoral factors, and gravity; most important vasodilators nitric oxide, endothelin, and prostacyclin; vasoconstrictors include thromboxane and leukotrienes; hypoxemia and hypoxic pulmonary vasoconstriction important trigger for controlling PVR; low O_2 directly closes potassium channels, leading to contraction of vascular smooth muscle; in fetus, hypoxic pulmonary vasoconstriction increases PVR so blood shunted across foramen ovale; in disease and one-lung ventilation, hypoxic pulmonary vasoconstriction shunts blood away from nonventilated parts of lung, improving ventilation perfusion matching in parts of lung receiving ventilation; hypercarbia, acidosis, and alpha-1 adrenergic stimulation (through norepinephrine) also increase PVR; beta-2 adrenergic

stimulation through epinephrine causes pulmonary dilatation

Effect of gravity: can alter regional PVR; in upright patient, distribution of blood flow changes according to the difference in hydrostatic pressure between apex and base of lung; functional differences in blood flow regions are described as West zones; in West zone 1, alveolar pressure at apex higher than arterial pressure, resulting in no flow; in West zone 2, alveolar pressure lies somewhere between pulmonary arterial and pulmonary venous pressures, acting as variable styling resistor that directly alters local PVR; in West zone 3, high pulmonary venous pressures determine resistance to flow, with venous pooling, distending pulmonary capillaries that can improve PVR by decreasing resistance or impair it through increasing hydrostatic pressure across capillary

Neural and Hormonal Regulators of Systemic Circulation

Autonomic control: autonomic nervous system has great influence over systemic vascular resistance and blood volume; with exception of capillaries, sympathetic nervous system innervates all blood vessels in nearly all organs apart from brain; because of preponderance of vascular alpha-1 adrenergic receptors, vascular constriction dominant effect of sympathetic stimulation; constriction in small arteries causes increase in SVR; increase in SVR especially prominent in kidneys, gastrointestinal (GI) tract, spleen, and skin (higher density of alpha-1 adrenergic receptors compared with other organs); in times of stress, stimulation of sympathetic nervous system causes vasoconstriction that can divert up to 50% of cardiac output to organs with higher demand; venoconstriction decreases caliber, reducing capacitance and redistributing volume to central blood volume compartment; while norepinephrine dominant sympathetic neurotransmitter, release of epinephrine can sometimes cause beta-2–mediated vasodilation, especially in coronary arteries and pulmonary vascular smooth muscles

Vasomotor center: several poorly defined regions within pons and medulla that control global systemic vasomotor tone and also receive information from pressure sensors within arteries; 3 components — vasoconstrictor area, in anterolateral part of upper medulla, sends efferent signals to preganglionic sympathetic vasoconstrictor neurons, causing vasoconstriction in nearly all systemic arterioles within ~5 to 10 secs; vasodilator area, in lower part of medulla, directly inhibits vasoconstrictor area; nucleus tractus solitarius receives afference via glossopharyngeal and vagus nerves from baroreceptors, which buffer arterial pressure against sudden changes in circulation

Other inputs to vasomotor center: come from hypothalamus, hippocampus, and parts of cerebral cortex; this location may explain how BP fluctuates with changes in memory or with emotions; vasomotor center itself sensitive to hypoxemia and hyperperfusion, which can stimulate powerful sympathetic discharge, causing BPs as high as 250 mm Hg, occluding vessels and some organs through vasoconstriction; this extreme hypertension seen in Cushing reflex in response to increases in intracranial pressure; extreme hypertension also seen in hyperacute phase of significant brainstem and spinal cord injury, emergency reflex to preserve cerebral perfusion in extremis

Baroreceptor reflex: maintains normal BP against fluctuations due to body posture or changes in cardiac output or regional vascular tone; baroreceptors, sensors for baroreflex; baroreceptors in carotid sinus ae innovated by glossopharyngeal nerve; baroreceptors in aortic arch innovated by vagus nerve; carotid baroreceptors most sensitive, responding to mean arterial pressures between 60 mm Hg and 180 mm Hg; baroreceptors in arch have higher response threshold by ~30 mm Hg; stimulus, arterial stretch; within normal mean arterial pressure ranges, baroreceptors are barely stimulated but at ~60 mm Hg to 80 mm Hg, they progressively send more rapid stimuli to nucleus tractus solitarius, inhibiting vasoconstrictor center and stimulate vagal parasympathetic outflow, causing vasodilatation and bradycardia; opposite occurs with hypotension and decreased stretch in baroreceptors; baroreceptors most responsive to sudden changes in stretch; sustained changes (*eg*, in chronic hypertension) lead to right shift in BP response curve; longer-term responses to chronic changes in BP or volume mediated by kidneys

Humoral regulators of circulation:

Angiotensin II: stimulated by renin; released in response to low sodium levels in macula densa in kidney or in response to beta-1 stimulation of juxtaglomerular apparatus; constricts arterioles to increase SVR; acts on adrenal cortex to release aldosterone, causing sodium and fluid retention and increasing blood volume and pressure over longer term; stimulates vasopressin release from posterior pituitary

Vasopressin: potent vasoconstrictor; acts fairly quickly; mediator for water reabsorption from renal tubules over long term

Regional blood flow: systemic circulation consists of panel of parallel circuits that each feed organ system with independent internal resistor; although these parallel circuits all see same cardiac output, distribution not uniform; under resting conditions ~30% of cardiac output goes to liver and splanchnic circulation, 25% to kidneys, 15% to brain, and 12% to skeletal muscle

Determining proportion of blood flow: measured through application of Fick principle; equation predicts blood flow through organ can be calculated by introducing tracer substance to organ; if tracer's content in feeding artery and in draining vein known, along with rate of trace uptake by organ, flow equal to uptake divided by arteriovenous difference of tracer content

Causes of differences in organ flow: organ size; vessel and capillary density within individual organ; extrinsic neural and hormonal influences that may divert blood away or toward organ at point in time; intrinsic regulation

Intrinsic Regulation

Autoregulation: most metabolically important organs show some form of intrinsic blood-flow regulation; blood flow in most organs (including brain, heart, and kidneys) maintained across a broad range of mean arterial pressures, reflecting changes in cardiac output and other organ resistance; myogenic autoregulation, response to high perfusion pressures, property of vascular smooth muscle that doesn't require extrinsic input; sudden stretch from increased perfusion pressures causes reflexive increase in arterial tone to decrease blood flow

Vasodilatory response: seen with decreased perfusion pressures; metabolic mediators play much bigger role in functional hyperemia, also known as flow-metabolism coupling; changes in metabolism within organ can dramatically alter its blood flow within short time; at rest, skeletal muscle receives only ~600 mL to 700 mL of blood flow per minute (10%-12% cardiac output) even though it makes up 30% to 40% of total body weight; during heavy exercise, blood flow to skeletal muscle can increase to match change in O_2 consumption with exercise, which can increase by up to 60 times that of resting levels; GI tract sees significant increases in blood flow after eating large fatty meal; within brain, areas of higher activity have more blood flow and metabolic activity than areas with lower activity

Internal mechanisms in autoregulation: while extrinsic neurohumoral factors affect individual organ blood-flow delivery, in most situations local metabolic control enough to match blood flow to metabolism; each organ has internal variable resistor at level of arterioles and precapillary sphincters; increased organ metabolism vasodilates these resistors

Vasodilator theory: increasing tissue metabolism generates more vasodilatory substances (*eg*, adenosine, CO_2, histamine, potassium, and hydrogen ions); these vasodilating substances diffuse to arterioles and precapillary sphincters to increase local blood flow

Hypoxic theory: lack of O_2 inhibits ability of vascular smooth muscle to contract, causing vasodilatation and increasing capillary blood flow; during periods of high demand, flow in other organs changes in response to autonomic nervous system control, especially those with higher density of alpha-1 adrenergic receptors; renal and splanchnic blood flow typically decreases, allowing up to 40% to 50% of cardiac output to be diverted to areas with greater need

Renal blood flow: of 25% of cardiac output kidneys receive, 80% goes to renal cortex (with abundant glomerular filtration); remaining 20% goes to renal medulla, which contains metabolically active nephrons; *tubuloglomerular feedback* — links urinary sodium and chloride levels with changes in renovascular resistance; in response to decreased urinary sodium, juxtaglomerular apparatus secrete renin and afferent glomerular arterioles dilate, decreasing renovascular resistance and enhancing filtration; renin secretion also stimulates angiotensin II production, which increases BP through global vasoconstriction; renin also has vasoconstrictor effect on efferent arteriole on glomerulus; because afferent arterial feeds into glomerulus, constricting when the efferent arteriole increases total glomerular filtration; in times of stress, renal blood flow falls as cardiac output diverted to other organs by extrinsic neural and hormonal control; this leads to oliguria and frees up nearly 20% of cardiac output to other organs with greater need

Cerebral blood flow: brain suspended within cerebrospinal fluid in relatively noncompliant cranial vault; because intracranial pressure (ICP) normally higher than CVP, it becomes Starling resistor for cerebral perfusion (difference between mean arterial pressure and ICP, unless CVP higher); factors that can alter intracranial pressure can also alter cerebral perfusion; increasing brain volume through edema, cerebral blood volume through hypercarbic vasodilatation, or increasing CSF pressure to decrease cerebral perfusion

Suggested Reading

de Gregorio C et al: Athlete's heart and left heart disease. Adv Exp Med Biol. 2018;1067:313-25; **Yeo JM et al:** Isolated heart models for studying cardiac electrophysiology: a historical perspective and recent advances. J Basic Clin Physiol Pharmacol. 2017;28(3):191-200; **Hoit BD:** Anatomy and physiology of the pericardium. Cardiol Clin. 2017;35(4):481-90; **Næsheim T et al:** Propulsion of blood through the right heart circulatory system**.** *Scand Cardiovasc J*. 2018;52(1):4-12.

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Renal Function, Fluid and Electrolyte Balance, and Intraoperative Fluid Therapy

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Overview: review function of the kidneys and their role in the maintenance of the body's fluid and electrolyte status; discuss appropriate intraoperative fluid therapy in a clinically relatable context

The Kidney

Overview: the kidney has many important functions, including maintaining fluid balance and blood pressure, excretion of unwanted metabolites, reuptake of conserved molecules, maintenance of long-term acid balance, and production of various hormonal mediators, including renin; renin is the first step in the renin-angiotensin-aldosterone axis (RAA) that helps maintain blood pressure, blood osmolarity, and body sodium; the kidney also aids in vitamin D synthesis and red blood cell formation

The nephron: the nephron is the basic functional unit of a kidney; the glomerulus is the interface between systemic blood and the filtration system of the nephron; renal blood flow is approximately 1200 mL/minute or about 20-25% of cardiac output; renal blood flow relatively well-regulated between mean blood pressures of about 80-180 mm Hg; within this range glomerular filtration rate (GFR) is held fairly constant; at perfusion pressures less than approximately 80 mm Hg, GFR becomes perfusion limited and falls linearly with arterial pressure; blood is supplied to the glomeruli by renal afferent arterioles to be filtered and collected via renal efferent arterioles; by differentially constricting these two separate arteriole beds, blood flow filtered by the glomerulus can be regulated precisely by means of the difference between the pressures in the two arterioles; assuming adequate perfusion, the smaller the difference in pressure between the two arteriole beds, the greater the filtration fraction and thus GFR

The filtration fraction: defined as a percentage of blood filtered to the glomerulus; decreases in renal blood flow via sympathetic vasoconstriction of both arterioles results in a GFR decrease with an increased filtration fraction; higher pressure in the efferent arterioles will decrease the gradient between the two beds, thereby increasing the filtration pressure and potentially GFR

Angiotensin II: preferentially vasoconstricts the efferent arterioles, which in the long term is detrimental to kidney function, but short term is one reason why intravenous (IV) angiotensin II might be helpful for kidney function in critically ill patients with impaired perfusion

The functional elements of the nephron: include the glomerulus, the proximal convoluted tubule, the descending and then ascending thin limbs of Henle, the thick ascending limb of Henle, the distal convoluted tubule, connecting tubule and collecting ducts; ultrafiltrate goes from the glomerulus, to the proximal convoluted tubule, to the loop of Henle, then the distal convoluted tubule, and finally to the collecting ducts; each segment of the nephron has specific transporters and permeability coefficients that aid in the optimal reabsorption of needed nutrients, excretion of toxins and unwanted metabolites, and regulation of ion concentrations and fluid volume

Renal filtration: for all substances, the maximum reabsorption is equal to the filtered load minus the excretion rate; the filtered load is defined by the concentration of the substance times GFR; the excretion rate depends on the filtered load minus maximum reabsorption; when the filtered load is increased beyond a certain threshold, the excretion rate then follows linearly; for example, normally glucose is not excreted in the urine but if the concentration of glucose in the blood and thus the filtrate is increased, at some point the ability of the kidney to reabsorb glucose, or its transport maximum, will be reached, and excess glucose will then be excreted in the urine; some substances excreted by the kidney are not reabsorbed; among these include bile salts, urate and oxalate, creatinine, and catecholamines

Medications and the kidney: examples of drugs and their metabolites that are renally excreted include diuretics, most antibiotics, some beta blockers, metformin, aspirin, and atropine; many opioids and their metabolites such as morphine, hydrocodone, meperidine, and tramadol are also renally excreted; therefore if kidney function is impaired, renally cleared drugs need to be dosed based on estimated GFR; creatinine is almost entirely excreted into the urine and therefore creatinine clearance is a useful measure of GFR; clearance of a substance is defined by the amount excreted per unit time, divided by plasma concentration; in practice GFR can be estimated using different equations that corporate serum creatinine including the Cockcroft-Gault equation and the Modification of Diet in Renal Disease (MDRD)

Fluid balance: The sodium ion is ubiquitous in the body and is closely associated with volume balance; the concentration of sodium in the plasma or urine in relation to the amount of water present is an indicator of volume status; patients can be hyper or hypovolemic in the setting of both hypo and hypernatremia

Fractional excretion of sodium (FENa): test to estimate volume status using the concentration of sodium in the blood and urine; provides a measure of the percentage

of sodium in the blood filtered by the kidney excreted into the urine; FENa is measured as the ratio of urinary sodium divided by urinary creatinine and plasma sodium divided by plasma creatinine; this is an estimate and is affected by variables such as diuretics, however it can be helpful as an indicator of volume status; if the FENa is less than 1%, the kidney is trying to preserve sodium suggesting a pre-renal state; an elevated FENa above 2%-3% suggests sodium wasting, such as can occur with acute tubular necrosis

Other substances to estimate volume status: urea, uric acid and lithium can also be used instead of sodium to estimate volume status; unlike the FENa, these ratios can be used in patients taking diuretics

BUN (blood urea nitrogen)-to-creatinine ratio: another method commonly used for estimating volume status; which can be taken directly from the chemistry panel; a BUN-to-creatinine ratio of >20 suggests a pre-renal state; a BUN-to-creatinine ratio of <10 suggests the possibility of intrinsic kidney disease or injury

Nephron anatomy: the glomerular interface is composed of fenestrated endothelium designed to keep larger macromolecules out of the nephron to avoid unnecessary loss of protein; normally, this filter functions well restricting the passage of macromolecules above about 50,000 molecular weight as well as negatively charged molecules such as albumin; however, this barrier can become compromised in preeclampsia, nephrotic syndrome, sepsis, certain autoimmune diseases, and other conditions; under normal conditions, of the blood filtered by the glomerulus approximately 99% of the fluid volume is reabsorbed by the kidney

Proximal tubule: distal to the glomerulus, filtrate reaches the proximal tubule where about 65% is then reabsorbed; sodium and other solutes are actively reabsorbed and water falls passively to maintain iso-osmolarity of the tubular fluid; among the ion transporters in the proximal tubule are the ubiquitous sodium-potassium ATPase(Na-K-ATPase) pumps, as well as hydrogen ion-potassium ATPase(H-K-ATPase) pumps; most of the sodium and potassium as well as calcium and bicarbonate are thus reabsorbed in the proximal tubules; bicarbonate is absorbed via reaction with carbonic anhydrase located on the luminal surface of the proximal tubule epithelium, and is a major contributor to the maintenance of blood acid-base balance; acetazolamide is a carbonic anhydrase inhibitor that decreases sodium bicarbonate and sodium reabsorption while also inhibiting the secretion of hydrogen ion; the net effect of acetazolamide is to alkalinize the urine and acidify the blood; other active transporters couple sodium ions to reabsorb metabolites such as amino acids, glucose, lactate, chloride, and phosphate; the kidney has ability to eliminate excess water rapidly and can dilute urine down to about 50 mOsm or approximately 20 mL/minute flow rate; this is done chiefly using the countercurrent concentrating mechanism

The loop of Henle: the loop of Henle is where the countercurrent concentrating mechanism is most efficient; osmolarity can change from about 300 mOsms upon entering the descending thin limb, and increase to about 1,200 mOsms at the tip; the ascending thin and thick loops are not permeable to water but sodium chloride will diffuse and is actively taken up in these limbs; one of the mechanisms for sodium reabsorption in the thick ascending limb is via the sodium-potassium-2 chloride pump (Na-K-2Cl); this is where furosemide (Lasix) works; these active transport pumps are among the most energy-consuming in the kidney, by inhibiting Na-K-2Cl, there may be a benefit to the oxygen-deprived kidney in critical illness, there is some data to suggest that furosemide may help to maintain kidney function by preserving normoxia of this mechanism; furosemide will tend to decrease serum sodium and potassium as the channels are inhibited; at a certain point in diuresis, however, serum sodium concentrations may begin to rise indicating that the concentrating limit of the kidney for sodium has been reached

The distal convoluted tubule: once the tubular fluid gets to the distal convoluted tubule, it begins once again to become hypotonic at about 100 mOsm; the distal convoluted tubule has further sodium chloride transporters that also lead to re-absorption of water; this is where thiazide diuretics act; they can cause hyponatremia as well as hypokalemia; thiazide diuretics may indirectly also lead to hypercalcemia via increased activity of basal-lateral sodium-calcium transporters; both loop and thiazide diuretics can cause a contraction metabolic alkalosis by indirectly increasing aldosterone levels which increase urinary hydrogen and potassium secretion

The collecting duct: the tubular fluid now leaves the distal convoluted tubule to enter the collecting duct, where urea diffuses into an increase in fluid osmolarity before finally being excreted as urine; the collecting duct is where anti-diuretic hormone (ADH) is active; ADH is one of the major regulators of fluid balance in the body; high levels of ADH released from the posterior pituitary in response to increased blood osmolarity and decreased blood pressure results in the tubular fluid losing water through aquaporin channels to be reabsorbed by the body; alcohol can directly inhibit ADH secretion; syndrome of inappropriate ADH secretion (SIADH) results in hyponatremia; inadequate ADH in diabetes insipidus causes the kidney to produce large amounts of dilute urine

The RAA axis and low-dose(renal-dose) dopamine: renin is released from the macula densa in the kidney where it cleaves angiotensinogen to angiotensin I; angiotensin I is cleaved by angiotensin converting enzyme to become angiotensin II, a more potent vasoconstrictor; angiotensin II activates aldosterone; aldosterone stimulates sodium reabsorption and potassium secretion in the collecting tubules via a number of mechanisms, with resultant water reabsorption; spironolactone is one of the diuretics that works at this site, often called a potassium-sparing diuretic for this reason; it is not recommended for patients with poor kidney function; dopamine has been previously used to increase urine output; it does increase urine output particularly in patients with higher baseline sodium levels by increasing sodium excretion from the kidney; fenoldopam, a dopamine A1 receptor agonist will do the same thing; unfortunately at suggested renal dosing of about 0.5-3 mcg/kg per minute, dopamine dilates both the afferent and efferent glomerular arterioles equally, resulting in increased renal blood flow but little increase in GFR; consequently, renal-dose dopamine is ineffective at

preventing kidney failure and may cause harm, so renal-dose dopamine should generally not be used

Intraoperative Fluid Therapy

Overview: fluid is given 1) to maintain circulating vascular volume both as a replacement for active as well as insensible losses; 2) to increase oxygen delivery and perfusion to tissues; and 3) as a carrier for medications; how much fluid, what kind of fluid, and when to give fluid continue to be the subject of debates; are colloids better than crystalloids?; is less fluid better than more fluid?; are certain kinds of crystalloids superior to others? blood-component therapy is outside scope of lecture; will be discussed only briefly

IV fluids: thoughtful consideration should occur before administering or withholding IV fluids; fluids are drugs, to be dosed as and when necessary; dosing and timing are important; intraoperative fluid requirements fall into the category of resuscitation; the choice of fluids should be made accordingly; all of the following patient and operative variables should be considered when determining patient intraoperative fluid management strategy; 1) is the patient healthy or sick? 2) malnourished or well fed? 3) dehydrated or fluid overloaded? 4) diabetic? 5) in renal failure? 6)what are the electrolyte, hemoglobin, other pre-operative laboratory values? 7) duration of procedure? 8) expected significant bleeding, fluid shifts, unusual or challenging electrolyte or medication-induced changes in the patient's condition? 9) presence of a Foley catheter? has the patient urinated before procedure?

Goal-directed fluid therapy: an integral component of the early recovery after surgery (ERAS) program; describes how to give the right amount of fluids and other necessary interventions and medications in order for the patient to optimally endure and recover from the procedure; optimization is different for each patient; difficult to define how to optimize patient outcomes because of the complexity of human physiology and a lack of basic understanding; there are a number of common elements to surgical procedures that remain more or less constant; 1) patients tend to be vascularly underfilled preoperatively, though efforts being made to combat this; preoperative fluid loading, particularly with medium-chain carbohydrate drinks, is part of ERAS program, despite paucity of data in support; 2) both preload and afterload, as well as inotropy, tend to fall in induction, leading to hypotension in susceptible individuals; 3) in large cases there can be significant fluid shifts that need to be addressed

Fluids and the different vascular spaces: can think of the intravascular space, the circuit that sends blood to the brain, heart and vital organs as being like a leaky bucket with the heart as a pump; this bucket will change in size and often during induction or sepsis will get larger; this is manifest by decrease in systemic vascular resistance(SVR); in hemorrhage, the amount of fluid in the bucket is decreased and the body compensates by making the bucket smaller, by increasing SVR or by circulating the tissue faster by increasing chronotropy and inotropy; to maintain the same relative amount of fluid in the bucket more fluid may be put in the bucket, or alternatively the bucket may be made smaller by using vasopressor agents; or make the amount of the fluid in the bucket seem greater by circulating it faster by using an inotrope or chronotrope; filling the bucket with more fluid is usually the initial approach; rationale for this is that the microcirculation, where tissue perfusion occurs, becomes vasoconstricted during all low flow states, including sepsis, where systemic vascular resistance (SVR) might be very low; thus the larger vessels are dilated, smaller vessels are vasoconstricted and end organ capillaries are receiving very little flow; therefore simply giving a vasoconstrictor agent in this case without putting additional fluid into the bucket would be to shut down the microcirculation even further; as fluid in the microcirculation relies on Stokes flow, increasing volume to the macrocirculation creates an increase in the pressure head to the microcirculation, resulting in increased flow to these small vessels; there is a strong rationale for correcting hemodynamic disturbances initially with fluids; whether to use vasopressors or inotropes next is a subject of debate; since our present world view is to look at blood pressure as a more important measure of hemodynamics than other parameters such as cardiac output, vasopressors usually second intervention chosen; they also require less cardiac energy

Water, electrolyte, and glucose requirements: what kind?, how much? and when?; there are many different algorithms for estimating fluid deficits including the 4:2:1 ratio and the Parkland Formula for Burns; these all right for late 20th century when fluid estimation necessarily empiric; today some sort of cardiovascular monitor should be used as a guide to hemodynamic management; whether it be esophageal doppler, intraoperative transesophageal echocardiography (TEE), arterial waveform cardiac output estimation, pulse pressure waveform measurements, or a central venous pressure (CVP) (or Swan-Ganz) catheter, some sort of objective data should be used as a guide; lecturer defends "much-maligned" Swan-Ganz catheter; criticism made that CVP doesn't correlate with fluid-responsiveness; lecturer points out that many studies looking at goal-directed therapy were done using CVP; device measures hydrostatic pressure of column of fluid from a central vein to a pressure transducer; not always possible to interpret data; fault of practitioner, not device; one of the interesting findings when using monitors of cardiac output or other hemodynamic parameters is observation that patients tend to be intravascularly under-filled on induction and therefore benefit from early initial fluid administration of between ~250 mL and 1 L early in the surgical procedure; fluid given as boluses rather than slow titration provides the benefit of increased intravascular volume and subsequent improvements in cardiac function; this limits amount of fluid given later in procedure and often the total amount of fluid given to patient; a possible target for intraoperative fluid administration is about 4 mL/kg/hour; a patient might require more or less but this is a reasonable target; if most fluid is given up front, it tends to improve hemodynamics and limit the amount of total fluid given; interestingly, hypertensive individuals tend to benefit from early fluid administration, contrary to what might be expected; although their initial blood pressure may be elevated, these patients tend to be intravascularly fluid depleted and dependent to some degree on sympathetic tone; fluid-repleting these patients can help dampen the excessive swings in blood pressure often seen in this patient population

Evidence from the literature: the implication is that we want to limit the amount of fluid given intraoperatively;

this is true within reason; famous curve from Bellamy et al. in *British Journal of Anaesthesia* (BJA) 2006 illustrates how hypovolemia and low blood volume lead to poor perfusion and poor tissue oxygenation; conversely, hypervolemia with ensuing tissue edema also leads to poor perfusion and tissue oxygenation; therefore aim is for patients to be normovolemic throughout procedure; lecturer argues that usually too much fluid is given; third-space losses can be sequel to even best-intentioned fluid strategies; although some studies argue more fluid is better in surgical cases, most of the literature from ARDSNet sepsis trials argues that fluid overload is an important predictor of poor outcome; a recent trial by Myles et al in *New England Journal of Medicine* (NEJM) 2018 reviewed the effect of a restrictive versus a liberal IV fluid strategy for patients at risk for poor outcomes after abdominal surgery; restrictive fluid group received a median 3.7 L over 24 hours during and after surgery compared to the liberal fluid group's median 6.1 L over the same time period; there was no statistically significant difference in disability-free survival at one year, but an increase in acute kidney injury (8.6% vs 5%) in favor of the liberal fluid group; the liberal fluid group also had lower rates of septic complications, surgical site infections, and use of renal replacement therapy; ARDSNet retrospective study and others suggest that patients with greater fluid balance had better cognitive outcomes than those in the restricted fluid group; (Mickelson et al in *American Journal of Respiratory and Critical Care Medicine (AJRCCM))*showed that the vigorous approach of zero net fluid balance might be just as deleterious to the patient as previously instituted practice of giving the patient excess fluid to compensate for perceived insensible losses

Fluid deficit estimation: estimation based on type of surgery, body weight, etc. is vestige of 20th century medicine and is not current standard of care, but is still often used and may be on board exam; the most common fluid estimation algorithm is the Holliday-Segar nomogram, or a 4:2:1 ratio; this comes from a 1957 pediatric paper; the authors estimated total water requirement necessary to offset urinary and insensible losses was approximately 100 ml per 100 kcal/day; the estimated replacement volumes are 4 mL/kg/hour for the first 10 kg, 2 mL/kg/hour for the second 10 kg and 1 mL/kg/hour for each kg after that; for a 70 kg adult this equals 110 mL/hour; whether this is the right amount of fluid depends on many factors

Parkland Formula: another commonly used formula; originally developed for estimation of fluid requirements in burn resuscitation; outdated and tending to overestimate the amount of fluid needed by about a factor of two, the formula is useful as a guide; 4 x patient weight (kg) x % total body surface area (BSA) of burn (estimate using rule of nines) = total fluid to be given within 24 hours (50% of fluid in first 8 hours, remainder in last 16 hours); anecdotally, overhydration of burn patients appears to be more of an issue than under-resuscitation

Summary: goal-directed therapy with a monitoring device or a dynamic parameter such as cardiac output or pulse pressure variation is the standard of care for determining fluid balance in medicine today; still, need to gather all data available; example — if hemodynamic monitor shows normal stroke volume variation, but patient's blood pressure is sagging and there has been no urine output for an hour, reasonable to conclude that patient is underfilled no matter what monitor shows

Third space losses: what are they really? simplistically, approximately 60% of body fluid is in the intracellular compartment and 40% extracellular; roughly 20% of the extracellular fluid is intravascular; intravascular volume can be estimated as 40% times 20% times 70 kg times 60% = 3.4 L for a 70 kg patient; and assuming a hematocrit 40%, a total intravascular fluid of approximately 4.7 L, or approximately 5 L; when the body becomes dehydrated, water moves out of the intracellular space to replete the intravascular space; likewise when fluid is given IV to a patient who is vascularly underfilled and dehydrated, the fluid (assuming it is crystalloid) will fill the intravascular space, leak into extravascular space, and replete the intracellular space; at a certain point, the intracellular space becomes replete and further IV crystalloid fluid that reaches the extravascular, extracellular, or interstitial space simply collects there; at this point, makes sense to switch from crystalloid to a colloid such as albumin; lecturer usually starts to consider this switch after giving around 3 L of crystalloid; colloids remain intravascular longer than crystalloids and draw extravascular fluid back into the vascular space or from the glycocalyx via osmotic forces; if only a colloid were administered or a colloid given first, less extravascular fluid would be available to draw back into the intravascular space and the extravascular space, particularly the intracellular space, would not be repleted; more recently, Starling equation has been reinterpreted; the glycocalyx, the fuzzy layer that covers the vascular endothelium, is the reservoir for fluid and supplies the osmotic gradient that controls fluid returned to the vasculature; in critical illness such as shock and burns, the glycocalyx is interrupted or removed, resulting increased third-spacing of fluid into the extravascular matrix; for practitioner, it is less important to know where the fluid actually goes than to understand ramifications of Starling hydrostatic and osmotic forces

The third space: the third space is the anatomical space that does not contribute to vascular perfusion and is extracellular, such as peritoneal or plural spaces and areas along fascial planes; it is any extracellular, extravascular, interstitial space where fluid collects; contrary to what has been suggested, the third space does exist; fluid-overloaded patients are intravascularly underfilled but whole-body fluid overloaded; eventually the average post-surgical patient will mobilize this fluid, partially via the lymphatics and possibly through postcapillary processes and urinate out excess; auto-diuresis typically takes about one to three days, assuming there are no other extenuating circumstances; post-operatively, blood pressure in this kind of patient can be supported on a nominal amount of pressor agent until the fluid returns to the vasculature and patient returns to his or her hemodynamic baseline; temptation to diurese these patients should be avoided, because even though they are whole-body fluid overloaded, their intravascular status is underfilled, and diuresis will exacerbate the situation; sometimes need to give fluid in order to maintain vascular volume, even though the patient is whole-body fluid overloaded; reasonable approaches can be undertaken with the use of dynamic and static indicators of fluid volume and responsiveness

Choice of fluid: normal saline, Ringer's lactate solution (LR), PlasmaLyte, dextrose 5% in water (D5W); choice of crystalloid is a controversial aspect of fluid management

Normal saline: few years ago racemic Ringers lactate use was discouraged because d-isomer was considered pro-inflammatory; recent studies suggest normal saline is associated with increased renal failure in patients; the SMART and SALT-ED trials reported in NEJM in 2018 found increased acute kidney injury in both critically ill (SMART trial) and non-critically ill (SALT-ED trial) patients; both large trials; patients were given either normal saline or balanced crystalloid (LR or PlasmaLyte); in the non-critically ill patient trial, there was an increase in major adverse kidney events (from 4.7% to 5.6%.); in the critically ill patient trial, 15.4% of patients treated with normal saline experienced a major adverse kidney event as compared to 14.3% in balanced crystalloid group, and these critically ill patients' in-hospital mortality at 30 days was 11.1% in the saline treated patients as opposed to 10.3% in the balanced crystalloids group; other trends included increased requirement for new renal replacement therapy and persistent renal dysfunction; alternatively, McIlroy et al. in *Intensive Care Medicine* in 2017 found there was no association between chloride-rich and chloride-poor IV fluids for acute kidney injury (AKI) and other kidney injury in patients undergoing cardiac surgery; currently, LR or PlasmaLyte appears to be the fluid of choice; are problems with all crystalloids, but inexpensive, and choice should not matter in healthy patients; NS may be preferred in patient with head trauma and low sodium states because the osmotic pressure of normal saline is 308 mOsms/L, which is slightly hyperosmotic compared to blood and more than LR, which is slightly hypo-osmotic at 273 mOsms per liter; normal saline has the potential for a hyperchloremic non-gap metabolic acidosis, and the association with decreased kidney function

PlasmaLyte: PlasmaLyte has more physiologic concentration of electrolytes and thus is theoretically the best crystalloid, but in the absence of any definitive data, cost should be considered; previous trials of PlasmaLyte compared to other crystalloids found worse outcomes in animal models of shock

Hypertonic saline: hypertonic saline useful in conditions of increased intracranial pressure; used along with mannitol to increase tonicity of plasma; draws fluid out of the brain parenchyma and decreases intracranial pressure (ICP); beneficial for resuscitation and shock, but clinical trials do not show any benefit

D5W: fluids such as D5W have no place in intraoperative theater unless glucose control is an issue; although nominally iso-osmolar upon infusion, D5W is very hypotonic and essentially only contributes free water to the body at large; 0.45% NaCl with 5% dextrose (D5 half normal saline) is reasonable as a pre-operative or post-operative maintenance fluid in hemodynamically fluid repleted patients; however, can lead to post-operative hyponatremia, which is otherwise rare in patients treated intraoperatively with standard crystalloid or colloid therapy; one study measured the prevalence of post-operative hyponatremia at only 4.4%, and of these, nearly all received inappropriate hypotonic solutions intraoperatively

Role of colloids vs crystalloids: controversial, but lecturer prefers colloids, specifically albumin 5% in normal saline for fluid repletion, occasionally 25% with furosemide to clear pulmonary edema; fills intravascular space better than crystalloid; only 20% of crystalloid volume remains in the intravascular space after about a half hour; blood loss is replaced by crystalloid in a 3:1 ratio; with a large amount of bleeding, crystalloid requirements can become considerable and contribute to dilutional coagulopathy; colloids are used in 1:1 ratio for blood loss replacement, so less fluid is required than those receiving only crystalloids; very difficult to prove in a randomized clinical trial that one is better than the other; research results mixed; empirically, albumin is the fluid of choice for patients with ascites after a paracentesis; post-hoc analysis of the SAFE trial suggests avoiding albumin for head trauma; otherwise it is useful when excessive amounts of crystalloids would otherwise be used; higher cost of albumin needs to be considered; the substituted starches and gelatins are other colloids that have the same volume-sparing effects as albumin but are largely no longer used in the US because of concerns about adverse kidney function in susceptible patients given these drugs; the hydroxyethyl starches are described by their concentration in the bag, their average molecular weight, and the ratio of hydroxyethyl groups that replace the glucose units; the newest hydroxyethyl starch is trade-named Voluven, (6% hydroxyethyl starch 130/0.4 in 0.9% NaCl); such fluids may return to clinical use in future, but currently risk:benefit ratio unfavorable; when resuscitating a patient intraoperatively, a possible approach is to use as few liters of crystalloid as necessary (probably LR) and then switch to colloids, albumin or fresh frozen plasma (FFP), if there are ongoing bleeding issues, and blood (which is a shear-thinning solution or suspension rather than a colloid)

Hemoglobin levels: general consensus in non-bleeding patients, patients with upper GI bleeds, and septic patients is that a lower threshold of about 7 g/dL of hemoglobin may be as good as 10 g/dL; the *NEJM* TITRe2 study, looking at outcomes after cardiac surgery in patients randomized to a hemoglobin nadir of 7.5 g/dL vs 9 g/dL, did not demonstrate any benefit to a lower transfusion threshold; those patients randomized to a lower transfusion threshold at 7.5 g/dL actually did worse and there were more deaths; in TRICC study, Hébert et al. 1999 described a cardiac subgroup of patients who appeared to do better with higher transfusion thresholds; data from Jehovah's Witness patients and other patients not transfused suggests that hemoglobin can drop to around 4 g/dL before life-threatening events occur; with bleeding patients keep hemoglobin ≥ 7 g/dL but not much more than 9 g/dL; in cardiac patients the hemoglobin may need to be higher; may be possible medical-legal issues when hemoglobin goes below 7 g/dL; based on anecdotal evidence, lecturer prefers to maintain Hb >8 g/dL in the care of frail and cachectic patients; with cancer there is also the possibility of adversely affecting immunologic function, and caution needs to be exercised before transfusing; studies suggest if giving more than a few units of packed red blood cells (PRBCs), ratio of 1:1:1 platelets to FFP to PRBCs is optimal; some retrospective studies suggest a more precise ratio of 1:1:1.2; Holcomb et al. reported results in 2015 from the PROPPR trial, comparing a 1:1:1 to a 1:1:2 ratio of platelets to FFP to PRBCs and mortality in patients

with severe trauma; no significant difference in mortality between the two groups, 12.7% vs 17%, but was less death from exsanguination in 1:1:1 group, 9.2% vs 14.6%, and hemostasis was more readily achieved; there is a tendency for rise in blood pressure with administration of pRBCs, presumably due to scavenging of nitric oxide; FFP has an effect much like colloid and tends to increase blood pressure, although not as much as with pRBCs; platelets are stored at room temperature and whether it is endotoxins or inflammatory lipids that frequently accompany them, they often result in blood pressure dips

Summary: 1) the kidney is integral to the efficient maintenance of fluid volume, elimination of metabolic waste products, maintenance of acid-base balance and production of various hormones; diuretics work in different segments of the nephron and can be useful in decreasing volume overload; 2) the kidney auto-regulates GFR over a wide range of arterial blood pressures; however, in low flow states, GFR may be flow-dependent resulting in inadequate filtration; it may be possible in the acute case that increasing efferent arterial pressure, may preserve GFR, and inhibiting sodium-potassium-2 chloride (Na-K-2Cl) pumps in the ascending limb may decrease oxygen requirements of the kidney, aiding in the preservation of nephron viability under low flow and ischemic conditions; 3) intraoperative fluid therapy in the 21st century should be guided by patient hemodynamic indices, preferably dynamic rather than formula-based; 4) there is no unequivocal evidence to favor colloids versus crystalloids, but most evidence and practitioners support the use of crystalloid initially, followed by colloid if fluid resuscitation requires fluid in excess of what is generally considered normal (about 3 L of crystalloid before switching to colloid is not unreasonable); LR appears to be superior to normal saline, although this is not universally agreed upon, and there are conditions where normal saline might be preferred; 5) the only colloid currently in use in the US is albumin; it should be noted that it is expensive and as a human derived blood component may not be acceptable to all patients; substituted starches now have a black box warning for increased susceptibility to kidney failure, and they are off the market; 6) blood component replacement should be carefully considered in the context of hemodynamic stability and ongoing bleeding; in massive hemorrhage, blood products should be given in a ratio of 1:1:1, platelets:FFP:PRBCs; a hemoglobin of approximately 7 g/dL normally adequate in a hemodynamically stable, non-bleeding patient; although there are caveats in patients with cardiac disease

Suggested Reading

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Hematology and Blood Component Therapy

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Anemia

≤30% of patients have anemia prior to surgery; more common among females and elderly; in 2015, nearly 15 million units of packed red blood cells (PRBCs) administered in United States

PRBCs: 1 bag contains ~200 mL of red blood cells (RBCs) and 5200 mL of plasma citrate and phosphate in citrate-phosphate-dextrose solution; hematocrit between 60% and 80%; shelf life maximum 42 days; multiple types of RBCs available, including leukocyte-poor washed RBCs and irradiated RBCs; during storage, changes occur in RBCs; from 5th to 42nd day, ~20% to ~80% abnormality in RBC shape; cells become more abnormal with number of days in storage; increase in hemolysis from ~1% on 5th day of storage to ~8% on 42nd day of storage; pH drops from ~6.6 to ~6.4 over 42 days

Transfusion goals: maximize O_2 transport to tissues; prevent end-organ damage from malperfusion; optimize hemodynamic stability; increase patient's likelihood of surviving encounter

Transfusion considerations: ABO and Rh needed for compatibility; type and cross-match with ABO and Rh; if unsure of patient's blood type or if emergency, give O-negative RBCs; for plasma administration, ABO compatibility matters but Rh does not; for platelet administration, Rh important and needs to be matched (preferred) but in life-threatening situations, any platelets can be administered (no ABO group needed); Rh-negative pregnant patients (main risk group) getting Rh-positive platelets will need Rho(D) immune globulin (*eg*, BayRHo-D, RhoGAM) after transfusion

Transfusion threshold: usually hemoglobin of 6 g/dL to 7 g/dL; some institutions with sicker cardiac patients use more conservative transfusion threshold of 8 g/dL to 10 g/dL; anemic patients have increased catecholamine demand, some tachycardia and ST segment alterations, new arrhythmias, compromised left ventricular contractility, lactate-associated acidosis, and increased total body O_2 extraction; definition of anemia, <13 g/dL in males and <12 g/dL in females (per World Health Organization)

Incidence of transfusion risks: blood given to wrong person (1 in 15,000) or incompatible transfusion (1 in 33,000); bacterial infections (1 in 500,000); hepatitis B (1 in 200,000); hepatitis C (1 in 1.5 million); HIV (1 in 2 million); based on 2014 data; increase in hypothermia, coagulopathy, acidosis, 2,3-DPG deficiency, hyperkalemia, and microaggregate delivery

Major transfusion risks: acute lung injury (antileukocyte antibodies and donor blood bind to circulating granulocytes in recipient); acute hemolytic reactions (antibodies in recipient bind to ABO surface antigens on donor cells)

Common transfusion risks: less serious; metabolic acidosis and hyperkalemia; hyperkalemia occurs because potassium level in PRBC storage bags can rise to 19 mEq/L to 35 mEq/L at ~21 days of storage

Hypovolemia: primary compensatory mechanism, increased myocardial contractility and decreased systemic vascular resistance; correction occurs over hematocrit range of 30% to 45%; below that, hypovolemic shock and shock states occur; may result from bleeding and repeated phlebotomy in hospitalized patients (average, 40 mL/day to 70 mL/day, 500 mL/wk)

Other transfusion risks: fluid overload, pulmonary edema, posttransfusion circulatory overload, and transfusion-related acute lung injury (TRALI) associated with acute respiratory distress syndrome (ARDS); fever, acute transfusion reactions, increased multiorgan failure, increased infection rate, transfusion-associated immunomodulation, transfusion-associated leukocyte microchimerism, human error

Transfusion studies:

TRICC trial (1999): 838 intensive care unit (ICU) patients in Canada with hemoglobin <9, <72 hours post admission; compared patients with hemoglobin of 7 g/dL to 9 g/dL with those with 10 g/dL; death primary outcome; cardiac and surgical patients excluded; concluded that hemoglobin of 7 g/dL to 9 g/dL reasonable target for transfusion; patients aged >55 yrs should be excluded from restrictive red blood cell therapy; low hemoglobin not bad but higher hemoglobin not any better

CRIT study (2002): published in *JAMA*; anemia and blood transfusion in critically ill patients; observational study; 2 arms, blood sampling and transfusion; blood-sampling group (1100 patients from 145 ICUs) had average of 4.6 blood draws per patient; another 3500 patients with anemia from ICUs identified; concluded that anemia common and should be expected in ICU patients; transfusions become more common with elderly patients and as patient length of stay increases; actual average trigger for transfusion 8.4 g/dL; transfused patients had higher mortality at every admitting hemoglobin level compared with nontransfused patients

Holcomb et al (2015): consider ratio in massive transfusion situations; study showed that transfusion ratio of 1 PRBC to 1 fresh frozen plasma (FFP) to 1 platelet did not result in significant differences in mortality at 24 hrs or 30 days

compared with 1 PRBC to 1 FFP to 2 platelets; normal ratio will be 1:1:1

Cost of blood transfusions: ~$500 per unit plus $1000 for transfusion setup; in surgical patients, these costs can increase up to $1000 per unit, owing to acquisition costs

Transfusion practice: becoming more conservative; administration of blood necessary to treat significant blood loss; in perioperative setting, conservative approach possible, but should be used in guarded fashion; to assess need for transfusion, must consider O_2 delivery and other hemodynamic factors in addition to hemoglobin and hematocrit

Anticoagulation and Coagulopathies

Background: chronic conditions requiring anticoagulation increasing; prevalence of atrial fibrillation predicted to increase from ~5.2 million in 2010 to 12.1 million in 2030; ~90,000 heart valves implanted in United States and 280,000 worldwide each year; half of implanted valves mechanical and patients need lifelong anticoagulation therapy; >600,000 percutaneous intervention procedures performed in United States in 2005 (need dual antiplatelet therapy for some time)

Classic coagulation cascade: partial thromboplastin time (PTT) gives information about intrinsic coagulation path; sensitive to inhibitors and deficiencies of all factors except 7 and 13; prothrombin time (PT) and international normalized ratio (INR) measure extrinsic factors (2, 7, 9, 10, and fibrinogen), used primarily to measure anticoagulant activity of warfarin and vitamin K antagonists; tests take ~45 minutes to 3 hrs to get results

Platelet activity: activation, aggregation, adhesion; *activation* — through von Willebrand factor and factors 2B and 3A; collagen and thrombin most potent platelet activators; *aggregation* — aggregation with adenosine diphosphate (ADP) and thromboxane; *adhesion* — via tissue factors from endothelium

Current tests: thromboelastogram (TEG), rapid thromboelastogram, rotational thromboelastometry (ROTEM); all give similar results

TEG and rapid TEG: monitor interaction of platelets within fiber and mesh of clot during clot formation and lysis over time; physical property of clot measured by using cylindrical cup that holds whole-blood sample at 37°C and oscillated with rotation cycle of 10 secs; *advantages* — assess viscoelastic properties of clot formation in fresh or citrated whole blood in real time; test synthesizes information obtained from multiple coagulation tests such as PT, PTT, thrombin time, fibrinogen level, and platelet count into single readout; *limitations* — inability to fully detect platelet inhibition

ROTEM: very similar; needle oscillates, instead of cup; as clot forms, torque of rotating cup transmitted to immersed pin; degree of pin rotation converted to electrical signal via transducer and monitored via chart recorder; strength of developing clot then increases magnitude of output; during clot lysis, bonds broken between cup and pin and signal decreases; generated forces used to measure clotting time, kinetics of clot initiation, clot strength, and clot lysis over time

Interpretation of TEG results: for prolonged R time (time to clot initiation), FFP recommended because contains all needed clotting factors; prolonged K time (reduced angle) correlates with decreased fibrinogen level or activity, cryoprecipitate recommended; for low maximum amplitude (MA), consider giving platelets or DDAVP because can be result of possible decreased platelet count or function; for elevated lysis >30%, consider antifibrinolytics

Antiplatelet and Anticoagulant Medications

Aspirin: mechanism of action, irreversible acetylation of cyclooxygenase 1 to inhibit platelet generation of thromboxane A2 to produce antithrombotic effect; for reversal, need 4 days until platelet will regain function; for emergency reversal, platelet transfusion needed

Clopidogrel (Plavix): active metabolite irreversibly blocks P2Y12 component of ADP receptors to prevent activation of glycoprotein (GP)IIb/IIIa receptor complex; reduces platelet aggregation; platelets blocked for remainder of lifespan (7-10 days); no reversal agents available; if patient has life-threatening bleed, platelet transfusion needed

Platelet mapping: specialized TEG required if patient on aspirin or clopidogrel; kaolin-activated sample produces strong thrombin response to maximally activate all platelets and cleave all available fibrinogen; shows TEG output that reflects what would be expected if patient not using aspirin or clopidogrel; 2 other TEGs run with ADP-activated receptor or thromboxane A2 receptor; will show aspirin and clopidogrel effects; graphs brought together and algorithm performed to show degree of platelet inhibition

Heparinoids: *unfractionated heparin* — binds antithrombin to increase activity to inactivate thrombin and factor 10A; monitor unfractionated heparins with PTT; reversal with protamine sulfate (1 mg per 100 U unfractionated heparin); if platelet count decreases, must consider diagnosis of heparin-induced thrombocytopenia; variable dose-response relationship based on location of heparin administration and metabolism in body; unfractionated heparins may be used in renal failure; *low-molecular-weight heparin*mechanism same as that of unfractionated heparin but monitor with anti-10A levels; only partially reversed with protamine sulfate; better correlation between dose and anticoagulant response but significant renal clearance; if creatinine clearance <30, change to unfractionated heparin; *fondaparinux (Arixtra)* — activates antithrombin, which inactivates factor 10A; very long half-life with once-daily dosing; does not interact with platelets or platelet factor 4; should not be used with creatinine clearance <30; no reversal agent

Direct thrombin inhibitors: *bivalirudin (Angiomax)* — reversible; inhibits thrombin enzymatic activity; used in liver dysfunction but not in renal dysfunction; half-life ~25 mins but up to 3.5 hrs if patient has renal failure; *argatroban* — direct, reversible, highly selective thrombin inhibitor; half-life is 40 mins to 50 mins but much longer in hepatic impairment; use in renal dysfunction but avoid in liver dysfunction

Warfarin: inhibits synthesis of vitamin K–dependent clotting factors (2, 7, 9, and 10) and anticoagulant proteins C and S; indications include venous thrombosis, pulmonary embolism (PE), atrial fibrillation, and mechanical cardiac valve

Reversal of warfarin-related bleeding: prothrombin complex concentrate (concentrate of factors 2, 7, 9, 10, and proteins C and S); variable doses based on

INR; administer intravenously (IV) slowly over 10 to 15 minutes; avoid repeated doses because of risk of thromboembolic events; minutes to take effect; *vitamin K* — 5 mg or 10 mg IV; several hours to take effect; *recombinant factor 7A* — minutes to take effect; *FFP* — if other medications not available

Newer oral anticoagulants: dabigatran (Pradaxa), rivaroxaban (Xarelto), apixaban (Eliquis); indicated for atrial fibrillation and thromboembolic events

Dabigatran: specific, reversible direct thrombin inhibitor; inhibits both free and fibrin-bound thrombin; *indications* — deep venous thrombosis (DVT) or PE, nonvalvular atrial fibrillation, or postoperative thromboprophylaxis; half-life ~12 hrs to 17 hrs; reversal agent idarucizumab (Praxbind)

Rivaroxaban and apixaban: 10A inhibitors; reversal agents currently under investigation; andexanet alfa (Andexxa) works in older, healthy patients within few minutes after administration for duration of infusion without evidence of clinical effects

Considerations for anticoagulant use: most newer agents have limited reversal agents available; surgical intervention may be needed for these patients; therefore, use conventional anticoagulants (*eg*, heparinoids, warfarin); if long-term follow-up needed or patient unlikely to follow up, newer agents (*eg*, apixaban, rivaroxaban, dabigatran) may be better choices

Thrombocytopenia

Background: platelet count <150,000; present in ~41% of ICU patients; drop in platelet count to ≤50,000 at admission associated with higher mortality rates, increased Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) II score, Simplified Acute Physiology Score (SAPS), and multiorgan dysfunction syndromes; <20,000 associated with increased risk of spontaneous bleeding; important to determine time course of decrease in platelets

Platelet concentrates: prepared from fresh whole blood; RBCs separated by centrifuging whole blood at low speed; then supernatant or platelet-rich plasma centrifuged at high speed to separate platelets; that platelet-rich plug then respun in small volume of plasma; each platelet concentrate contains 50 billion to 100 billion platelets in ~50 mL of plasma (random-donor platelet concentrates); rich in leukocytes (100 leukocytes per U), responsible for the high incidence of fever associated with platelet transfusions; platelets may be stored for ≤7 days, but viability begins to decline after ~3 days; platelet transfusions usually given as multiples of 4 to 6 platelet units

Causes of thrombocytopenia: *outpatient* — pregnancy, immune thrombocytopenic purpura, myelodysplastic syndrome, hypertension, and antiphospholipid antibody syndrome; *ICU* — drug effects, disseminated intravascular coagulation, dilutional thrombocytopenia; *coronary care unit* — exposure to heparin, GPIIb/IIIa receptor antagonists, mechanical devices (*eg*, coronary artery bypass pump, continual renal replacement therapy, intra-aortic balloon pumps); *emergency department* — acute alcohol toxicity, thrombocytopenic thrombotic syndromes, immune thrombocytopenic purpura, drugs; *common hospital drugs* — heparin, phenytoin, ranitidine, vancomycin, piperacillin, sulfonamides, thiazide diuretics

Heparin-induced thrombocytopenia: described as 50% decay rate of platelets; usually occurs 5 days to 10 days following exposure; 5% to 10% of patients develop cutaneous lesions; *thrombosis* — ≤75% of patients develop thrombosis (50% DVT of lower extremities, 10% DVT of upper extremity, ≤25% develop acute PE); *diagnosis* — using 4T system (timing of onset, severity of thrombocytopenia, presence of thrombosis, and rule out other causes of thrombocytopenia); most common test ELISA (rapid but not specific); confirm with serotonin-release assay with radiolabeled serotonin mixed with platelets, then heparin added for confirmatory test; *treatment* — remove heparin or low-molecular-weight heparin; use another anticoagulant (*eg*, argatroban, bivalirudin); provide supportive care

Suggested Reading

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The Central and Peripheral Nervous System

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Basic anatomy overview: the brain, encased in the cranium; the spinal cord comes off the brain and exits the foramen magnum; it is protected by the vertebral column; the coverings of the central nervous system include the pia mater, which is directly adherent to the spinal cord and the brain, the subarachnoid space, where the CSF is located; outside of the subarachnoid space is the arachnoid mater; outside of the arachnoid mater is the subdural space; in the brain, the subdural space encases the bridging veins; at the level of the spinal cord this is a potential space; next is the dura mater, adherent to the skull and the cranium and running down to S2, to the point of the filum terminale; in the epidural space, the area outside the dura mater, is a collection of fat, blood vessels, and lymphatic tissue; below the midbrain, the arachnoid and the dura fuse to form the theca

Epidural space: in the epidural space, the cranial aspect is a potential space between the dura and the skull; bleeding or an abscess will cause expansion of this area and results in compression; at the level of the brainstem or the spinal cord, it is a real space, between the thecal sac and the ligamentum flavum and on the anterior aspect between the thecal sac and the posterior spinal ligament; the epidural space runs from the foramen magnum to the sacrococcygeal ligament; the contents of the epidural space are blood vessels, lymphatics, and nerve roots; the subdural space is a potential space between the dura mater and the arachnoid mater; there are no contents in the subdural space; in the cranium the bridging veins pass through; it is possible for this area to expand

Subarachnoid space: this is another real space between the arachnoid mater and the pia mater; cerebrospinal fluid (CSF) and trabeculae from the pia mater are found here

Spinal cord: has its own unique anatomy and blood supply; the bony spine protects the spinal cord; it allows for a rigid method of posture along with your central muscles; the spinal cord exits the foramen magnum; this goes to L1 or L2 in adults; this level changes as you grow; in a first trimester fetus, the spinal cord will extend to sacral level 5; in newborns the spinal cord comes to L2-4, whereas the conus medullaris in the adult is at L1-L2; from the conus, the cauda equina descends into the thecal sac and out at individual levels

Bony spine: comprised of seven cervical vertebrae, twelve thoracic vertebrae, five lumbar, five sacral, and a coccygeal component that is from three to five bones; multiple ligaments are involved in holding the vertebral bodies together; on the anterior aspect of the spinal cord, two major ligaments, the anterior and posterior longitudinal ligaments; these run anterior and posterior to the vertebral body; in between these vertebrae from C1 to S1, is a disc; the intervertebral disc is comprised of a firm outer fibrous dense layer with a soft gelatinous nucleus pulposus on the inside; posterior to the spinal cord are the supraspinous ligaments, which are most superficial to the skin; your needle would then traverse to the interspinous ligament and then ligamentum flavum; the flavum is the last stop before the dura or theca; once you puncture the theca, you will find the CSF

Bony and cartilaginous landmarks of the spine: the foramen magnum, which is the point where the spinal cord leaves the cranium, estimated at the level of the mastoid process (cervical level 0); there are a couple cartilaginous landmarks in the neck that give indication of level; C4 approximated by the laryngeal cartilage; C6 approximated by the cricoid cartilage; T1 or vertebral prominence is the most prominent palpable spinous process in the back of the neck; T7 approximated by the apex of the scapula; L4-L5 is at the level of the iliac crest, known as Tuffier's line

Blood supply of the spine: the blood supply of the spinal cord breaks down into the anterior two-thirds and the posterior one-third; the anterior two-thirds is primarily motor function and is supplied by the single anterior spinal artery, which is a branch off the vertebral arteries; there are several radicular arteries off the aorta, the most famous being the artery of Adamkiewicz at about the level of T11 or T12, serving the thoracolumbar aspect of the spinal cord; known for being vulnerable during abdominal aortic aneurysm repair surgery, with the potential complication of anterior spinal artery (ASA) syndrome, resulting in flaccid paralysis in the legs; sensory function is intact because the posterior one-third of the spinal cord is supplied by two posterior spinal arteries, which branch off the vertebral arteries

Spinal nerves: there are eight cervical spinal, twelve thoracic, five lumbar, and five sacral nerves; all are paired; the anterior spinal cord develops and gives off the motor ramus while the posterior spinal cord is the origin of the sensory ramus of the nerve root; nerve roots C1 to C7 come off above the vertebrae that they are named for; however, due to C8, all the resultant nerve roots below that, T1 to S5, exit below the vertebrae for which they are named; almost all of these nerves supply a sensory skin dermatome and a muscular myotome; C1 to C3 is the side of the neck; C3 to C5, the upper aspect of the shoulders; C5 to T1, the arms, the hands, the brachial plexus; T1 to T12, the thorax and abdomen, notably the nipple at T4, the umbilicus at approximately T10; T12 to L4, the lumbar plexus which supplies the anterior medial lateral thigh and the medial aspect of the ankle; L4 to S1-S2, supplies the sacral plexus, sciatic, posterior thigh, leg, and foot

Physiology of Nervous System

Brain: the cerebrum contains the cerebral cortex and the subcortical areas

Cerebral cortex: broken down into the frontal, parietal, temporal, and occipital lobes; frontal lobe houses the precentral gyrus, known as the primary motor cortex; discerns good from bad, can anticipate consequences of actions and can suppress actions; responsible for short term memory; important in interpreting social cues; the parietal lobe has sensory aspects or postcentral gyrus, known as the primary somatosensory cortex; deals with recognition and point discrimination; temporal lobe manages the more important aspects of language, audio and visual processing, and creating new memories; the occipital lobe primarily functions as the visual cortex; the cortical areas are all easily visible from the outside

Subcortical aspect of the cerebrum: houses the basal ganglia, which are important in motor control, cognition, and emotion; the thalamus, which controls audio and visual processing, sleep-wake cycles, hunger and satiety; the internal capsule is found subcortically and is largely comprised of the corticospinal tract, helping to carry motor neurons from the precentral gyrus; there are two cranial nerves that come off the cerebrum, cranial nerve I and cranial nerve II, the primary olfactory and optic nerves

Cerebellum; located below the cerebrum and posterior to the brainstem; associated with motor control, attention, and language management

Ventricles: in the brain there are two lateral ventricles, one third ventricle, and one fourth ventricle; all are filled with CSF and play a role in creating, reabsorbing and circulating CSF

Brainstem: the first area below the cerebrum and anterior to the cerebellum is the midbrain, associated with vision, sleep-wake, and temperature regulation; it is the origin of cranial nerves III and IV, the oculomotor nerve and the trochlear nerve; the pons, which is further caudad of the midbrain, is involved in facial motor and sensory function, special senses like taste, and audio and visual processing; the pons is the origin of cranial nerve V (trigeminal), cranial nerve VI (abducens), cranial nerve VII (facial), and cranial nerve VIII (vestibulocochlear); lower down is the medulla, the site of cardiac centers, respiratory centers, a few other chemoreceptors, and the area postrema or vomiting control center; the medulla gives rise to cranial nerve IX (glossopharyngeal), cranial nerve X (vagus), cranial nerve XI (spinal accessory nerve), and cranial nerve XII (hypoglossal); the brainstem communicates closely with the autonomics to control regulation of body functions and responses to endogenous catecholamines and parasympathetic responses

Reticular activating system (RAS): responsible for the regulation of sleep and wake cycles; it helps to maintain attention; there are several structures involved in these functions that run from brainstem to cortex and back; these include the midbrain, the reticular formation, the thalamic intralaminar nucleus, and the dorsal hypothalamus

Respiratory center: located in the medulla; in healthy patients, should be stimulated by carbon dioxide (hypercarbia); CO_2 detected in the carotid body in aortic arch, helps to control the rate and depth of diaphragmatic movement; can be suppressed by many common medications, including opioids and inhaled anesthetics; mechanical insults can alter the effect and function of the respiratory center in cases of trauma or tumor mass effect

Blood supply to the brain: four arteries enter the skull, two internal carotid arteries and two vertebral arteries; the carotid artery, before entering the skull, splits at the C3 level from a common carotid artery into the external and internal carotid arteries; the external carotid artery supplies the facial tissues, the skull, and the meninges; the internal carotid artery enters the skull via the carotid canal and makes multiple branches; the subclavian arteries give rise to the vertebral arteries, which run lateral to the cervical vertebrae in the transverse foramen of the vertebrae; the vertebral arteries enter the skull through the foramen magnum and unite at the level of the pons to form the basilar artery, which sits on the pons

Circle of Willis: the anastomosis of the internal carotid arteries and the vertebral arteries; the internal carotid arteries primarily manage the anterior perfusion of the brain and the anterior circulation of the Circle of Willis, including primarily giving off the middle cerebral arteries and the anterior cerebral arteries; the anterior cerebral arteries are connected by anterior communicating arteries; the vertebral arteries combine to form the basilar artery, which gives off the posterior cerebral and cerebellar arteries; these are connected by the posterior communicating arteries off the internal carotid arteries

Ring formation: sometimes, via anastomoses, the other vessels can make up for the loss of perfusion from one vessel and allow the full brain to be perfused; this is not always the case; areas supplied by the primary cerebral arteries — the anterior cerebral artery supplies the medial frontal, parietal, and the olfactory bulb; the middle cerebral artery supplies the lateral aspect of the frontal lobe, part of the parietal lobe, and the anterior temporal lobe; the posterior cerebral artery supplies the posterior temporal lobe, the occipital lobe, and the thalamus; based on the sidedness of an infarction or a reduction in perfusion, the symptomatology will be different with occlusions of each of these arteries

Venous anatomy of brain: the deep and superficial venous drainages of the brain are different; the deep drainage comes from traditional veins, which come together at the vein of Galen behind the midbrain, which joins the inferior sagittal sinus to make the straight sinus; the straight sinus drains into the confluence of sinuses; the superficial drainage which sits just under the cranium is comprised of multiple dural venous sinuses; the walls of these are the dura, and receive blood from veins; CSF enters from the subarachnoid space and is filtered out

Sinuses: there is a superior sagittal sinus, two transverse sinuses, a straight sinus, and the occipital sinus; these form to make the confluence of sinuses linking up with the deep drainage; the transverse sinus gives off the sigmoid sinuses forming the internal jugular veins, eventually draining into the superior vena cava and returning to the heart

Perfusion within the brain: regulation of cerebral perfusion not fully understood; functions by autoregulation; task of regulation is to maintain a consistent cerebral blood flow (CBF)over areas with varied perfusion pressures; normal blood flow is 45 to 65 mL per hundred grams of brain tissue per minute; a normal cerebral metabolic rate is 3.5 mL of O_2 per hundred grams per minute; when cerebral blood flow and cerebral metabolic rate are working together, known as coupling, that ratio, CBF to metabolic

rate, is between 14 to 18; cerebral perfusion pressure is the mean arterial pressure minus the intracranial pressure; a normal cerebral perfusion pressure is 50 to 100 mm Hg

Autoregulation: classically described as a plateau where with maps between 60 and 150 mm Hg, there is the same cerebral blood flow; however, everyone has their own autoregulation plateau; too low a cerebral perfusion pressure results in ischemia due to reduced cerebral blood flow; a cerebral perfusion pressure that is too high for a personal autoregulation plateau may result in hyperemia and increased intracranial pressure (ICP)

Autoregulation mechanism: the exact mechanism is not known; however, it is hypothesized that pH is involved, that hydrogen ions directly affect smooth muscle in arterial walls, that CO_2 crosses the blood-brain barrier causing vasodilation, that with a higher pH there is less cerebral blood flow, and with a lower pH there is increased cerebral blood flow; $PaCO_2$ has a marked effect on cerebral blood flow; going from a $PaCO_2$ of 20 to 80 results in about a four-fold increase in cerebral blood flow; oxygen saturation and oxygen partial pressure also have an effect; if PaO_2 is less than 50 mm Hg can expect a large increase in cerebral blood flow; other instances that will increase cerebral blood flow will be metabolic rate of oxygen; if high, as with seizures, CBF will have to increase to meet it; in conditions of low metabolic rate, less cerebral blood flow is needed because the two are coupled; an example is clinical or induced hypothermia

Anesthetics and autoregulation: different medications have different effects on CBF autoregulation; inhaled anesthetics typically alter this in a dose-dependent manner; at high dose, reduced cerebral oxygen consumption, vasodilation, which may result in uncoupling, where there is a lot of cerebral blood flow but not a lot of metabolism occurring in the brain; this could cause an unnecessary increase in ICP; propofol will show vasoconstriction and reduced cerebral blood flow and a reduced cerebral metabolic rate; etomidate reduces the cerebral blood flow and the cerebral metabolic rate; ketamine increases cerebral blood flow and the metabolic rate; opioids show no clear alteration of cerebral blood flow or cerebral metabolic rate

Steal and inverse steal: based on path of least resistance; regular steal is increased $PaCO_2$ (hypercapnia) causing vasodilation to all of the brain, flooding the brain but avoiding narrowed vessels, areas that are sensitive or already ischemic; inverse steal ("Robin Hood effect") is a result of a decreased $PaCO_2$; decreased $PaCO_2$ will cause vasoconstriction, drop ICP, and decrease cerebral blood flow; vasoconstriction occurs in normal vessels, while ischemic areas, in which vessels do not constrict normally, have maximal vasodilation and thus maximal perfusion, which can be beneficial

Cerebrospinal fluid (CSF): the CSF is 99% water, comprised of electrolytes, protein, glucose, neurotransmitters, and amino acids; the CSF volume in a person with normal ICP of 5 to 15 is around 100 to 150 mL; the body replaces it every six hours; formation occurs in the choroid plexus in the ventricles and is an ultrafiltrate of plasma; absorption happens at the arachnoid villi, lymphatics, and in the cerebral microvessels; the normal levels of glucose are 50 to 80 mg/dL and the protein should be 15 to 60 mg/dL; acid-base status is an important aspect of CSF; however, the acid-base status lags behind the serum; CSF acidosis or alkalosis takes a while to develop; important to avoid, eg, a CSF alkalosis in patient who retains CO_2 from obstructive sleep apnea OSA)or chronic obstructive pulmonary disease (COPD); can lead to hypoventilation syndrome

Blood-brain barrier: CSF is protected by the blood-brain barrier, which is not the same as the blood-CSF barrier, which is at the choroid plexus; the blood-brain barrier separates the circulation from the brain extracellular fluid; done by capillary endothelial cells at tight junctions, which do not exist in the regular circulation; it is comprised of astrocyte end-feet and a basement membrane; it shows high electrical resistivity; however, it will allow passive movement of some things, typically uncharged molecules, water, some gases, including oxygen and carbon dioxide, and some lipid-soluble medications; the things that are actively pumped across the blood-brain barrier are glucose and proteins; very few drugs penetrate; many are not very lipid soluble; if these medications are in an ionized state, it is extremely difficult for them to cross; the blood-brain barrier can be interrupted by head trauma, aneurysm, brain masses like astrocytomas, abscesses, glioblastoma, infection and meningitis, and procedural interruption

Pathophysiology of the CNS: the brain at no point stores oxygen; it is acutely sensitive to hypoxia and ischemia

Global hypoxia: global hypoxia is a complete loss of brain perfusion; can be due to systemic hypoxemia, or to a low perfusion state resulting in low cerebral perfusion pressure and low cerebral blood flow; conversely, hypoxia can be due to an acute increase in ICP, making it difficult for blood to flow into brain; if hypoxia is prolonged, often results in mentally and physically disabling syndrome that is acutely deadly

Focal hypoxemia and ischemia: usually the result of a loss of perfusion to one of the arteries or arterioles that supply the brain; could be due to hemorrhagic or infarctive cerebrovascular accident (CVA) or to thrombotic (possibly due to atrial fibrillation), infectious, or air embolism; these will typically present with specific symptoms that help localize where the ischemia and hypoxia have occurred

Cerebral blood flow: normally is about 50 mL/100 gm of brain tissue/min; cerebral impairment is seen at around 25 to 30 mL/100 gm/min; the isoelectric electroencephalogram (EEG) is seen around 15 to 20 mL/100 gm/per min; and irreversible damage is seen around 10 mL/100 gm/min; in hypoxia or ischemia, glucose needs to be watched closely and managed; the blood sugar should be 100 to 180 mg/dL; goal is somewhere from 140 to 180 mg/dL; if the glucose control is too tight (eg, <119) there is an increased risk of hypoglycemia; hypoglycemia and hyperglycemia are bad for areas that have experienced tissue hypoxemia

Traumatic brain injury: number one cause of death from blunt trauma; approximately forty percent of trauma deaths are the result of traumatic brain injury, accounts for 20% of deaths in those aged 5 to 45; this is the number two cause of death in that age group; there are some predictors of poor outcomes with traumatic brain injury — being older than 55 years old, a blood glucose greater than 200, poor pupillary reaction when presenting to healthcare providers, a Glasgow coma scale score ≤ 8, hypotension upon presentation, and hypoxemia upon presentation; the

pathophysiology of a TBI starts with the primary insult; the secondary insult is the edema that results from that trauma that leads to intracranial hypertension; intracranial hypertension or increased ICP makes the brain more difficult to perfuse; in this situation, any bout of systemic hypotension will result in decreased cerebral perfusion pressure; even one episode of systemic hypotension in a situation of high ICP greatly increases mortality; the swelling and decreased cerebral perfusion pressure results in ischemia and hypoxia; that makes any injury to the head or brain that much more severe if there are instances of ischemia and hypoxemia; increase in cerebral metabolic rate (eg, from hyperthermia)can compound this

How to avoid a secondary insult: maintain blood pressure, maintain cerebral perfusion pressure, and reduce ICP; the goal is to avoid ischemic or hypoxic insult; the ICP may need to be aggressively reduced with multiple interventions, possibly including surgery

Intracranial pressure: a result of the cranium having a fixed volume; it contains three things, the brain, CSF, and blood; the Monro-Kellie doctrine states that in the setting of a non-distensible cranial vault, blood, CSF, and brain tissue must be in equilibrium; if any is in too great supply, then others get pushed out to accommodate the problem; too much CSF, hydrocephalus; too much blood, hematoma; there is always the potential of tumors or edema; these cause something to be thrown off, whether it is brain, CSF, or blood, and one, two, or even all three are moved out of the cranium; the factors influencing ICP include CSF quantity and distribution; carbon dioxide, which has the most effect on cerebral blood flow — higher $PaCO_2$ leads to increased cerebral blood flow; position affects ICP — supine positioning leads to higher ICP, upright position, lower ICP; increased mean arterial pressure results in increased cerebral perfusion pressure and increased cerebral blood flow, especially if the patient is outside of their autoregulation plateau; space-occupying lesions, hematomas, tumor, abscesses will push CSF out, and as they grow, they can reduce the ability of the body to perfuse the brain; edema will push CSF out of the cranial vault; a normal ICP is 5 to 15 mm Hg; if it increases, there is minimal compensation; CSF is almost always pushed out first; it is pushed into the thecal sac, which helps, and it will temporarily help reduce the ICP; however, if there is a further increase, it will result either in reduced perfusion or herniation of the brain tissue

Management of Elevated ICP

Hyperventilation: some patients may have to be intubated; the hope is that the intubation can be done deep to depress laryngeal reflexes and to depress the hypertensive response from intubation that can further increase intracranial pressure; hyperventilation is another, though temporary, fix; typically, the $PaCO_2$ is brought down to around 30, and this will increase cerebral vasoconstriction; important to remember the delayed CSF response to acid-base status changes; hyperventilation and reduction in cerebral blood flow only works until there is a normalization of CSF pH, at which point the vessels return to a normal caliber, as this is a normal perfusion state as far as the brain is concerned

Other therapy for increased ICP: elevate the head of the bed, if possible; reduce cerebral metabolic rate; this can be done with medications, like propofol or etomidate, or with hypothermia; while in this acute setting, try to maintain a cerebral perfusion pressure above 60 in order to maintain stable cerebral blood flow and avoid the secondary insult of hypoxemia and ischemia; mannitol is a medication that can, as long as it is given slowly, help to increase diuresis and reduce the amount of fluid in the brain; this should be done only if there is an intact blood-brain barrier; if there is a severe head injury, mannitol may not be an option; another option is 3% sodium chloride given to achieve a serum sodium of 145 to 155 mEq/L, with the intention of drawing fluid away from the brain; sedation and paralysis may be needed to reduce ICP and patient straining

Intracranial arteriovenous malformation (AVM): an abnormal connection between an artery and a vein; can lead to increased intracranial pressure; the artery connects to a low-pressure system (the vein); this can result in acute hemorrhage, seizure, focal neurologic deficits, global neurologic deficits, and the potential of death; potential treatments include embolization, radioablation, or craniotomy to correct the aneurysm; however, correction does not completely resolve the problem; the arterial vessel that had been connected to the vein and had been subject to relatively low pressures now experiences higher pressures; normal perfusion pressure may result in a breakthrough at the area that had been corrected; AVMs can sometimes result in regional hyperemia, which may result in edema or hemorrhage; these cases require very tight blood pressure control, especially at the time of emergence and extubation

Cerebral protection, an area of controversy: prevention of neuronal damage or stopping neuronal damage where it has occurred; best method is maintaining cerebral perfusion, keeping the secondary insult from occurring by maintaining systemic hemodynamics, oxygenation, and ventilation; hypothermia can also be used; the reason for hypothermia is to reduce the cerebral metabolic rate of O_2 ($CMRO_2$); each degree Celsius reduction drops $CMRO_2$ by about 7%; mild hypothermia (33-34°C) significantly reduces $CMRO_2$ and cerebral blood flow; moderate hypothermia (26-31°C) produces greater effects, but important to prevent shivering and the adverse intracranial pressure effects that can result; neuromuscular blockade may be needed; can also use medications and anesthetics for cerebral protection, trying to temporize the patient and reduce the effect of the injury; this can include propofol sedation, which reduces the cerebral metabolic rate and cerebral blood flow

Tumors and tumor management: surgical positioning is often fanatical to facilitate the approach to tumors, causing anesthetic issues; prevent facial trauma, as the surgeon has the head; protect the eyes and as soon as the surgeons take over the eyes, instruct them to protect; maintain cerebral blood flow despite a space-occupying lesion; some patients may have intracranial hypertension, a high ICP; some may have herniation; important to review CTs; note level of consciousness of patient; another situation that can happen with tumors is the potential for venous air embolism; this is typically seen with patient in the sitting position for a posterior fossa tumor

Air embolism: venous air embolism is typically thought to be a massive air embolus that can cause immediate right heart failure and loss of perfusion to the rest of the body, but even microemboli can be dangerous; a patent foramen ovale can result in a paradoxical air embolus; these are most dangerous for a patient in the lateral position; they

are often subclinical, as opposed to large venous air embolisms, and are typically diagnosed postoperatively

Spinal cord and the organization of the spinal cord: comprised of the white matter and the gray matter; white matter is myelinated axons running in tracts between the brain and the periphery; the gray matter is neuronal cell bodies, dendrites, and glial cells; this is where a lot of the synapses occur between different nerve roots; spinal cord is organized into tracts that are in very specific aspects of the cord, these are similar neurons that carry information from the periphery to the brain in groups or from the brain to the periphery; afferent nerves arriving at the spinal cord or brain, going from the periphery to the brain; efferent nerves exiting the spinal cord, going from the CNS to the peripheral nervous system; the primary tracts that are grouped together in the spinal cord are the dorsal columns or medial lemniscus; these carry fine touch, proprioception, vibration, and two-point discrimination; two other sensory tracts are the anterior spinothalamic tract, which carries crude touch, and the lateral spinothalamic tract, which carries most of the pain and temperature sensation; the motor efferents are comprised largely of the anterior corticospinal tract and the lateral corticospinal tract; the anterior corticospinal tract deals with central muscles; the lateral corticospinal tract deals with peripheral muscles; the spinothalamic tract carries somatic afferents from the periphery to the brain (somatosensory cortex of postcentral gyrus); the corticospinal tract carries the somatic efferent from the brain (precentral motor cortex)to the periphery

Spinal Reflex: an interneuron bypasses the standard spinothalamic tract; at the synapse of the primary and secondary neuron, the interneuron will synapse with a motor efferent to cause an immediate reflex response; reflex responses occur in the absence of cortical input, speeding up the response to an injury and reducing the injury

Neural Monitoring (evoked potentials): a stimulus is applied to a nerve, and a resulting potential is followed on EEG or an electromyogram (EMG) or electrophysiologic recording; periodic or continuous neural monitoring is done to monitor the spinal cord during surgery to see if anything has changed during the procedure for worse or better; the sensory system is typically watched with SSEPs (somatosensory evoked potentials); this starts with a skin stimulation of peripheral nerves; responses to peripheral stimulation are received in the somatosensory cortex and recorded at the level of the scalp; they are heavily affected by halogenated gas or nitrous oxide, where latency and amplitude can be abolished; they need total intravenous anesthesia (TIVA); along with sensory, watch motor evoked potentials (MEPs); that is done in a reverse manner, a transcranial stimulation of the precentral gyrus with intent to assess motor response from peripheral muscles; this is why neuromuscular blockade is avoided in these patients; it is typically a good idea to have some sort of method of depth monitoring to reduce the duration of the residual anesthetic; purpose of monitoring to be sure that the synapses are functioning normally, neurotransmitters are being released, and responses are being generated; synaptic transmission occurs at the synapse of two nerves; the presynaptic nerve is carrying a threshold-achieving, action-potential stimulus to the postsynaptic nerve, which receives the information via neurotransmitters that are released by the presynaptic axon terminal; the dendrites on the postsynaptic receptor at the synaptic cleft then cause further transduction of information and further release of neurotransmitters

Neurotransmitters: common neurotransmitters: acetylcholine, GABA, dopamine, glutamate, aspartate, substance P, glycine, and catecholamines; motor neurons at a neuromuscular junction release acetylcholine, which is stimulating nicotinic acetylcholine receptors, resulting in muscle stimulation and contraction; this is where you get excitation, contraction, coupling; there's a release of calcium from the sarcoplasmic reticulum; sarcomeres, which are muscle subunits, shorten and cause contraction of the muscle

Sarcomeres: comprised of myosin, which is a thick filament, and actin, which is a thin filament; the head of the myosin attaches to the actin filament and then adenosine triphosphate (ATP) allows myosin heads to release during contraction and further shorten the sarcomere by binding the actin further back; to complete the whole cycle at the end of contraction, calcium is pumped out of the cytoplasm back into the sarcoplasmic reticulum so that this can happen again

Suggested Reading

Ashwell KWS, Waite PME. Chapter 2 — Development of the Peripheral Nervous System. The Human Nervous System (Third Edition), Academic Press. 2012;14-30; **Catala M, Kubis N.** Gross anatomy and development of the peripheral nervous system. Handb Clin Neurol. 2013;115:29-41; **Mandal PK, Saharan S, Penna O, Fodale V.** Anesthesia issues in central nervous system disorders. Curr Aging Sci. 2016;9(2):116-43.

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ANESTHESIOLOGY
Board Review

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Lower-extremity Regional Analgesia

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Topics: lower-limb regional anesthesia; *hip and femur* — quadratus lumborum blocks for hip surgery; suprainguinal fascia iliaca compartment block; regional analgesia before and after hip fracture; lateral femoral cutaneous nerve block; *knee* — adductor canal block vs femoral triangle block; infiltration between popliteal artery and capsule of knee (IPACK); ultrasound-guided local infiltration analgesia

Hip and Femur

Quadratus lumborum block for hip surgery: relatively recent; transversus abdominus plane (TAP) block used for few years; abdominal wall has 3 layers (external oblique, internal oblique, transversus abdominis); if local anesthetic injected in plane between internal oblique and transversus abdominus, anesthetic will diffuse and block nerves originating from intercostal wall and cover part of abdominal wall

Anaesthesia (2011): Carney, with others including John McDonnell (pioneer in field of TAP block), explain that, if clinician aims posterior at point where those muscles resolve into aponeurosis, can inject in that area; corresponds to old landmarked block where clinicians inject in triangle of Petit and attempt to feel 2 pops (aponeurosis corresponding to external oblique at internal oblique), after which local anesthetic injected; quadratus lumborum located more medially, rectangular muscle that spreads from lower ribs and inserts onto pelvis; if injecting near this muscle or toward lateral border, equivalent of TAP block with possibly better spread; this block used for abdominal wall anesthesia and analgesia; different approaches described; quadratus lumborum in cross-section has slightly triangular shape; can inject at lateral border and get similar result to TAP block, or near posterior aspect of muscle and rely on spread to achieve blockade of nerves; some clinicians have described injecting anteriorly to muscle, placing injection site between quadratus lumborum and psoas muscle

BioMed Research International (2017): Ueshima *et* reviewed anatomy and techniques; contains good pictures showing fascial planes; if injecting anteriorly, close to psoas muscle as well as site where psoas compartment block or posterior lumbar plexus block traditionally performed; in that respect, achieve more of lower extremity block and less of TAP block of abdominal wall

Anesthesia & Analgesia (2017): La Colla *et al* published 2 cases in (1 hip fracture, 1 revision total hip arthroplasty); instead of doing psoas compartment block and inserting catheter, performed anterior quadratus lumborum block; saw patients had good analgesia for ~18 hrs; mixture of ropivacaine, dexmedetomidine, dexamethasone injected; dexmedetomidine and dexamethasone not FDA approved for peripheral nerve blocks; patients had no quadriceps weakness; clinicians said they now use this block instead of continuous lumbar plexus block; issue with continuous lumbar plexus block, femoral nerve blocked, so weakness of quadriceps, making it more difficult, possibly more dangerous, for patients to walk and risk of falling; billing another possible issue, since number of units allowed to be billed for quadratus lumborum block lower than inserting psoas compartment catheter; however, seems to have clinical advantage

Regional Anesthesia and Pain Medicine (2017): retrospective cohort study; 9000 patients who underwent 11,000 procedures included in study; no infections related to block; only 1 hematoma; 60 perioperative nerve injuries, of which 43 were sciatic nerve injuries; only 9 cases deemed to be attributable to block (equating to 0.08%, very low complication rate)

Anesthesiology (2002): study by Auroy *et al*; had hotline patients could call when experiencing complications from peripheral nerve blocks; obviously contains reporting bias; out of 394 posterior lumbar plexus blocks, 1 cardiac arrest, 1 death, 2 cases of respiratory failure; complication rate not insignificant with this block; may be the reason many practitioners who used this block have abandoned it; however, not all have abandoned it (still reliable in expert hands), but potential for severe complications; further studies needed to confirm efficacy and lack of side effects

Fascia iliaca compartment block for hip surgery: variation in which injection performed much more proximal than in regular fascia iliaca compartment block; when Wenny described femoral nerve block as paravascular approach, called it 3-in-1 block; by injecting in groin area, local anesthetic would travel into psoas sheath proximally and block not only femoral nerve but also lateral femoral cutaneous nerve, and traveling medially, would also block obturator nerve; clinicians now know obturator nerve actually almost never blocked by this approach; Wenny thought it blocked, because he tested skin of medial thigh (in most patients, covered by femoral nerve); to test for obturator blockade, power of abductor muscles must be tested; femoral block very popular for while

Dalens et al (1989): described alternative approach called fascia iliaca compartment block; used in children, where most blocks performed under general anesthesia or very

deep sedation; concern that injection possibly performed inside nerve, and since patient under general anesthesia, anesthesiologist may not recognize until too late; idea that, by injecting more laterally but under fascia iliaca, local anesthetic would be in right compartment and would diffuse to femoral nerve and lateral femoral cutaneous nerve, blocking both without risk of intraneural injection; ultrasound not used for regional anesthesia at that time; clinician would locate proper area using landmarks and feel 2 pops (fascia lata and fascia iliaca) being pierced by needle, after which dose of local anesthetic injected; Dalens compared femoral block with fascia iliaca compartment block; of 60 patients, all had complete sensory block of femoral nerve innervation, but only 9 had complete sensory block of lateral femoral cutaneous nerve in femoral nerve block group, while 55 out had complete block of sensory area in fascia iliaca compartment block; conversely, complete quadriceps block in only 1 patient; in 37 patients, no block of quadriceps; block from motor site less deep with fascia iliaca compartment block

Anesthesia & Analgesia (1998): similar findings by Capdevila *et al*; compared 3-in-1 block and fascia iliaca compartment block in adults; in 3-in-1 block group, 90% of patients had blockade in femoral nerve area, while 62% had blockade in lateral femoral cutaneous area; in fascia iliaca compartment block group, 88% had block of femoral nerve area, while 90% had block in lateral femoral cutaneous area

Anaesthesia (2011): Hebbard *et al* described block that would be fascia iliaca compartment block but performed above inguinal ligament; once clinician had view of iliopsoas muscle and fascia iliaca using ultrasound probe, probe rotated 90° in parasagittal orientation; would try to bring needle dissecting with fluid as proximal as possible in plane under fascia iliaca, between fascia iliaca and iliopsoas muscle; more proximal, more small branches innervating hip blocked, resulting in better analgesia of hip than performing block under inguinal ligament; initial study was only concept and cadaveric evaluation (no patients); must be careful not to pop through fascia and deep circumflex iliac artery, which lies just superficial to iliopsoas muscle and under abdominal-wall muscles

Journal of Ultrasound Medicine (2017): study by Bullock *et al*; series of 5 patients undergoing total hip replacements who received suprainguinal fascia iliaca technique; all patients had anesthesia in area of lateral femoral cutaneous nerve and anterior femoral cutaneous nerve branches; however, intravenous (IV) morphine equivalents after 24 hrs showed patients had received between 20 mg and 50 mg of morphine equivalents, so does not seem to show analgesia very effective

Journal of Clinical Anesthesia (2016): case report by Alameida *et al*; 3 patients received either clopidogrel or ticlopidine, thus at high risk for bleeding if spinal anesthesia performed; obviously very sick patients so clinicians did not want to give general anesthesia; used fascia iliaca compartment block using the suprainguinal approach; used ropivacaine and mepivacaine, propofol infusion, fentanyl boluses; able to have femoral fixation in those intertrochanteric hip fracture patients performed using no other anesthesia

Acta Anaesthesiologica Belgica (2015): Kumar *et al* compared conventional infrainguinal vs modified suprainguinal approach of fascia iliaca compartment block for patients undergoing total hip replacement; 40 patients randomized to either technique; 40 mL 0.2% mepivacaine; suprainguinal patients had lower visual analog scale (VAS) scores at 6 hrs but no difference at 12 hrs or 24 hrs; significant difference in time to first patient-controlled analgesia (PCA) morphine demand as well as cumulative morphine consumption in first 24 hrs; patients also had lower risk of nausea and vomiting

Conclusions: theoretically, makes sense that more proximal injection will provide better analgesia for hip surgery; more evidence needed to determine if valid approach

Regional analgesia for hip fractures:

Anesthesiology (2003): study by Matot *et al*; 68 patients with hip fracture randomized to epidural or conventional analgesia upon arrival to emergency department (ED); patients had known coronary artery disease (CAD) or at risk for CAD; patients randomized to either intramuscular meperidine or epidural analgesia; of 34 patients in each group, 7 in conventional analgesia group had cardiac events vs none in epidural analgesia group; 7 events consisted of 3 fatal myocardial infarctions, 1 fatal congestive heart failure (CHF), 1 nonfatal CHF, and 2 episodes of new-onset atrial fibrillation; providing analgesia before patient goes to surgery can reduce adverse events; since typically elderly patients with multiple comorbidities, makes sense that, instead of opioids, regional analgesia could be helpful; increasing numbers of teams aiming to provide regional analgesia as soon as patient arrives in ED and diagnosed with hip fracture; logistical issues (*eg*, manpower, equipment, other) exist; other than Matot paper, little evidence exists showing difference in outcomes

Journal of Orthopaedics and Traumatology (2009): Greek study; Mouzopoulos *et al* assessed hip fracture patients at risk for delirium; patients broken down into 3 groups (low, intermediate, and high risk for delirium), based on severity of illness, preexisting cognitive impairment measured using a Mini Mental State Examination, index of dehydration, and visual impairment; 207 intermediate- and high-risk patients randomized to either fascia iliaca compartment block or placebo; rate of delirium lower with fascia iliaca compartment block (10.78% vs 23.8% in placebo group); however, statistical significance only among patients at intermediate risk, not high risk

Pain Research and Management (2015): study by Nie *et al*; 104 patients with hip fracture randomized to either fascia iliaca compartment block or fentanyl IV PCA; patients in regional group reported less pain than those in PCA group; however, 19.6% of patients in fascia iliaca compartment group developed delirium vs 5.7% in PCA group; statistically significant but opposite that of what would be expected; patients in regional group developed delirium more often than those who received fentanyl PCA

Journal of Acute Care Surgery: retrospective review; 108 patients aged >60 yrs with hip fractures; 64 patients received only analgesics, 44 received continuous fascia iliaca compartment block; median time between arrival to ED and block placement >12 hours; patients received block at lower pain-score ratings, however, no differences in inpatient morbidity and mortality; patients

who received block discharged home more often; difficult to draw conclusions because no randomization, only retrospective review

Conclusions: not much other published evidence found comparing regional analgesia with conventional analgesia following hip fracture; no clear evidence that regional analgesia improved outcomes; need more research needs to develop clearer idea of impact

Place for lateral femoral cutaneous nerve block: many clinicians ask if still needed; lateral femoral cutaneous nerve often blocked when femoral nerve block or fascia iliaca compartment block performed; using ultrasound, lateral femoral cutaneous nerve block simple to perform; probe placed in position where femoral nerve block normally done and then moved laterally; sartorius muscle, which typically has teardrop shape, will become visible quickly with round side being medial and pointy side being lateral; following sartorius towards its lateral edge, space seen between pointy side of sartorius and more lateral muscle (tensor fasciae latae); often in that space, small triangular fascial recess where lateral femoral cutaneous nerve lies can be seen; nerve small and often difficult to see clearly but, depending on patient, can sometimes be seen well; if not seen well, area between 2 muscles can be infiltrated, reliably resulting in good block

Journal of Pain Research (2017): Elsey *et al* performed prospective double-blinded randomized comparison of ultrasound-guided femoral nerve block with lateral femoral cutaneous nerve block vs standard anesthetic management (*ie*, general anesthesia with IV opioids) for pediatric patients undergoing surgical repair of traumatic femur fracture; 17 patients in study; 10 randomized to regional group, 7 to IV opioid group; maximal postoperative pain median score 0 in regional group vs 3 in IV opioid group; no significant differences for intraoperative anesthetic requirements, opioid requirements either intraoperatively, in PACU or on floor, or time to first opioid requirements; somewhat surprising results but shows regional anesthesia not always better

Anaesthesia and Intensive Care (2014): Davies *et al* studied 20 volunteers who received ultrasound-guided lateral femoral cutaneous nerve block; orthopedic surgeon drew incision lines showing where he would perform incision for anterolateral, lateral, and posterior approaches for hip arthroplasty; >10 of 20 patients in whom 0% of incision would be covered by block regardless of approach; demonstrates that lateral femoral cutaneous nerve block does not seem to be of obvious usefulness

Acta Anaesthesiologica Scandinavica (2016): Thybo *et al* explored whether lateral femoral cutaneous nerve block had positive effect on analgesia after total hip replacement; included 60 patients with VAS >40 mm after total hip replacement on postoperative day 1 or 2; in first group, patients given block with ropivacaine and after 45 mins, block repeated using normal saline; in second group, patients had block with normal saline and then block with ropivacaine; difference in pain scores relatively minimal; 17 mm in VAS during 30° flexion of hip 45 mins after first block; 42% of patients deemed nonresponders; difference <15 mm

Conclusion: some effect but minimal

Knee

Adductor canal block: goal to inject local anesthetic under sartorius muscle; similar to 1 technique to block saphenous nerve

Differences between block only intended to block saphenous nerve (*eg*, to supplement popliteal sciatic block) and adductor canal block: — 1) when saphenous nerve block done, only that nerve should be blocked; thus, inject as distally as possible to block less of quadriceps of vastus medialis, since nerve to vastus medialis also travels in adductor canal; conversely, when doing adductor canal block for knee analgesia, should inject fairly proximally, typically about mid-thigh, to get spread into canal and block other branches that will contribute to innervation of knee and provide knee analgesia; 2) volume; for saphenous nerve block, typically 5 mL to 10 mL enough; for adductor canal block in average-sized patient, ~30 mL of local anesthetics used; if patient very short, less may be used but must be enough to fill canal and block smaller branches, including some branches of femoral nerve; down canal toward bottom, posterior branch of obturator nerve also crosses canal and will be blocked if you enough local anesthetic given; 3) saphenous nerve block aims only at blocking saphenous nerve; adductor canal block aims at providing analgesia after knee surgery, mostly on anterior aspect of knee; *typical technique* — take ultrasound probe about mid-thigh, slide on medial side of thigh and try to locate sartorius muscle (typically trapezoidal) and femoral vessels (artery and vein) underlying it; artery typically round and pulsatile; vein can be compressed if pressed firmly with probe; near those structures some white hyperechoic tissue, may or may not be nerves, typically seen; small nerves and often difficult to see until local anesthetic injected and area dissected

Technique: this anesthesiologist's personal bias to go in plane between vastus medialis and sartorius muscle, although other clinicians cross sartorius; crossing sartorius can be more painful for patient, but if using small needle for single-injection block, probably acceptable; important not to penetrate vessels, but goal to inject close to vessels; typically, distinct pop felt as probably vastoadductor membrane crossed, fascial layer that goes from vastus medialis to adductor muscles (on posterior side of thigh); inject ~30 mL fractionated with aspiration every few mL; be sure to see nice spread; if no spread, tip of needle might be in vein being compressed because using too much pressure with probe, stop injecting and reassess position of vein and position of needle; if doing saphenous nerve block, can go more distal and vessels will be lost; femoral vessels cross adductor hiatus to become popliteal vessels, but plane between vastus medialis and sartorius muscle still there; in that plane lies saphenous nerve, so inject there and block very little of nerve through vastus medialis

Possible issues with adductor canal: canal has 2 ends and proximally may be spillover to femoral nerve; usually, as some tracer and dye studies have shown, local anesthetic will follow vessels and thus not get to femoral nerve, but femoral nerve blockade possible resulting in quadriceps weakness and risk of fall; conversely, possibility of distal spillover and some of local anesthetic can get

into popliteal fossa; some cases have described sciatic tide blockade with foot drop and weakness of muscle of lower leg; typically, dose of anesthetic that actually reaches those areas quite low, so block will not last as long as main block where dose actually administered; risk of blocking other things when performing adductor canal block

Volunteer studies have shown that adductor canal block spares quadriceps:

Anaesthesiology (2013): Jaeger *et al* compared motor strength of quadriceps muscle as percent of baseline in patients who received placebo injection, adductor canal block, or femoral nerve block; graph in study showed that after ~3 hrs, patients who received femoral nerve block with 30 mL of 0.1% ropivacaine (very dilute anesthetic) lose ~60% of motor strength of quadriceps, while patients who received adductor canal block drop by ~10% of baseline

Regional Anesthesia and Pain Medicine (2013): study by Quoffi *et al* had similar findings; femoral nerve block drops knee extension power to ~10% of baseline after 30 mins, while little change in patients who received adductor canal block; study also evaluated hip adduction (ie, blockade of obturator nerve), with no change from baseline in either group; volunteer study, so finding does not necessarily hold true in patients who have had knee replacement (major surgery with much disruption of proprioception, innervation of knee) and can have some muscle stunting and muscle spasm

Regional Anesthesia and Pain Medicine (2013): study by same team with Jaeger *et al* showed that patients who had total knee replacement and got either adductor canal or femoral nerve block actually lost significant quadriceps muscle strength; median loss ~50% in adductor canal group and ~80% in femoral nerve block group; little change in adductor muscle strength, although not quite normal (~70%–80% of baseline)

Anesthesiology (2014): Kim *et al* studied patients with knee replacement; power of quadriceps measured in kg-force; showed baseline ~15 kg-force in both groups; however, after 6 hrs to 8 hrs, patients with femoral nerve block dropped to ~2 or 2.5 compared with ~7 or 8 in adductor canal group; at 24 hrs and 48 hrs, power significantly reduced in both groups; remember that patients who have had knee replacement will not have normal quadriceps strength regardless of block used

Difference between adductor canal block proper vs femoral triangle block: brought up by team from Denmark; discussed that, from anatomic standpoint, vastoadductor membrane actually starts only in lower third of thigh, really anatomic definition of adductor canal; above level of vastoadductor membrane, sartorius overlies vessels and nerves, but should be called femoral triangle; relevant from anatomic standpoint because different nerves included in those compartments; *femoral triangle* — saphenous nerve, nerve to vastus medialis, some branches such as medial retinacular nerve and medial femoral cutaneous nerve; *adductor canal* — nerve to vastus medialis actually not included in adductor canal proper; nerve to vastus medialis stays superficial to vastoadductor membrane, saphenous nerve still there as well as posterior branch of obturator nerve; spillover possible if injection done distally to popliteal sciatic nerve; therefore, seems blocks obtained by injecting in one location vs other somewhat different; in one case, more anteromedial block, in other case, more medioposterior block; not clear whether injecting in one vs other or maybe both locations would provide best analgesia for knee replacement; needs further investigation; *knowing where vastoadductor membrane starts* sometimes difficult to determine; membrane probably too thin to be visible on ultrasound, but Danish team found anatomic landmark can be used to determine where adductor canal starts; need to look more posteriorly; often clinicians don't look toward posterior edge of sartorius when performing adductor canal block, but if probe moved more medially or more posteriorly, can see adductor muscles; depending on level, will see different muscles; more seen proximal to the adductor longus; *mnemonic to remember order of adductor muscles* — "ALABAMA"; AL=adductor longus, AB=adductor brevis, AM=adductor magnus; order in which muscle stack seen from anterior to posterior; moving up and down thigh, adductor longus will be seen, first wider than sartorius when more proximal; moving farther down the muscle gets smaller and ends up inserting on femur; point where edges visible; lateral and posterior edges of those 2 muscles meet=point where adductor canal proper and vastoadductor membrane start; can use as landmark to decide where to inject

Conclusion: data lacking for best location to inject for knee analgesia; more studies probably published soon, but interesting concept that injecting more or less proximally or distally in same canal can end up with very different distributions of the block

IPACK block and ultrasound-guided local infiltration analgesia: developed by Sinha (Hartford Hospital, Connecticut); goal to inject between vessels and capsule and provide analgesia to posterior aspect of knee without having to perform either sciatic or tibial nerve block that will have motor effect, cause foot drop, or cause sensory blockade of foot and lead to problems when patient tries to walk; Sinha also described ultrasound-guided local infiltration analgesia in which clinician infiltrates several nerves anteromedially, avoiding common peroneal nerve; analgesia quite similar to what surgeons achieve when they infiltrate intraoperatively

Technique: often with patient lateral, although can be done supine if leg elevated similar to popliteal block; attempt to locate popliteal vessels in popliteal area, but instead of targeting tibial nerve (typically superficial to those vessels), try to insert needle between femur and capsule of knee and those vessels; go as far as possible, then inject local anesthetic while pulling out needle; try to infiltrate whole area; will cause blockade of all branches that go into knee, into posterior aspect of knee without blocking any components of sciatic nerve that go into lower leg; initially, Sinha described performing selective tibial nerve block; idea that most of that innervation carried by tibial nerve; if only tibial nerve blocked, no foot drop and patient still able to walk; small percentage of patients who receive selective tibial block still get some diffusion to peroneal nerve and have foot drop, but fairly uncommon; however, some patients will describe some numbness on sole of foot, feeling of walking on cotton, so gait not quite normal after knee replacement,

can sometimes be problem; therefore, Sinha developed IPACK technique

Conclusions: no motor block or sensory disturbances seen with use; reliable but still remains to be fully validated in terms of analgesia after knee surgery

Summary

Cutting-edge topics in regional anesthesia of lower limb: *quadratus lumborum blocks* — possibly helpful for hip surgery; still need large study demonstrating that they work well with no adverse effects; *suprainguinal fascia iliaca compartment block* — few studies; makes sense anatomically but remains to be demonstrated if actual difference compared with regular infrainguinal fascia iliaca compartment block; *regional anesthesia after hip fracture and before surgery beginning in ED* — makes sense; patients more comfortable, receive less opioids; patients typically have multiple comorbidities; more studies needed to determine if it prevents delirium; *lateral femoral cutaneous nerve block* — easy block but questionable benefit; *adductor canal block vs femoral triangle block* — proof of concept exists (anatomic distinction); remains to be seen if difference in knee analgesia*; IPACK and ultrasound-guided local infiltration analgesia for knee surgery* — operator dependent, needs to be learned well; IPACK straightforward; anterior infiltration trickier; operator dependent; some patients very comfortable, some in significant pain; has learning curve

Suggested Reading

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ANESTHESIOLOGY
Board Review

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Physiology of the Endocrine Systems

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Pituitary Gland

Sits in sella turcica at base of brain above sphenoid bone, below hypothalamus

Anterior Pituitary Gland

Overview: "master gland;" trophic cells produce peptide hormones, regulate hormone secretion from thyroid gland, adrenal cortex, ovaries, and testes; other cells produce hormones regulating growth and lactation; some of these hormone-producing cells are themselves regulated by highly specific releasing factors secreted by the hypothalamus, a brain region directly above the pituitary; thyrotroph cells, controlled by hypothalamic thyrotropin releasing hormone (TRH), secrete thyrotropin (thyroid stimulating hormone, TSH); TSH released into circulation by anterior pituitary gland stimulates production and release of thyroxine by thyroid gland; negative feedback system mediated by peripheral thyroid hormones tightly controls thyrotroph cells to inhibit TSH secretion, example of hypothalamic-pituitary-peripheral gland axis; corticotroph cells, controlled by hypothalamic corticotropin releasing hormone (CRH), secrete adrenocorticotropic hormone (ACTH) into the circulation, stimulating the adrenal cortex to release cortisol; negative feedback system mediated by cortisol tightly controls corticotroph cells (hypothalamic-pituitary-adrenal axis (HPA)); ACTH molecule is cleaved from precursor protein composed of melanocyte-stimulating hormone and analgesic peptide endorphin; somatotroph cells in anterior pituitary release growth hormone (GH) when stimulated by growth hormone releasing hormone (GHRH) produced by the hypothalamus; not subject to negative feedback; instead, the hypothalamic peptide somatostatin inhibits GH secretion; somatostatin is also secreted by pancreatic D cells and regulates release of insulin and glucagon; octreotide, a synthetic analogue of somatostatin, is used in treatment of carcinoid syndrome and in management of gastric and pancreatic secretions; lactotroph cells in anterior pituitary release luteinizing hormone (LH) and follicle stimulating hormone (FSH), which share common subunit with TSH ,upon stimulation by hypothalamic gonadotropin releasing hormone (GnRH); receive negative feedback by sex steroids from periphery; prolactin is another anterior pituitary hormone; over- or underproduction of FSH, LH, prolactin rarely impact anesthetic management

Anterior Pituitary Dysfunction

Pituitary macroadenomas: diameter >1 cm; can compress adjacent structures; visual disturbances, seizures, or increased intracranial pressure; compression of optic chiasm causes bitemporal hemianopsia; acute bitemporal hemianopsia occurs with apoplexy of pre-existing pituitary adenoma, warrants urgent or emergent surgery; many macroadenomas produce only parts of TSH, LH, or FSH molecules; termed nonfunctioning; other anterior pituitary disorders involve hyper-or hypofunction; Most common examples of hyperfunction are excesses of prolactin, growth hormone, and cortisol; acromegaly and Cushing disease most relevant to anesthesia

Acromegaly: somatotroph hyperfunction, excess GH production, secretion; GH-secreting pituitary tumor; GH stimulates bone, cartilage, and soft tissue growth; overgrowth of membranous mandibular bones, prognathism, and soft-tissue overgrowth of lips, tongue, epiglottis, and glottic structures can result in challenging airway management; connective tissue overgrowth can cause recurrent laryngeal nerve paralysis, carpal tunnel syndrome, other peripheral neuropathies; anatomic changes are slow and often go unnoticed; patients can develop glucose intolerance, muscle weakness, arthritis, osteoporosis, hypertension, obstructive sleep apnea (OSA), congestive heart failure, dysrhythmias, coronary artery disease; primary treatment is surgical removal of pituitary tumor; medical management if symptoms persist after surgery includes radiation, dopamine agonist (eg, bromocriptine, cabergoline), somatostatin analog (eg, octreotide); excision often transsphenoidal; soft-tissue, metabolic effects may resolve after surgery, but bony changes will persist

Anesthesia issues in patients with acromegaly: patients should be evaluated for other endocrinopathies and cardiac disease preoperatively; airway management is major anesthetic concern; difficult establishing conventional mask airway; extra-large oral airways or extra-large face masks may be helpful; endotracheal intubation challenging; external airway assessments may fail to detect hypertrophy of tissues in posterior pharynx or immediate supraglottic area; reassuring external assessment of eg, neck mobility or Mallampati class possibly misleading; ensure advanced airway and tracheostomy equipment available; consider awake fiberoptic intubation; may need small-diameter endotracheal tubes; because expert assistance and advanced airway equipment may be needed, good idea to line these up in advance and avoid providing anesthetics outside of OR; closely monitor blood glucose; osteoporosis and increased susceptibility to peripheral neuropathies warrant careful positioning; patients with

OSA at high risk for postoperative airway obstruction; monitor muscle relaxant effects via peripheral nerve stimulator, titrate; respiratory depression effects of narcotic analgesics may be severe; in presence of airway abnormalities, consider opioid-sparing analgesics

Cushing disease: Clinical presentation of corticotroph hyperfunction, resulting in unregulated excess secretion of ACTH and excess secretion of cortisol by adrenals

Anterior pituitary hypofunction: mass effect due to large pituitary adenoma most common cause; other causes are trauma, radiation, apoplexy, tumors, infiltrative disease, and surgical hypophysectomy; in Sheehan syndrome, hemorrhagic shock during parturition causes vasospasm and subsequent pituitary necrosis postpartum; severe manifestations of adrenal insufficiency (eg, hypotension) typically develop over 4-14 days after anterior pituitary destruction; in conditions of stress from surgery, glucocorticoid supplementation may be warranted; half-life of thyroid hormone 7-10 days, symptomatic hypothyroidism unlikely until 3-4 weeks after pituitary surgery or apoplexy

Pituitary surgery: gland usually accessed by trans-sphenoidal approach through the nose or beneath the upper lip; anesthesiologist thus has little access to airway during the case; endotracheal intubation warranted; airway management challenging; potential for bleeding from cavernous sinus; invasive monitoring and large bore intravenous (IV) access not typically needed; medical condition of patient may warrant use of arterial line; possibility of conversion to open craniotomy, though unusual, should be included in contingency planning; intraoperative magnetic resonance imaging (MRI) may be used, thus must plan for safety needs of this modality

Posterior Pituitary Gland

Overview: composed of nerve terminals of neurons originating in hypothalamus; is extension of the brain and secretes directly into circulation; 2 types of posterior pituitary cells; one stores and secretes peptide antidiuretic hormone (ADH); other secretes oxytocin

Antidiuretic hormone(vasopressin): regulates plasma osmolarity and extracellular fluid volume; facilitates renal tubular water resorption; intravascular hypovolemia, pain from trauma or surgery, nausea, and positive pressure airway ventilation stimulate secretion; is also vasoconstrictor

Diabetes insipidus (DI): kidney unable to retain free water; causes polydipsia and polyuria, dilute urine, high serum osmolarity, urine output >2 L/day; central and peripheral causes; central DI, insufficient vasopressin secretion by posterior pituitary; caused by intracranial trauma, hypophysectomy, metastatic disease; in peripheral DI, no renal response to vasopressin (thus called nephrogenic DI), due to hypokalemia, hypercalcemia, obstructive uropathy, chronic renal insufficiency; mild DI defined as daily urine volume 2-6 L; if adequate thirst mechanism, mild DI requires no treatment; but fasting DI patient can rapidly develop volume depletion and hypernatremia; direct management at hypovolemic hypotension; use normal saline, Ringers lactate, or other fluids of near-normal tonicity; significant volume often required to achieve normal volume and normal osmolarity; monitor and titrate urine output, plasma volume, sodium, and osmolarity in immediate perioperative period; for acute or advanced central DI, treat with synthetic vasopressin analog desmopressin (DDAVP); can be used IV or subcutaneously; consider use intraoperatively and immediately postoperatively; side effects include hyponatremia, hypertension, and coronary artery vasospasm; anesthesiologist less likely to need to treat nephrogenic DI; need to manage volume and electrolyte status if patient fasting; vasopressin and analogues ineffective

Syndrome of inappropriate release of antidiuretic hormone (SIADH): persistent secretion of vasopressin in absence of osmotic stimulus; caused by malignancy, certain drugs, CNS disorders (eg, trauma, infection, and tumor); associated with pulmonary conditions (eg, tuberculosis, pneumonia, positive pressure ventilation, chronic obstructive pulmonary disease); urine osmolarity greater than serum osmolarity; urine sodium >20 mEq/L; serum sodium <120 mEq/L; if serum sodium <110 mEq/L, cerebral edema and seizures may result; fluid restriction primary medical treatment for mild hyponatremia; asymptomatic chronic hyponatremia rarely fatal, often treated with demeclocycline, which antagonizes vasopressin on renal tubules; IV resuscitation with fluids containing high concentrations of sodium reserved for symptomatic, severe hyponatremia (ie, serum sodium <120 mEq/L); hyponatremia corrected no faster than 0.5 mEq/L/hr to prevent irreversible central pontine myelinolysis

Oxytocin: stimulates uterine contraction and milk ejection; exogenous oxytocin administered to contract uterus following cesarean section; rapid administration prior to delivery can cause uterine tetany and compromised utero-placental blood flow; rapid administration postpartum after cesarean can cause hypotension

Thyroid Gland

Overview: thyroid disease second most common endocrine disorder encountered perioperatively (diabetes mellitus first); present in ~1% of adult population, with female:male ratio 5-10:1

Thyroid anatomy**:** gland sits at base of neck just inferior to cricoid cartilage; two lobes, one on either side of trachea, connected by thyroid isthmus; parathyroid glands are immediately behind thyroid as are recurrent laryngeal nerves, which control glottis and vocal folds; these nerves at risk for damage during thyroid and parathyroid gland surgeries, thus possible airway obstruction from medialized vocal cords factors into decisions about extubation; thyroid gland originates in fetus in foramen cecum at back of the tongue, then descends into lower anterior neck; thyroid tissue may persist between tongue and lower neck, including in airway; this tissue is highly vascular and injury during airway management (eg, mechanical trauma from laryngoscopy) can result in significant bleeding; thyroid tissue may also extend into the anterior mediastinum (substernal thyroid tissue) and may require more extensive and complicated surgery; large thyroid masses may displace, compress, or invade trachea and compromise airway; review of plain films and neck or chest CT scans very important in planning airway management; emergency tracheostomy may be difficult with large thyroid masses

Thyroid physiology: TSH (anterior pituitary) stimulates thyroid gland to uptake iodine and produce hormones T3

and T4; 80% of T3 produced by conversion from T4 in peripheral tissues; T3 20-50 times more potent than T4 but has shorter half-life; T3 and T4 extensively bound to plasma proteins, (up to 99%); only free or unbound thyroid hormone biologically active; T3 and T4 major regulators of metabolic activity; alter speed of biochemical reactions, total body oxygen consumption, and heat production; thyroid function tests (TFTs) include serum TSH, currently best initial screen for function evaluation; TSH increases with hypothyroidism, decreases with thyrotoxicosis; starvation, glucocorticoids, stress, dopamine, and fever may suppress TSH level; thus, assess total T4, free thyroxine index, and total T3 in sick patients

Hyperthyroidism: excess secretion of thyroid hormone by thyroid gland; etiology of thyroid surgery patient's hyperthyroidism likely to have been explored by endocrinologist; good to consult with endocrinologist about patient's medical management and its effectiveness; thyrotoxicosis is excess thyroid hormone from causes other than new hormone synthesis by thyroid gland, most commonly excess ingestion of exogenous thyroid hormone; signs and symptoms of excess thyroid hormone include muscle weakness, leukopenia, anemia, thrombocytopenia; low clotting factor concentrations from increased metabolism may cause increased sensitivity to anticoagulation therapy; hyperthyroidism may cause dysrhythmias and is a leading cause of sinus tachycardia, atrial fibrillation, palpitations, hypertension, and high output or ischemic congestive heart failure; ophthalmic disease with proptosis and periorbital edema only with Graves disease; chronic treatment of excess thyroid hormone production by thyroid gland includes gland ablation via surgery or radioactive iodine; medical management includes inhibition of hormone production with anti-thyroid drugs (eg, propylthiouracil [PTU], methimazole); up to 4-12 weeks required to normalize hormone levels; side effects of antithyroid medications include hepatitis and agranulocytosis

Thyroid storm: endocrine emergency; physiologic decompensation due to high thyroid hormone level; infection, surgery, trauma, cessation of anti-thyroid medications, excess iodine, iodinated IV contrast agents, and amiodarone may precipitate; may occur up to 6-18 hours postoperatively; manifestations include diarrhea, vomiting, hyperpyrexia, hypovolemia, tachycardia, congestive heart failure, hypotension, shock, weakness, irritability, delirium, and coma; may mimic malignant hyperthermia, neuroleptic malignant syndrome, sepsis, hemorrhage, pheochromocytoma crisis, or transfusion or drug reaction; mortality rate if untreated >20%; treatment includes blocking thyroid hormone synthesis and release, blocking T4 to T3 conversion, suppressing sympathetic responses with beta-adrenergic blockade, and supportive therapy (eg, active cooling, meperidine to attenuate heat production from shivering, vigorous hydration, electrolyte replacement); steroids indicated if suspicion of adrenal insufficiency, including cardiovascular decompensation

Anesthesia considerations: ideally, patient should be euthyroid prior to surgery to avoid thyroid storm; anti-thyroid drugs, pharmacologic iodine doses, and beta-adrenergic antagonist medications should be continued through surgery; in emergent situations, thyrotoxic patients can be prepared for surgery in <1 hr with high-dose IV propranolol or esmolol, titrated until heart rate <100 bpm; propranolol, beta-adrenergic receptor blocker, inhibits peripheral conversion of T4 to T3; consider generous sedative premedication unless there is concern for airway compromise; avoid sympathetic stimulation from pain, beta-adrenergic agonists, or ketamine; regional anesthesia beneficial to prevent sympathetic responses; addition of epinephrine to local anesthetics risky because systemic uptake could worsen tachycardia and hypertension; thrombocytopenia may occur; perform platelet count before initiating regional anesthetic; patients may be hypovolemic due to hypertension, diarrhea, or perspiration; hypotension treated with vasopressors and fluid therapy; anticipate brisk tachycardic response to anticholinergic drugs; with Graves disease, protect proptotic eyes, which may not fully close; drug metabolism and anesthetic requirements often increased; however, myasthenia gravis may occur with Graves disease, up to 30-fold increased incidence, titrate muscle relaxants carefully

Hypothyroidism: low level of thyroid hormone; may be congenital or result from surgical damage, medication side effects, iodine deficiency, radioiodine ablation, radiation, or secondary to pituitary disease; autoimmune Hashimoto thyroiditis common cause of hypothyroidism in adults; associated with other autoimmune processes such as systemic lupus erythematosus, rheumatoid arthritis, primary adrenal insufficiency, pernicious anemia, type 1 diabetes, and Sjogren syndrome; clinical features of hypothyroidism include impaired mentation, periorbital edema, facial edema, enlarged tongue, ascites, normochromic normocytic anemia, coagulation abnormalities, delayed gastric emptying; potential cardiovascular and hemodynamic complications include diastolic hypertension, pericardial effusion, bradycardia, intravascular hypovolemia, diminished baroreceptor reflexes, reversible cardiomyopathy, conduction abnormalities; there may be hyponatremia, fluid overload from decreased water excretion and reduced glomerular filtration rate (GFR), SIADH, and increased risk of autoimmune adrenal destruction with decreased cortisol and aldosterone production; treatment is thyroid hormone supplementation; T4 once daily, requires 7-10 days for effect, 3-4 weeks for stable state; T4 dose adjusted every 4-6 weeks based on serum TSH level; T3 not routinely used because of short half-life, but cautious T3 dosing may be used to hasten recovery; IV thyroid hormone requires caution in presence of coronary artery disease; may induce cardiac ischemia; daily IV dose 50%-60% of oral dose

Myxedema coma: profound hypothyroidism with physiologic decompensation; surgery, drugs, trauma, and infection can precipitate; clinically, decreased mental status associated with hyporesponsiveness to carbon dioxide (CO_2), congestive heart failure, hypothermia, and exaggerated symptoms of hypothyroidism; treatment includes IV T3, passive rewarming, supportive care, (eg, intubation, ventilation, correction of electrolyte abnormalities, glucocorticoid therapy, management of hypotension, congestive heart failure, and effusions); identify and treat precipitating cause (eg, myocardial infarction (MI), cerebral vascular accident, infection); active rewarming will cause vasodilation and hypotension

Surgery and hypothyroidism: only severe hypothyroidism requires postponing elective surgery; securing airway may be difficult if enlarged tongue, relaxed oropharyngeal

tissues, goiter, or poor gastric emptying; prone to hypotension from hypovolemia and blunted baroreceptor reflexes, especially with cardiac depressants and vasodilators; possible CO2 insensitivity and increased sensitivity to central nervous system (CNS) depressants and paralytic medications; corticosteroid supplementation needed if there is concomitant autoimmune adrenal insufficiency; increased likelihood of congestive heart failure, hypothermia, hypoglycemia, hyponatremia, and delayed emergence

Thyroid surgery: indications include neoplasms, thyroid malignancy, hyperthyroidism resistant to medical management, retrosternal goiter, and goiter causing obstructive or cosmetic symptoms; general anesthesia with endotracheal intubation is most common anesthetic technique; preoperatively, assess thyroid function and prepare for potentially difficult airway management; some surgeons monitor recurrent laryngeal nerve integrity with electromyography (EMG); recording electrodes inserted into laryngeal muscles or external electrodes fitted onto endotracheal tube detect laryngeal muscle activity in response to nerve stimulation; alternatively, laryngeal mask airway (LMA) may be used for airway management; this allows intraoperative visualization of vocal cord function with fiberoptic scope; neuromuscular blockade must be avoided or minimized; acute airway obstruction earliest and most critical postoperative complication, causes include bleeding, edema, exacerbation of pre-existing tracheomalacia, or bilateral recurrent laryngeal nerve paresis; anticipate need for urgent or emergent re-intubation or emergent return to operating room; phrenic nerve injury or pneumothorax other causes of early respiratory compromise; later, hypocalcemia from hypoparathyroidism; typically no immediate need for thyroid hormone replacement; typically no major postoperative pain, but may be nausea; prophylactic antinausea agents may be beneficial

Parathyroid Hormones and Calcium

Overview: calcium essential for neuromuscular excitability, cardiac automaticity, coagulation, muscle contraction, neurotransmitter and hormone secretion and action, and enzyme activation; parathyroid hormone (PTH) and vitamin D maintain extracellular calcium concentration within narrow range; the 4 parathyroid glands produce PTH in response to levels of ionized calcium and magnesium; PTH increases intestinal calcium absorption and increases osteoclastic release of calcium and phosphorus from bone; decreases renal clearance of calcium and enhances formation of biologically active 1,25-dihydroxyvitamin D by kidneys; vitamin D augments effects of PTH, necessary for calcium absorption from gastrointestinal (GI) tract; 1,25-dihydroxyvitamin D made in skin after sun exposure and activated by hydroxylation in liver and kidneys; calcitonin from thyroid C cells lowers calcium and phosphorus concentrations by inhibiting renal calcium reabsorption and osteoclast activity; calcitonin has limited physiologic role in humans; serum calcium divided into bound and unbound forms; principal binding protein is albumin; phosphate, citrate, and other anions complex roughly 6% of total serum calcium; hypoalbuminemia decreases total calcium approximately 0.8 mg/dL for each g/dL of albumin below normal (ie, 4.0 g/dL); unbound form called free calcium or ionized calcium; acidosis increases and alkalosis decreases ionized calcium, due to alterations in albumin binding; ionized calcium physiologically important form can be measured directly in whole blood

Hypercalcemia: causes include hyperparathyroidism, malignancy, immobilization, granulomatous disease, vitamin D intoxication, renal disease, and adrenal insufficiency; hyperparathyroidism characterized by hypercalcemia, hypophosphatemia, and elevated PTH; usually caused by parathyroid adenoma; parathyroid hyperplasia also associated with pituitary adenoma and increased tumors in multiple endocrine neoplasia, type 1 (MEN I), or medullary thyroid carcinoma and pheochromocytoma in MEN, type 2A (MEN IIA); parathyroid carcinoma is rare cause of hyperparathyroidism and hypercalcemia; hypercalcemia of malignancy due to release of PTH-like molecules from tumors and cytokine-mediated or direct bony destruction, results in resorption of calcium from bones; clinical features of hypercalcemia include nausea, vomiting, osteoporosis, muscle weakness and atrophy, fatigue, pancreatitis, seizures, depressed mental status, dehydration, hypertension, dysrhythmias, catecholamine resistance, anemia, and/or thrombosis; mild hypercalcemia often asymptomatic; total serum calcium >13 mg/dL, increased risk of end-organ calcification, renal calculi, and nephrocalcinosis; total serum calcium >14-15 mg/dL considered emergency, may see uremia, coma, cardiac arrest, and fatality; acute treatment includes hydration with normal saline to maintain urine output of 100-150 mL/hr; for volume overload administer furosemide; monitor for hypokalemia, hypomagnesemia, fluid overload, and diuresis-induced hypovolemia; if renal or cardiac failure, consider dialysis; medical management includes bisphosphonates, gallium nitrate, or glucocorticoids; effects require several days; calcitonin may be used acutely but effects are transient; hypercalcemia >12 mg/dL warrants correction preoperatively; intravascular volume and electrolyte abnormalities require normalization and monitoring; unpredictable effect on neuromuscular blockade, titrate muscle relaxants carefully; muscular weakness may worsen respiratory function; careful positioning warranted because of possible osteoporosis; patients predisposed to digitalis toxicity, conduction abnormalities; avoid hypoventilation because acidosis increases free calcium

Hypocalcemia: serum calcium, corrected for albumin levels, <8.5 mg/dL in the absence of hypoalbuminemia or pH abnormalities; major cause is hypoparathyroidism due to underproduction of PTH; rarely, end-organ tissues may resist PTH effects; PTH underproduction may occur after gland damage during neck surgery; symptoms may be seen immediately postoperatively or days to weeks later; other causes of PTH underproduction include radiation, hemosiderosis, infiltrative processes like malignancy and amyloidosis, severe hypomagnesemia; less common causes include severe vitamin D deficiency, sequestration of calcium (eg, from extensive burns, fat emboli, or pancreatitis), furosemide, hyperphosphatemia, and antiepileptic drugs; in OR, massive transfusion, especially with liver failure, results in hypocalcemia when citrate binds to calcium; often asymptomatic until total calcium <7 mg/dL or ionized calcium <2.8 mg/dL, especially if onset insidious; level of ionized calcium is sometimes

reported in mmol/L; reference range is 1.14-1.30 mmol/L; chronic hypocalcemia causes lethargy, muscle cramps, prolonged QT interval, renal failure, cataracts, dementia, personality changes; acute hypocalcemia produces neuromuscular irritability with muscle cramps and hand, foot, and circumoral paresthesias; facial nerve irritability to percussion (Chvostek sign); carpal spasm with tourniquet ischemia for 3 minutes (Trousseau sign); severe hypocalcemia results in stridor, laryngospasm, tetany, apnea, coagulopathy, hypotension with catecholamine resistance, psychosis or confusion, and seizures unresponsive to conventional therapy; severe or symptomatic hypocalcemia should be treated with IV calcium; administer centrally when possibly because irritant to veins; 10 mL ampule of calcium gluconate contains 93 mg elemental calcium, 10 mL ampule of calcium chloride contains 273 mg; less urgent situations treated with infusion of elemental calcium over 8-12 hours; monitor calcium, creatinine, electrocardiogram (ECG), and hemodynamic status during therapy; in anesthesia, assess and correct calcium, electrolyte abnormalities, respiratory or metabolic alkalosis, hypothermia; rapid infusions of blood products (especially with hepatic insufficiency) and renal dysfunction can worsen hypocalcemia; follow coagulation status; may see hypotension with insensitivity to beta-adrenergic agonists; can be prolonged QT interval, advanced atrioventricular block, and digitalis insensitivity; response to neuromuscular blocking drugs unpredictable; careful positioning required because of possible osteoporosis

Parathyroid surgery: anesthetic considerations and surgical complications like those for thyroid surgery; general anesthesia or regional techniques used; may perform recurrent laryngeal nerve monitoring intraoperatively; blood may be sent intraoperatively for PTH levels, with 50% reduction predictive of surgical success; circulating half-life of PTH is minutes; no major postoperative pain; nausea common, administer prophylactic anti-nausea agents

Adrenal Cortex

Overview: adrenal gland cortex secretes glucocorticoids, mineralocorticoids, and androgens; adrenal medulla secretes catecholamines; glucocorticoids, mineralocorticoids, and catecholamines maintain homeostasis in stress

Glucocorticoids: cortisol principle glucocorticoid hormone, produced daily in diurnal manner in response to ACTH;, required for converting norepinephrine to epinephrine in adrenal medulla and for producing angiotensin; acts as anti-inflammatory agent and has multiple effects on carbohydrate, protein, and fatty acid metabolism; stress increases cortisol release; cortisol raises blood pressure by augmenting catecholamine-induced vasoconstriction

Cushing syndrome: glucocorticoid excess; most common cause is exogenous steroid administration, eg, chronic treatment with prednisone for inflammatory conditions; endogenous causes include excess ACTH secretion from the anterior pituitary, ACTH secretion from tumors elsewhere, and excess cortisol secretion secondary to adrenal adenoma or adrenal hyperplasia; clinical features include truncal and facial obesity, gastroesophageal reflux disease, hypernatremia, hyperglycemia, hypokalemia, excess intravascular volume, refractory hypertension, hypercoagulability, muscle wasting and weakness, skin fragility, and osteopenia or osteoporosis; endogenous glucocorticoid excess can result in hypertension refractory to treatment; excess intravascular volume can be reduced with diuretics, but potassium must be replaced; monitor and manage serum glucose levels; careful positioning necessary due to osteoporosis; may be unrecognized coronary artery disease; consider venous thrombosis prophylaxis if glucocorticoid excess; adrenalectomy is performed for adrenal adenoma or hyperplasia, may be open or laparoscopic; excess ACTH secretion treated by tumor excision; start glucocorticoid replacement postoperatively for unilateral and bilateral adrenalectomies; mineralocorticoid replacement only necessary if bilateral

Glucocorticoid deficiency: causes include loss of ACTH secretion by pituitary gland, drug side effects, and destruction by infection, metastatic tumor, autoimmune processes, or hemorrhage; long-term exogenous steroid administration may suppress HPA axis within 2 weeks of high-dose therapy and suppression can persist for up to 12 months after treatment stopped; no suppressant effects on mineralocorticoids from exogenous glucocorticoid treatment; glucocorticoid deficiency symptoms may include episodic fever, abdominal pain, and hypotension; presentation may appear as acute surgical abdomen; primary adrenal insufficiency known as Addison disease; associated with both low cortisol and low aldosterone levels, resulting in weight loss, weakness, nausea and vomiting, abdominal pain, and postural hypotension; mineralocorticoid deficiency will lead to decreased urinary sodium conservation, decreased response to circulating catecholamines, and hyperkalemia; treatment of primary adrenal insufficiency requires both glucocorticoid and mineralocorticoid therapy; secondary adrenal insufficiency precipitated by abnormalities in ACTH secretion; results in low cortisol level but normal aldosterone function; may have panhypopituitarism with symptoms of TSH, growth hormone, or gonadotropin deficiency; excess exogenous glucocorticoid therapy will also cause secondary adrenal insufficiency; secondary adrenal insufficiency requires glucocorticoids; mineralocorticoids not required because adrenal gland normal (ie, issue is deficient ACTH)

Addisonian crisis: acute adrenal insufficiency; medical emergency; can be due to stress such as surgery, trauma, or infection; features include tachycardia, hypotension unresponsive to fluids, nausea, abdominal pain, and mental status changes; at basal conditions, hydrocortisone replacement dose 10-20 mg daily (eg, 10-15 mg upon awakening and 5-10 mg at 4:00 PM); increase glucocorticoid dose during stress; many reference tables available listing relative potencies of different synthetic glucocorticoids along with their mineralocorticoid activities; treatment includes fluids, steroid replacement, inotropes as necessary, and electrolyte correction; may note hypoglycemia and changes in mental status; determine and treat precipitating cause; anesthetically, evaluate and treat volume, hemodynamic, glucose, and electrolyte status as necessary; avoid etomidate because of potential for further adrenal suppression; may see marked sensitivity to sedative, anesthetic, or vasodepressor drugs; titrate drug doses carefully to avoid cardiovascular depression; chronic exogenous steroid therapy may result in adrenal suppression, but for routine perioperative situations, steroid supplementation is controversial and should be individualized; if patient has received >14 day course of

supraphysiologic steroid treatment in past year, may need glucocorticoid supplementation perioperatively; for minor surgery, such as inguinal herniorrhaphy, minor urologic or gynecologic procedures, oral or minor plastic surgery, consider hydrocortisone 25 mg or typical daily steroid dose (whichever higher) preoperatively and resume usual regimen postoperative day one; moderate surgery, such as open cholecystectomy, joint replacement, or extremity revascularization, consider hydrocortisone 50-75 mg or usual daily dose (whichever higher) preoperatively, taper for 24 hours, then resume usual regimen on postoperative day two; major surgery, such as cardiothoracic or major abdominal procedures, consider hydrocortisone 100-150 mg or usual daily dose (whichever higher) within 2 hours preoperatively, then taper over 2-3 days; dexamethasone dose to prevent nausea and vomiting (4 mg) provides considerable glucocorticoid activity and is equivalent to prednisone 25 mg

Mineralocorticoids: aldosterone principal hormone; major regulator of extracellular fluid volume and potassium homeostasis; production regulated by renin-angiotensin system and blood potassium; aldosterone causes reabsorption of sodium and excretion of potassium and hydrogen ion in distal renal tubule

Conn syndrome: excessive and unregulated secretion of aldosterone; causes include aldosterone-producing adrenal adenomas or aldosterone excess from bilateral adrenal hyperplasia; clinical features include diastolic hypertension, hypokalemic alkalosis, headaches, and muscle weakness; treatment for aldosterone-producing adrenal adenomas is adrenalectomy; treatment for bilateral adrenal hyperplasia is aldosterone receptor inhibitor (eg, spironolactone)

Primary adrenal insufficiency: both glucocorticoid and mineralocorticoid production inadequate and replacement of both required; dexamethasone has little or no mineralocorticoid activity, inadequate replacement therapy in primary adrenal insufficiency; fludrocortisone must be given in addition to dexamethasone; alternatively, steroid hormone with both glucocorticoid and mineralocorticoid activity (eg, hydrocortisone)

Secondary adrenal insufficiency: caused by lack of ACTH; mineralocorticoid replacement usually unnecessary; with bilateral adrenalectomy, both glucocorticoid and mineralocorticoid activity must be replaced, if unilateral, mineralocorticoid replacement may be unnecessary

Adrenal Medulla

Overview: preganglionic fibers of sympathetic nervous system stimulate release of catecholamines from adrenal medulla; peripheral effects include chronotropic and inotropic stimulation of heart, vasomotor changes, enhanced hepatic glycogenolysis, and inhibition of insulin release; biotransformed in kidney and liver to metanephrine, normetanephrine, and vanillylmandelic acid

Pheochromocytoma: catecholamine-secreting adrenal medulla tumor; secretes epinephrine, norepinephrine, and dopamine independent of neurogenic control; rare cause of hypertension (0.1% incidence); part of MEN IIA and MEN IIB; association with neurofibromatosis, tuberous sclerosis, Von Hippel-Lindau disease, and Sturge-Weber syndrome; 10% extra-adrenal (ie, paraganglioma); clinical features due to excess catecholamine release, include palpitations, headache, and diaphoresis in episodically hypertensive patient (10% of patients not hypertensive); also see anxiety, tremors, hyperglycemia, orthostatic hypotension, weight loss, dehydration and hemoconcentration; screen with 24 hour urine collection for catecholamines and metabolites

Anesthetic considerations**:** initial acute intraoperative presentation associated with high morbidity; treatment is excision; preoperative recognition of end-organ damage important; dilated or hypertrophic cardiomyopathy occurs in 20%-30% of patients; also see congestive heart failure, hypovolemia, intracranial hemorrhage, hyperglycemia, renal failure; comorbid endocrinopathies should be looked for and treated; preoperatively, restore intravascular volume and reduce end-organ effects of catecholamines; begin alpha receptor blockade with oral phenoxybenzamine, a long-acting, irreversible alpha-1 and alpha-2 adrenergic blocker, or with prazosin or doxazosin, short-acting, competitive alpha-1 blockers; achieving adequate alpha blockade may require up to 14 days; surgery risk acceptable if blood pressure <165/95 mm Hg, postural hypotension, maximum 1 premature ventricular contraction every 5 minutes, no ECG changes for 1-2 weeks, and nasal congestion; discontinue prazosin, doxazosin 12 hours prior to surgery and phenoxybenzamine 48 hours prior; adequate volume repletion achieved if weight gain and decreased hematocrit; beta blockade used with caution because of cardiomyopathy, start after adequate alpha blockade to prevent unopposed vascular alpha receptor stimulation and worsening hypertension; a less common preoperative management strategy is to deplete adrenal medulla of stored catecholamines with metyrosine, a catecholamine synthesis inhibitor; clinical endpoints are same as with prazosin, doxazosin, and phenoxybenzamine

Anesthetic goal: to avoid hypotension or sympathetic outflow to prevent adrenergic crisis; consider preoperative sedation; avoid sympathetic, vagolytic, or histamine-releasing drugs, sympathetic responses to induction, intubation, pneumoperitoneum, and surgical stimulation; combined technique for open procedures with epidural is effective for ablating sympathetic responses but not catecholamine surges; avoid hypotension, use direct blood pressure measurement; other invasive monitoring depends of individual patient status; magnesium blocks catecholamine receptors and release from the adrenal medulla and peripheral adrenergic nerve terminals; can be useful adjunct with loading dose followed by an infusion, with intermittent boluses as needed, but may delay emergence and cause muscle weakness; dysrhythmias and severe hypertension may occur intraoperatively; treatment may include IV boluses of sodium nitroprusside, nicardipine, magnesium, or phentolamine; after hypertension has been treated, beta blockade with labetalol or esmolol may then be required; after tumor venous supply ligated, there may be acute drop in blood pressure from decreased catecholamine level and residual alpha and beta blockade; treat with volume support, direct-acting vasopressor (eg, phenylephrine); vasopressin may be helpful; monitor glucose perioperatively as patients may have hyperglycemia preoperatively, hypoglycemia postoperatively; endogenous catecholamine level normalizes quickly; blood pressure may take much longer; ICU care may be needed postoperatively for unstable patients

Key Points

1. Anterior pituitary gland functions as the master gland.
2. Antidiuretic hormone regulates salt and water balance. Also known as vasopressin, ADH causes vasoconstriction and increases blood pressure.
3. Hypothyroidism and hyperthyroidism warrant careful anesthetic management.
4. Adrenal cortex and medulla affect major conditions within the body. Adrenal glands release glucocorticoids, mineralocorticoids, and catecholamines, which maintain homeostasis during stress

Suggested Reading

Patel H et al: Physiology, Posterior Pituitary. 2018 Sep. StatPearls. Treasure Island (FL): StatPearls Publishing; 2018 Jan; **Pirahanchi Y et al:** Physiology, Thyroid. 2018 Sep. StatPearls. Treasure Island (FL): StatPearls Publishing; 2018 Jan; **Yasir M et al:** Corticosteroid Adverse Effects. 2018 Sep. StatPearls. Treasure Island (FL): StatPearls Publishing; 2018 Jan.

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Board Review

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Physiology and Pharmacology of the Autonomic Nervous System

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Introduction: anesthesiologists, autonomic physiologists; turn off, turn on, block, stimulate, manipulate; generally interfere with autonomic nervous system (ANS) in every case; general anesthesia shuts off breathing, blood pressure (BP) control, temperature control; anesthesiologists take over for the medulla oblongata, then turn it back on, controlling response to surgery; eliminating autonomic response major goal of anesthesia; when ANS eliminated, anesthesiologist controls these processes (breathing, cardiovascular (CV) system, respiratory system, gastrointestinal (GI) system, temperature regulation, renal and bladder functions, sexual function); autonomic system=body's power, light, heat, water, and sewage system; temperature control through vasodilation of skin and other processes; O_2 delivery by controlling blood flow to periphery; major problems if these don't work

ANS Physiology

ANS: includes sympathetic and parasympathetic nervous system

Neurotransmitters: *acetylcholine* — neurotransmitter to ganglion for sympathetic nervous system; *norepinephrine* — postganglionic fiber mostly uses norepinephrine (generally, norepinephrine transmitter in periphery); when considering action of blocking receptor, consider whether nicotinic or muscarinic; nicotinic receptor for both parasympathetic and sympathetic in ganglion; nicotine affects ganglion in periphery and can stimulate it; muscarinic in periphery at end organ for parasympathetic; end organ for sympathetic uses norepinephrine

Synthesis and metabolism of norepinephrine and epinephrine transmitters: *synthesis* — phenylalanine converted to tyrosine in liver, then metabolized into dopa and then dopamine; dopamine in storage vesicles, and eventually gets converted into norepinephrine and epinephrine; *metabolism* — converted by monoamine oxidase inhibitor (MAOI) into vanillylmandelic acid; MAOI increases norepinephrine and epinephrine; may be problematic; MAOI may need to be stopped prior to surgery

Sympathetic nervous system: most cells originate in medulla, extend to T1 to T12, then to sympathetic chain ganglion and out to system; preganglionic fiber synapse in ganglion close to intermediolateral column of spinal cord, in gray matter, between T1 and T12; postganglionic fiber, long fiber goes out to periphery; if thoracic epidural administered, consider effect on sympathetic nervous system (profound vasodilation may result, needing BP support); cardioaccelerator fibers in levels T1 to T5; lower you go, less effect; below T12 (even less if don't drive level up), preganglionic neuron from intermediolateral column synapses in ganglion (usually sympathetic chain ganglion along periphery); then postganglionic fiber (long, small fiber) that goes out to periphery to places such as heart, smooth muscles, glands; neurotransmitter in sympathetic chain ganglion, acetylcholine and neurotransmitter in the periphery in most situations norepinephrine; norepinephrine (in periphery, except for sweat glands) makes sympathetic nervous system work

Effects on body: eyes, salivary glands, heart, lungs, pancreas, upper GI tract, liver, abdominal blood vessels, bladder; *consider what happens when frightened or hurt* — contraction of pupils and muscles, salivation, increased heart rate and contractility, bronchoconstriction or bronchodilation, changes insulin secretion, affects sphincter tone in gut, gluconeogenesis and glyconeogenesis, constricted blood vessels and increased blood pressure, increased urge to urinate, sphincter contraction

Sweat glands: different; preganglionic, in intermediolateral column from T1 to T12, and then synapses in ganglion (acetylcholine receptors), but postganglionic fiber goes out to sweat glands and, unlike other areas, uses acetylcholine as transmitter; atropine can affect sweating (especially in person of short stature)

Adrenal medulla: sympathetic neuron from T1 to T12, synapses in adrenal medulla (adrenal medulla essentially ganglion), transmitted by acetylcholine in adrenal medulla, releases epinephrine and norepinephrine into bloodstream; in response to stress, adrenal medulla releases epinephrine and norepinephrine, increasing BP and heart rate

Parasympathetic nervous system: starts in medulla, in midbrain; nerves III, VII, IX, become vagus nerve, control eyes, salivary glands, heart, bronchioles, stomach, other areas through vagus nerve, and also work through pelvis, affecting kidneys, sexual function, intestines, and genitalia; preganglionic fiber or neuron in brainstem; has synapse in ganglion in the periphery; postganglionic fiber extends to heart, smooth muscles, or glands, and acetylcholine transmitter at end

Effects on body: ciliary ganglion contracts iris sphincter and ciliary muscles; salivation, heart rate, lung, pancreas, intestine, and bladder; parasympathetic agents slow things down; heart rate, conduction velocity, and contraction reduced; bronchoconstriction, insulin

produced, gut function improves, sphincter relaxes; c*onsider what happens in vasovagal episode* — bradycardia, fainting, etc

Synapses in the Sympathetic Nervous System

Postsynaptic effect: norepinephrine descends sympathetic nerve to presynaptic nerve terminal, released into nerve terminal and, depending on postsynaptic cell, causes different effects; could be alpha-1 receptor (may produce vasoconstriction), beta-1 receptor or beta-2 receptor (may produce vasodilation or contractility effects); alpha-1, beta-1, and beta-2 in postsynaptic part of cell

Presynaptic effect: norepinephrine enters receptor and then feeds back on itself to alpha-2 receptor; alpha-2 receptor then inhibits it and causes reduction in norepinephrine transmission; consider alpha-2 agonist medications such as clonidine, dexmedetomidine, mivazerol (predominantly alpha-2 agonists); dexmedetomidine ~1500:1 (alpha-2:alpha-1), therefore causes reduction from alpha-2 in presynaptic as well as stimulus with alpha-1; in summary, alpha-2 agonists cause reduction in release of these transmitters; *norepinephrine reuptake* — norepinephrine not just synthesized and used once, but taken back up into receptor, recycled and used again; several drugs prevent reuptake of norepinephrine and therefore potentiate its effect; important to consider that when released into periphery, norepinephrine causes contraction if alpha receptor; changes in potassium concentration or hydrogen ion concentration can inhibit effect of adrenergic nerve terminal; acetylcholine, histamine, serotonin, can all inhibit action of norepinephrine at nerve terminal; therefore, excessive histamine, serotonin, prostaglandin E (PGE), or changes in pH or osmolality will inhibit effect of norepinephrine in periphery; in patient with low pH, their norepinephrine and epinephrine may not work well and it will not be as efficient

Receptor function:

Sympathetic nervous system: agonist goes to adrenergic receptor (alpha or beta), through membrane works through G-protein to convert ATP to cyclic AMP (cAMP), and cAMP turns on system; "turns off," when cAMP broken down by phosphodiesterase (PDE) into AMP; therefore, turning it off can be affected by phosphodiesterase inhibitors; many drugs that affect the breakdown of cyclic AMP; PDE *inhibitors types 1 through 5* — type 1, caffeine; type 2, theophylline or aminophylline; type 3, milrinone or amrinone; type 4 not commonly used; type 5, sildenafil and vardenafil; possible interaction between sympathetic and parasympathetic nervous systems; vagal nerves working as muscarinic receptors may have some negative effects on beta-adrenergic receptors; *2 systems* — vagus synapsing with muscarinic receptors and sympathetic synapsing with adrenergic receptors; they turn on conversion of ATP to cyclic AMP

Pharmacology

Sympathomimetics: ephedrine, phenylephrine, metaraminol, mephentermine, and methoxamine; ephedrine and phenylephrine predominantly used; both have carbon-ring structure with some side groups

Catecholamines: *5 predominant catecholamines* — dopamine, norepinephrine, epinephrine, isoproterenol, dobutamine; all look similar apart from carbon group on side; various discussions about difference among them; some have mixed effects; dopamine has some alpha, beta, and dopa effects; norepinephrine has alpha-1 and beta effects; epinephrine has slightly less alpha effect; isoproterenol and dobutamine have predominantly beta effects; dobutamine has no dopaminergic effect; name "dobutamine" confusing; more like isoproterenol than dopamine (both predominantly beta, cause tachycardia and vasodilation); dopamine works on dopaminergic receptors

Muscarinic and nicotinic effects in ANS

Muscarinic effects: *heart* — reduced heart rate, decreased inotropic effects and conduction; standard agonist methacholine; standard antagonists atropine, scopolamine, glycopyrrolate; *other effects* — effects cause constriction of bronchioles; salivary stimulation; contraction and relaxing of sphincters in intestines; contraction and relaxing sphincters in bladder causing urge to urinate

Nicotinic effects: work through autonomic ganglia; standard nicotinic agonist succinylcholine or nicotine; antagonists include curare, pancuronium, vecuronium, rocuronium, pipecuronium, atracurium, cisatracurium, mivacurium, and doxacurium; *nondepolarizing muscle relaxants and heart rate* — glycopyrrolate, scopolamine, and atropine increase heart rate, but nondepolarizing drugs predominantly nicotinic; pancuronium used to cause slight increase in heart rate, then no longer used; vecuronium, rocuronium, and cisatracurium used instead; they have very little effect at muscarinic receptors; therefore, they don't affect heart rate; *muscle weakness with glycopyrrolate, scopolamine, atropine* — do not cause weakness because they work at muscarinic receptors; these drugs block acetylcholine, increase heart rate, and reduce salivation

Blood-brain barrier: atropine and scopolamine cross blood-brain barrier; can have profound effects on central nervous system (CNS); scopolamine can affect memory, cause confusion; atropine can cause confusion; glycopyrrolate does not cross blood-brain barrier because quaternary molecule, charged; therefore, affects heart but has no CNS effects

Adrenergic receptors:

Beta-1 receptors: found in heart; increase heart rate, contraction, conduction (ionotropic); *beta-1 receptor agonists* — dopamine, dobutamine, isoproterenol; *beta-1 receptor antagonists* — metoprolol, esmolol, propranolol, timolol, labetalol, atenolol, propranolol

Beta-2 receptors: found in adipose cells, blood vessels, bronchioles, uterus, kidney; *effects* — lipolysis in fat cells; dilation of blood vessels; dilation of bronchioles; relaxation of uterus; renin secretion in kidney; glyco- and gluconeogenesis in liver, insulin secretion in pancreas; *beta-2 agonists* — albuterol, etc; *beta-2 antagonists* — propranolol, timolol, labetalol; (remember that agonists stimulate receptors and antagonists block them)

Alpha-1 receptors: found in blood vessels, pancreas, intestines, bladder; alpha-1 constricts and inhibits insulin; secretes, relaxes, constricts; *standard alpha-1 agonist* — phenylephrine; works in blood vessels and increases BP through vasoconstriction; *alpha-1 antagonists* — prazosin, phentolamine, labetalol; prazosin used for treating pheochromocytomas, but also used in bladder disorders and hypertension; therefore, for patients taking prazosin, always consider indication

Alpha-2 agonists: work in CNS; inhibit norepinephrine and epinephrine release; *classic alpha-2 agonists* — clonidine, dexmedetomidine, mivazerol
Clonidine: not available as intravenous (IV) preparation in United States; clonidine regarded as antihypertensive, but has both alpha-1 and alpha-2 effects; alpha-2 effects ~ 40:1 over alpha-1; clonidine IV given to hypertensive patient, first effect would be increased in BP, because of alpha-1 effects; when it reaches CNS and alpha-2 effects predominate, BP would reduce; only works as antihypertensive when given slowly, so that it gets into CNS slowly; causes reduction in epinephrine and norepinephrine and reduces BP
Dexmedetomidine: works same way, ~1500:1 alpha-2:alpha-1; given slowly, can lower BP, heart rate, etc; always ensure rate programmed correctly via pump so administered safely and appropriately
Alpha-2 antagonists: yohimbine, phentolamine; phentolamine sometimes used to treat pheochromocytoma; yohimbine not used often

Dopaminergic drugs: dilate blood vessels; *standard agonist* — dopamine; *standard antagonist* — droperidol; work at dopamine 1 and 2 receptors; droperidol previously used commonly and successfully as antiemetic; however, prolonged QT syndrome and may have led to arrhythmias; also caused profound dysphoria in patients; direct agonists bind receptor and turn receptor on; indirect agonists increase endogenous neurotransmitter activity and increase release of norepinephrine, decrease reuptake of norepinephrine; *eg*, drugs such as phenylephrine (direct agonist), causes vasoconstriction, raises systemic vascular resistance (SVR), increases BP; *agonists* — clonidine, dopamine, dobutamine

Downregulation and upregulation of receptors: after administering drug that stimulates receptor, either alpha or beta, body reacts; will probably downregulate; *eg*, after beta agonist, few hrs later, receptor population looks different, and person not as responsive to drug; when drug stopped, may need to be weaned; if blocking drug administered, body increases number of receptors and; when drug stopped, withdrawal phenomenon occurs; be careful turning on and turning off these drugs, and wean them carefully

Hypotensive agents:
Nitric oxide (NO): half-life of ~2 secs in bloodstream; inhaled NO selective pulmonary vasodilator; by time it gets into bloodstream and reaches heart, it's gone; can improve ventilator-to-perfusion (V/Q) mismatch in lung, can dilate pulmonary vasculature; *problems* — only lasts 2 secs, gone as soon as turned off; tachyphylaxis; hard to prove that as beneficial drug
Nitroprusside: also works through NO system; *problems* — very effective, potent drug, so caution required; can cause profound hypotension; directly breaks down into NO and can cause acute cyanide toxicity; interferes with hypoxic pulmonary vasoconstriction
Nitroglycerin: metabolized into NO, which requires going out to periphery; vasodilates; more effects on preload reduction; assumed nitroglycerin given systemically will improve coronary blood flow but does not; if given systemically, BP lowers, which lowers heart's O_2 consumption, and coronary blood flow maintained
Other hypotensive agents: fenoldopam, hydralazine (can cause reflex tachycardia when withdrawn), adenosine; (formerly, theory that dopamine or fenoldopam could be given to protect the kidney; dopamine can raise BP and improve blood flow, but debatable whether or not this improves kidney function); *many different inotrope and vasoactive agents* — phenylephrine, methyldopa, clonidine, ephedrine, epinephrine, norepinephrine, dopamine, fenoldopam, methylhexamine, dobutamine, isoproterenol, terbutaline, amrinone, milrinone, sildenafil, nitroglycerin, nitroprusside; consider all drugs and whether alpha-1 or alpha-2, beta-1, beta-2, dopamine
Mechanism of action: consider how these drugs work; PDE inhibition (*eg*, amrinone, milrinone, sildenafil); work through NO (*eg*, nitroglycerin or nitroprusside); effect on heart rate, BP, cardiac output and SVR
Dosing: choose each drug based patient's particular condition; should have experience with all of them, know how to use; does patient have vasodilation, problem with inotropic state, problem with volume status, ischemia?; choose appropriate drug based on physiology; trying to raise resistance, trying to raise inotropic state, change heart rate, change blood volume?

Adrenergic antagonists: alpha and beta antagonists; *alpha antagonists* — prazosin, phenoxybenzamine, phentolamine; used mostly in patients who have bladder problems or pheochromocytoma; *beta antagonists* — labetalol, atenolol, metoprolol, esmolol, propranolol; consider what you're trying to do
Atenolol: excellent drug, inexpensive and effective; half-life 6 hrs to 7 hrs, once-daily drug; reduces mortality
Metoprolol: available in 2 forms (tartrate and succinate); tartrate form has half-life of 3 hrs to 4 hrs, therefore given twice daily; succinate form has longer half-life, can be given once daily
Mortality rate for metoprolol tartrate, metoprolol succinate and atenolol: mortality rate for metoprolol tartrate about double that of metoprolol succinate; harder to remember to take drug twice daily, easier to take succinate form once daily; mortality rate for atenolol about half that of metoprolol; atenolol once-daily drug; also, metoprolol metabolized through CYP450 system in liver, and if patient takes another interacting drug (eg, antidepressant), it increases metabolism and therefore reduces metoprolol level; atenolol renally excreted, not affected by liver metabolism, or by metabolism of other drugs, safe drug
Esmolol: metabolizes through acetylcholinesterase, lasts ~5 mins; however, ANS responds better when blocked for long time; use extreme care when using esmolol; tendency to overdose or give too rapidly; better to have "long-term commitment" to beta blockade; safer to use metoprolol, propranolol; however, esmolol infusions useful in critically ill patients in whom uncomfortable need to be cautious giving a beta blocker; expensive compared with oral beta blocker
Propranolol: crosses blood-brain barrier; favorable drug; comes in an extended-release form; affects dreams and sleep; may be useful for treating posttraumatic stress disorder (PTSD)

Phosphodiesterase inhibitors: if phosphodiesterase blocked, cAMP increased; effect of cyclic AMP

increased; caffeine (type 1 PDE inhibitor), increases alertness; theophylline or aminophylline (type 2) causes bronchodilation; milrinone or amrinone (type 3) increases contractility; vardenafil and sildenafil (type 5) involved in conversion of cyclic GMP (cGMP to cAMP; t*ype 5 receptors* — different; receptor on endothelial cell; when activated, L-arginine converts to L-citrulline, which releases NO, which diffuses across and affects conversion of GTP to cGMP; turned off by PDE; PDE causes cGMP to convert to GMP, block this with PDE inhibitors (sildenafil, vardenafil); in person taking PDE inhibitor, more cGMP and more vasodilation; do not give nitroglycerin in home setting to patient taking sildenafil or vardenafil; patient will vasodilate, get dizzy, etc; however, combination of these medications can be managed in operating room, where fluid administration possible; sildenafil and vardenafil useful for treating patients with severe pulmonary hypertension; also has tendency to lower coronary vascular resistance

Methylene blue: not standard recommendation, however 10-mg bolus will shut off conversion of GTP and cGMP and sometimes normalize BP in patient with septic shock when every other drug has been tried; give infusion of ~5 mg/hr

CV control: ANS has target BP controlled in nucleus tractus solitarius (NTS); sends out signals to CV system through sympathetic, parasympathetic nervous systems; interactions between left and right baroreceptors (take over for each other if one of them denervated or open to air, or if other one won't work); also many receptors in heart , all send signals to nucleus tractus solitarius and out to system; occasionally someone pulls on carotid, causing body to think BP quite high, and thus BP will reduce significantly; to solve that problem, put small amount of lidocaine on baroreceptor

Issues to Avoid

Hypotension: increased mortality rates when hypotension lasts >~15 mins; if diastolic pressure <30 mm Hg, or systolic pressure <60 mm Hg, effects on 2-day, 30-day, and 1-yr mortality; therefore, fix hypotension quickly

Hypertension: less of problem; if diastolic pressure >120 mm Hg, or systolic pressure >200 mm Hg, effects on 2-day, 30-day, and 1-year mortality at ~15 mins, but effects less dramatic than with hypotension

Tachycardia: bigger problem; heart rate >120; effects on mortality in ~ 5 mins; avoid tachycardia in patients, especially smokers or those with coronary disease, hypertension chronic obstructive pulmonary disease, benign prostatic hyperplasia, hiatal hernia, diabetes, older age etc

How to prevent tachycardia: blocking ANS with beta blockers reduces mortality; reduces 30-day mortality, 2-year mortality; *atenolol* — study showed that atenolol administered to patients reduced short- and long-term mortality, compared with those who did not take it; heart rate in atenolol-treated group ~75, ~85 in placebo group; real difference in peak heart rate; peak heart rate in atenolol-treated group never >120; aim not to maintain very low heart rate, but rather to prevent tachycardia; limit high heart rate; tachycardia leads to ischemia, ischemia leads to myocardial infarction (MI), MI leads to death; beta blockers reduce mortality in heart failure, after MI, for patients having heart surgery, many other situations; *clonidine* — study on showed 7-fold reduction in 30-day mortality, 50% reduction in 2-year mortality; blocking release and effect of catecholamines can improve survival

Beta blockers and other antihypertensives in perioperative period: giving beta blockers to patients using protocol, if add or continue drug, reduction in mortality of ~35%; if drug withdrawn in perioperative period, 2- to 4-fold increase in mortality; if patient on beta blocker before surgery, should continue it perioperatively (Level 1 standard indication); withdrawal of vasoactive agents (eg, beta blockers, calcium channel blockers, nitrates, alpha-2 agonists, ACE inhibitors) in perioperative period increases mortality for MI, congestive heart failure, ventricular tachycardia; all patients with risk for coronary disease should continue vasoactive medications perioperatively

Catecholamines: useful when need to maintain life; however, cause myocardial necrosis, tachycardia, MI, tissue necrosis, arrhythmia, hypokalemia, hyperglycemia; try to avoid using inotropes unless really needed; inotropes can lead many problems, so use caution; antagonists prolong life but agonists, in this situation, don't

ANS and memory: epinephrine released in stressful situations increases BP; increases heart rate; activates platelets to reduce bleeding; however, epinephrine in brain has effect on memory; "if you scare people, they dream about it, and if you hurt people, they can develop PTSD"; PTSD associated with surgery can cause serious problems; PTSD associated with dementia, hippocampal injury; ~40% develop diabetes; higher mortality rates, early coronary disease; PTSD essentially causes neural injury from hyperstimulation; epinephrine released during stressful events makes memories more important

Propranolol and PTSD: crosses blood-brain barrier; blocks beta receptors; may be able to prevent PTSD after acute events; studied in patients after traumatic car accidents; seems to reduce the instance of PTSD, may also be useful for reducing old PTSD memories

Cocaine: prevents reuptake of epinephrine and norepinephrine in CNS; makes memory of cocaine experience more significant; high epinephrine levels, epinephrine makes memory more permanent; propranolol has been used to treat cocaine addiction; crosses blood-brain barrier, blocks receptors, and edits memories from being epinephrine-associated memories to just "boring," normal memories

Summary

ANS very important; however, aim for "boring and slow;" rapid-onset, rapid-metabolizing drugs (remifentanil, desflurane, rapacuronium, esmolol, dexmedetomidine) come on and go away quickly; hard to show reduction in mortality rate with those drugs because they stimulate ANS very quickly; desflurane stimulates receptors; irritant, raises pulmonary blood pressure, causes tachycardia; rapacuronium causes lethal bronchospasm; "boring," "slow" things (eg, transcutaneous clonidine, atenolol) preferred; unblocked ANS can be lethal during surgery, but so can blocked one; be careful

Suggested Reading

Hunter MJ et al: Methylene blue for vasoplegic syndrome after cardiac operation: early administration improves survival. *Ann Thorac Surg*. 2017;104(1):36-41; **Mangano DT et al:** Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. Multicenter Study of Perioperative Ischemia Research Group. *N Engl J Med*. 1996;335(23):1713-20; **Glick D:** Autonomic Nervous System. In: Miller RD at al. *Basics of Anesthesia*. 6th ed. Philadelphia, PA: *Elsevier/Saunders*; 2011:66-77; **Mudumbai SC et al:** Effectiveness of preoperative beta-blockade on intra-operative heart rate in vascular surgery cases conducted under regional or local anesthesia. *Springerplus*. 2014;3:227; **Wallace AW et al:** Association of the pattern of perioperative β-blockade and postoperative mortality. *Anesthesiology*. 2010;113(4):794-805; **Wallace AW et al:** Clonidine and modification of perioperative outcome. *Curr Opin Anaesthesiol*. 2006;19(4):411-7; **Wallace AW et al:** Perioperative β-blockade: atenolol is associated with reduced mortality when compared to metoprolol. *Anesthesiology*. 2011;114(4):824-36.

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Risks, Benefits, and Selection of Inotropes

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Introduction: choice of inotrope depends on medical subspecialty; cardiologists choose dobutamine for congestive heart failure (CHF); anesthesiologists choose epinephrine or similar for CHF; cardiologists treat awake patients with CHF, who have elevated systemic vascular resistance (SVR); anesthesiologists commonly treat unconscious people with CHF, who have low SVR; anesthesiologists treat low cardiac output (CO) with low SVR and cardiologists treat low CO with high SVR; choice of drug different in those situations; choice of inotrope should depend on patient's physiology (SVR, blood volume, heart rate (HR), inotropic and lusitropic state); important to look at effect of drug on mortality rates rather than surrogate markers (*eg*, CO, end systolic wall stress, length of stay, diastolic pressure); use caution in pharmacologic management of patient, and should not be based on specific service of patient's physician

Risks associated with inotropes: inotropes cause myocardial necrosis, tachycardia, increase myocardial oxygen consumption, increase risk of myocardial ischemia, myocardial infarction (MI), cardiac arrest, arrhythmias, death in MI, CHF, and coronary artery bypass grafting (CABG)

Epinephrine: standard animal model for CHF involves epinephrine infusion for ~1 mo leading to profound, permanent heart failure (HF); epinephrine infused for that period of time caused myocardial necrosis and heart failure (HF); in patient accidentally injected with 5 mg epinephrine subcutaneously, and after ventricular tachycardia and ventricular fibrillation and left ventricular assist device (LVAD) placed, patient survived, but ejection fraction 10%; epinephrine causes myocardial necrosis; when epinephrine given as bolus and blood pressure (BP) rises to 250/150 mm Hg, not good for heart; mortality rate for 5 mg of epinephrine ~50%, and people who survive have profound HF

Catecholamines: elevated levels of catecholamines in HF lead to myocardial necrosis; blocking with beta blockers leads to recovery of myocardial function, longer survival; pheochromocytoma, which has elevated catecholamines, leads to HF

Methamphetamines: prevent reuptake of epinephrine; cause tachycardia, arrhythmias, MI, and HF

Ephedra: often thought to be performance-enhancing drug, but does not improve performance; side effects include irregular HR, seizures, MI, stroke, and death

Catecholamines and beta blockers: giving beta blockers to people with HF prolongs life while giving catecholamines shortens life (cardiac output goes up, end diastolic pressure goes down, but death results)

Studies showing risks associated with inotropes: *Martinez et al (2010)* — studied myocardial necrosis and severe biventricular dysfunction in context of chronic ephedra abuse; ephedra caused dilated cardiomyopathy; patients had partial recovery of ejection fraction after 5 yrs of total cessation, but ephedra caused neuropathy, myopathy, psychosis, addiction, stroke, insomnia, myocarditis, arrhythmias, MI, and death; *Andraws et al (2005)* — comprehensive review of cardiovascular (CV) effects of ephedra alkaloids; adverse effects included stroke, MI, and sudden death; US Food and Drug Administration (FDA) banned those substances because associated with serious problems; 2*016 study of goal-directed therapy* — less favorable outcome seen with use of inotropes; *Belletti et al (2015)* — effects of inotropes and vasopressors on mortality meta-analysis by; inotrope not associated with improved survival; *current use of vasopressor and inotrope in cardiogenic shock* — adrenaline use associated with excess organ injury and mortality; use of adrenaline associated with worsening in cardiac and renal biomarkers; *Osinaike et al (2015)* — role of perioperative factors in prolonged intensive care unit (ICU) stay after coronary bypass; concluded left ventricular (LV) support with inotrope as only independent predictor of prolonged ICU stay after CABG surgery

Managing Hemodynamics

Heart: physical system with inputs and outputs, outputs into systemic vasculature

Impedance: in any physical system, optimal energy transfer when output impedance of system equals input impedance of system being pumped into; want to match impedance of heart to vasculature; analogous to 2 dancers where impedance of arms has to match between dancers to be able to transfer energy from one to another, stretchiness of heart needs to match stretchiness of vasculature; stretchiness of veins has to match diastolic stretchiness of heart so it can fill; output impedance of heart ~2 mm Hg/mL, and input impedance of systemic circulation ~2 mm Hg/mL; in normal state, output impedance of heart equals input of systemic vasculature, so balanced, and optimal energy transfer results; output impedance of venous system ~0.1 mm Hg/mL, and input to heart in diastole ~0.1 mm Hg/mL, so input impedance of heart matches output impedance of venous system in normal state; for hemodynamic management, input impedance of the arteries should be 2, and output impedance of the veins should be ~0.1, resulting in

optimal energy transfer when vasculature reasonable compared with heart and those impedances match

Potential problems: include blood volume effects, systemic vascular effects, lusitropy (diastolic dysfunction), contractility effects of systolic function, chronotropic effects (HR), left HR, right HR, pulmonary hypertension, myocardial ischemia, valvular problems; many things to fix in little time ~30 secs before bad result; use of inotropes tried in various situations; with inotrope use after MI, beta blocker decreases mortality, beta agonist increases mortality, and placebo neutral; same result in 15 different studies in CHF; cardiac surgery like MI with CHF; beta blockers decrease mortality, giving inotropes increased mortality; 100% of people undergoing CABG surgery release troponin; common for people having CABG surgery to have some myocardial injury; in this case as well, beta blocker decreases mortality and beta agonist increases mortality

Afterload: "afterload" term from frog musculature experiments; take sartorius muscle from frog, put it on hook, put weight on it; initial weight, preload; it stretches it to original length, then add another weight that muscle has to pick up once it starts contracting, afterload; so afterload in heart=BP; want to match output impedance of vasculature to input impedance of systemic vasculature; SVR probably easiest thing to adjust; SVR should be reasonable

Preload: term refers to little weight on frog muscle to return to initial length; heart essentially fancy blood vessel; in diastole, heart has compliance that looks like vein (vein has compliance of 0.1 mm Hg/mL, and slope of diastolic pressure volume relationship 0.1 mm Hg/mL); in systole, that compliance changes, ejecting blood, and at end systole, end-systolic pressure-volume relationship (ESPVR) has slope of 2 mm Hg/mL and has gotten stiffer

Pressure-volume loops: width of loop indicates stroke volume, and multiplying stroke volume (SV) times HR yields CO; area of loop (stroke work) proportional to amount of O_2 heart uses for each beat, to pump blood out; little triangle on lefthand side, between end-systolic volume and zero, potential energy, amount of O_2 for just basal requirements (to allow heart to function); little square or loopy part, amount of O_2 to pump blood; total O_2 consumption, little triangle plus little loopy part; heart, time-varying blood vessel that changes its impedance (or elasticity) from looking like vein in diastole (so it can fill), to looking like an artery in systole (so it can eject), over and over again; complicated system; O_2 consumption related to area of those loops and pressure-volume loops; efficiency of heart, little loopy part divided by whole part, so amount of O_2 to pump divided by potential energy and external work; in normal, balanced person, potential energy and external work sufficiently

Managing low blood volume and SVR: low blood volume and septic shock (low SVR) most common problems CV system has learned to deal with over time; rare for animal to die of coronary artery disease; CV system optimized to deal with volume and resistance; first, need to make volume and resistance reasonable; if still have problems, consider using inotrope; *phenylephrine* — when phenylephrine given to normalize resistance, has tendency to drop SV and CO, raise O_2 consumption, and decreases efficiency; however, still used to make BP reasonable; *nitroprusside* — lowers BP and end systolic volume, raises SV and CO, lowers total O_2 consumption, improves efficiency; but may make BP too low; need vasculature to be reasonable; resistance ~1200 in most people, want normal BP, need to adjust resistance and blood volume reasonable levels; if resistance too high, raises O_2 consumption; if resistance too low, may not have adequate perfusion to brain; important to balance those 2 things; *O_2 consumption* — if HR raised, total O_2 goes up but coronary blood flow drops; threshold for ischemia in young, healthy person HR of ~200 bpm to ~220 bpm; ~170 bpm to ~180 bpm in normal person; ~120 bpm in at-risk person (*eg*, smoker, COPD, diabetes) with ischemia; different with BP; when BP raised, O_2 consumption also raised, but also coronary blood flow simultaneously increased; lowering or raising the BP does not rapidly lead to ischemia because O_2 comes and goes with it

Drugs: phosphodiesterase (PDE) breaks down adenosine triphosphate (ATP) into cyclic adenosine monophosphate (cAMP) into AMP, and AMP gets recycled; PDE inhibitor stops breakdown of cAMP; 5 types of PDE inhibitors; *type 1* — caffeine; works in brain; *type 2* — theophylline, aminophylline; work in lung, avoid bronchospasm; *type 3* — milrinone, amrinone; work in heart; synergistic agents, increase CO; *type 4* — unknown; *type 5* — vardenafil, sildenafil; work with cyclic guanosine monophosphate (cGMP); work on blood vessels, vasodilators; type 5 PDE inhibitors different from types 1 through 4; work with receptor, which turns on nitric oxide (NO) synthase; L-arginine converted to L-citrulline, producing NO; NO turns on conversion of guanosine triphosphate (GTP) to cGMP; cGMP relaxes blood vessels; cGMP broken down by type 5 PDE into GMP, then recycled into GTP; *turning process on and off* — nitroprusside breaks down spontaneously into NO and turns this on; nitroglycerin metabolized by sulfonylation into NO and turns this on; can be blocked by methylene blue (10 mg IV), which will shut down conversion of GTP to cGMP, and will raise BP

Inotropes: include phenylephrine, methyldopa, clonidine, ephedrine, norepinephrine, dopamine, fenoldopam, dopexamine, dobutamine, isoproterenol, terbutaline, others; important to think about receptor type, if it works through PDE inhibitors, or through NO, what drug does to mean arterial pressure, HR, CO, SVR, bronchodilation, renal blood flow, pulmonary vasculature, and where it works; these drugs should be chosen intentionally, not casually by just picking favorite drug

Isoproterenol: beta agonist, raises HR and CO, lowers SVR; inotrope

Dobutamine: beta agonist; raises HR, lowers SVR, raises CO; no dopaminergic effects; inotrope

Dopamine: alpha, beta, and dopaminergic effects, somewhat dose dependent; raises HR, BP, SVR, CO; inotrope

Epinephrine: alpha and beta effects; raises HR, BP, SVR, CO; inotrope; basically escape mechanism; secreted by adrenal medulla

Norepinephrine: alpha and beta effects, but more alpha; raises HR, BP, SVR, CO; inotrope; norepinephrine

neurotransmitter used everywhere; potent; vasoconstrictor; probably correct first-line drug in septic shock

Phenylephrine: alpha effects; raises BP and SVR; drops CO; effect on HR depends on other drugs given, whether person conscious or unconscious; should always think about how these drugs work when person awake and when asleep, when SVR low or high; may get very different response

Nitroprusside: works through the NO system; nitroprusside spontaneously breaks down into NO; drops BP and SVR; raises CO

Nitroglycerin: also works through NO system; broken down by metabolism (sulfonylation into NO); drops BP and SVR; may not affect CO much (less blood volume available because of vasodilation); although thought to raise coronary blood flow, it does not; if given down coronary vessel directly, vasodilates and more coronary blood flow results, but if just given systemically, drops allover BP, with no net improvement in coronary blood flow; when dropping BP systemically, total O_2 consumption lowered, improving relative O_2 availability, but not increasing coronary blood flow specifically (not selective coronary vasodilator); coronary blood flow remains constant while dropping total O_2 consumption in heart

Milrinone: type 3 PDE inhibitor; causes drop in BP and in SVR, elevation of CO and inotropic state; very good synergism with either epinephrine or norepinephrine; some suggest that can give milrinone by itself without other drugs; in lecturer's clinical experience in cardiac anesthesia, milrinone leads to vasodilation, and other agents needed to control resistance; if person unconscious, need epinephrine or norepinephrine along with milrinone to adjust resistance

Sildenafil: type 5 PDE inhibitor; drops pulmonary vascular resistance in about one-third of people, lowers coronary vascular resistance (CVR); very good pulmonary vasodilator; when given to patients, will cause small drop in SVR (~3-5 mm Hg), which can be seen on computer, but very small effect; nitroglycerin taken with type 5 PDE inhibitor at same time will lead to vasodilation and dizziness, and should not be taken at home; okay to give in standard anesthesia monitoring setup with art-line and IV; drops CVR and pulmonary vascular resistance, improves coronary blood flow; very effective for pulmonary hypertension

Methylene blue: one of few agents that block NO effects; blocks conversion of GTP to cGMP, and raises resistance; in study done in Argentina, administered methylene blue to people in vasoplegic shock; cured vasoplegic shock and reduced mortality; should be thought of as 12th-line agent, nothing else worked

Vasopressin: works at vasopressin receptors; raises SVR, drops CO; discovered ~1898; took pituitary, ground it up, gave it IV, and BP went up, so they named it "blood-pressure-go-up"; normal vasopressin levels ~2 pg/mL to ~10 pg/mL; if dehydrated, may be 30 pg/mL; in operating room (OR), will go to 200 pg/mL; on cardiopulmonary bypass, will go to 1000 pg/mL; if vasopressin given at beginning of day, receptors will not have decreased in density because vasopressin levels low, and it will work quite well; if given at end of day, patient with septic shock or some other problem may not have many vasopressin receptors, so drug less effective; depends on background levels; in study with hypophysectomized animals (hypophysectomy caused them to have low vasopressin levels), vasopressin acts like normal drug; but in nonhypophysectomized animal, depended largely on clinical state; correct place for vasopressin in clinical armamentarium unclear; could be very effective if low vasopressin levels at baseline

"Rocket fuel" (combination of epinephrine and milrinone): if in cardiac OR and CO and ejection fraction very bad, and you may not be able to get patient off the table, place balloon pump, which will raise diastolic BP and improve coronary blood flow, and administer epinephrine; if still no contractility, add milrinone; milrinone synergistic with epinephrine; epinephrine stimulates beta receptors and raises HR, BP, SVR, CO, and inotropic state; milrinone lowers BP and SVR, raises CO and inotropic state; for patient with poor ejection fraction and not going to come off pump, get epinephrine and balloon pump, administer milrinone, synergism between these 2 agents will result, and heart will beat better; "rocket fuel" not good for patient, but patient avoids death that day

Considerations for Choosing an Inotrope

O_2 consumption and CO: if need to raise BP, phenylephrine good drug, but recognize that it drops SV and CO, raises total O_2 consumption, and decreases efficiency; nitroprusside potent drug, raises SV and CO, drops total O_2 consumption, and improves efficiency; think about this in terms of optimizing CO by making vasculature reasonable; want resistance to be ~1200 in adult, and want to optimize efficiency; PDE inhibitors good drugs; if you need to wake up and drive to work, need type 1 (caffeine); if you need to stop bronchospasm, need type 2 (theophylline, aminophylline); if you want stronger heartbeat, type 3 (milrinone or amrinone); remember that these drugs need to be used in combination with epinephrine, norepinephrine; make sure resistance normal; these agents synergistic; amrinone or milrinone with epinephrine synergistic; vardenafil and sildenafil (type 5) very good drugs for vasodilating pulmonary vasculature based on coronaries, and have little effect on systemic vasculature; giving methylene blue blocks this action, as will nitroglycerin and NO

Hemodynamics: hypotension bad; looked at 50,000 people and in VA system, ~11% of people had diastolic BP <30, ~12% had systolic BP <60; when that pressure extended beyond ~15 mins, started affecting 2-day, 30-day, and 1-yr mortality; do not let hypotension persist; fix quickly; 15 mins long time, and effects set in; hypertension lesser problem; occurs more commonly, diastolic BP >120 in 16% of people, systolic BP >200 in ~16% of people; after 15 mins start having problems, but less dramatic effects; tachycardia major problem; HR >120 bpm leads to increases in 2-day, 30-day, and 1-yr mortality; occurs in ~8% of patients; *persons at risk* — age 65 yrs and smoker, elevated cholesterol, diabetes, hypertension, coronary disease, vascular disease, or look like they might have those things; don't let those people have HR >120 bpm

Summary and Conclusions

Catecholamine infusions — useful when needed to maintain life; cause myocardial necrosis, tachycardia, MI, tissue necrosis, arrhythmia, hypokalemia, hyperglycemia; do not use inotropes unless really needed; antagonists prolong life, agonists shorten it; catecholamines essentially like ejection seat in plane (designed for escape from dangerous situation); "rocket fuel" used when heart needs to pump; milrinone synergistic with epinephrine and prolongs effect of cAMP produced with epinephrine; milrinone leads to profound vasodilation, needs to be adjusted; may need to give norepinephrine with it to get resistance to 1200; if you need get heart to pump and heart not pumping, turn on epinephrine, put in balloon pump, turn on some milrinone, make the SVR 1200; choose inotrope to fix what's broken; *for volume* — give volume; *if SVR* — fix SVR; make it reasonable; *if chronotropy* — ensure correct HR; told in school that CO equals SV times HR; mathematically, that means that raising the HR yields more CO; probably true in baby, if baby's HR is 50 bpm and you make it 150 bpm, will raise CO; but in normal adult, HRs between probably 60 bpm and 90 bpm don't do much to CO; when HR raised, stroke volume goes down; if HR is 20 bpm and you make it 60 bpm, will going to raise CO, but if HR between 60 bpm and 90 bpm, not much effect; also, making HR much higher (~150 bpm) may lower CO; relationship not simple straight line, and equation you've been told repeatedly, CO equals stroke volume times HR, suggests straight line, but not so; depends on patient and on what level you're at; at low HR, raising works somewhat; at medium HR, probably not; at high HR, will make it go down; fix HR, then fix diastolic function; *if tamponade* — nothing you do will work except fixing tamponade; *inotropes* — use inotropes when you need them, but be cautious; if HR too low, fix it, but remember it's nonlinear; not just "higher HR better"; depends on achieving optimal HR for patient; inotropes not good for patient, only stopgap measure; if person has tamponade, give volume, give inotrope, get them to OR, drain tamponade; not going to solve that problem; "rocket fuel" not good for patient, but they need it to get to tomorrow

Suggested Reading

Andraws R et al: Cardiovascular effects of ephedra alkaloids: a comprehensive review. *Prog Cardiovasc Dis*. 2005;47(4):217-25; **Belletti A et al:** The effect of inotropes and vasopressors on mortality: a meta-analysis of randomized clinical trials. *Br J Anaesth*. 2015;115(5):656-75; **Hensley FA et al:** The Practice of Cardiac Anesthesia. 1st ed. Philadelphia, PA: Lippincott Williams & Wilkins; 1990; **Martínez-Quintana E et al:** [Myocardial necrosis and severe biventricular dysfunction in the context of chronic ephedrine abuse]. [In Spanish.] *Addiciones*. 2010;22(1):25-8; **Nativi-Nicolau J et al:** Pharmacologic therapies for acute cardiogenic shock. *Curr Opin Cardiol*. 2014;29(3):250-7; **Osinaike BB et al:** Prolonged intensive care unit stay after coronary artery bypass graft surgery: role of perioperative factors. *Niger Postgrad Med J*. 2015; 22(4):213-6.

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Pain Mechanisms and Pathways, Management of Chronic Pain

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Pain Generation, Regulation, and Perception

Overview: complex subject; International Association for the Study of Pain defines as "unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"; tissue damage not required to feel pain; acute, following traumatic event, or chronic, due to disease conditions

Acute vs chronic pain: *acute* — primitive sensation, protects organism from further damage; transient or persists until damaged tissue heals; *chronic* — no protective function; persists beyond tissue repair; may cause additional comorbidities (*eg*, psychiatric conditions, muscle atrophy, arthritis)

Types of pain: somatic pain from tissues (*eg*, skin, periosteum, joints, muscles); neuropathic pain from damaged nerves (*eg*, diabetic neuropathy); visceral pain from visceral damage, follows separate pathway to brain

Somatic pain: signals from noxious stimuli generated by extremes of temperature, pressure, chemicals; perceived by sensory neurons with free nerve endings; pain sensory receptors (nociceptors) normally silent, generate pulses only when activated by stimuli; tissue damage releases certain chemicals, activating nerve signal terminals releasing neurotransmitters (*eg*, substance P, glutamate, calcitonin gene-related peptide [CGRP])

Perception of pain: requires complete neural circuit from periphery to somatosensory cortex in brain; initiation of somatic pain signal highly complex mechanism; several chemicals initiate pain transduction at nociceptor neurons, which transmit to spinal cord and higher centers; nociceptor neurons express wide variety of protein receptors, which form ion channels present throughout nerve endings; important in detecting and transforming noxious stimuli into electrical impulses, which then travel along nerves, synapses; different mechanisms for mechanical and chemical stimuli for initiation of pain signals; when noxious stimuli cause damage to cells, cells release chemical mediators (*eg*, prostaglandins, bradykinin, serotonin, substance P, potassium, histamine); transduction of pain impulse due to high-threshold chemical, thermal, or mechanical stimuli, directly or indirectly activating cationic channels and free nerve endings

Protein receptor types: different stimuli types use different protein receptor types; most important type involved in detection, transmission of noxious stimuli, transient receptor potential (TRP) channel family of receptors; 28 types of TRP molecules, 6 subgroups (canonical [TRPC], vanilloid [TRPV], ankyrin [TRPA], melastatin [TRPM], polycystin [TRPP], mucolipin [TRPML]); these channels nonselective for cations, but usually affinity for calcium ions

Vanilloid receptors (TRPV): mediate nociceptor transmission, form cationic channels; type 1 (TRPV1) responds to noxious heat stimulation >45°C, capsaicin sensitive; type 2 (TRPV2) responds thermal stimulation >52°C, capsaicin insensitive; cold receptor CMR-1/P8 responds to noxious cold (8°C–25°C); both channels respond to temperature fluctuations, leading to membrane depolarization and transduction of pain signals

Ankyrin (TRPA): mechanical damage to tissues releases bradykinin, indirectly activates TRPA1 channel

Melastatin (TRPM): inflammatory and neuropathic pain transmission; upregulated in presence of inflammation; high-threshold compression or tactile mechanical stimuli produce currents of cations leading to action potential generation; influx of sodium, calcium ions releases intracellular calcium stores, increasing calcium concentration to engage signaling systems, mediating short-term functional changes, decreased nociceptor threshold; may explain sensitization of peripheral nerves; high-threshold imports can also disrupt neuronal and nonneuronal membranes, release fatty acids, cations; fatty acids catalyzed by phospholipase A2 to produce arachidonic acid, leading to induction of isoenzyme cyclooxygenase-2 (COX-2) to accelerate prostaglandin formation; prostaglandin E2 (PGE2) acts on nociceptors, increase adenylyl cyclase to activate cyclic AMP (cAMP), activating protein kinase A and C, which phosphorylate prostanoids; kinin and amine receptors in ion channels can increase responsiveness of primary nerves to any stimuli, results in hyperpathia, analgesia, allodynia

Pain perception terminology: algesia, pain; esthesia, sensation; "an-," absence of; anesthesia, absence of sensation felt by brain; analgesia, perception of no pain; hyperpathia, abnormally painful reaction to stimulus, especially if repetitive, and increased threshold, increased latency; usually results from nerve damage and subsequent repair; hyperalgesia, increased pain from stimulus that normally provokes mild or no pain; allodynia, pain due to stimulation that does not normally provoke any pain

Types, Structure, and Function of Pain Afferent Neurons

Pain transmission from periphery to spinal cord: primary conductors of pain signals, first-order neurons

A delta and C fibers: small-diameter fibers; *A delta fibers* — myelinated, 1 µm to 5 µm diameter, transmission 5 m/sec 30 m/sec; conduct initial noxious

stimulation; classified based on response to heat, mechanical stimuli; *C fibers* — thinner (0.25 µm to 1.5 µm diameter), nonmyelinated, transmission 0.5 m/sec to 2 m/sec; classified based on response to various stimuli, such as temperature, mechanical stimulation (CMH, heat; CMC, cold; CMHC heat and cold); first-order neurons synapse in spinal cord dorsal horn; gray matter here has specific laminae in posterior aspect where neurons enter (Rexed laminae [I–X]); C fibers terminate in laminae I, IIA, II; A delta fibers terminate in laminae I, V; upon transduction of high-threshold stimuli, nociceptive signal transmitted by primary nociceptor afferents, where sodium (Na)-dependent depolarization mediated by isoforms of Na ion channels; majority tetrodotoxin (TTX) sensitive, but inflammation and exposure to certain substances may lead to increased expression of TTX-resistant Na channels, with lower Na conductions; at dorsal horn, synapses, modulation; A delta, C fibers terminate into nociceptor-specific or wide–dynamic-range neurons; fibers may ascend ipsilaterally within spinal cord, but most project contralaterally, form spinothalamic tract; nociceptor-specific neurons in laminae I, II, V get input from A delta and C fibers; central region responds to high-intensity stimulation, outer region responds to nonnoxious input; wide–dynamic-range (WDR) neurons in laminae I, II, V, VI receive input from A delta, A alpha, A beta, C fibers; WDR neurons in laminae I, II respond to nonnoxious (*ie*, low-tensile, -thermal, -mechanical) input; laminae V, VI, high-threshold stimulation; WDR neurons generate prolonged "after" responses ("wind-up"), depending on input extent, frequency, causing continued nociceptor transmission and sensation

Wind-up phenomenon: WDR neurons, continued nociceptor reception due to repeated stimulation through afferent C fibers; central sensitization, (wind-up phenomenon), similar process; N-methyl-D-aspartate (NDMA) receptor, contributing factor (explains effect of NMDA-blocking agents in pain relief); normally, WDR neurons, moderate-sized receptive field, but persistent nociceptor input may increase it

Spinal pathway phase: after synapse at dorsal horn level, second motor neurons mostly travel to contralateral side, form spinothalamic tract, in anterolateral column; some fibers ascend on ipsilateral side, in ventrolateral aspect; axons from laminae I, II form neospinothalamic tract, transfer nociceptor-specific signals; axons from lamina IIa, V form paleospinothalamic tract, transmit WDR neuron signals; second-order neurons end in thalamus; neospinothalamic tract ends in caudoventral posterolateral nucleus of thalamus; paleospinothalamic tract ends in medial and intralaminal nuclei of thalamus; thalamic neurons retain many characteristics of nociceptor-specific and WDR neurons; from thalamus, third-order pain-transmission neurons (supraspinal tracts) project into somatosensory cortex, S1 and S2 regions; projections from thalamic, ventral, posterolateral nuclei (primarily nociceptor-specific signals) end primarily in S1; intralaminal and medial nuclei end bilaterally in S2; some fibers end in other areas, mainly receiving input from their counterparts; majority of nociceptor signals end in deeper layers of cortex, while superficial layers primarily receive nonnociceptor signals; further projections of these neurons to anterior and posterior cingulate gyrus, play major role in pain perception and related behavioral responses, relayed to hippocampus, thalamic nuclei and mediate neural, endocrine, and autonomic responses to pain; primarily responsible for nonopioid and hormone-related analgesia; efferent signals from anterior cingulate gyrus to other nuclei (*eg*, caudate, putamen, accumbens) responsible for motor responses to pain signals

Modulation of pain: occurs at supraspinal level via several factors; pain results from activation of sensory receptors to protect against actual or impending tissue damage; no direct correlation between nociception and sensory perception of pain; patient response to pain perception of interpretation may vary dramatically depending on emotional state, level of anxiety, past experiences or memories, tension, distraction; forms basis of pain treatments (*eg*, biofeedback); endogenous regulation well-established, accepted phenomenon; pain modulation exists in form of intermediary pathways; input to pathways arises from brain regions (*eg*, hypothalamus, amygdala, rostral anterior cingulate gyrus), which project into periaqueductal gray (PAG) brain matter, primary control center for pain modulation, projects signals to medulla; medullary nuclei including nucleus raphe magnus, projects to spinal, medullary dorsal horns, enhance or diminish nociceptive transmission, altering pain perception; this descending intermediary circuit opioid sensitive, responsible for responses to opioids, cannabinoids, nonsteroidal anti-inflammatory drugs (NSAIDs), serotonin and norepinephrine reuptake inhibitors (SNRIs)

Pain matrix: complex pain matrix in brain activated by noxious stimulation, includes somatosensory cortex (S1 and S2), insula, amygdala, hippocampus, thalamus, PAG, which regulate pain behavior, moderate pain perception, and emotional, motor, cognitive, and behavioral responses; pharmaceutical agents, behavioral management, act on various aspects of matrix to regulate pain perception; PAG plays major role in analgesic responses (primary area for opioid-generated analgesia); electrical stimulation of PAG produces similar results, but with significant side effects (*eg*, anxiety, distress, migraine-like headaches), uncommon method for analgesia; deep brain stimulation controls pain centrally; amygdala plays significant role in emotional response to pain (*eg*, anxiety, stress, fear); activation of alpha-2 adrenergic receptors inhibits nociceptor transmission, mainly at spinal cord level via presynaptic activity, inhibits release of excitatory neurotransmitters from primary efferent terminals and through postsynaptic activation of alpha-1 adrenergic receptors, causing depolarization of neurons, demonstrating additional mechanism for enhancing inhibition of pain; *hormonal regulation of pain* — hypothalamic-pituitary axis (HPA) partially responsible for analgesic response, through corticotrophin-releasing factor and adrenocorticotropic hormone (ACTH); sympathetic stimulation of chromaffin cells in adrenal cortex, release of endorphins and encephalin

Autonomic Nervous System and Contribution to Pain

Autonomic nervous system: involved in transmission, regulation of pain (primarily visceral); visceral pain arises from ischemia, inflammation, or distension of hollow viscera; some viscera (*eg*, liver) feel no pain; viscera normally insensitive to stimuli (*eg*, cuts, burns); visceral pain diffuse in nature, poorly localized, frequently referred

(*ie*, to somatic tissues; *eg*, cardiac ischemic pain felt in left arm, shoulder pain after distension or inflammation of diaphragm); pain poorly localized because of low-density of nociceptors; visceral pain acute or chronic; acute pain arises from activation of high-threshold nociceptors; chronic from sensitization of both high- and low-threshold mechanoreceptors; nociceptors project into laminae I, V, but not II; thus different from somatic afferent fibers; in laminae I, V convergence of inputs from viscera, somatic tissues in spinal cord and higher levels explains perception of referred pain; transmission of nociceptor impulses from viscera via autonomic, sympathetic, parasympathetic nerves; dual sensory innervation with slow unmyelinated C fibers, primary reason visceral pain effectively treated with sympathetic nerve blocks; some spinal afferent fibers travel along hypogastric, lumbar colonic, splanchnic nerves, terminate in thoracolumbar regions as part of sympathetic innervation; traverse prevertebral, paravertebral ganglia into spinal cord; vagal and pelvic afferents terminate in brainstem and lumbosacral cord, contribute to parasympathetic innervation; spinal and vagal afferent fibers convey sensory information from upper gastrointestinal (GI) tract to central nervous system (CNS); vagal afferents transmit predominantly physiologic information, spinal afferents transmit noxious information; spinothalamic tracts major pathways for visceral nociception; dorsal column and ventral posterolateral column primarily involved in visceral pain transmission

Complex Regional Pain Syndromes

History: 1864, "causalgia" described in Civil War soldiers with nerve injuries; symptoms included burning, pain, edema, vasomotor and sudomotor changes, progressive loss of function, psychologic disturbances; 1986, sympathetically maintained pain hypothesized; 1993, complex regional pain syndrome (CRPS) types 1 and 2; type 1 historically known as reflex sympathetic dystrophy (RSD), type 2, causalgia

CRPS: progressive, chronic illness; pathogenesis poorly understood; also known as RSD, reflex neurovascular dystrophy, causalgia, algoneurodystrophy, sympathetically maintained pain, clenched-fist syndrome, Sudeck atrophy; similar sympathetic pain syndromes include phantom pain, herpes zoster, metabolic neuropathies, neuralgias, complex regional pain syndrome; although syndromes sympathetic, response to sympathetic block may vary among patients; pain typically has sympathetically maintained and sympathetically independent components

Pathophysiology of sympathetic pain: formation of normal circuit in nervous system after injury, forms cycle of afferent sensory input, efferent increased sympathetic output; sympathetic fibers may act as efferents, impairing circulation, ischemia (especially in late phases of disease), generating more somatic pain, thus more ischemic cell damage; degrees of neuroexcited chemicals at nerve endings, plus involvement of central mechanisms (explains increased pain during emotional stress); pathogenesis of CRPS theorized as disease process of peripheral nerves, peripheral soft tissues, or spinal cord itself; vasomotor, sudomotor control substantially altered

Complex regional pain syndrome type 1: usually develops after initial injury; male:female incidence 1:3; pain, allodynia, hyperalgesia, soft tissue edema, vasomotor and sudomotor changes in regional pain

CRPS type 2: signs and symptoms similar to CRPS 1; develops after major nerve injury

CRPS phases: *stage 1* — acute phase; sympathetic underactivity; increased blood flow, affected extremity warm, dry, shiny, edematous; increased hair and nail growth; burning pain, allodynia, avoidance behavior (protecting extremity); *stage 2* — dystrophic phase; sympathetic overactivity; decreased blood flow, vasoconstriction, ischemic edema of extremity; extremity cold, cyanotic, pale, sweaty, mottled skin; brittle nails, muscular atrophy; range of motion of extremity decreased due to pain, diffuse osteoporosis due to reduced blood flow; burning pain, allodynia, activity avoidance, extremity protection, joint pain; *stage 3* — atrophic phase; sympathetic overactivity with CNS involvement; skin atrophy, loss of fat pad, muscular wasting, severe contracture; significantly reduced range of motion; pain spreads more proximally, may involve other limbs; extremity protection, no voluntary activity of limb

Diagnosis: typically clinically made on examination; testing may include skin-temperature testing, blood-flow measurements using thermography, cold stress response, digital plethysmography, oscillometry; radioisotope scanning may show increased uptake in bones, especially small joints, suggesting increased osteoblastic activity, which causes reduced bone density (rate correlates with duration of disease); bone microdensitometry useful for assessment, treatment evaluation; neuroimaging, ~50% patients show abnormalities in spinothalamic, trigeminothalamic, and corticospinal function, may represent dysfunction of medulla; may show pathologic changes in spinal cord, brain; majority have measurable abnormalities of sensory, motor systems on neuroimaging, evidence of spinal cord, brain dysfunction; chronically, efferent nerve fibers histologically unaffected compared with afferents; only C fibers, histopathologic abnormalities; histopathologic muscle changes similar to diabetes

Treatment: complex, challenging; combine various modalities; sympathetic blockade, physical therapy current mainstay; interventional pain treatments include sympathetic chain blockade, neurolytic blockade of sympathetic fibers at affected limb; *sympathetic blockade* — performed at level of stellate ganglion (stellate ganglion block), at thoracic level, lumbar level; *intravenous (IV) regional blocks* — with reserpine, guanethidine, helpful; IV phentolamine may be helpful; *surgical sympathectomy* — no longer common; *pharmacologic agents* — *eg*, tricyclic antidepressants, clonidine, propranolol, gabapentin, NSAIDs, useful; *physical therapy* — mainstay of treatment; active and passive range of motion improvement, occupational therapy helpful; also improves blood flow to affected extremity; *regional anesthetic blocks or somatic blocks* — facilitate physical therapy; *long-term epidural infusions* — used along with oral analgesics; *behavioral medicine* — *eg*, coping skills, biofeedback, relaxation techniques, group therapy, integral part of treatment; if no good response to treatment, *spinal cord stimulation* — percutaneously placed epidural stimulating electrodes or surgically placed electrodes

Neuropathic Pain

Neuropathic pain: pain arising from damaged nerve; normally, nerve fibers only conduct signals, do not generate pain signals; damaged nerve inappropriately discharges impulses at random; pain burning, shooting, sharp, lancinating; *anatomic classification* — mononeuropathy, affecting 1 nerve; polyneuropathy, affecting >1; *etiologic classification* — metabolic, traumatic, infectious, postinfectious, neoplastic, paraneoplastic, toxic; mononeuropathy often also entrapment neuropathy, injury from scar formation, pressure from adjacent structures; often results from trauma, surgery, after infection (*eg*, herpes zoster, causing postherpetic neuralgia); polyneuropathy common with diabetes, alcoholism, human immunodeficiency virus (HIV), syphilis, or centrally located (*eg*, autonomic neuropathy, Guillain-Barré syndrome, multiple sclerosis); diabetic neuropathy, "glove-and-stocking" distribution, hyper- or hypoesthesia; hyperesthesia, during ischemic phase, hypoesthesia if nonfunctional nervous tissue; in diabetes, peripheral neuropathy, autonomic neuropathy, and/or focal neuropathy affecting eyes, ears, hearing; autonomic neuropathy causes lack of anginal pain during cardiac ischemia; alcoholic neuropathy, primary axonal sensorimotor peripheral neuropathy (axonal degeneration, nutritional deficiencies cause sensory, motor deficiencies); HIV neuropathy, distal sensory polyneuropathy caused antiretroviral toxicity or by opportunistic infections (*eg*, cytomegalovirus, herpes zoster)

Diagnosis: mainly clinical; assess for diabetes, vitamin deficiency, other illness; electromyogram, nerve conduction velocity studies

Treatment: focus on cause and neuropathy itself; remove scar tissue, tumors; correct or stabilize disease states (*eg*, HIV, diabetes); address side effects of pain, dysfunction

Treating Pain

Overview: can be treated by level of origin, pain transmission, and level of interpretation

Level of origin: local anesthetic infiltration, topical local anesthetics, clonidine patches, depletion of pain transmitters (*eg*, substance P, using capsaicin), NSAIDs, neurolysis

Pain transmission: peripheral neuromodulation, central neuromodulation (spinal cord, deep brain); neuroablative techniques

Level of interpretation: cerebral level; pharmaceutical agents (*eg*, tricyclic antidepressants, gabapentin, pregabalin, duloxetine); analgesics (opioid, nonopioid); complex pain symptoms require multimodal approach including physical therapy, behavioral management, and interventional pain treatments

Opioids (Opiates)

Pharmacodynamics (PD): pharmaceutical agent's effects on organism; pharmacokinetics (PK), organism's methods for metabolizing, excreting pharmaceutical agent

DEA classification: controlled substances, defined by United States Drug Enforcement Agency (DEA); 5 categories of controlled substances (schedules), based on acceptable medical use, potential for dependence or abuse; most medically used opioids Schedule II, some Schedule III; individual states regulate dispensing, prescribing (most require controlled substances license and DEA license to prescribe); *opioids with no clinical use, schedule I* — heroin, lysergic acid diethylamide (LSD), 3,4-methylenedioxy-methamphetamine (MDMA, ecstasy), methaqualone, peyote; marijuana, Schedule I, acceptable analgesic in many states

Types of opioids: originate from natural opium alkaloids, found in poppy seeds; these include heroin, morphine, codeine, thebaine, papaverine; opioids can be natural, synthetic, or semisynthetic compounds, similar in structure and function; bind to opiate receptors; variable potency; specific affinity to certain opiate receptors; many synthetic, semisynthetic opioids (*eg*, meperidine, fentanyl, hydrocodone, hydromorphone, methadone); semisynthetic opioid hydromorphone contains natural alkaloid morphine, hydrocodone contains codeine, oxymorphone and oxycodone contain thebaine; body secretes endogenous opioids in response to pain, exercise; these include endorphin, enkephalin, dynorphin

Opioid classification: by affinity to opioid receptors (agonists, antagonists, agonist-antagonists); 4 different classes; *phenanthrenes — eg*, morphine, codeine, hydrocodone, levorphanol, hydromorphone, oxycodone, oxymorphone, buprenorphine; those with 6-hydroxyl group in chemical structure (*eg*, morphine, codeine), higher incidence for nausea, hallucinations than those without (mostly synthetic); *benzomorphans* — pentazocine (agonist-antagonist, high incidence of dysphoria); *phenylpiperidines — eg*, fentanyl, meperidine; fentanyl, highest affinity for mu receptors; *diphenylheptanes — eg*, propoxyphene, methadone; also classified according to affinity for mu receptors; strong affinity by agonists (*eg*, morphine, fentanyl, beta-endorphin, leu-enkephalin); strong agonist affinity for kappa receptors (*eg*, beta-endorphin, leu-enkephalin); moderate affinity for kappa receptors (*eg*, pentazocine); weak affinity for kappa receptors (*eg*, morphine, fentanyl, buprenorphine); strong affinity for delta receptors (*eg*, beta-endorphin, leu-enkephalin); weak affinity for delta receptors (*eg*, morphine, fentanyl); naloxone, naltrexone have strong affinity for mu receptors, antagonistic, moderate affinity for kappa and delta receptors; strong-potency opioids include morphine, fentanyl, sufentanyl, alfentanil, etc; moderate-potency opioids include buprenorphine, pentazocine, butorphanol; codeine, weak potency; opioids may be combined with acetaminophen or ibuprofen

Opioid site of action: neuronal cell bodies possess opioid receptors on cell surface (primarily delta, kappa, mu); opioids exert specific actions through these receptors on cell membranes; mu receptors named for affinity for morphine, kappa receptors for affinity to ketocyclazocine, delta receptors for discovery on mouse vas deferens; more recently discovered, less well-known opioid receptors include sigma, epsilon, zeta, lambda; principal concentration of opioid receptors in CNS, also in peripheral afferent nerves and terminals, other organs (primarily GI tract); *opioid receptor structure* — inhibitory G protein-coupled receptors (GPCR); discovery of endogenous ligands for these receptors led to different nomenclature, nociception and orphanin FQ (N/OFQ), product of precursor protein encoded by normal gene with significant sequence homology to genes encoding prodynorphin, proenkephalin, and proopiomelanocortin; 2 *major branches in opioid peptide N/OFQ receptor*

family — main branch comprises mu, delta, kappa receptors (naloxone acts as antagonist); second branch, receptor for N/OFQ, negligible affinity for naloxone; opioid receptors, group of 7 amino acid chains in helical structure, span across neuronal cell membrane, connected through 3 extracellular and 3 intracellular loops; external end (N-terminus) where ligands bind; internal terminal (C terminus), coupled with G protein

Mu, delta, kappa receptors: *mu receptor* — 3 subtypes (mu_1, mu_2, mu_3); mu_1 responsible for analgesia, physical dependence; mu_2, for respiratory depression, miosis, euphoria, physical dependence, reduced GI motility; mu_3, possible vasodilatory effect; mu receptors distributed throughout CNS areas involved in regulation of pain, analgesia; highest concentration of mu receptors in thalamus, amygdala, cordate putamen, neocortex, interpeduncular complex, nucleus accumbens, inferior and superior colliculi; moderate distribution of mu receptors in PAG and raphe nuclei; mu, delta, and kappa receptors also present in Rexed lamina I and II; physiologic functions regulated by mu receptors include respiratory and cardiovascular functions, intestinal motility, mood, thermoregulation, hormone secretion, immune functions, also responsible for effects of opioids; *delta receptors* — 2 subtypes; produce analgesia, antidepressant effect, convulsant effect, physical dependence, respiratory depression; olfactory bulb, neocortex, cordate putamen, nucleus accumbens, amygdala have high concentration; hindbrain (*eg*, thalamus, hypothalamus) have low concentration; present in Rexed lamina; role in GI motility, mood, behavior, cardiovascular regulation; *kappa receptor* — 3 subtypes (k_1, k_2, k_3); produce analgesia, anticonvulsant effects, depression, hallucinations, miosis, diuresis, sedation, stress (*ie*, some anti-delta effects); located predominantly in occipital cortex, nucleus accumbens, hypothalamus, claustrum; regulate nociception, diuresis, feeding, neuroendocrine and immune system functions

Mechanisms of action: inhibitory action on presynaptic and postsynaptic neurons; opioid action dependent on receptor density on neuron; presynaptic action, inhibition of neurotransmitter primary effect, can also block release of inhibitory neurotransmitter; action on postsynaptic neuron also present; overall action analgesia; presynaptic neuron inhibition action prevents release of neurotransmitters (*eg*, noradrenaline, acetylcholine, substance P); as pain impulse arrives at dorsal horn, neurotransmitter (*eg*, substance P, glutamate) release inhibited by opioids, thus blocking further impulse transmission; impulse transmission of pain dependent on calcium channels; direct action on these channels reduces calcium entry into cells, indirect action reduces outward movement of potassium ions; both actions via G-coupled proteins; opioids also have intracellular effect on inhibition of adenylyl cyclase (converts adenosine triphosphate [ATP] into cyclic adenosine monophosphate [cAMP], necessary for neurotransmitter release); G-protein uncoupling occurs after prolonged exposure to opioids explains drug tolerance resulting from desensitization of these receptors; downregulation of opioid receptors, decreased production of endogenous opioids also contributes to tolerance; physical dependence usually masked by presence of opioid ligand or receptor, unmasked by antagonist (*eg*, naloxone), competitively displaces opioid from receptor, reverses effects, leads to withdrawal symptoms

Effects: vary by organ system; major action on CNS; analgesia primary effect; more effective on somatic than neuropathic pain (but does reduce intensity of neuropathic pain); *CNS* — sedation, euphoria, dysphoria, hallucinations (more common with kappa receptors), tolerance, dependence; *cardiovascular* — decreased sympathetic outflow from reduced pain; direct effect on sinoatrial (SA) node, causing bradycardia; peripheral vasodilation from reduced sympathetic outflow, histamine release, may also result in decreased blood flow, blood pressure; *respiratory* — mu receptors in brainstem responsible for depression of respiratory centers, bradypnea; respiratory rate more affected than tidal volume; carbon dioxide sensitivity in brain also reduced, reduced respiratory drive; concurrent use of other CNS depressants (*eg*, benzodiazepines) can cause severe respiratory depression, death) main cause of opioid-overdose deaths); opioids suppress cough reflex; codeine (less potent than morphine), similar effect on cough; *GI tract* — stimulation of chemoreceptor trigger zone (CTZ) leads to nausea, vomiting; receptors in GI tract responsible for decreased peristalsis, leading to constipation, and increased smooth muscle tone, responsible for biliary duct obstruction (from spasm of sphincter of Oddi); *ocular* — mu, kappa receptors in Edinger-Westphal nucleus, pupil constriction (*ie*, miosis), common sign of opioid abuse, overdose; *endocrine* — release of ACTH, prolactin, gonadotropin, antidiuretic hormone; *other* — histamine release from mast cells, itching, hypotension, bronchospasm; generalized muscle rigidity, especially thoracic muscles (more vulnerable to this effect), can cause difficulty in ventilation of intubated patient, requiring increased pressure during resuscitation; opioids cross placenta, if given during final stages of labor can lead to neonatal respiratory depression

Naturally occurring endogenous opioids: peptides; similar in action to exogenous opioids; *3 types* — beta-endorphin, leu-enkephalin and met-enkephalin, dynorphin A and B, newly discovered endomorphin-1, endomorphin-2; ~70% of action at presynaptic level; dynorphin acts on alpha receptors leading to gamma-aminobutyric acid (GABA) release, hyperpolarizes dorsal horn neurons, preventing activation by arriving pain impulse, thus reducing pain input; variable affinity for opioid receptors; beta-endorphin binds equally to mu, delta receptors; endomorphins bind primarily to mu receptors; dynorphin, preference for delta receptors; enkephalin, preference for kappa receptors

Antagonists: naloxone, naltrexone; competitive antagonists, block effect of opioids on cell membrane by occupying opioid receptors but not activating them; stronger affinity for mu receptors than agonists; naloxone more effective parenterally, shorter acting, may not provide reversal for longer-acting opioids; naltrexone effective orally, longer effect, more useful in detoxification from longer-acting opioids; agonist-antagonist opioids (*eg*, pentazocine, nalbuphine, nalorphine), poor affinity for mu receptors, act as mu antagonists, kappa agonists; ceiling effect, prevents further action at increased doses; pure agonists, no ceiling effect

Key Points

1. Pain transmission, interpretation, and perception as well as origin of pain are very complex and involve intricate interaction between chemicals, nervous tissues, and muscular tissues.
2. Opioids can be classified in several ways, including pharmacologically, by therapeutic need, and potential for abuse.
3. Neuropathic pain arises from damaged nerves and has a complex pathogenesis as well as multimodal treatment.
4. Complex regional pain syndrome is associated with sympathetic pain. Treatment is by a multimodal approach.

Suggested Reading

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ANESTHESIOLOGY
Board Review

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Postoperative Care and Management of Complications

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Overview: standards for postoperative care, supervision of patients, complications of anesthesia and their avoidance

Postoperative Care

Standards of postoperative care: American Society of Anesthesiologists (ASA) updated 5 standards of postoperative anesthesia care October 2014

1. All patients who have received general anesthesia, regional anesthesia, or monitored anesthesia care shall receive appropriate postanesthesia management
2. Patient transported to the postanesthesia care unit (PACU) shall be accompanied by member of anesthesia care team knowledgeable about patient's condition
3. Upon arrival in PACU, patient shall be reevaluated and verbal report provided to responsible PACU nurse by member of anesthesia care team accompanying patient
4. Patient's condition shall be evaluated continually in PACU
5. Physician responsible for discharge of patient from PACU

PACU report — on arrival, provided to receiving PACU nurse by the anesthesia provider; should include preoperative history (patient's medications, relevant allergies, past medical history, underlying diagnosis, any premedications given prior to procedure), intraoperative history (procedure performed, type of anesthesia delivered, medications and fluid given, estimated blood loss, urine output, any notable intraoperative events or problems, as well as range of vital signs), patient's current status (airway; size and location of lines, catheters, or invasive monitors; level of consciousness; pain level; intravascular volume status; overall impression), any planned postoperative instructions (acceptable ranges for blood loss, vital signs, urine output, potential cardiovascular or respiratory problems, contact information for responsible team, lab or diagnostics studies, *eg*, chest X-ray, postoperative ECG)

Postoperative Complications in PACU

Respiratory: *airway obstruction* — most frequent; causes include airway edema, trauma, vocal cord paralysis, arytenoid dislocation, secretions, foreign body in airway, laryngospasm, anxiety; tongue falling against posterior pharynx most common airway obstruction; clinical signs include sonorous respiration (partial obstruction), absent breath sounds, and often paradoxical movement of the chest with respiration (complete obstruction); *respiratory insufficiency* — caused by hypoventilation and hypoxemia; *causes of hypoventilation* — residual anesthesia or muscle relaxant, use of postoperative opioids, splinting secondary to pain, tight abdominal binder, obstructive sleep apnea; can occur in premature infants or neonates; *cause of hypoxemia* — atelectasis, exacerbation of asthma or COPD, congestive heart failure or fluid overload, pulmonary embolus, acute lung injury, aspiration, pneumothorax or hemothorax, diaphragmatic injury or paralysis, pneumonia

Diagnosis and management of respiratory insufficiency: start by assessing airway breathing and circulation, then increase FiO_2 delivered to patient; increase rate of O_2 being delivered; nonrebreather or shovel mask; jaw thrust or chin lift and placement of oral or nasal airway; positive-pressure ventilation with bag-valve mask; intubation or use of noninvasive ventilation (*eg*, continuous positive airway pressure [CPAP] or bilevel positive airway pressure [BiPAP]); consider patient's history, operative course, fluid status, and any medications administered; obtain arterial blood gas or chest X-ray to rule out pneumothorax or pulmonary edema

Hypoventilation: inadequate ventilation to allow sufficient gas exchange can lead to increased $PaCO_2$ and respiratory acidosis

Causes and treatment**:** *residual inhalational or IV anesthesia* — try to arouse patient and provide support; *residual muscle relaxant* — administer reversal agent such as neostigmine (Bloxiverz, Prostigmin) or sugammadex (Bridion); *postoperative opioid administration* — consider administering naloxone (Narcan, Evzio); *splinting secondary to pain* — initiate pain control, consider patient-controlled analgesia (PCA) or regional anesthesia; *tight abdominal binder* — release binder and consult surgeon; *obstructive sleep apnea* — try repositioning patient or administering BiPAP; *hypoventilation in premature infant* — provide supplemental O_2, consider giving acetaminophen (*eg*, Mapap, Paracetamol, Tylenol), regional anesthesia instead of further opioids

Fluid overload or pulmonary edema: recognize hypoxemia on arterial blood gas or through recognition of high central venous pressure or pulmonary capillary wedge pressure; chest x-ray may show increased pulmonary vasculature, increased interstitial or alveolar fluid, pleural effusion, or fluid in fissure

Treatment: stop IV fluids; administer diuretics (*eg*, furosemide (Furocot, Lasix) 20 mg to 100 mg intravenously [IV]); provide supplemental O_2; consider noninvasive mechanical ventilation

Atelectasis: recognized by decreased breath sounds or opacifications on chest x-ray

Treatment: incentive spirometry; reposition patient; administer CPAP or BiPAP; remove impacted secretions via bronchoscopy; chest physiotherapy; positive pressure ventilation with positive end-expiratory pressure (PEEP)

Asthma or COPD exacerbations: recognized by wheezing on auscultation

Treatment: albuterol (*eg*, Proventil, Ventolin), steroids, cromolyn sodium (Intal); CPAP or BiPAP, if necessary; in severe bronchospasm, patient may need reintubation

Pulmonary embolus: recognized on electrocardiogram (ECG); combination of sinus tachycardia with an S1Q3T3, or through ultrasound of lower extremities demonstrating clot; D-dimer typically not helpful for diagnosis in PACU; use transthoracic or transesophageal echocardiogram to rule out central pulmonary embolus or assess right ventricular (RV) dysfunction; obtain chest CT scan or pulmonary angiogram if patient stable

Treatment: cautious fluid resuscitation; supportive inotropes and vasopressors; thromboembolectomy or catheter-directed thrombolysis; provision of anticoagulation in consultation with surgeon; inferior vena cava (IVC) filter

Aspiration: common occurrence in postoperative setting; chest x-ray may reveal foreign body infiltrates, atelectasis, or collapse; typically may not see anything at all on chest x-ray

Treatment: supportive care for small aspiration with limited respiratory compromise; for large aspiration event, rapid sequence intubation, gastric decompression, and mechanical ventilation with high amount of PEEP; prophylactic antibiotics and steroids ineffective; no evidence to support bronchoalveolar lavage and routine suction; aspiration can be prevented via elevation of head of the bed, avoidance of oversedation, and placement of an nasogastric (NG) tube in patients with gastric compression

Upper airway obstruction or stridor: caused by airway edema or trauma, vocal cord paralysis, dislocation of arytenoid, secretions, or foreign body

Treatment: remove secretions by suctioning; administer glycopyrrolate (typically 0.2 mg IV); severe edema or trauma may necessitate reintubation; for vocal cord paralysis, dislocation of arytenoid or presence of foreign body, consult otolaryngologist; use of racemic epinephrine (Asthmanefrin, Micronefrin, Nephron), dexamethasone (Decadron, Dexamethasone Intensol, Dexasone), humidified air, or heliox, can be helpful

Pneumothorax, hemothorax or pleural effusion: diagnosed by chest x-ray

Treatment: needle decompression of chest at second intercostal space in midclavicular line, or through placement of chest tube; for large hemothorax or ongoing bleeding, exploratory thoracotomy may be indicated

Diaphragmatic injury or paralysis of the diaphragm: elevated hemidiaphragm seen on chest x-ray; paralysis secondary to a regional block usually temporary

Treatment: supportive treatment with an increased FiO_2; reassure patient; large diaphragmatic injury may require surgical repair

Laryngospasm: uncontrolled contraction of laryngeal cords; diagnosed by clinical signs of high-pitched "crowing," or silence if glottis totally closed; more common after airway trauma, repeated instrumentation, or patients who have copious secretions (*eg*, blood, vomit) in airway

Treatment: positive-pressure mask ventilation; placement of oral or nasal airway; suctioning; small dose of succinylcholine (Anectine, Quelicin) if refractory; intubation if necessary; cricothyroidotomy or jet ventilation can be rescue approach for patients who cannot be intubated or ventilated

Hemodynamic: most common causes of hemodynamic compromise in PACU can be differentiated based on problems with preload, left ventricular (LV) and RV function, and afterload

Hypotension: decreased preload common underlying cause of hypotension; decreased preload causes include hypovolemia (from third spacing or fluid sequestration, bleeding, or wound drainage), venodilation (from spinal or epidural anesthetic), presence of pericardial tamponade, tension pneumothorax, or air embolus; other hypotension causes include LV dysfunction or impaired contractility caused by severe metabolic derangement (*eg*, acidosis, sepsis, hypoxemia), myocardial infarction, volume overload, or dysrhythmia; arterial vasodilation or decreased afterload can be caused by inflammatory response or be related to anesthetic; clinical signs include drop in blood pressure (BP), disorientation, nausea, change in level of consciousness, decreased urine output, and angina

Initial diagnosis and management: start with examination and stabilization of patient; checking airway, breathing, and circulation; if considering resuscitating patient with fluid, ensure adequate venous access; review patient's history, anesthesia record, surgical procedure, estimated blood loss, and other data from PACU; consider obtaining laboratory studies; arterial blood gas can be helpful to assess oxygenation and acid-base status; complete blood count can be helpful to assess hemoglobin and platelet levels; consider coagulation studies; ECG can help assess for arrhythmia; chest x-ray can help assess for pneumothorax, hemothorax, or evolving cardiomegaly; transthoracic or transesophageal echocardiogram can help assess cardiac contractility, function of left and right ventricles, assessment of LV filling, presence of IVC collapse, or new valvular abnormalities

Treatment: consider invasive monitoring (*eg*, placement of arterial catheter or central venous line); initiate vasopressor or inotropic support with phenylephrine, norepinephrine, or dopamine as necessary; consult with cardiology, intensive care unit (ICU), or surgery as indicated

Hypotension from hypovolemia: diagnosed via presence of tachycardia and with hypotension, low central

venous pressure or pulmonary capillary wedge pressure; respiratory variation in arterial wave form or recognition of IVC collapse or underfilled LV on an echocardiogram; treat hypotension caused by hypovolemia through fluid resuscitation and assessment for cause (*eg*, ongoing bleeding, diuresis, high NG tube output)

Hypotension from bleeding: diagnosed via recognition of tachycardia along with anemia, hypovolemia, and sanguineous drain output; treat hypotension from bleeding via fluid resuscitation, blood transfusion as appropriate, correction of coagulopathy or thrombocytopenia, treatment of hypothermia; consider returning to operating room (OR) if surgery needed to stop bleeding

Hypotension resulting from sepsis: diagnosed via presence of fever, leukocytosis, tachycardia, hypovolemia, and lactic acidosis; treat with fluid resuscitation, obtain blood cultures, and initiate broad-spectrum antibiotics

Hypotension caused by myocardial infarction or myocardial ischemia: diagnosed via 12-lead ECG, use of transthoracic or transesophageal echocardiogram, obtaining cardiac enzymes; treat with cautious fluid resuscitation, aspirin; consult with cardiologist and surgeon to describe role of heparinization or cardiac catheterization and use of antiplatelet agents; consider use of appropriate inotropes or vasopressors; balloon pump support may be helpful; after blood pressure stabilized, beta blockade should be initiated

Hypotension from arrhythmias: relatively common source of hypotension in PACU; diagnosed via 12-lead ECG; treat following advanced cardiovascular life support (ACLS) protocol; tachyarrhythmias may require electrical or chemical cardioversion or correction of electrolyte abnormalities; bradyarrhythmia may be treated with atropine, epinephrine, dopamine, or transcutaneous venous pacing; consult cardiologist

Hypotension from pulmonary embolus: diagnose via recognition of S1Q3T3 sign on ECG or through diagnostic criteria on echocardiogram; treat with cautious fluid resuscitation, thromboembolectomy, or catheter-directed thrombolysis and anticoagulation

Hypotension from anaphylaxis: diagnosed via tachycardia in combination with vasodilatory shock; decreasing systemic vascular resistance and increased cardiac output; check serum tryptase and eosinophil count; treatment includes removal of causative agent, resuscitation with fluids, provision of diphenhydramine (*eg*, Benadryl), steroids, and epinephrine as necessary

Hypotension from pericardial tamponade: rare but important cause of hypotension in PACU; caused by postcardiac surgical bleeding, trauma, or dissecting thoracic aneurism; it may be procedural related (*eg*, after placement of central venous catheter); diagnosed via Beck's triad (hypotension, jugular venous distension, and muffled heart sounds); nonspecific ST segment changes or low-voltage QRS complex on ECG; enlarged cardiac shadow on chest x-ray; echocardiogram best for diagnosis; treat with fluid resuscitation, pericardiocentesis, or surgical repair of bleeding vessel

Hypotension from bleeding: most common cause of ongoing hypotension in PACU bleeding from surgical site, coagulopathy, or uncorrected thrombocytopenia; bleeding may be obvious or occult; examine surgical site and drains in patients with ongoing hypotension; may or may not be signs of hypovolemia; manage ongoing bleeding by early consultation with surgeon and placement of large-bore IV access in initiation of fluid resuscitation

Postoperative hypertension: occurs relatively frequently in in PACU; common causes include incisional pain, irritation from endotracheal tube, distended bladder, previous history of hypertension, fluid overload, metabolic derangements (*eg*, hypoxemia, hypercapnia, acidosis), and intercranial hypertension; clinical signs and symptoms include elevated blood pressure, headache, bleeding, vision changes, angina, or ST segment changes on ECG; start treatment with draining bladder, providing appropriate analgesia, or correcting underlying metabolic derangement; beta blockers, calcium channel blockers, nitro paste, or hydralazine (Apresoline) can be given for mild to moderate hypertension; IV antihypertensive infusion such as nicardipine (Cardene), nitroglycerin, or nitroprusside can be given for more severe or refractory hypertension; keep in mind patient's baseline preoperative BP as relative target for titration

Postoperative tachycardia: typically mediated by parasympathetic output or caused by medications (*eg*, atropine, glycopyrrolate, or muscle relaxants); clinical signs and symptoms may include hypertension or hypotension and angina; treat underlying cause, potentially providing fluid bolus, draining bladder, or providing pain control; symptomatic treatment of tachycardia may be necessary to allow offending medication to wear off; cardiac arrhythmias also common causes of tachycardia; if atrial fibrillation occurs, use beta blockade, calcium channel blocker, or cardioversion if patient becomes hemodynamically unstable

Postoperative bradycardia: most commonly caused by increased parasympathetic flow or decreased sympathetic output, which may manifest as hypotension concomitant with bradycardia; in case of suspected increased parasympathetic output, consider muscarinic blocking agents (*eg*, atropine, glycopyrrolate [*eg*, Cuvposa, Glycate, Robinul); for decreased sympathetic output, betamimetic agents (*eg*, ephedrine [Akovaz, Corphedra]) most useful

Myocardial ischemia: should always be part of differential in any postoperative patient with hemodynamic compromise; risk factors include congestive heart failure, valvular disease, low ejection fraction, history of smoking, anemia, hypertension, or undergoing emergency surgery; causes may include tachycardia, which decreases time and diastole, leading to coronary hypoperfusion, hypotension, or hypoxemia; clinical signs include angina, ECG changes, and dysrhythmias; cardiac enzyme and troponin levels should be evaluated; treat underlying cause, such as pain, fluid bolus, or anxiolysis; give O_2, aspirin, nitroglycerin, beta blockade, and morphine

Other Complications

Postoperative nausea and vomiting (PONV): ~20% to 30% of surgical patients experience some degree of PONV; several risk factors; *patient related* — young women, hiatal hernia, obesity, history of postoperative nausea or motion sickness, and nonsmoker; *surgical related* — otolaryngology, abdominal, and gynecologic procedures; extraocular muscle traction, middle ear irritation, peritoneal or intestinal irritation, and dental procedures; *anesthesia related* — gas in stomach from face mask ventilation; use of nitrous oxide, parenteral opioids, etomidate [Amidate]; and hypotension concurring after spinal or epidural anesthesia; *postoperative related* — use of parenteral opioids and postoperative oral fluid intake; strategies to reduce baseline risk of PONV include avoidance of general anesthesia by using regional technique, use of propofol [Diprivan, Propoven] for induction and maintenance of anesthesia, avoiding nitrous oxide, avoiding use of volatile anesthetics, minimizing intraoperative and postoperative opioids, and ensuring adequate patient hydration

Treatment: multimodal treatment best strategy for; treating underlying risk factor (*eg*, hypotension, hypoglycemia, elevated ICP, GI bleed) essential part of treatment; serotonin receptor blockers (eg, ondansetron [Zofran, Zuplenz], 4 mg IV) at end of surgery have few side effects and commonly used; dexamethasone (steroid given as 4 mg to 8 mg IV just after induction) also useful antiemetic, although exact mechanism of action unclear; droperidol (Inapsine) useful for breakthrough nausea but may lead to sedation and currently has FDA-mandated black box warning because of QT interval prolongation; some physicians have substituted 1 mg of IV haloperidol (Haldol) for droperidol; prochlorperazine (Compazine), metoclopramide (Reglan), and promethazine (Phenergan, Phenadoz, Promethegan) also options; using drugs from several different classes as well as prevention effective for overall PONV treatment

Delayed awakening: most common cause residual anesthetic, sedative, or analgesic; less-common causes include hypothermia, metabolic derangement, or stroke; management includes treating underlying causes (*eg*, applying forced-air warming blanket), correcting metabolic disturbance, or providing reversal of medication; naloxone reverses opioid effects, although patient may need repeated doses if half-life of opioid longer than that of naloxone; flumazenil (Romazicon) can be used to reverse effects of benzodiazepines

Altered mental status or emergence delirium: common causes include hypoxemia, underlying metabolic derangement, cerebral hypoperfusion, extremes of age, emotionally significant operation, presence of intraoperative recall, use of scopolamine or atropine, using substances or undergoing pain, nausea, or pruritus; emergence delirium resolves in 10 to 15 mins; management includes verbal reassurance, adequate analgesia, correction of underlying metabolic derangements, supplemental O_2, of benzodiazepines, physostigmine [Antilirium] to treat essential anticholinergic syndrome if reaction thought to be related to scopolamine or atropine

Postoperative neuropathies: less common in PACU; spinal cord injuries can occur with positioning during intubation or with hematoma after placement of neuraxial anesthesia, however, both complications rare; peripheral nerve injuries common and can affect ulnar nerve (from compression of ulnar nerve at postcondylar groove of humerus), peroneal nerve (from compression of nerve against fibular head while patient in lithotomy), femoral nerve (due to exaggerated lithotomy position with use of candy-cane stirrups), brachial plexus (due to overabduction of the arms past 90° in supine position or neck being too far to one side), or long thoracic nerve (problems during pneumonectomy, leading to winged scapula and paralyzed serratus anterior muscle); most symptoms of postoperative neuropathy resolve within 6 to 12 wks, although permanent injuries can occur

Corneal abrasions: caused by ocular drying, which can happen if eyes left open during procedure, contact with eye during face mask ventilation or intubation, or scratching eye upon awakening; patients told not to rub eyes while waking up; clinical signs and symptoms include excessive tearing, photophobia, or decreased visual acuity; treat with artificial tears, eye closure, sometimes ocular antibiotics; most corneal abrasions heal within 72 hrs

Postoperative weakness: caused by residual neuromuscular blockade (most common cause), cerebrovascular accident, or preexisting neuromuscular disorder; symptoms and signs include poor respiratory effort, shallow breathing, rapid respiratory rate, or subjective scalable muscle weakness; treatment includes administration of neuromuscular reversal agent or reintubation until weakness resolves

Pain management in PACU: plan for controlling postoperative pain depends on patient and factors related to surgery; IV administration typically preferred because medications can be given in smaller dose, have more reliable uptake, and are more easily titrated; fentanyl (eg, Abstral, Duragesic, Subsys), hydromorphone (Dilaudid, Exalgo ER), meperidine (Demerol), and morphine (*eg*, Duramorph, Infumorph P/F, MS Contin) most commonly used opioids; most centers have moved toward multimodal analgesic approach, including use of nonsteroidal anti-inflammatory drugs (NSAIDS), acetaminophen, or COX-2 inhibitors; benefit, reducing overall opioid requirement, decreasing incidence of nausea and vomiting, and fewer gastrointestinal side effects; ketorolac (Acular, Acuvail, Toradol) popular analgesic, but side effects include platelet dysfunction and nephrotoxicity, should be used with caution in renal dysfunction patients, elderly, or those at increased risk of bleeding

Postoperative hypothermia and shivering: common in PACU; caused by distributive heat loss, evaporation because of skin preparation used during surgery, impaired function of normal thermoregulation because of anesthetic, and higher rate of heat loss from patients who have undergone burn injury, trauma, or cachexia; important effects include increased O_2 consumption and increased CO_2 production, elevated peripheral vascular resistance, impaired platelet function and decreased clotting factors, and increased rate of infection and cardiac dysrhythmias; important effects of shivering include increased O_2 consumption (up to 200%), increased CO_2 production, difficulty in using appropriate physiologic monitors, may lead to myocardial ischemia, and can precipitate ventilatory compromise; treatment includes use

of forced-air warming devices, patient reassurance, and meperidine in severe cases of shivering

Discharging patients from PACU: criteria are usually based on a modified Aldrete score; assessment parameters include vital signs, mental status, respiratory status, activity, surgical site status, control of pain, recovery from regional anesthesia, and treatment and management of postoperative nausea and/or vomiting; clinical judgment should always supersede any particular score or preexisting criterion

Postanesthesia recovery: typically divided into 2 phases; *phase 1* — starts with patient entering PACU from OR until criteria met for transfer to phase 2; patients should not be discharged home from phase 1; *phase 2* — starts with completion of phase 1 and ends with patient being discharged to home; phase 1 PACU recovery has monitoring and staffing ratios equivalent to ICU, whereas phase 2 transitional period; for some patients who have received monitored anesthesia care or regional block, possible to fast-track them, essentially bypassing phase 1; to discharge patient from phase 2 to home, should be documentation of vital signs and overall postoperative recovery; surgical site should be in acceptable condition; patient should have adequate pain control, should be able to ambulate, should have recovered from regional anesthesia (unless peripheral nerve block), and should be discharged to responsible individual

Suggested Reading

Carron M et al: Role of sugammadex in accelerating postoperative discharge: a meta-analysis. *J Clin Anesth*. 2017;39:38-44; **Mitra S et al:** New advances in acute postoperative pain management. *Curr Pain Headache Rep*. 2018;22(5):35; **Royster RL et al:** Postoperative atrial fibrillation. *Anesth Analg*. 2017;125(1):10-2; **Tateosian VS et al:** What is new in the battle against postoperative nausea and vomiting? *Best Pract Res Clin Anaesthesiol*. 2018;32(2):137-48.

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Monitored Anesthesia Care and Sedation

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Monitored anesthesia care (MAC) vs general anesthesia: 2013 American Society of Anesthesiologists (ASA) position statement defines MAC as specific type of anesthesia service for diagnostic or therapeutic procedure by anesthesiologist or physician to individual patient; includes all aspects of perianesthesia care; general anesthesia, state in which patient loses consciousness and ability to respond purposefully, irrespective of whether airway instrumentation required; MAC involves varying levels of sedation, analgesia and anxiolysis

Levels of sedation: knowing patient's level of sedation requires examination of 4 key parameters; these include responsiveness, airway, spontaneous ventilation, and cardiovascular function; comparison of these 4 qualities reveals depth of sedation correlates with patient's dependence on practitioner to intervene and preserve normal physiologic state; in transition from minimal- to moderate-sedation analgesia, eliciting patient response may require escalating stimulation from verbal to tactile, without much compromise in ability to maintain patent airway, spontaneously ventilate, and preserve cardiovascular function; as patient transitions to deep-sedation analgesia, patient's ability to purposefully respond diminishes, requiring repeated or painful stimulation; patient may require assistance in maintaining patent airway and spontaneous ventilation; cardiovascular function remains largely intact; general anesthesia requires active involvement of practitioner (*eg*, maintaining patent airway, providing positive pressure ventilation, and cardiovascular support in unarousable patient) even with painful stimulation

Role of the anesthesiologist: MAC has distinct requirements from monitored sedation analgesia (service commonly provided by nonanesthesiologists); requires anesthesiologist to conduct preanesthetic evaluation, obtain patient or guardian consent, and develop plan of preoperative, intraoperative, and postanesthetic management while considering patient's underlying medical condition and potential problems during procedure; anesthesiologist must be prepared and qualified to convert to general anesthesia when necessary; must be able to rescue patient's airway from any sedation-induced compromise (different from moderate sedation, in which physician does not intend to induce depth of sedation that would impair patient's ability to maintain patent airway); physicians providing moderate sedation must be qualified to recognize deep sedation, manage its consequences, and titrate to lesser sedation level; MAC often utilizes sedatives, hypnotics, and analgesics commonly used during general anesthesia; patients sensitive to sedation analgesia medications, such as severely debilitated patients, those with respiratory issues (*eg*, obstructive sleep apnea), or those at extremes of age, may require minimal sedation level; sometimes patient's condition and/or procedure may require deep sedation level or transient period of general anesthesia for successful completion of procedure; MAC also involves *postanesthesia care responsibilities* — ensuring patient returns to full consciousness, has stable vital signs, relief from pain and postoperative nausea and vomiting (or to help prevent them), side effects or complications addressed; other components of MAC include personally administering, or medically directing anesthesia care maintaining continuous physical presence or designate anesthesia trainee, nurse anesthetist, or anesthesiologist assistant to be immediately available to diagnose and treat medical emergencies; MAC best managed by anesthesiologist so sedation level can be matched to patient needs and procedural requirements

Standardized monitoring practices: patients monitored according to the ASA Standards for Basic Anesthetic Monitoring at all levels of sedation and anesthesia care; 2 monitors integral for patient safety, pulse oximetry and capnography

Pulse oximetry: quantitative method for continuous real-time monitoring of arterial oxygenation; provides early warning of the effects of sedatives and opioids on respiratory system

Capnography: can monitor respiratory rate; aid in detection and management of airway obstruction; can be adapted for face masks, nasal cannulas, and nasal airways; can help reduce risk associated with sedation in both adult and pediatric patients; required for assessing adequacy of ventilation when endotracheal tube or laryngeal mask airway placed

Temperature: many patients receiving MAC cared for in offsite locations, deliberately kept cold for cooling equipment; adverse effects of hypothermia include increased bleeding tendency and transfusion requirements, wound infection, delayed wound healing, and adverse cardiac events; hypothermia can be problem, especially with high-risk patients unable to adequately regulate own body temperature; MAC may blunt response to hypothermia and, combined with neuraxial technique, may predispose (especially elderly and children) to hypothermia through blunting or ablation of thermoregulatory mechanisms; warming equipment may not be available in remote locations

Continual observation of qualitative clinical signs: personal observation via visual, tactile and auditory cues

allows for assessment of patient's condition throughout procedure; should be continuous or at least frequent

Patient selection: evaluate ability to understand procedure, as well as their role, and maturity to cooperate with procedure; also important to evaluate for any hearing or visual disability or cognitive deficits; inability to communicate may suggest general anesthesia more appropriate for some procedures; verbal communication allows assessment of level of sedation, answer questions and reassure patient, and inform patient when cooperation is needed

Factors affecting drug choice: *goals of MAC* — provide patient comfort, maintain cardiorespiratory stability, improve operating conditions, prevent recall of unpleasant perioperative events; to achieve these goals, MAC may involve single or combination of analgesic, amnestic, and hypnotic medications, ideally with minimal side effects; rapid and complete recovery from sedation; drug choice for sedation should take pharmacokinetics and pharmacodynamics of coadministered drugs as well as underlying medical condition of patient into consideration

Context-sensitive half-time: time required for plasma-drug concentration to decline by 50%; reflects combined effects of distribution and metabolism on drug disposition; may be more reliable (than elimination half-time) to predict duration of action for continuous infusions; allows better understanding of pharmacokinetics during continuous infusions, making it more clinically relevant; increases as infusion duration increases (*eg*, fentanyl has shorter elimination time than sufentanil, but context-sensitive half-time twice that of sufentanil at 2 hrs, because fentanyl continuously being redistributed from peripheral tissues); cannot be used for recovery time

Effect-site equilibration and concentration: effect-site equilibration time represents delay between drug administration and initial drug effect; drugs with short equilibration half-time (*eg*, propofol) will equilibrate rapidly with brain and have shorter delay and onset, while midazolam and fentanyl have longer onset times; recovery from sedation dependent on rate of decrease of drug concentration the effect site(*ie*, brain); equilibration half-time can be used to determine bolus dosing intervals for different medications; insufficient time for drug dose to reach effect site may cause adverse effect from delayed cumulative effect (*eg*, oversedation); optimized drug administration by titrating in small increments at appropriate intervals, or using continuous infusion method with adjustable rate more reliable for maintaining therapeutic drug concentration

Combination therapy: goal to provide anxiolysis, analgesia, amnesia, hypnosis using specific medications; propofol/fentanyl combination by infusion associated with more rapid recovery and better stress response than each drug alone; however, risk for cardiorespiratory depression remains; dose range of opioids(*eg*, fentanyl) used for MAC can have potentiating effect with coadministered sedatives; steep dose-response curve within dose range used for MAC and small increments can have profound sedative effect; drug combinations must be cautiously used, since may have synergistic effect and may result in life-threatening complications of respiratory and cardiac depression, such as with midazolam and fentanyl

Medications

Propofol: sedative hypnotic; white lipid emulsion; administered intravenously; common complaint pain on injection; can be resolved by administration of intravenous (IV) lidocaine, either prior to or together with propofol; context-sensitive half-life is short even after prolonged administration; short effect-site equilibration time makes it easy to titrate; minimal analgesic effect at typical dosages of 25 µg/kg/min to 75 µg/kg/min; associated with less postoperative pain and opioid use in combination therapy; less postoperative sedation, drowsiness, confusion, and nausea and vomiting; 2009 study examining adverse events during pediatric sedation anesthesia with propofol for procedures outside operating room (OR) found no deaths, 2 reports of CPR, and 4 reports of aspiration in ~50,000 cases; more common, but less serious, adverse events (AEs) included transient hypoxemia, central apnea, airway obstruction, stridor, laryngospasm, excessive secretion, and vomiting

Benzodiazepines: anxiolytic, amnestic, and hypnotic properties; provide early amnesia, reduce preoperative anxiety, improve patient comfort; relatively short elimination half-time; may cause significant psychomotor and cognitive impairment; age-dependent response; study demonstrated 50% of elderly patients unresponsive to verbal command despite having one-third of therapeutic plasma concentration of midazolam found in middle-aged patients; another study in healthy volunteers demonstrated propofol reduced distribution and clearance of midazolam in concentration-dependent manner; midazolam has antagonist, flumazenil, but resedation may occur ≤90 mins after flumazenil administration

Opioids: can provide analgesic component; can supplement ineffective regional or local anesthetic technique; blunt hemodynamic and physiologic responses; can provide pain relief for prolonged positioning, injection pain, or tourniquet pain; fentanyl and remifentanil typical opioids used; adverse effects include respiratory depression, muscle rigidity, nausea, vomiting; oversedation from coadministered sedatives may be resolved with antagonist, naloxone

Remifentanil: potent, ultra–short-acting analgesic agent for painful procedures under MAC; equilibration time of 1 to 2 mins makes it easy to titrate; minimal change to context-sensitive half-time of 3 to 5 mins with infusion; metabolized by nonspecific esterases resulting in rapid clearance and termination of effect; drug of choice for patients with significant liver or renal disease; concomitant administration of midazolam decreases remifentanil dose requirements by ≤50%; leads to increased patient satisfaction and amnesia, decreased nausea, vomiting, and anxiety; disadvantages include increased risk for respiratory depression, apnea, and excessive sedation; bolus administration of remifentanil associated with increased incidence of respiratory depression and chest wall rigidity

Ketamine: phencyclidine derivative; provides intense analgesia; routes of administration can be oral, intramuscular (IM), or IV; along with dissociative state (patient's eyes may remain open, with nystagmus), low dose (0.25-0.5 mg/kg) associated with minimal respiratory and cardiovascular depression; commonly used with other sedatives for deep sedation and/or general

anesthesia; side-effect profile can often be mitigated by administrating antisialagogue (*eg*, glycopyrrolate) for excessive salivation; benzodiazepine (*eg*, midazolam) to reduce hallucinations; when combined with propofol, reduces propofol dose, preserves hemodynamics, decreases nausea, vomiting, and airway complications, and improves procedural conditions; however, elevates intracranial and intraocular pressure; 2009 study found risk factors that predict ketamine-associated airway and respiratory AEs include high IV doses, children aged <2 yrs or >13 yrs, and use of coadministered anticholinergics or benzodiazepines

Dexmedetomidine: selective alpha-2 receptor agonist; depresses central sympathetic function; produces sedation and analgesia; potentiates opioid-induced analgesia, benzodiazepine-induced hypnosis; potent MAC-sparing effects with volatile agents; minor effects on respiratory function; lack of pain on injection, analgesia, and minimal adverse respiratory effects make it useful alternative to propofol; commonly used for sedation during instrumentation of difficult airway; in children having MRI and CT procedures, loading dose was 2 µg/kg to 3 µg/kg over 10 mins, followed by infusion of 1 µg/kg/hr to 2 µg/kg/hr; young, healthy volunteers with high vagal tone, particularly during rapid IV or bolus administration, experienced significant episodes of bradycardia and sinus arrest

Risks Associated with MAC

Upper airway patency: upper-airway dilator muscles sensitive to sedative hypnotic drugs (*eg*, midazolam) that can increase inspiratory subglottic airway resistance 3- to 4-fold

Protective airway reflexes: protective laryngeal and pharyngeal reflexes can be depressed by anesthesia and sedation; also compromised by advanced age and debilitation

Respiratory control: opioids suppress ventilatory response to hypercarbia and hypoxemia; combination of opioids and benzodiazepines negatively impact respiratory responsiveness

Local anesthetic toxicity: MAC often provided to elderly or debilitated patients when general anesthesia (using inhalation agent and airway instrumentation) contraindicated; patients receive local anesthetic for nerve block or local infiltration of surgical site; need to be observant for systemic local anesthetic toxicity; effects of local anesthetic on brain concentration dependent; low concentrations cause sedation and numbness of tongue, circumoral tissues, and metallic taste; higher concentrations cause restlessness, vertigo, tinnitus, and difficulty focusing; even higher concentrations may result in slurred speech, skeletal muscle twitching (which may precede onset of tonic-clonic seizure), and cardiovascular collapse; MAC can also depress cardiac function (especially in patients with congestive heart failure), resulting in less hepatic blood flow to clear local anesthetic drugs; compromise of respiratory drive may result in respiratory acidosis, increasing cerebral blood flow and leading to more local anesthetic exposure to brain; changes in intracellular pH result in more trapping of local anesthetic; hypercarbia, acidosis, and hypoxia may potentiate cardiovascular effects of local anesthetics

MAC and Outcomes Outside OR

Pediatric patients:

Coté (2000): examined adverse sedation events in children from Food and Drug Administration's database and from survey of pediatric specialists; of 95 children aged 1 through 20 yrs, 51 died and 9 experienced permanent brain injury; 71% of AEs associated with drug overdose; use ≥3 sedatives, and nitrous oxide in combination with any sedative, associated with adverse outcomes; 93% occurred in non–hospital-based facilities and with dental practitioners; contributing factors included lack of standardized drug administration practices, including appropriate monitoring and lack of trained personnel in sedation and advanced skills to rescue airway

Cravero (2006): examined incidence and nature of AEs among 30,000 cases submitted to Pediatric Sedation Research Consortium Database from 2004 to 2005; findings concluded >50% care provided by intensivists and emergency department (ED) doctors, 19% by anesthesiologists; radiologic procedures comprised majority (62%) of cases; propofol was most commonly used drug, followed by midazolam and ketamine, with fentanyl as most common opiate in 8% of all sedations; 80% healthy, ASA status 1 or 2, with 76% aged <8 yrs; majority of complications, adverse respiratory events, with desaturations <90% (most common), and stridor, laryngospasm, wheezing, or apnea occurring in ~1 in 400 procedures; 1 in 200 sedations required airway and ventilation interventions, ranging from bag-mask ventilation and oral airway placement, to emergency intubation; overall complication rate of 5.3%; no deaths reported

Beach (2016): examined procedural sedation anesthesia encounters between 2007 and 2011, using data from Pediatric Sedation Research Consortium; out of ~139,000 encounters, 0 deaths, 3 cardiac arrests, 10 aspirations, 62 unplanned admissions (75 major complications); low relative incidence of aspiration, (1 per 10,000); risk of major complication increased for patients with an ASA physical status of 3 or 4, gastroenterology (GI) diagnosis, airway or GI procedure; infants 3-fold higher risk

Adult patients:

Metzner (2009): analyzed data from ASA Closed Claims Database; compared patterns of injury and liability between anesthesia claims from remote locations and OR; found that patients tended to be older(aged >70 yrs), sicker (69% with ASA status 3-5), with more undergoing emergent procedure in remote locations compared with OR; age and ASA class also associated with increased risk for adverse airway and respiratory events in other studies, along with depth of sedation and time of day; MAC occurred 8 times more often in remote locations; most commonly involved facilities included gastroenterology suite and cardiology catheterization or electrophysiology lab, representing more than half of all cases; risk of death and adverse respiratory events in remote locations 2 times that of OR; inadequate oxygenation/ventilation most common (7 times more frequently than in OR); substandard anesthesia care found in >86% of remote-location claims, of which 62% preventable by better monitoring (*eg*, pulse oximetry or capnography); propofol(alone or in combination) most

commonly used sedative associated with oversedation in remote location claims; overall, respiratory depression leading cause of AEs due to oversedation, along with substandard monitoring

Karamnov (2017): retrospective study; reported similar findings; of 52 cases, 58% experienced oversedation leading to apnea; 56% required use of reversal agent; risk factors included age, body mass index, comorbidities, female sex, and GI suite procedures

Bellolio (2016): meta-analysis of AEs in adults undergoing procedural sedation in ED reviewed 55 articles, totaling 9600 procedural sedations; most AEs reported included laryngospasm, intubation, and aspiration; recommended propofol, etomidate, and ketamine alone or in combination with propofol

Guidelines for procedures performed outside OR: published by ASA October 2013; outlines basic requirements for remote anesthetizing locations

Equipment: anesthesia machine or equivalent, checked daily for functionality; age-appropriate, self-inflating hand resuscitator bag capable of administering at least 90% O_2 while delivering positive pressure ventilation; adequate, reliable primary O_2 source as well as backup tanks; adequate, reliable systems for scavenge of anesthetic gases; adequate, reliable suction to clear airway of secretions; anesthesia drugs for intended anesthesia care; monitoring equipment to meet basic standards for monitoring patient; flashlight or another form of battery-operated illumination device, aside from laryngoscope

Physical location: sufficient number of electrical outlets, clearly labeled as having backup to emergency power supply; sufficient space to accommodate necessary equipment and personnel to allow expeditious access to patient, anesthesia machine, monitoring equipment; immediate availability of emergency cart with defibrillator, emergency drugs, and other equipment adequate to provide cardiopulmonary resuscitation; reliable means of 2-way communication to request assistance (*eg*, wired or wireless telephone, intercom, code button); trained staff to support anesthesiologist; provision of appropriate postanesthesia management and adequate numbers of trained staff to safety transport patient to postanesthesia care unit; observation of all applicable building and safety codes, as well as facility standards

Standardized Practice for Nonanesthesiologists

Deep sedation: ASA advisory (2010) concerned granting privileges to nonanesthesiologists; framework to identify physicians, dentists, oral surgeons, or podiatrists potentially qualified to personally administer or supervise administration of deep sedation; required to demonstrate ability to recognize when patient has entered state of general anesthesia and maintain patient's vital signs until sedation level recovered to appropriate level; education and training for safe administration of sedative and analgesic drugs to establish deep sedation level, and to rescue patients from potential harm, secondary to deeper-than-intended sedation level; nonanesthesiologists would have same responsibilities as anesthesiologist caring for patient (including completing preanesthetic evaluation, obtaining informed consent from patient, and developing perianesthetic plan), with exception of practicing unrestricted general anesthesia; patient's ASA physical status and risk for aspiration of gastric contents determined as part of the patient assessment, as well as appropriateness of assignment to provider; nonanesthesiologists expected to understand pharmacology of all sedation drugs and antagonists, and have proficiency using advanced airway equipment, managing patient's airway, and benefits and risks of supplemental O_2; education and training also focused on learning about basic requirements for patient monitoring, including recovery period, physical presence, and documentation of patient vital signs and administered drugs; certification in advanced life support skills, participation in quality-assurance programs and knowledge of CMS regulations pertaining to deep sedation such as pre- and postanesthesia evaluation, and intraoperative anesthesia record also required; special training not intended to grant privileges for providing general anesthesia, but only to learn safe administration of deep sedation

Guidelines for moderate procedural sedation and analgesia: released by ASA in 2018 for adult and pediatric patients applicable during preoperative, intraoperative, and postoperative phase of moderate sedation analgesia; reflected understanding that sedation and analgesia represented continual state, independent of route of drug administration; 7 new recommendations detailed below:

1. Patient evaluation and preparation: nonanesthesiologists to evaluate relevant medical history, such as cardiac or pulmonary disease, obstructed sleep apnea, prior anesthesia experience, current medications (potential for drug interaction), and allergies; focused physical examination to be conducted especially for difficult airway, and review of relevant laboratory test results; patient preparation includes determination of urgency of procedure, obtaining informed consent, instructions regarding nothing by mouth (NPO), and consulting with medical specialists as necessary
2. Patient's respiratory status continually monitored with capnography to supplement standard monitoring by observation and pulse oximetry; in light of many studies, this demonstrated the efficacy of capnography and reduction in hypoxemic events during moderate sedation for procedures
3. Presence of individual other than proceduralist with knowledge and skills to recognize and treat airway complications; same individual may assist with minor, interruptible tasks once patients level of sedation analgesia and vital signs stable
4. Sedatives and analgesics not intended for general anesthesia (*eg*, benzodiazepines, dexmedetomidine, remifentanil) used in combination for sedation or analgesia, should be titrated in small, incremental doses, or by infusion via secure IV route, while allowing sufficient time to elapse between doses or rate changes
5. Sedatives and analgesics intended for general anesthesia (*eg*, propofol, ketamine, etomidate), alone or in combination with opioids or other sedatives, to be administered in small, incremental doses, or by infusion via secure IV route, while allowing sufficient time to elapse between doses or rate changes; patient care should be equivalent to that for patients receiving general anesthesia
6. Care focused on potential for residual sedation and cardiorespiratory depression during recovery period;

continued observation and monitoring until patient meets appropriate preestablished discharge criteria

7. Creation and implementation of quality improvement processes to improve safety documentation; strengthen patient-safety culture through team training and simulation drills; create emergency response plan

Moderate sedation by nonanesthesiologists: ASA released statement in 2016 on granting privileges to nonanesthesiologist sedation practitioners (*eg,* physicians, dentists, podiatrists) for administration of moderate sedation; supervised sedation professional defined as registered nurse or physician assistant who would administer sedative and analgesic drugs under supervision of nonanesthesiologist sedation practitioner or anesthesiologist, and monitor patients during moderate sedation

Requirements: sedation practitioners expected to satisfactorily complete formal training program in safe administration of sedative and analgesic drugs used to establish level of moderate sedation, use of reversal agents for opioids and benzodiazepines, monitoring of patient's physiologic parameters during sedation, and recognition of abnormalities and monitored variables that require intervention; elements of training and education, along with licensure, practice patterns, performance improvement, required of both nonanesthesiologist and supervised sedation professional; both only required to have proficiency in basic airway skills; neither bound by Centers for Medicare and Medicaid Services (CMS) regulations related to anesthesia care or participation in quality assurance system; CMS regards general anesthesia, MAC, deep sedation, and regional anesthesia under anesthesia services that must be provided by qualified anesthesiologist or nonanesthesiologist sedation practitioner; moderate and minimal sedation fall under analgesia services; additional guidance provided by 2016 ASA statement on anesthetic care during interventional pain procedures for adults; noted provision of moderate sedation and/or anesthesia as separate and distinct service from pain procedure; during moderate sedation, patient to be responsive during critical portions of procedure and to report any procedure related change in pain intensity, function, and/or paresthesia; many pain procedures do not always require sedation(*eg*, epidural steroid injections, epidural blood patch, trigger-point injections); however, significant anxiety, procedures requiring patient to remain motionless for prolonged period, and/or to remain in painful position may require sedation or anesthesia services

Sedation of children different from that of adults: ability to cooperate depends on chronologic age and cognitive and emotional development; American Academy for Pediatrics and American Academy of Pediatric Dentistry released guidelines for safe sedation in children; clarify use of monitors, especially regarding continuous, expired CO_2 measurement (shown to reduce incidence of hypoventilation and desaturation from 7% to 1%); children with developmental disabilities have 3-fold increase in incidence of desaturation; children aged <6 yrs or with developmental delay more susceptible to sedative effects on respiratory drive, airway patency, and protective airway reflexes, especially when using ≥2 sedating medications;

Requirements and recommendations: emphasis on safe sedation practice competency to recognize various levels of sedation, provide age-appropriate cardiopulmonary support, airway management, selection of medications to match procedure (*eg*, opioids or ketamine for painful procedures, sedative hypnotics for CT and MRI procedures), titration of medications to avoid oversedation, appropriate selection of ASA class 1 or 2 patients for different levels of sedation, review of past medical history and focused physical examination, along with preparation of child (especially NPO instructions); absolute risk of aspiration during elected procedural sedation not known (reported incidence varies between studies); guidelines recommend facilities, personnel and equipment to manage emergency and rescue situations, and for proper documentation and continuous quality improvement; *deep sedation* — guideline recommends assigning dedicated staff member to constantly observe patient's vital signs, airway patency, and adequacy of ventilation, as well as be trained in pediatric advanced life support (PALS) and capable of assisting with emergency events; responsible practitioner must be present, trained in and capable of providing PALS, and skilled to rescue child with apnea, laryngospasm, and/or airway obstruction, including performing tracheal intubation and obtaining vascular access; electrocardiographic monitoring and defibrillator along with IV access recommended for deep sedation

Dental office–based settings: ASA 2017 statement on sedation and anesthesia administration in dental office-based settings emphasized that education in sedation and anesthesia management in such settings should be subject to same rigorous requirements for credentialing and privileging as in non–office-based facilities; provider should complete training in age-appropriate resuscitative and related emergency measures; more stringent selection criteria in children aged <6 yrs, patients with major medical problems, patients needing prolonged and extensive procedures, and individuals other than proceduralist be responsible for monitoring patient during procedure; age-appropriate equipment and facilities compliant with sedation and/or anesthesia care standards; development of quality-improvement process for capturing clinical performance, patient outcomes, and adverse events

Suggested Reading

American Society of Anesthesiologists Standards and Guidelines: https://www.asahq.org/standards-and-guidelines. Accessed October 26, 2018; **Beach ML et al:** Major adverse events and relationship to nil per os status in pediatric sedation/anesthesia outside the operating room: a report of the Pediatric Sedation Research Consortium. *Anesthesiology*. 2016;124(1):80-8; **Bellolio MF et al:** Incidence of adverse events in adults undergoing procedural sedation in the emergency department: a systematic review and meta-analysis. *Acad Emerg Med*. 2016;23(2):119-34; **Coté CJ et al:** Adverse sedation events in pediatrics: a critical incident analysis of contributing factors. *Pediatrics*. 2000;105:805-14; **Cravero JP et al:** Incidence and nature of adverse events during pediatric sedation/anesthesia for procedures outside the operating room: report from the Pediatric Sedation Research Consortium. *Pediatrics*. 2006;118(3):1087-96; **Cravero JP et al:** The incidence and nature of adverse events during pediatric sedation/anesthesia with propofol for procedures outside the operating room: a report from the Pediatric Sedation Research Consortium. *Anesth Analg*. 2009;108(3):795-804; **Green SM et al:** Predictors of airway and respiratory adverse events with ketamine sedation in the emergency department: an individual-patient data meta-analysis of 8,282 children. *Ann Emerg Med*. 2009;54(2):158-68; **Karamnov S et al:** Analysis of adverse events associated with adult moderate procedural sedation outside the operating room. *J Patient Saf*. 2017;13(3):111-21; **Metzner J et al:** The risk and safety of anesthesia at remote locations: the US closed claims analysis. *Curr Opin Anaesthesiol*. 2009;22(4):502-8.

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Ethics, Patient Safety, and Medicolegal Issues

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Ethics

Four principles of bioethics: autonomy, beneficence, non-malfeasance, justice; *autonomy* — emphasizes respect of patient's wishes, values, religious beliefs, and patient's right to initiate, continue, or withdraw medical treatment; patient's decision should be free from controlling influences by others, free from limitations that prevents patient's thorough understanding of circumstance; *beneficence* — moral obligation to act for benefit of others; requires preventing and removing harm, promoting good; *non-malfeasance* — obligation not to inflict harm on others; *justice* — fair and equitable distribution of benefits and burdens to all individuals in society; these principles integrated in process of making treatment decisions

Decision-making capacity: when obtaining informed consent, physician first determines if patient has decision-making capacity; distinguished from legal term, competence, determined by court of law; decision-making capacity determined by physician; patient able to understand clinical situation and information about tests or treatment, appreciates significance of decision, reasons for making decision, can communicate choice; if unsure if patient has decision-making capacity, should obtain psychiatry consult

Informed consent: after determining decision-making capacity; *components* — 1) competence, decision making; 2) disclosure (*ie*, providing information on risks, benefits, alternatives of treatment, procedure, or anesthetic); 3) understanding (*ie*, patient has understanding of treatment and/or anesthetic); 4) recommendation of plan; 5) voluntariness, implies absence of controlling influences, control exerted by other individuals; 6) decision for or against plan; 7) authorization

DNR/DNI: patient with Do-Not-Resuscitate (DNR) and/or Do-Not-Intubate (DNI) order entering operating room (OR), may present unique circumstance; *eg*, some surgeries require tracheal intubation; administration of anesthesia may necessitate administration of vasoactive medications, interventions that may be considered resuscitation in other clinical settings; patients or their surrogate decision makers must be educated regarding differences between resuscitation in OR vs elsewhere and potential iatrogenic issues (*eg*, hemodynamic changes); both surgeon or proceduralist and anesthesiologist must review and clarify patient's wishes for resuscitation during anesthetic procedure and postoperative period; clarifications or modifications of patient's resuscitation wishes must be documented in medical record and communicated to all involved health care providers; if patient chooses to suspend DNR order for perioperative period, time at which DNR order to be reinstated needs to be discussed with patient, communicated to team members, and documented in medical record; automatic suspension of DNR order does not respect patient's right to self-determination or autonomy; American Society of Anesthesiologists (ASA) guidelines for ethical practice of anesthesiology supports respect of patient's right to self-determination; as stated in ASA Guidelines for Anesthesia Care of Patients with Do-Not-Resuscitate Orders or Other Directives That Limit Treatment, "If a physician does not feel comfortable proceeding with the procedure respecting the patient's wishes, then the physician should withdraw from the care of a patient and provide another provider in a timely manner. If another provider cannot be present in a timely manner, then the care of the patient should proceed with reasonable adherence to the patient's wishes"

Patient Privacy

Health Insurance Portability and Accountability Act of 1996 (HIPAA): includes compliance requirements to protect patient health information; standards for privacy of individually identifiable health information (*ie*, HIPAA privacy rule); HIPAA privacy rule applies to health care plans, providers, health care clearinghouses, and protected health information (PHI) in any form, including paper, oral, digital information; PHI includes patient name, address, birth date, social security number, physical or mental condition, any health care provided to patient, payment information that could be used to identify patient; if PHI deidentified, use and disclosure of information not restricted; if patient PHI breached or patient not allowed access to PHI, fines and/or criminal penalties could be instituted from Health and Human Services (HHS) Office for Civil Rights, which enforces HIPAA

HIPAA privacy rule permits disclosure of PHI without individual's authorization or permission to persons or entities in following circumstances: 1) specific situations where required by law (*ie*, by statute, regulation, or court order); 2) public health authorities given authorization to collect or receive PHI to prevent or control disease, injury, or disability; 3) reports of child or adult abuse, neglect, domestic violence; 4) Food and Drug Administration (FDA)–regulated products to track products with regard to quality, safety, effectiveness; 5) public health authorities to prevent spread of communicable diseases; 6) employers concerning medical surveillance or employee work-related illness or injury to extent that employer can comply with Occupational Safety and Health Administration (OSHA)

standards; 7) health oversight activities, including investigations for government benefit programs; 8) judicial and administrative proceedings; 9) situations of serious threat to health or safety to individual or public; 10) PHI of individuals deceased >50 years; 11) cadaveric donation of organs or tissues; 12) worker compensation as allowed by worker compensation laws; 13) research purposes with institutional review board approval

Professionalism: in addition to respecting patient's privacy, physicians accountable to patients by maintaining professionalism and licensure; *principle of professionalism* — no one universally accepted definition; incorporates, in addition to other aspects, personal values, personal traits, maintaining one's own emotional, physical, and mental health, and ethics principles; includes physician's commitment, first and foremost, to care of the patient; also commitment to improve health care of society, commitment to maintain skills and competence for welfare of patients, including licensure; 2002, American Board of Internal Medicine, American College of Physicians, European Federation of Internal Medicine worked together to develop Medical Professionalism in the New Millennium: A Physician Charter; >100 organizations have endorsed it; charter includes 3 fundamental principles, 9 professional commitments

Three principles: 1) principle of primacy of patient welfare, 2) principle of autonomy, 3) principle of social justice in which physician promotes fair distribution of resources for health care

Nine professional commitments: 1) commitments to professional competence, 2) honesty with patients, 3) patient confidentiality, 4) maintaining appropriate relations with patients, 5) improving quality of care, 6) just distribution of finite resources, 7) scientific knowledge, 8) maintaining trust by managing conflicts of interest, 9) professional responsibilities including collaborative, respectful relationships with colleagues and self-regulation

Impairment: physician's responsibility to patient health care may be compromised by impairment; 1973, American Medical Association (AMA) report, *The Sick Physician*, defined impairment as "a physician who is unable to provide care to patients with reasonable skills and safety due to, for example, physical or mental illness, declining abilities from the aging process, loss of motor skills, abuse of narcotics, drugs, alcohol or other drugs"

Aging: physiologic changes accompanying aging may contribute to impairment of physician's ability to practice medicine with appropriate skill and safety to patients; deterioration of short-term memory, problem-solving ability, hearing and vision, rapid processing and applying of new knowledge, physical strength, and stamina during night shifts of work are some changes that may occur during aging; state licensure and hospital privileges generally do not specify age at which physicians should stop practicing medicine; federal laws address rights of aging physicians, including Age Discrimination and Employment Act of 1967, Employee Retirement Income Security Act

Fatigue: can compromise physician's well-being and patient care; physician's responsibility to maintain own health and well-being and to communicate fatigue to supervisor

Substance use disorder: may also contribute to impairment of physician's ability to practice medicine and provide safe care to patients; may also have serious consequences for physician; *Diagnostic and Statistical Manual of Mental Disorders* diagnostic criteria for substance use disorders includes 9 classes of drugs (alcohol, cannabis, hallucinogens, inhalants, opioids, sedatives, hypnotics and anxiolytics, stimulants [including amphetamine-type substances, cocaine], tobacco, and other or unknown substances); *criteria for substance use disorder* — 1) taking substance in larger amounts or over longer time than initially intended, with thus impaired control; 2) expressing desire to reduce or regulate use of substance or reporting multiple attempts to achieve reduction or discontinuation of use of substance; 3) spending majority of daily activities obtaining substance, using substance, or recovering from effects of substance; 4) craving substance to point where desire for drug predominates other thoughts; 5) failing to fulfill occupational, social, and/or family responsibilities; 6) using substance despite being aware of negative physical or psychological effects of drug; 7) developing tolerance or developing withdrawal symptoms; mild substance use disorder, presence of 2 to 3 symptoms; moderate, 4 to 5 symptoms; severe, ≥6 symptoms

Drug abuse in anesthesiology: incidence of drug abuse in anesthesia personnel suggested at 1% to 2% per survey studies; anesthesiologists and anesthesiology residents have access to opioids, other controlled substances; there may be diversion of controlled substances from patients to individual for elicit use; in past 10 yrs, abuse of propofol increased in academic anesthesiology; while abuse of inhalational agents low, incidence appears to be increasing over time, low likelihood of those affected returning to work; considerable mortality risk

Signs of substance abuse: wearing long sleeves, mood changes, increased signout of opioids from pharmacy, frequent breakage of narcotic vials, decreased work efficiency and clinical skills, missing work, shaking, pinpoint pupils, behavioral changes (including wide mood swings), coming to work early and leaving late, frequent bathroom breaks, preferring to be alone;

Warner *et al* (2013): retrospective study of anesthesia residents from 1975 to 2009; found 0.86% of anesthesia residents with substance use disorder during training; actual prevalence may have been higher, as cases in study were only confirmed cases of substance abuse disorder; of anesthesia residents with substance abuse, 8% women; median age 31 yrs; initial rate increase followed by lower rates from 1996 to 2002, with highest rates occurring since 2003; most commonly, intravenous opioids including fentanyl, followed by alcohol, marijuana or cocaine, anesthetics or hypnotics, and oral opioids involved in initial substance use disorder episode; 15% of residents with substance use disorder had prior history involving alcohol, marijuana, cocaine, other drugs; 11% of anesthesia residents with substance use disorder died from substance use (7% during, 4% after, training)

Warner *et al* (2015): nested matched-cohort study, reported following risk factors for United States anesthesiology residents for developing substance use disorder: male

sex and residents who attended United States medical school; authors noted period of lower incidence rates of substance use disorder corresponded to time when proportion of individuals in medical school training outside of United States enrolled in anesthesia residency programs peaked; no difference in in-training exam scores in clinical base yr between controls and anesthesia residents with substance use disorder, but significantly less by CA-1 yr for anesthesia residents with substance use disorder; residents with substance use disorder less likely to complete primary board certification or subspecialty certification; also had higher mortality rate; Americans with Disabilities Act (ADA)considers history of chemical dependence as disability, but does not provide protection for individuals currently using drugs; individuals who have successfully undergone treatment and able to return to work may be considered qualified individuals under ADA

Addressing impairment: AMA Code of Medical Ethics states, "When physician health or wellness is compromised, so may the safety and effectiveness of the medical care provided. To preserve the quality of their performance, physicians have a responsibility to maintain their health and wellness, broadly construed as preventing or treating acute or chronic diseases, including mental illness, disabilities, and occupational stress"; physicians unable to provide care to patients with reasonable skills and safety due to impairment may be identified by colleagues as impaired if physician unable or unwilling to recognize impairment; decisions for treatment and limiting or suspending privileges should be addressed on individual basis

Patient Safety

Medical error: Institute of Medicine report, *To Err Is Human: Building a Safer Health System*, definition, "the failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim"; medical errors include serious errors, minor errors, and near misses

Adverse event (AE): injury caused by medical management rather than patient's underlying disease; sentinel event, patient safety event not related to natural course of patient's illness or underlying condition that results in death, permanent harm, or severe temporary harm

Medication errors: may occur by commission (*ie*, performing the wrong action) or omission (*ie*, not performing a correct action); *errors related to medications can occur at any of following steps* — 1) ordering or prescribing medication including dose, frequency, and duration; 2) transcribing medication order so prescription read and interpreted correctly; 3) dispensing medication and confirming drug-drug interactions and medication allergies patient may have; 4) administration (*ie*, correct medication and dose must be administered to correct patient at correct time and by correct route); most medication errors occur at step 4

Medication error-reduction suggestions: medication reconciliation; automated alerts in anesthesia information systems regarding dose, allergy, and drug-drug interactions; standardization of drug trays in anesthesia carts; labeling tray divisions in clear manner; preference for single-use vials; discarding multiple-dose vials at end of case; provision of high-risk drugs by pharmacy (*eg*, heparin, insulin); alert labels on high-concentration or high-risk drugs; separate regional cart for regional drugs; labeling every medication; standardized handoff of care; use of smart pumps

Prospective observational study: demonstrated 1 in 20 perioperative medication administrations involved medical error and/or adverse drug event, with patient harm observed in more than one-third of these errors; more recommendations include barcode-assisted drug labeling; dose calculators; reminders to redose antibiotics; connect infusions to dedicated carrier line and at most proximal port to reduce inadvertent boluses of infusions

ASA statement on labeling of pharmaceuticals for use in anesthesiology recommendations: 1) label content; should include generic name and concentration for syringe labels and total volume of contents of infusion bags; 2) font; text on label should follow American Society for Testing and Materials international standards for font size, use of emphasis for distinctive syllables for drugs with similar names, and availability of space on label around drug name; 3) contrasting background; should be maximum contrast between text and background (*eg*, if white background, text should be blue or black); 4) color; standard background color for labels for 9 classes of commonly used drugs in anesthesiology (*eg*, red label for muscle relaxants); 5) label enhancements; may include barcoding, label material, facilitating writing of information on label with pen or marker, printing in black bold type (except succinylcholine and epinephrine, printed as reverse-plate letters); tall-man lettering

Medical error procedure: if error occurs, should be disclosed to patient; explanation of how error occurred should be explained to patient as well as how effects of error addressed or will be addressed, and what actions by physician or organization will be taken to prevent future error; since 2001, the Joint Commission requires disclosure of unanticipated outcomes of care; 10 states (since 2002) mandate disclosure of unanticipated outcomes to patients and/or their families; 36 states have apology laws, which prohibit certain statements, expressions, or other evidence related to disclosure from being admissible in lawsuit (*eg*, North Carolina, rule 413 states, "Statements by a healthcare provider apologizing for an adverse outcome in medical treatment, offers to undertake corrective or remedial treatment or actions, and gratuitous acts to assist affected persons shall not be admissible to prove negligence or culpable conduct by the healthcare provider in an action brought under article 1B of chapter 90 of the General Statutes"); confirm specifics of state statutes

AE procedure: Joint Commission encourages, but does not require, accredited organizations to report sentinel events; when AEs occur, Joint Commission requires establishment of reporting system for accredited organizations for AEs; all sentinel events must be reviewed by hospital and comprehensive systematic analysis, and corrective action plan must be completed; comprehensive systematic analysis may involve root cause analysis (*ie*, structured analytic process to identify causes or contributing factors to problems or incidents that have already occurred); after root causes or contributing factors identified, corrective action plan identified and implemented to minimize recurrence

Barriers to reporting medical errors: include attitudinal errors, helplessness, uncertainties, and fears/anxieties; attitudinal barriers may include physician's pride, allowing competition with peers; helplessness may involve lacking institutional support or support of colleagues after disclosure, or feeling helpless about errors, as practitioner feeling loss of control of system in which he or she practices; uncertainties may include being uncertain about which errors to disclose and how to disclose errors; fears/anxiety may be loss of self-esteem, fear for loss of respect of colleagues, fear of legal ramifications and financial liability

Patient Safety and Quality Improvement Act of 2005: provided authority to create patient safety organizations in order to improve patient safety; patient safety organizations provide environment in which clinicians and organizations can voluntarily report, aggregate, and evaluate data to improve patient safety in legally secure environment; Anesthesia Quality Institute listed as patient safety organization by Department of HHS; established by ASA in 2008 as source of information to facilitate education and feedback in quality improvement of practice of clinical anesthesiology; since 2010, Anesthesia Quality Institute home to National Anesthesia Clinical Outcomes Registry (NACOR); collection of data designated by Centers for Medicare and Medicaid Services as qualified registry and qualified clinical data registry; can provide anesthesia groups with benchmarks to compare strengths and weaknesses with other anesthesia groups and facilities to improve quality of practice of anesthesiology

Quality improvement projects: organizations and individuals may develop quality-improvement projects for health care; may be designed and implemented by identifying issue and delineating goal to be accomplished; next, baseline measurements secured and appropriate measures identified to determine if changes implemented resulted in improvement; then, changes implemented and Plan-Do-Study-Act cycle utilized to design and test changes

Lean Six Sigma principles: industry has also utilized principles to reduce errors, reduce waste; these Lean Six Sigma principles have also been utilized in health care; Six Sigma quality improvement projects utilize DMAIC, 5-phase process to define, measure, analyze, improve, and control, thus improving existing processes; quality improvement continuous project, identifying issue, acquiring data, analyzing data, introducing opportunities for improvement, and reassessing change, which will hopefully improve and advance performance in patient safety

Infection

Infection control: can be institution quality improvement project; 1 in 31 United States patients contracts ≥1 infection in association with care received in hospital; standard precautions to reduce risk of passing infectious agents from patient to patient, health care team members to patient, and patient to health care team members should be applied to all patients

- Wearing gloves: for contact with blood, nonintact skin, mucous membranes, and body fluids (except for sweat); change gloves if gloves become soiled or when contact with noncontaminated body part follows contact with contaminated body part; minimize contamination of environment with soiled gloves; remove gloves after patient contact; perform hand hygiene following removal of gloves
- Hand hygiene: essential for infection control to comply with frequent and effective hand washing; soap and water most effective at removing spores; ethanol has more antiviral activity than isopropanol; antiseptics with ethanol germicidal, yet antiseptic effects not persistent
- Use personal protective equipment (PPE) as appropriate: PPE may include gloves, gowns, mask, and eye protection
- Obey isolation signs
- Follow respiratory cough etiquette
- Surgical masks: wear surgical mask when placing central line or performing neuraxial block
- Proper handling of needles and other sharps: do not recap needles; dispose of sharps in puncture-resistant sharp containers; do not bend or break sharps that have been used; Employee Health Services or designee must be contacted immediately for needle sticks and exposure to body fluids; never allow sharp boxes to become more than two-thirds full
- Other precautions: contact, droplet, and airborne precautions; should place sign outside door indicating level of precaution; communicate necessary precautions to health care providers who may come in contact with patient; *contact precautions* — wear gown and place gloves upon entering room as well as with patient or environment contact; if risk of being splashed or sprayed, use face and eye protection; before exiting room, remove gloves and gown, perform hand hygiene; clean equipment prior to use of equipment by other patients; *droplet precautions* — separate patients by 3 ft; keep curtains drawn between patients; wear standard surgical mask, gloves, gown, and eye protection; patient should wear standard mask if being transported; use respiratory hygiene and cough etiquette; *airborne precautions* — patient should be placed in airborne-infection isolation room with door closed, including in postanesthesia care unit; N95 respirator mask must be worn when in same room as patient; postpone elective procedures until airborne precautions no longer necessary; procedures should be scheduled to reduce exposure of other patients and staff

OR protocol: OR designed to have positive pressure in relation to environment; portable negative-pressure isolation chamber should be placed in OR, or OR should have antechamber, which can be used for patients requiring airborne precautions going to OR

Central line–associated bloodstream infections: *recommendations to reduce incidence* — perform hand hygiene before and after central line insertion; sterile gloves, sterile gown, face mask with eye shield, and bouffant cap worn; full-body, sterile drape placed over patient prior to insertion of central line or changing of central line over guide wire; prior to managing central line (*eg*, when administrating medications or assessing central line), perform hand hygiene and use clean gloves; prior to central line insertion and dressing changes, apply antiseptic to skin (*ie*, alcoholic chlorhexidine with chlorhexidine concentration >0.5% in alcohol, unless contraindication to chlorhexidine); antiseptic must be dry prior to placing central line; for daily care, alcohol-impregnated port protectors may be used on access ports; prior to accessing

hub, perform hand hygiene, wear clean or sterile gloves, scrub hub with 70% alcohol or chlorhexidine with alcohol for 15 sec, allow hub to dry; do not allow hub to touch other surfaces while drying; access port with sterile devices; discard gloves, perform hand hygiene when finished; daily baths with 2% chlorhexidine may reduce risk of central line–associated bloodstream infections for patients aged >2 mos; change gauze dressings every 2 days, clear dressings every 7 days; if dressings soiled, damp, or loose, perform dressing changes more often

Malpractice

Definition: malpractice results if patient injured because of negligence or omission of action; to be considered medical malpractice, must be violation in provision of standard of care to patient, with patient's injury resulting in significant damages (*eg*, disability, loss of income, future or past medical expenses, pain and suffering), and that deviation from standard of care caused said injury

Lawsuit: lawsuit regarding medical practice begins with patient filing complaint; physician may have previously received formal notice of complaint; during process of pretrial discovery, written discovery, deposition of parties and witnesses, and perhaps deposition of expert witnesses proceed to share information between plaintiff's attorneys and defendant's attorneys; after pretrial discovery phase, many cases may be settled or dropped; for cases that go to trial, physician will go to court and testify in front of judge and often jury

Impact of errors on physicians: study found that, after medical errors, physicians experience increased anxiety, loss of confidence, difficulty sleeping, and decreased job satisfaction; >90% of physicians felt their organization or hospital did not support them sufficiently in addressing stress experienced after medical error

Database for medical malpractice: medical malpractice awards in addition to clinical privilege restrictions and adverse actions regarding licensure are listed in National Practitioners Data Bank, run by Department of HHS; access not available to general public; provided to hospitals, professional societies, health care organizations, federal or state licensing authorities, and entities administrating federal or state health care programs

Suggested Reading

Nanji KC et al: Evaluation of perioperative medication errors and adverse drug events. *Anesthesiology.* 2016;124(1):25-34; **Wahr JA et al:** Medication safety in the operating room: literature and expert-based recommendations. *Br J Anaesth*. 2017;118(1):32-43; **Warner DO et al:** Risk and outcomes of substance use disorder among anesthesiology residents: a matched cohort analysis. *Anesthesiology.* 2015;123(4):929-36; **Waterman AD et al:** The emotional impact of medical errors on practicing physicians in the United States and Canada. *Jt Comm J Qual Patient Saf*. 2007;33(8):467-76.

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Essentials of Neuroanesthesia: Part 1

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Physiology: most important is to review cerebral blood flow and factors controlling cerebral blood flow; brain is only 2% of body weight; receives 15%–20% of cardiac output, utilizes 20% of oxygen, utilizes 25% of glucose used by the whole body at rest; high blood flow due to high metabolic demand and lack of substrate storage; high metabolic function devoted to synaptic activity (50%), maintenance of ionic gradient (25%), and biosynthesis of cellular material (25%); precise control of cerebral blood flow is essential

Anatomy: brain is supplied by two internal carotid arteries (anterior circulation) and two vertebral arteries that join to form basilar artery posterior circulation; anterior circulation is heavily supplied by sympathetic nervous system; posterior circulation is less supplied or less protected by the sympathetic nervous system; autoregulation of posterior circulation is less active than for anterior circulation; therefore, posterior circulation is more prone to being disturbed by surging blood pressure as with preeclampsia and uncontrolled hypertension; leads to posterior cerebral edema; temporary loss of vision

Circle of Willis: anastomosis in the interpeduncular cistern formed between the anterior and posterior circulation as well as between arteries of two cerebral hemispheres; was thought to prevent ischemia if supply of any major blood vessels compromised; now thought that it serves to reduce pressure within arterial system; pressure gradient exists because pulse wave and pulse flow arrive to skull through the different cerebral arteries asynchronously due to arterial tree asymmetry; Circle of Willis protects cerebral artery and blood-brain barrier from hemodynamic stress; formed by anterior cerebral arteries on either side, anterior communicating artery, internal carotid bifurcation, posterior communicating artery, and posterior cerebral artery; posterior cerebral artery is part of posterior circulation and the rest belongs to the anterior circulation; Circle of Willis is only complete in about 40% of population; therefore, ischemia can develop in the brain despite good perfusion in one side; be careful about proper maintenance of brain perfusion because Circle of Willis is sometimes incomplete and unable to compensate for blood supply in other side of the brain if 1 side disturbed

Venous system: cranial veins are classified into 3 systems; superficial drains scalp, muscles, and tendons; intermediate drains bone, diploë, and dura mater and consists of emissary and diploic veins, meningeal vein, and venous sinuses; deep system veins drain brain; scalp veins normally drain mostly to extracranial venous system and partly through emissary veins to dural venous sinus; with raised intracranial pressure (ICP), there is retrograde flow from intracranial to extracranial venous system, resulting in dilation of scalp veins and emissary veins; diploic and scalp veins are collateral between superficial sagittal sinuses to extracranial veins and the veins of the brain from the superficial and deep venous system

Superficial veins: include cortical veins; drain to superior sagittal and transverse sinus; veins of medial and inferior cortical surface drain to vein of Galen; anastomotic channels are between the superficial and deep venous systems; include occipital vein, posterior [occipital] vein, [posterior communicating vein], and basal vein of Rosenthal

Deep venous system: consists of internal vertebral vein, thalamostriate veins, and vein of Galen; drains inferior sagittal sinus to straight sinus; straight sinus and veins of inferior infratentorial compartment form a network that drains to straight or transverse sinus

Physiology: during resting conditions, venous system has 70%–80% of cerebral blood volume; controlled by cervical sympathetic system; when ICP increases, activation of sympathetic system results in venoconstriction and drives blood away, offsetting effect of raised ICP; little evidence of metabolic and myogenic control; with hypercapnia, pial venules dilate in response to increased arterial flow produced by arterial dilatation; as $PaCO_2$ increases, increase in sympathetic activity causes pial venoconstriction and tries to offset increased ICP; acute arterial hypertension causes areas of cortical venous dilatation due to increases in blood flow; venous transmural pressure may be higher than ICP; can lead to prevenicular disruption of blood-brain barrier

Cerebral Blood Flow

Overview: normally 50 to 55 mL per 100 g/min; distribution not uniform; gray matter receives about 80 mL per 100 g/min; white matter receives about 20; blood flow <20 mL per 100 g/min considered critical; irreversible cell death can occur

Control: cerebral blood flow usually remains constant despite variation of many local and systemic factors; ability to maintain constant flow with variation of cerebral perfusion pressure is called cerebral autoregulation

Cerebral perfusion pressure: calculated by mean arterial blood pressure (MAP) minus ICP, assuming that venous pressure in brain is less than ICP; if venous pressure higher than ICP, then cerebral perfusion pressure calculated as MAP minus venous pressure

Autoregulation: since 1959, assumed that autoregulation maintained between MAP of 50 and 150 mm Hg; now know that autoregulation is individualized; disturbed in patients with hypertension so that autoregulation curve is shifted to right; assessment of autoregulation using near-infrared spectroscopy sometimes defective in some people; blood pressure has to be individualized to patient to maintain within 10% of preoperative to maintain proper perfusion

Myogenic theory of autoregulation: proposed by Bayliss in 1902; autoregulation caused by stretching of smooth muscles of vessels, leading to vasoconstriction; mechanism is calcium-mediated pathway in vascular muscle as it is inhibited by calcium-channel blockers; there is an opening of voltage-gated calcium channels following stretch, leading to calcium entry and vasoconstriction

Neurogenic control of autoregulation: extensive arborization of perivascular nerves plays a role; extrinsic prevascular innervation refers to vessel innervation outside brain parenchyma; 3 main sources of extrinsic prevascular innervation identified — trigeminal ganglion, superior cervical ganglion, and sphenopalatine ganglion; carry sensory sympathetic-parasympathetic nerves; hypothesized main role of sympathetic nerve is to offer increased tone to maintain blood pressure below upper limit of autoregulatory mechanism; parasympathetic system felt to play a role primarily in pathological state because trigeminal vascular system important in pain sensation; early focus for migraine; discovered that calcitonin gene-related peptide, a potent vasodilator, is released from trigeminal nerves; once blood vessels dive deep into parenchyma and leave Virchow-Robin space, they lose extrinsic innervation and the intrinsic innervation begins; nerves take over that arise from distant pathways and local interneurons; majority do not act directly on blood microvasculature themselves, but connect to astrocyte foot processes; nucleus basalis, locus coeruleus, and raphe nuclei implicated as sources of innervation of cerebral microvasculature; stimulation of local gabaminergic interneurons causes vasodilatation of regional microvessels

Endothelin: binds to endothelin B receptor in intact endothelium and causes vasodilatation; in denuded endothelium, binds to endothelin A receptor and causes vasoconstriction; vasodilatory effect of endothelin B receptors is mediated by nitric oxide; balancing between constricting action of endothelin with nitric oxide-mediated vasodilatation; endothelin antagonist has been used to treat cerebral vasospasm after subarachnoid hemorrhage; thought that endothelin not major contributor to resting cerebral blood flow under normal physiological conditions, but important in several conditions, notably cerebral ischemia and vasospasm

Astrocytes: end-feet around endothelium and small blood vessels involved in integrity of blood-brain barrier; astrocytes also control blood flow at level of synapses; unique anatomical position to affect blood flow; processes extensively ensheath capillaries, link microvasculature with synapses; primary role was thought to involve extracellular potassium buffering; with synaptic activity, astrocytes produce glutamate; glutamate stimulates subtype of astrocytes, leading to increased intracellular calcium in end-feet of astrocytes, which in turn leads to increased extracellular calcium; stimulation increases uptake through potassium-dependent calcium channels; potassium channel-dependent calcium leads to increase of potassium uptake into end-feet of astrocytes and accumulation of potassium in astrocytes; leads to leakage into endothelium and vasodilatation

Summary: sympathetic and parasympathetic nervous systems control only the large vessels of the brain; microvasculature controlled by vascular smooth muscle, endothelin (in pathological states only), and especially by astrocytes

Partial pressure of arterial CO_2: affects cerebral blood flow; cerebral circulation very sensitive to levels; 3%–6% increase in P_aCO_2 leads to 1%–3% decrease of flow per 1 mm Hg in P_aCO_2; 1 mm Hg positive change in P_aCO_2 increases cerebral blood flow by 3%–6%; 1 mm Hg negative change in P_aCO_2 leads to decrease of cerebral blood flow by 1%–3%; all vessels of cerebral circulation are sensitive; P_aCO_2 activity on microvasculature in gray matter is greater than on white matter, which has relatively less vasculature

Mechanism: not known; assume that P_aCO_2 and dissolved bicarbonate in blood affect flow; CO_2 diffuses through blood-brain barrier; bicarbonic anhydrase in brain; changes into bicarbonate and H ion;, increase in P_aCO_2 or CO_2 in blood leads to increase of acidosis in brain, increasing nitric oxide, leading to vasodilatation

Reactivity: maintained within P_aCO_2 range between 30 and 50 mm Hg; usually blunted during severe hypotension because vessels are already maximally vasodilated

Partial pressure of oxygen: blood flow changes under conditions of normal oxygenation are less pronounced compared with reactivity to P_aCO_2; when PO_2 below 50 mm Hg, there is cerebral vasodilatation; hypercapnia increases and hypocapnia decreases cerebral vascular sensitivity to hypoxia; proposed mechanism is adenosine

Age and gender: age is important; there is decrease in mean flow velocity (cerebral blood flow as measured by transcranial Doppler) with increased age; mean velocity, used as surrogate for cerebral blood flow, decreased from 74 cm/second at 20 to 39 years to 58 cm/second in persons older than 60 years; peak systolic and diastolic flow decrease; pulse volatility index (resistance of small blood vessels of brain) and resistance index increase with age; difference in flow velocity is exaggerated with subarachnoid hemorrhage; females up to 60 years have higher flow velocity than males; after that, differences are abolished

Hypothermia: causes reduction in cerebral blood flow; maximum reduction at 18°C; below this temperature, suppression of metabolism; temperatures below 18°C associated with loss of autoregulation and vulnerability to ischemia

Hyperthermia: dangerous and destructive to brain; malfunction of enzymes and loss of autoregulation; hypothermia can be used as a neuroprotective; hyperthermia is neurotoxic

Preserving Cerebral Blood Flow and Perfusion Pressure During Neuroanesthesia

Introduction: most common complication is increased ICP; controlling high ICP or preventing further increases is essential to avoid even short periods of insufficient perfusion; degree of midline shift and histopathological

diagnosis of glioblastoma or metastasis are independent risk factors for intraoperative brain swelling; increased ICP >30 mm Hg can produce brain swelling; reverse Trendelenburg position, head elevation help to decrease ICP and reduce swelling; avoid hypercarbia, hypoxia; avoid obstruction of venous drainage by extreme head position, endotracheal kinking or obstruction during craniotomy

Supratentorial tumors: cerebral autoregulation measured by transcranial Doppler and CO_2 activity is usually preserved if tumor is medium size (less than 40 cubic cm) and midline shift is 5 mm or less on perioperative CT scan or MRI

Drugs to reduce ICP: presence of cyclooxygenase enzyme with arachidonic acid can produce prostaglandin, prostacyclin (a brain vasodilator); can enhance ICP; the cyclooxygenase inhibitor indomethacin is a cerebral vasoconstrictor and reduces cerebral blood flow without affecting cerebral oxygen metabolism; injection of indomethacin reduces ICP and improves cerebral perfusion pressure in patients with intracranial tumors during isoflurane anesthesia; also useful in patients with severe head injury; bolus of 0.2 mg/kg followed by infusion of 0.2 mg/kg per hour during propofol anesthesia in patient subjected to craniotomy for supratentorial brain tumor produced no evidence of brain ischemia as assessed by diffusion-weighted imaging

Diuretics: can be used intraoperatively to decrease ICP; mannitol is osmotic diuretic widely used during neurosurgery to reduce ICP; effective when some degree of blood-brain barrier integrity is preserved in significant portion of brain; dose varies between 0.25 g to 1 g/kg; during administration, especially with multiple doses, no further doses should be given if serum osmolarity is ≥320 mOsm/L to avoid hyperosmolar acute kidney injury; administer by infusion over 10 to 15 min; sudden exposure of cerebral circulation to extreme hyperosmolarity can have vasodilator effect; can produce brain engorgement and further increase ICP; this does not occur with slower infusion

Loop diuretics: effect of mannitol can be enhanced and rebound brain swelling reduced by adding a loop diuretic such as furosemide; two mechanisms involved; first, loop diuretics enhance water excretion, helping to maintain gradient between intravascular compartment and brain parenchyma across blood-brain barrier; second, furosemide inhibits chloride channels in neurons and glial cells, reducing their ability to re-accumulate idiogenic osmoles like chloride ions; inhibits ability to draw water into intracellular space to restore original size

Hypertonic saline: in critical situation can be used instead or in combination with mannitol; initial ICP effects of the equiosmolar smaller doses of mannitol and hypertonic saline are very similar; can be used in 3%, 7.5%, 15%, and 23.4% concentrations; monitor osmolarity; don't give if serum sodium is more than 150 mmol/L

Measurement of ICP: can use fluid-filled external pressure transducer; similar to arterial pressure and central venous pressure monitoring; catheter inserted through lateral ventricle; connected by transducer Wheatstone bridge through fluid-filled tubing; simple and cost effective; zero calibration possible; therapeutic and cerebral blood fluid can be withdrawn; can add antibiotics; can study pressure-volume index curves; disadvantage is difficult placement in slit-like ventricles; when ventricles are very small, can cause infection or hemorrhage

Intraparenchymal catheters: can insert into parenchyma; easier to place; accurate; fewer complications such as infection and hemorrhage; after insertion, cannot re-zero; expensive; fiberoptic Camino; sensor of catheter tip uses light source; pressure change causes change in light reflection; quantitative for pressure change

Cross-cranial Doppler: noninvasive technique; measures optic nerve sheath: normal diameter up to 0.4 cm; if increased more than 0.6 cm, means increased ICP; usually measured using ultrasound; versatile in emergency situation or emergency room for rapid diagnosis

Normal ICP values: 5–15 mm Hg in healthy adults in supine position; 3–7 mm Hg in children; 1–5 mm Hg in infants; cutoff values for treating ICP depend on intracranial pathology; for head injury, usually treat when ICP exceeds 20–25 mm Hg; keep below 20 mm Hg in operating room (OR)

ICP waveforms: three components — arterial vascular component, cerebrospinal fluid circulatory component, and cerebral venous outflow component; normal waves usually have 3 peaks; percussion is P1; tidal is P2; dicrotic is P3; according to Monro-Kellie doctrine, volume of outer cranium is constant; there is period of compliance during which increased brain volume due to increased ICP can be compensated for by shifting venous blood out of cranium; once there is reduced compliance of the brain, P2 merges with P1 or exceeds P1; with sufficient ICP, normal waveforms change

Pathological waveforms: Lundberg waveforms (three types) encountered during increased ICP; A waves (plateau waves) in patients with reduced intracranial compliance; systemic hypotension results in cerebral vasodilatation leading to increased cerebral blood volume, and hence, increased ICP; increased ICP can reach up to 40 mm and stays there for 5–15 min; when duration of plateau exceeds 30 min, there is high risk of cerebral ischemia; if there is intact autoregulation, and blood pressure rises, the effect is reversed; treat to prevent cerebral ischemia and herniation syndromes

P waves: have frequency 0.5–2 per min with amplitudes up to 20–30 mm Hg; indicate vasomotor center inability due to low cerebral perfusion pressure at lower end of cerebral autoregulation

C waves: frequency about 4–8 per min with amplitudes around 20 mm Hg; have been documented in healthy individuals

Pressure-volume index: with a catheter, such as intraventricular catheter, in brain, can draw a pressure and volume relationship; intracranial compliance defined as change of volume related to increased pressure; inverse of compliance is elastance — increased volume associated with increased pressure; relationship is non-linear; slope of this relationship in the logarithmic scale is linear; pressure-volume index (PVI) — volume required to change ICP by tenfold (logarithmic tenfold); normal value is about 20–25 mm; to increase volume by 20–25, can increase pressure inside the cranium by log of 10; calculate by

withdrawing around 2 mL of CSF and noting pressure change; procedure is repeated multiple times with aspiration and injecting saline into the catheter, with pressure change noted; reduced compliance occurs even before ICP values go high; high PVI values can be seen in patient with normal perfusion pressure but defective cerebral autoregulation; very important in patient with traumatic brain injury; with intact cerebral autoregulation, if you enhance cerebral perfusion pressure, blood vessels will constrict, cerebral blood volume and ICP will be reduced; with impaired cerebral autoregulation, increased cerebral perfusion pressure will lead at first to cerebral vasodilation and increased cerebral blood volume and increased ICP

Pressure reactivity index: if enhancing cerebral perfusion pressure with intact cerebral autoregulation, the blood vessels will constrict, then decrease cerebral blood volume and ICP; with impaired cerebral autoregulation, increasing cerebral blood perfusion pressure leads to further blood vessel vasodilation, increased cerebral blood volume, and consequently increased ICP; pressure reactivity index, if negative, means intact autoregulation and is good sign; if pressure reactivity index is positive, means that you are increasing cerebral perfusion pressure; will lead to increased cerebral blood volume and increased ICP; enhanced mortality rate because autoregulation is defective

Anesthetics: volatile anesthetics have dual effect on cerebral vasculature; low concentrations are the same; isoflurane and sevoflurane constrict cerebral vessels secondary to suppression of metabolism; at high concentration, varied vasodilator effect increases cerebral blood flow and ICP; in pigs, 1 minimal alveolar concentration (MAC) of desflurane has most profound vasodilator effect, resulting in increased cerebral blood flow and ICP; in humans undergoing craniotomies for supratentorial mass lesions who receive 1.2 MAC of either desflurane or isoflurane for maintenance of anesthesia, desflurane and isoflurane had similar effects in cerebral perfusion pressure and MAP; with desflurane in setting of hyperventilation and P_aCO_2 of 30 mm Hg, no significant changes were seen in lumbar CSF pressure; patients undergoing craniotomy for supratentorial tumors randomized to receive 1.2 MAC of sevoflurane or desflurane; desflurane had shorter extubation and recovery time but similar intraoperative and postoperative complications versus sevoflurane

Comparisons: sevoflurane has fewer cerebral vasodilator effects than isoflurane at same anesthesia depth; cerebral vasodilatory potency of halothane is higher than enflurane, which is higher than desflurane; desflurane equal to isoflurane; isoflurane and desflurane higher than sevoflurane; sevoflurane most suitable for neuroanesthesia

Cerebral blood flow and cerebral metabolic rate for oxygen: sevoflurane 1.5% volume compared with propofol 3.7 mcg/mL; reduction of cerebral blood flow with propofol is associated with decreases in jugular bulb venous oxygen saturation close to lower threshold of 50 mm Hg; with further vasoconstriction during hypocapnia, PCO_2 of 33 mm Hg, propofol reduces jugular venous oxygen below 50%, indicating critical cerebral perfusion; with sevoflurane, decreases in jugular bulb venous oxygen saturation do not occur with normo- or hypocapnia; at equipotent concentrations, cerebral metabolism is reduced to same extent with same anesthetics

Cerebral metabolic rate of oxygen ($CMRO_{2)}$: coupling between original cerebral blood flow and $CMRO_2$ is maintained with sevoflurane and propofol as long as you keep sevoflurane up to 1.2 or 1.3 MAC; above that, there is asynchrony between cerebral blood flow and $CMRO_2$; $CMRO_2$ will be much less than cerebral blood flow; can increase cerebral blood volume and cerebral arterial vasodilatation

Conclusions: all inhalational anesthetics up to 1 MAC can maintain cerebral autoregulation and matching between cerebral oxygenation, $CMRO_2$, and cerebral blood flow; above 1 MAC, only inhalation anesthetic up to 1.3 MAC that can maintain cerebral autoregulation and matching between cerebral blood flow and $CMRO_2$ is sevoflurane

Neuroprotection

Introduction: no definitive answer about protecting brain cells; most important is maintaining oxygen supply and oxygen perfusion of brain, especially during perioperative period and in intensive care unit (ICU)

Neuronal injury: necrosis thought to occur at acute phase in core of cerebral infarct; apoptosis is predominant mechanism of neuronal death in penumbra or area surrounding infarct; therapeutic aim is to perfuse penumbra and maintain healthy penumbra to overcome extensive neuronal injury; can't get back necrotic area; by preventing injury or further necrosis or apoptosis of penumbra, can enhance survival of penumbra and decrease influence of the neuronal injury

Mechanism: increased permeability of mitochondrial membrane leads to influx of sodium and calcium to mitochondria and results in depolarization; increased permeability of mitochondrial membrane leads to release of cytochrome c into cytoplasm, which activates caspase enzyme system; this leads to programmed cell death (apoptosis); to prevent, important to maintain the integrity of the mitochondrial membrane during ischemia and reperfusion

Immunological response: occurs in response to release of cytokines such as interleukin-1, contributing to neurodegenerative process; within minutes of vessel occlusion, increase in expression of transcription factors such as c-Fos and c-Jun; second wave of heat shock proteins increases expression up to 2 days; increase in chemokine expression, eg, tumor necrosis factor (TNF), interleukin-1, interleukin-6, has usually been observed within 24 hours; ischemia in deep white matter generally severe due to lack of collateral blood supply; inflammation may promote repair through ability of T cells to produce neurotrophic factor such as brain-derived neurotrophic factors, growth factors, and neutrophins, which facilitate neuronal cell proliferation and differentiation; macrophages or microglial cells may play role through secretion of cytokines, chemokines, and TNF alpha

Microglial cells: important in death or regeneration of brain; work like macrophages in brain; two phenotypes; type M1 are neurotoxic and neuro pro-inflammatory; type M2 are anti-inflammatory, neuroprotective, and help in repair; balance between M1 and M2 is important in healthy brain; in neurodegenerative disease (eg, multiple sclerosis,

Alzheimer's, amyotrophic lateral sclerosis [ALS]) there is an imbalance between M1 and M2, with predominance of M1; leads to continuous or chronic inflammation, leading to neurotoxicity; M2 engulfs and cleans toxic materials like beta amyloid and like alpha-synuclein in Parkinson's

Angiotensin receptor blockers: ARBs; neuroprotective agents being used for chronic degenerative disease; have partial agonistic effect in peroxisome proliferator-activated receptor gamma; there are nuclear receptors; can help change type M1 to M2; patients taking ARB blockers are less likely to develop Alzheimer's and Parkinson's disease; are in early stages of use as neuroprotective agents but promising

Anesthetic-induced neuroprotection: barbiturates can produce isoelectricity in electrocorticogram or EEG; were studied extensively in early 1970s; methohexital was first used as a neuroprotective agent; barbiturate-induced EEG burst suppression does not reduce ischemia and ischemic injury; EEG is rendered isoelectric rapidly after global ischemia; mechanism of the neuroprotection of barbiturates can be attributed to glutamate receptor blockage, potentiation of gabaminergic activity, and inhibition of calcium influx similar to other anesthetic agents; magnitude of protective effect is modest; doses that produce burst suppression of EEG may not be necessary to achieve protection; 1/3 of the dose required to achieve EEG suppression yielded injury reduction similar to that achieved with larger doses; administration of barbiturates for neuroprotection has many disadvantages, including potential need for inotropes or vasopressors to maintain blood pressure and possible need for postoperative mechanical ventilation secondary to delayed emergence from anesthesia; other complications include dysglycemia, bone marrow suppression, and increased rates of infection

Propofol: neuroprotective in vivo in animal models of focal and global cerebral ischemia in addition to decreased $CMRO_2$; neuroprotection has been attributed to antioxidant effects enabled by phenolic hydroxyl group or effects on glutamate uptake, dopamine release, or GABA receptors; no clinical data exists on neuroprotection in humans

Alpha-2 agonists: dexmedetomidine had neuroprotective effect in animal models of ischemia; exerts neuroprotective effect via myriad mechanisms; lowers plasma catecholamine levels and improves neurological outcome in rat models of ischemia; assists functionally and histopathologically; enhances astrocyte uptake and metabolism of glutamate; maintains integrity of mitochondrial membrane during ischemia by upregulating expression of anti-apoptotic factor Bcl-2 (B-cell lymphoma 2) and downregulating the expression of apoptotic factors

Ketamine: potentially neuroprotective because NMDA (N-methyl-D-aspartate) receptor antagonist; psychotomimetic side effects associated with vacuolation of neurons in the posterior cingulate and the retrosplenial cortex; side effects may worsen during ischemia; causes concern about use as neuroprotectant; however, low dose recently shown helpful in rat hippocampal cells in traumatic brain injury; might be helpful for microglia

Etomidate: used in past as neuroprotective agent during cerebral aneurysm clipping; increased volume of brain infarction; worsened neuronal injury by reducing nitric oxide levels in ischemic brain tissue, reducing blood supply and resulting in greater reduction in tissue PO_2; no longer recommended for use as a neuroprotective

Lidocaine: channel blocking effect; reduced extent of cerebral infarction; improved neurological outcome; neuroprotective effects accompanied by preservation of mitochondrial membrane integrity; reduced release of cytochrome c and caspase-3 activation; reduced apoptosis cascade; not widely accepted as a neuroprotective in operative setting

Volatile anesthetics: reduce ischemia, decrease glutamate transmission, antagonize postsynaptic glutamate receptors, and enhance GABA A-mediated hyperpolarization; increase levels of anti-apoptotic factors like Bcl-2 that reduce mitochondrial membrane permeability, and consequently release of cytochrome c to cytoplasm; have preconditioning effect; in animals, administration immediately or up to 1–4 days before induction of ischemia attenuates neuronal injury; preconditioning has been demonstrated for isoflurane and sevoflurane; mechanism for anesthetic preconditioning includes volatile anesthetic activation of sarcoplasm, sarcolemma, and mitochondrial potassium ATP channels; also adenosine receptors, signaling cascades, protein kinase C, and other factors; isoflurane-mediated preconditioning may be more effective in men than women; part of neuroprotective and anesthetic effects of volatile anesthetics have been attributed to their agonistic effect on TREK-1, a subtype of the potassium two-pore channels; leads to presynaptic terminal hyperpolarization by TREK-1 activation, thus reducing the neurotransmitter release; hyperpolarization of the post-synaptic cell might reduce calcium influx via dependent calcium channels and NMDA receptors

Harm to growing brain from volatile anesthetics: A-receptor blocking during synaptogenesis in immature brain can induce widespread neural degeneration; NMDA-antagonist effects of volatile anesthetics may cause cerebral damage in neonates

Xenon: exerts anesthetic effect by noncompetitive antagonism of NMDA receptors; in studies of neonatal hypoxic ischemic encephalopathy models, use of xenon improved neurological outcomes and led to histologic protection; can precondition brain against ischemic injury; potential as neuroprotective agent during ischemia

Other neuroprotective agents: other agents may be of value in future; lithium improves neurological outcome and can inhibit neurotoxic effects of volatile anesthetics in the growing brain; lithium downregulates tau, a phosphoprotein involved in the pathophysiology of Alzheimer disease in cultured cortical neurons; this effect may explain the efficacy of lithium in treatment of neurological disorders such as ALS

Erythropoietin (Epogen): important role in neuroprotection and neurogenesis and acts as a neurotrophic factor in the brain; exhibits anti-inflammatory and angiogenic properties; encouraging clinical results for

neuroprotection in acute stroke and brain trauma; there are derivatives without hematopoietic properties

Minocycline: in early clinical trials for neuroprotection; offers benefit in animal models of brain injury and chronic disease; inhibits cytochrome c

Dexamethasone: inhibits caspase-3 activity in rats with brain injury secondary to meningitis

Albumin: exerted neuroprotection in models of focal ischemia; antioxidant and scavenging properties; modulates apoptosis; enhances microcirculatory blood flow by enhancing nitric oxide production by endothelial glycocalyx; decreases leukocyte rolling and adherence, reducing inflammatory response; administration of doses up to 1.25 g/kg body weight per day for 7 days tolerated with subarachnoid hemorrhage; potential neuroprotective effects maintained by reducing delayed cerebral ischemia from vasospasm

Suggested Reading

Eltin JWJ et al: Dynamic cerebral autoregulation estimates derived from near infrared spectroscopy and transcranial Doppler are similar after correction for transit time and blood flow and blood volume oscillations. *J Cereb Blood Flow Metab* 2018 Oct 24 [Epub ahead of print]; **Endesfelder S et al:** Neuroprotective effects of dexmedetomidine against hyperoxia-induced injury in the developing rat brain. *PLoS One* 2017 Feb 3;12(2):e0171498; **Farrell D and Bendo AA:** Perioperative management of severe traumatic brain injury: What is new? *Curr Anesthesiol Rep* 2018;8(3):279-89; **Kapoor A et al:** Serum albumin marker in spontaneous subarachnoid hemorrhage: More than a mere nutritional marker! Br J *Neurosurg* 2018 Feb;32(1):47-52; **Kooi EMW et al:** Measuring cerebrovascular autoregulation in preterm infants using near-infrared spectroscopy: An overview of the literature. *Expert Rev Neurother* 2017 Aug;17(8):801-18; **Rivera-Lara L et al:** Validation of near-infrared spectroscopy for monitoring cerebral autoregulation in comatose patients. *Neurocrit Care* 2017 Dec;27(3):362-9; **Suarez MD et al:** The albumin in subarachnoid hemorrhage (ALISAH) multicenter pilot clinical trial: Safety and neurologic outcomes. *Stroke* 2012 Mar;43(3):683-90; **Sun WH et al:** Time dependent neuroprotection of dexamethasone in experimental focal cerebral ischemia: The involvement of NF-κB pathways. *Brain Res* 2018 Dec;1701:237-45.

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Essentials of Neuroanesthesia: Part 2

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Overview of hypothermia: considered both globally and focally neuroprotective; mild hypothermia shown to protect brain, recommended in comatose survivors of out-of-hospital cardiac arrest

Studies: new studies of out-of-hospital cardiac arrest with loss of consciousness found achievement of "target management temperature" of 36°C had same effect as mild hypothermia of 32°C; most important during neuroanesthesia or neuro-intensive care is avoiding hyperthermia, maintaining normothermia; do not exceed 36°C; studies in traumatic brain injury didn't find benefit of hypothermia in adults or children; some showed harmful effects of mild hypothermia compared with normothermia; only case hypothermia shown to increase survival is in neonatal encephalopathy; can increase neuronal survival and improve neurological outcomes

Recommendations: mild hypothermia to 32°C reserved for patients with increased or refractory intracranial hypertension; mild degree of hypothermia can decrease intracranial pressure (ICP), especially when combined with other measures; use slow rewarming, guided by ICP; rapid warming harmful; if induce hypothermia, must maintain for a long time and use slow rewarming; may explain why Intraoperative Hypothermia for Aneurysm Surgery trial (IHAS study) found that mild hypothermia failed to significantly improve neurological outcome after aneurysm surgery; if used, mild hypothermia should be induced very early or even before ischemia happens; maintain for reasonable time; rewarm very slowly

Glycemia: preferable to maintain blood sugar below 140 to 150 mg/dL, while avoiding hypoglycemia, which can also be harmful; NICE (Normoglycemia in Intensive Care Evaluation) trial was largest ICU trial; maintaining up to 150 mg/dL usually tolerated with no effect on neurological outcome; extremes of blood sugar can have deleterious neurological effects

Monitoring: for anesthetic management during craniotomy, apply standard ASA monitors; essential to have intra-arterial catheter to measure arterial blood gases; central venous catheter not routinely used except with high risk of venous air embolism (as with sitting position), lack of proper peripheral IV access, or craniotomies for larger tumors with expected major blood loss; lecturer prefers to use it for all aneurysm clipping; allows good access to add vasopressors and vasodilators and if there is risk of bleeding; for straightforward craniotomy for manageable tumor good peripheral IV access is sufficient

Maintenance of anesthesia: can use sevoflurane; for cases of severe intracranial hypertension, propofol and remifentanil preferred; usually prefer sevoflurane as inhalation anesthetic in neuroanesthesia; during sevoflurane anesthesia, CO_2 reactivity is preserved up to 1.3 MAC without major ICP effects; reverse Trendelenburg head position should be considered to reduce ICP; usually maintain $PaCO_2$ between 30 and 35; use hyperventilation to 25 to 30 only as transient means to control ICP in cases with severe intracranial hypertension with immediate risk of herniation; blood pressure should be tightly controlled to maintain cerebral perfusion pressure, especially if increased ICP; arterial pressure usually zeroed at level of external auditory meatus

Fluid management: be careful during craniotomy to provide proper tissue perfusion, avoiding increased ICP and cerebral edema; use balanced crystalloid solution, like lactated Ringer's or PlasmaLyte; saline can produce hyperchloremic acidosis and injure kidney; saline in reasonable amount is usually safe; may use crystalloids for maintenance; maximum about 1 mL per kg body weight per hour; compensate losses by blood transfusion or colloid; prefer to use albumin 5% as colloid; hydroxyethyl starch solution, even the new molecular weight solution, may have undesired effects on coagulation process; maintaining normal coagulation crucial during and after brain or spine surgeries

Supratentorial craniotomy: incision of temporalis muscle can be associated with limitation of mandibular opening and pseudoankylosis of temporomandibular joint; may result in difficult intubation if subsequent surgery is required within short interval

Cerebellar hemorrhage: not uncommon following supratentorial craniotomy; serious complication; no single pre-surgical factor can regularly predict occurrence; early detection is the key to minimizing sequelae

Post-operative pain control: easily accomplished using acetaminophen; like to use intravenous acetaminophen; can add tramadol or nalbuphine

Meningiomas: can be complicated by hemorrhagic postoperative manifestations; probably due to abnormal hyperfibrinolysis

Positioning for Craniotomies and Spine Surgery

Overview: pressure points such as sacrum, ischium, trochanter, and heel should be well padded by placement of viscoelastic gel pads to redistribute mechanical pressure; contact of patient skin with metal surfaces should be avoided to prevent burns from use of diathermy;

thromboembolic deterrent stockings and sequential compression devices are applied in patients undergoing prolonged procedures

Head: ideal position provides optimal surgical approach to target area with minimal pressure and minimal trespass on normal brain; based on 2 principles: imaginary trajectory from highest point of skull surface to area of interest of brain should be shortest distance, and exposed surface of skull (imaginary perimetry) should be parallel to floor

Rotation: can be turned between 0° and 45° lateral to right and left from body's sagittal axis; if more than 45° required, ipsilateral shoulder is raised on pillow or roll to maintain access; cervical strain may occur with extreme rotation; occasionally may have extremely deleterious effect on vascular structures of neck; may decrease blood flow in ipsilateral vertebral arteries; narrow foramina and transverse processes along cervical spine; may impair venous return from internal jugular veins, leading to increased ICP and brain swelling, increasing bleeding; flow more often reduced on contralateral side of rotation and intracranial part compared to cervical part; mechanical compression of extracranial vertebral artery during neck rotation has been described; those with associated risk factors such as cervical spondylosis, vertigo, atherosclerosis, osteoarthritis, and greater age more likely to have compromised vertebral blood flow with lateral rotation of neck; such preoperative signs of possible vertebrobasilar insufficiency can help neurosurgeon and anesthesiologist in positioning the neck; hyperflexion of head can also lead to decreased blood flow in vertebral and carotid arteries; may lead to brainstem and cervical spine ischemia

Additional complications: reduces anteroposterior size of hypopharynx; causes ischemia of base of tongue, leading to pharyngeal and tongue edema; may be accentuated by placement of other devices in oral pharynx, such as transesophageal echo probe or oral airway

Positioning: neck flexion at least 2 to 3 finger breadths between chin and chest or chin and sternum to avoid ischemia of cervical spine and upper airway edema

Case report of quadriplegia with patient in sitting position, severe flexion of neck compromised blood supply to cervical spinal cord

Fixation of head: variety of fixation devices; most common is Mayfield-Keys skull fixation device; Mayfield holder consists of clamp with 3 sterile pins; inserted into skull in bend-like area just above orbits and pinna; take care to avoid frontal sinus and temporal bone; position so no interference with cranial incision that facilitates the attachment of halo self-retaining retractor; when the clamps are squeezed together, gears slide until pins are seated in skull; knob is tightened; each ring exerts about 20 pounds of pressure; 80 pounds allowable in adults; 30 to 40 pounds is preferable limit in pediatric population; clamped on head frame assembly attached to table

Complications: some associated with Mayfield-Keys; pressure necrosis, perforation of skull, injury to medial meningeal artery leading to hematoma or arteriovenous fistula; extradural hematoma removed from pin site; scalp and eye laceration due to slippage of head holder; bleeding from pin site, air embolism, malposition, poor fixation, infection, and cervical spine injuries due to inadvertent patient movements

Sugita multipurpose head frame uses 4 pins to position head; ideal when maximum support necessary; allows for 360° rotation of frame and adjustment of angle of head during surgery; head holder consists of 4 pins; frame assembly consists of basal frame that is mounted to head holder

Horseshoe head rest: shaped with both vertical and lateral adjustment; provides flexibility in patient positioning in supine and prone positions; has gel pads that make it comfortable; absolute contraindication of any pressure on eye; risk of central retinal artery occlusion and postoperative vision loss if there is pressure; scalp alopecia is a known complication in a patient positioned supine in the horseshoe head rest for prolonged period

Supine position: well known; no special precautions

Lateral position: hemodynamic parameters minimally changed; mild decrease in stroke volume and cardiac output; increase in systemic and pulmonary vascular resistance; leads to modest decreases in systolic blood pressure and mean arterial blood pressure compared with supine

Ventilation: mild increase in the PaO_2 compared to supine with normal value of $PaCO_2$; perfusion best in dependent lung zone; non-dependent lung better ventilated; causing mild ventilation-perfusion (V/Q) mismatch if abdominal excursions are free

Limb positioning: apply axillary roll under thorax below axilla to prevent compression; dependent shoulder brought beyond cephalic edge of operating table; dependent arm rested on low padded arm rest between table and head fixation; lower limbs positioned with pillow between legs; dependent extremities flexed to avoid pressure over fibula head and peroneal nerve

Complications: brachial plexus injury; vascular compromise to dependent upper extremity; ear and eye injury; injury to suprascapular nerve of dependent shoulder

Park bench position: modification of lateral; provides better access to low-lying cranial lesions; access to interior brain stem, foramen magnum, and cerebellopontine angle tumors

Positioning: trunk rotated 15° from lateral; upper arm along lateral trunk; upper shoulder taped toward table; dependent shoulder and arm are positioned outside table; arm supported by sling; lower extremity slightly flexed; pillow between knees; do not tape shoulder tightly or drop neck too much

Prone position: common during spine surgery; understanding physiological changes reduces complications; can be associated with decreased cardiac index and venous return; knee-chest position decreases cardiac output by 20%; pelvic props for modified Relton-Hall frame under anterior superior iliac spine and padded support under the chest decreases by 17%; onto evacutable mattress is 11%; 1 pillow under the thorax and under the abdomen, leaving the abdomen free to move, is 3%; key during prone position is to avoid decreasing cardiac output and to increase venous return by leaving abdomen free to move; study found prone position caused left ventricle end compliance decrease;

changes attributed to decreased venous return due to inferior vena cava compression and left ventricular decreased compliance due to increased intrathoracic pressure in prone position; confirmed by studies using thermodilution pulmonary artery catheters to measure cardiac index when transferring from supine to prone; cardiac output decreased 17% to 24%

Increased intraocular pressure: increased intrathoracic pressure decreases venous return of head, leading to engorgement of ophthalmic veins and resulting in drainage of aqueous from eye, leading to increased intraocular pressure; with time, if blood pressure is decreased and intraocular pressure is increased, ocular perfusion pressure is disturbed; may contribute to post-operative vision loss (POVL)

Abdominal compression: possible cause of spinal cord ischemia causing neurological deficit after cervical laminectomy; avoid abdominal compression and hypotension, especially in myelopathic patients, for whom spinal cord perfusion very important

Ventilation: position very helpful; better ventilation-perfusion matching; free abdominal movement; reason prone position used in ICU in patients with ARDS (acute respiratory distress syndrome) or hypoxia due to ARDS; perfusion more evenly distributed in prone position; recruitment of dorsal airways results in increase in lung units and increased functional residual capacity with near ventilation-perfusion matching and reduction in shunt; similar effects to positive end-expiratory pressure (PEEP) without barotrauma risk or interference with cardiac function

Sitting position: optimum access to midline lesions; improves cerebral venous decompression, lowering ICP; decreases need for cerebral retraction; promotes gravity-assisted drainage of blood and cerebrospinal fluid (CSF), enabling a clean surgical field, visualization of bleeding points, and unobstructed view of patient's face, permitting observation of motor responses due to cranial nerve stimulation; significant venous pooling in lower extremities due to gravity, leading to decrease in cardiac output; arterial hypotension, heart rate and systemic vascular resistance increase; stroke volume and cardiac index decrease; increase in functional residual capacity and total lung capacity observed; perfusion is limited; no measured benefit of oxygenation observed; ventilation-perfusion mismatch; increasing ventilation is counteracted by decrease in perfusion; arterial blood pressure usually reduced by 0.77 mm Hg for each transmitter cm gradient above heart; decrease in cerebral perfusion pressures after positioning; leads to possible development of cerebral ischemia; ICP reduced

Lounging position: modified semi-sitting position; aims to create a positive pressure in transverse and sigmoid sinuses; lower head, legs elevated above level of head; decreases incidence and severity of venous air embolism in sitting position

Procedure: as patient sits, operating table is flexed, elevating thighs; foot of table is dropped; flex knees to prevent sciatic nerve stretching; pillow may be placed under knees; table tilted backward as flexed; neck in neutral core flex; avoid flexing more than 2 to 3 finger breadths between chin and sternum to avoid ischemia of cervical spine and edema of upper airway; secure arms across body or in arm rest to prevent downward drooping of shoulder, compressing brachial plexus; feet should not hang off table; ankles should be rested to prevent Achilles tendon injury; head holder frame clamped to side rails of back section to lower head end in case of air embolism; can apply CPR in this position

Hemodynamic changes: changes may be influenced by patient characteristics such as intravascular volume status, pre-existing hypotension, and BMI; positioning patient with flexion of hips, elevating knees to level of heart, help to minimize hypotension; slow stage positioning after adequate volume hydration over 5 to 10 minutes, with intermittent boluses of vasopressors as required to prevent any abrupt changes in blood pressure

Complications: venous air embolism; can occur when pressure within open blood vessel is sub-atmospheric; significant venous air embolism is rare unless surgical site is elevated more than 20-40 centimeters above heart; risk increases when open veins cannot collapse; encountered with injury to venous sinuses, cerebellar branching veins, epidural veins, emissary veins, and marrow spaces in skull or cervical vertebrae; during fossa procedure in sitting position, venous air embolism is detected by precordial doppler in about 40% and by transesophageal echocardiography (TEE) in 76%

Venous air embolus: if large and cannot be cleared, will result in occlusion of pulmonary vascular bed, resulting in increased pulmonary vascular resistance and pulmonary artery pressure, consequent rise in ventricular afterload; if severe obstruction, cardiac output will fall, caused by airlock in right ventricle; right ventricular failure or impaired left ventricular filling, caused by displacement of interventricular septum by distended right ventricle

Monitoring and detection: TEE and precordial Doppler can be used; TEE is most sensitive; right atrial catheter is helpful; usually use multi-orifice catheter; allows effective air aspiration; tip of catheter should be at juncture between superior vena cava and right atrium; proper position can be detected by TEE, ECG, or chest x-ray; in TEE, bicaval view determines proper position of catheter tip by visualizing superior vena cava and right atrium; in chest x-ray, proper position of catheter tip should be at level of carina; prefer chest x-ray method as it is accurate and universally available; in ECG technique, right arm lead of standard ECG monitor is attached to catheter via fluid column; use sodium bicarbonate; catheter advanced until biphasic p-wave is seen, then withdrawn until p-wave slightly shorter than r-wave

Paradoxical air embolism: potential for passage of air from right to left of heart with subsequent entry into coronary or cerebral circulation; can occur in pulmonary vascular bed; more commonly occurs via patent foramen ovale (PFO); paradoxical air embolism occurs only in context of major embolic events; increase in right atrial pressure is predicting factor for occurrence

PFO: detect pre-operatively by contrast bubble studies using pre-operative transthoracic echocardiography or intra-operative TEE; detection is crucial before institution of PEEP in sitting position to prevent paradoxical air emboli; PEEP increases right atrial pressure in relation to left atrial pressure and increases incidence of paradoxical air embolism in presence

of PFO; even when mean left atrial pressure exceeds mean right atrial pressure, paradoxical air embolism can occur, because transient reversal of intra-atrial pressure gradient can occur during each cardiac cycle; transpulmonary air passage can occur in absence of PFO; more likely when large volumes of air are present; threshold for transpulmonary passage may decrease in presence of pulmonary vasodilators, including inhalation anesthetics

Hypotension: 20% incidence of hypotension requiring vasopressors in sitting position; measures to avoid hypotension include predisposing hydration, wrapping of the legs with elastic bandages to counter venous pooling in legs, and use of vasopressor to maintain adequate cerebral perfusion pressure

Pneumocephalus: occurs to some degree in all craniotomies performed in sitting position and in other post-operative craniotomy patients and other surgical positions; avoid nitrous oxide during craniotomies to avoid development of tension pneumocephalus; tension pneumocephalus difficult to diagnose; should be suspected when patient fails to awaken after uneventful procedure, deteriorates after awakening, or suffers unexplained cardiovascular catastrophe; if suspected, should do CT scan to confirm; treat by observation, administration of higher oxygen concentration, or surgical evacuation if severe

Quadriplegia and paresis: cases in sitting position; cervical spinal cord compression and extreme neck flexion can reduce arterial perfusion to cervical spinal cord

Other complications: peripheral nerve injuries and severe swelling of the base of the tongue, soft palate, and pharynx have been described after posterior fossa craniotomies; nerve injuries can be minimized by careful positioning and padding; main cause of tongue and upper airway edema is impairment of head venous return due to extreme head flexion; avoid extreme flexion by allowing an adequate distance between chin and sternum; usually put soft bite block of rolled gauze between the teeth to avoid biting of the tongue and to help to decrease incidence of tongue edema

Upper Airway Management

Introduction: understand movement of cervical spine during intubation; primary force applied during intubation for cervical spine surgery is upward lift with a bit of angular force; up to 50 to 70 Newtons; 40N can lift 10 pounds; the more difficult the exposure, the greater the applied force

Direct laryngoscopy for intubation: extension of occiput on C1 combined with flexion at lower vertebrae; fulcrum usually at C7 to T1; direct laryngoscopy with MAC 3 blade, near-maximum extension at occiput and C1 with posterior arch of C1 touching skull

Comparison of devices: study of upper cervical motion during intubation with 3 intubation devices found mean motion at C1 and C2 was 10.2° for direct laryngoscopy, 5° for intubating laryngeal mask, and 1.6° for fiberoptic intubation; fiberoptic method was found to produce least motion and considered most suitable when movement not desired; C1 and C2 extension is a few degrees smaller when straight blade used, but probably not clinically meaningful; during intubation under general anesthesia with neuromuscular blockage and manual in-line stabilization, use of GlideScope produced better glottic visualization; cervical spine movement was eliminated; study — Keller implanted microchip sensor into pharyngeal surfaces of C2 and C3 in 20 cadavers to determine pressure exerted against cervical spine by laryngeal mask airway (LMA) and intubating LMA; concluded that devices exerted high pressure against upper cervical spine vertebrae during insertion, during inflation, and while in situ; could produce anterior displacement of upper cervical spine

Manual in-line stabilization and cricoid pressure: goal of manual in-line stabilization is to apply force to head and neck equal in magnitude and opposite to the direction of those generated by laryngoscopists, limit movement that results during airway management, avoid traction forces; manual in-line stabilization failed to reduce movement at site of instability in cadaver models; cricoid pressure, if not excessive, did not cause movement in cadaver model in injured upper cervical spine as long as injury is not at C6

Blood flow: maintaining head in neutral or near-neutral position important in maintaining blood flow to upper cervical cord; spine flexion causes elongation of cord with narrowing of diameter of longitudinal vessels; extension causes increase in diameter of cervical cord and folding of ligamentum flavum, which may exert pressure on cord and auxiliary longitudinal vessels; during intubation, maintain neutral head position of cervical spine with minimal movement, especially in cases with cervical spine injury or spondylosis

Neck motion: needs to be as minimal as possible during induction; avoid hypoxia in traumatic situation; fiberoptic or sleeve fiberoptic can be helpful when in doubt about integrity of cervical spine; LMA can be used in emergency airway management, such as in awake craniotomy in emergent situation after surgery

Monitoring

Electroencephalogram: EEG; recording of spontaneous electrical activity of cerebral cortex; recorded from surface of scalp; continuous and noninvasive indicator of cerebral function; summation of excitatory and inhibitory postsynaptic potential produced from pyramidal cells; usually use pair of electrodes, called a montage; can be either bipolar or referential

Bipolar montage: both electrodes active; electrodes lie in cerebral cortex; capable of recording electrical activity of cortex; voltage difference between the 2 electrodes is recorded

Referential montage: 1 active electrode; other, referential, electrode is commonly in mastoid, earlobe, or shoulder

Comparisons of montages: focal lesions are better detected by bipolar; diffuse lesions or changes better detected by referential; bipolar montage common for intraoperative monitoring; 10- to 20-electrode placement commonly employed; 10% or 20% of nasion line or perpendicular line or hemispherical circumference line; midline electrodes are designated as "Z"; right-side electrodes as even numbers; left-side electrodes as odd numbers

Plots: beta waves are fastest; alpha are slower; also theta and delta waves; normal EEG is plot of voltage versus time; usually about 1 to 35 Hertz frequency; waveform is classified into different bands; beta are highest and delta are lowest; automated analyses used; synchronized EEG activity with higher amplitude seen during sleep or general anesthesia; deep anesthesia produces burst

suppression; awakening produces dyssynchronization with higher frequency and lower amplitude; the higher the complexity of the function, the higher the frequency and the lower the amplitude with lesser synchronization

Electrocorticogram: recording from spontaneous electrical activity of brain from cortical surface or depth; wave forms better localized and delineated; used to delineate seizure focus and area of surgical resection; sometimes, great electrode is placed on cortical surface in surgery and recorded post-operatively to locate seizure focus

EEG uses: helpful to detect ischemia; shows abnormal changes in cerebral blood flow less than 20 mL per 100 gram per minute, before level at which cellular integrity is threatened (at 12 or 15 mL per 100 gram per minute)

Somatosensory evoked potential: SSEP; following peripheral stimulation, electrical activity travels along posterior column; proprioception, mechanoreception, spinal-thalamic pathways (nociception and thermal) are supplied by posterior spinal artery at level of brain stem; supplied by vertebral arteries and perforating arteries; at level of sensory cortex, vascular supply is anterior cerebral artery for lower limb and middle cerebral artery for upper limb, face, and trunk; electrical activity recorded along sensory pathways via dorsal column in spinal cord and scalp overlying sensory cortex; stimulation site should be below area at risk of ischemia from surgery; recording site should be above; neuronal pathway should travel through area at risk

Factors that affect SSEP: halogenated compounds, inhalation anesthetics increase latency and decrease amplitude; nitrous oxide also increases, delays latency and depresses amplitude; IV anesthetics (barbiturates, propofol) at low doses can cause many changes; cause delayed latency and suppressed amplitude at higher doses; etomidate and ketamine augment amplitude; opioids, given as bolus, cause depression, while low-dose continuous infusion causes many changes; alpha agonists compatible with intraoperative SSEP recordings; minimal depressant effects of benzodiazepines except in high doses; neuromusculars do not directly affect SSEPs; mild hypothermia produces increased latency of cortical SSEPs; with profound hypothermia, cortical potential disappears followed by increased latency and reduced amplitudes of subcortical potential, finally leading to disappearance of potentials; perfusion of neuronal pathways can affect SSEP recordings; ischemia can result in prolonged latency and reduced amplitude; severe anemia can affect SSEPs; increase in ICP can reduce amplitude and prolong latency of cortical SSEPs

Notification: notify surgeon if latency increases by more than 10% and amplitude decreases between 40% to 50% of baseline

Uses: spinal surgery, intramedullary tumors, scoliosis, and spine stabilization; cerebral vascular surgery where specific pathways are affected by ischemia, intracranial aneurysm; indicators — median and ulnar nerves for mid-cerebral artery territory, posterior tibial nerve for anterior cerebral artery territory; during carotid endarterectomy in tumor surgery to locate junction of sensory and motor cortex, to identify patient position related to nerve injury

Limitations: does not monitor spinal cord supply by anterior spinal artery; intraoperative SSEP does not rule out occurrence of post-operative paraplegia

Brainstem auditory evoked potential: recorded activities of neuronal generators of auditory pathways following stimulation of cochlear nerve

Early latency: first 10 milliseconds; represents activities up to brain stem; uni- or singular synapses; resistant to anesthetic effect; used for brain stem integrity

Mid-latency: up to 80 milliseconds; represents cortical activity; used like BIS (bispectral index) monitor; monitor depth of anesthesia; sensitive to anesthetic medications

Late latency: beyond 80 milliseconds; cortical association areas

Mechanisms: cochlear nerve activated by stimulation; electrical impulses travel along vestibulocochlear nerve to brain stem, mid-brain, and then primary auditory cortex; auditory stimuli have bilateral representation in cortex; usually elicited by clicks through ear; detect brainstem integrity during ear surgery; can be used to detect damage to cochlear vessels and brainstem during surgery in cerebellopontine angle, brainstem procedures, and posterior circulation vascular surgeries

Visual evoked potential: records electrical activity from neuronal generators along visual pathway; after light stimuli, retinal receptors are activated; electrical activity travels along optic nerve, optic chiasm, optic tract, and lateral geniculate body; reach visual projection areas in occipital cortex; initiate using stimulus light source, white or red LED-loaded goggles; used to detect ischemia of retina or for surgery of occipital cortex; visual evoked potential responses usually affected by halogenated compounds to greater extent; low-dose opioids, benzodiazepines, and low-dose propofol do not affect responses; opioids cause pupillary constriction, resulting in reduced light transmission to retina; can reduce visual evoked potential, so can use mydriatics at beginning of surgery; reduced core temperature causes prolonged latency, 20% reduction at 35°C

Motor evoked potentials: follow electrical or magnetic stimulation of motor cortex; usually magnetic in awake patients, electrical in anesthetized patients; magnetic are very sensitive to anesthetics and can be completely abolished; electrical impulses travel along corticospinal tract, descend to level of brain stem, travel down to anterior funiculi of spinal cord, and result in muscle activity; with change in stimulus, parameters should produce similar responses in particular group of muscles, provided no change in anesthetic depth and no use of muscle relaxants; significant when there is increased requirement of stimulus, more than 50 volts, to produce same response or there is decrease in amplitude more than 50%; used in spinal cord procedures as supplement to SSEPs, scoliosis correction surgery, and surgery for intramedullary tumors; can test integrity of anterior 2/3 of spinal cord because supplied by anterior spinal artery; intracranial tumors with motor cortex involvement; in thoracic aneurysm surgery, can be used to test blood supply of spinal cord in thoracic region; sensitive to inhalation anesthetics and nitrous oxide; maintained by low dose of inhalation anesthetics or TIVA (total intravenous anesthesia); ketamine good to maintain amplitude and latency

Suggested Reading

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Essentials of Neuroanesthesia: Part 3

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Bispectral index monitor: BIS monitor; for testing anesthesia depth; examines relationship synchronization among waves; utilizes various subparameters in time, frequency, and bispectral domains; different factors are weighted separately, fed into equation to produce a dimensionless number (BIS) that ranges from 100 (awake) to 0 (isoelectric EEG); as patient is sedated, BIS value drops to less than 90; values 60 to 40 are considered adequate hypnosis component of general anesthesia; value less than 40 is deeply anesthetized

Transcranial Doppler: most commonly used instrument to measure cerebral blood flow; reflected waves from object moving away are at lower frequency than origin frequency; ultrasound waves used to measure cerebral blood flow velocity at basal arteries; RBCs in vessel act as objects moving toward or away from probe; measures blood flow velocity as surrogate of cerebral blood flow; assumption that vessel diameter remains constant; debatable; few studies have shown that vessel diameter remains constant in many conditions; angle of insonation must remain constant to compare measurements; usually measure with probe of 2 megahertz keeping probe perpendicular to skin; frequently at level of just above zygomatic arch; 1 to 2 cm anterior to tragus, usually encounter middle cerebral artery, which is identified with flow toward probe at depths of 50 to 60 mm with characteristic flow sound; from there, with slight manipulation, can trace back to internal carotid bifurcation, anterior cerebral artery, and posterior cerebral artery

Pulsatility index: peak systolic to lowest diastolic flow with constant cerebral perfusion pressure; change reflects change in cerebrovascular resistance of small blood vessels; the higher the cerebral vascular resistance, the higher the pulsatility index; normal is 0.5 to 1 (dimensionless number); calculate high velocity systolic minus diastolic velocity, then divide by mean of flow velocity

Use in diagnosis: used in subarachnoid hemorrhage to diagnose and monitor cerebrovascular vasospasm; flow velocity above 120 cm/s, with pulsatility index above 1.5 diagnostic of vasospasm; used in carotid endarterectomy after clamping to assess flow velocity on other side; if flow velocity reduced >40% of baseline in contralateral side, shunt usually inserted; some recommend if >20%; detect emboli after carotid endarterectomy; predicts cognitive dysfunction

Jugular venous oximetry: measures oxygen saturation of venous blood at jugular bulb; represents global oxygenation extraction of cerebral tissues; oxygen delivery to cerebral tissues depends on cerebral blood flow and arterial oxygen content; usually about 50 to 60 mm Hg; right-to-left side difference is between 5 and 15; dominant jugular vein is cannulated retrograde; catheter tip is placed at jugular bulb; position confirmed by skull x-ray; in lateral x-ray skull view catheter tip should lie cranial to C1-C2 interspace; in AP x-ray view, catheter tip should lie cranial to line joining the 2 mastoid processes and caudal to lower margin of orbit; dominant side of jugular vein is defined by size of jugular foramen in the CT of the head and the intracranial pressure response to jugular vein pressure; if catheter tip lies within 2.5 cm of jugular bulb, chance of extracerebral contamination is minimal; normal value of arterial-venous O_2 content difference is 2.2 to 3.3 micromillimoles per mL; between arterial and venous O_2 content is 5 to 7.5 volume percent; jugular venous concentration is 60% to 75% and can be used in patient with head injury to identify secondary neuronal injury; in subarachnoid hemorrhage, can differentiate vasospasm from hyperemia [?]; transcranial Doppler helpful to identify difference and titrate hyperventilation therapy; if inducing hyperventilation in hypercapnia, don't decrease jugular venous bulb saturation below 60% or could induce cerebral ischemia

Near infrared spectroscopy: NIR; measures regional cerebral oximetry; light can penetrate tissue, including bone; oxygen binding to hemoglobin affects absorption; by measuring light absorption at 2 or more wave lengths, can measure concentration of oxy- and deoxyhemoglobin; peak absorption for reduced hemoglobin is around 740 nanometers; for oxyhemoglobin around 850 to 1000 nanometers; at 810 nanometers, absorption spectra of oxy- and deoxyhemoglobin are similar; called isosbestic point; technology based on the Lambert-Beer equation; calculates absolute concentration of chromophore, provided that sampling volume and path length followed by the light source are known; for given cortical tissue, cerebral vascular bed is about 70% to 85% venous and capillary; remaining is arterial; cerebral oximetry measurement predominantly reflects concentration and saturation of hemoglobin in venous and capillary bed; cerebral oximetry provides continuous bedside noninvasive measurement of focal oxygenation states

Interventions to improve oxygenation: can be assessed by corresponding changes from original oxygen saturation values; sensor placed over forehead on either side of midline, few cm above eyebrow to avoid contamination

by sagittal and frontal sinuses; look at x-ray and CT of head to examine frontal sinus before placing sensors; protect sensors from external light source to prevent contamination

Hemoglobin volume index: used to evaluate cerebral autoregulation; software is attached to NIR; measures hemoglobin volume in brain in relation to blood pressure; if index <0.3, blood pressure is at optimum autoregulation; if >0.3, blood pressure is not optimal and not in autoregulation curve; clinical outcome is impaired with higher postoperative complications, especially in cardiac surgery; in bypass situation, using NIR and hemoglobin volume index, can identify pressure with optimal autoregulation of brain to have less neural injury and less acute kidney injury; normal adult NIR values 71% to 76%, ±6%; children are 71%; neonate is 76%; values independent of hemoglobin or hematocrit values as long as hematocrit >30%

Transsphenoidal Surgery

Overview: transsphenoidal approach through sella turcica is used for excision of tumors within sella or environs; majority arise from pituitary gland; most common are prolactin-secreting microadenomas and nonsecreting macroadenomas; patients with former usually women who present with secondary amenorrhea and galactorrhea; nonsecreting adenomas manifest with mass effects, headache, visual disturbance, and hypopituitarism; nonsecreting adenomas typically larger at diagnosis; hypopituitary states may result from dysfunction of gland and closed compression of tumor mass; 3 less common tumors; growth hormone-secreting lesions cause acromegaly; adrenal corticotropic hormone (ACTH)-secreting tumors cause Cushing disease; preoperatively, pituitary lesion generally expands and compresses pituitary tissue and normal gland neural function is compromised; hormonal function is lost in following sequence: gonadotropins, growth hormone, ACTH, and thyroid stimulating hormone

Decrease in ACTH secretion: hypoadrenal status; risk of Addisonian crisis, especially under stress of surgery; correct profound hypocortisolism with hyponatremia preoperatively

Pituitary hypersecretion: other manifestations common; hypertension, diabetes, and central obesity common, concomitant of ACTH-secreting adenomas

Securing the airway: in acromegaly can develop larger tongue, narrow glottis; evaluate airway accordingly; those with Cushing disease and acromegaly can be difficult candidates during securing of the upper airway; careful examination of upper airway is very important; might do awake fiberoptic intubation

Techniques: straightforward for transsphenoidal resection of pituitary tumors; intravenous monitoring with arterial cannula is important to maintain minute-to-minute blood pressure; take blood sample to measure sodium, potassium, and blood sugar; can have diabetes insipidus; weight management crucial; patients with Cushing disease usually have fragile subcutaneous tissue because of hydrocortisone; may have difficult peripheral access and central venous catheter can be inserted; can have increased intracranial pressure (ICP); surgery usually performed in supine position; usually some degree of head-up posture to avoid venous engorgement; pharyngeal pack prevents blood accumulation in stomach, which could cause vomiting, or glottis, which could cause coughing and extubation; secure endotracheal tube at lower jaw at corner of mouth opposite surgeon's dominant hand; mucosal surfaces in nose infiltrated with local anesthetic and epinephrine solution; observe for dysrhythmia; surgical CO_2 management preferences vary; hypocapnia sometimes requested to reduce brain volume and minimize degree to which arachnoid bulges into sella; avoid opening arachnoid membrane, leading to CSF leakage; postoperative leaks can be persistent and associated with meningitis risk; with suprasellar extension of the tumor, a normal CO_2 level helps deliver lesion to sella for excision; some pump saline into lumbar CSF space

Anesthesia emergence: smooth emergence important; avoid coughing and bucking; patient should be completely recovered from muscle relaxant and regain whole train-of-four ratio; give 1.5 mg lidocaine prior to extubation to smooth extubation and avoid coughing; boluses of labetalol or esmolol helpful; bucking or coughing or repeated Valsalva maneuvers may contribute to reopening of CSF leak and worsen meningitis risk; clear airway of debris, including formed clots; if concern that persistent CSF leak may occur, surgeon may place lumbar CSF drain to maintain CSF decompression in early postoperative period; in postanesthesia care unit (PACU), avoid higher pressure mask ventilation; valve effect can induce tension pneumothorax; upper airway care of these patients postoperatively very crucial; if upper airway obstruction, better to insert LMA or re-intubate patient emergently than to use mask ventilation with higher pressure; object to avoid disruption of CSF leak site, especially if surgeon has sealed it with Fibrin glue or by packing the sphenoid sinus with fat or muscle

Cerebral aneurysm and subarachnoid hemorrhage: follow standards for craniotomy to maintain cerebral perfusion pressure; smooth induction and recovery; for cerebral aneurysm clipping, very important to avoid hypertension surging to avoid aneurysm rupture; if surgeon is applying temporary clipping of major vessel before clipping of aneurysm, important to induce hypertension, about 150 to 160, or MAP (mean arterial pressure) about 90% to 95%, to enhance perfusion; temporary clipping should not last >20 minutes to avoid permanent ischemia

Cerebral aneurysm repair techniques: microsurgical clipping or endovascular coiling

Complications after subarachnoid hemorrhage: cerebral vasospasm and delayed cerebral ischemia (DCI)

Delayed cerebral ischemia: occurs in 20% to 40% of patients; associated with increased incidence of cerebral infarction and mortality; usually caused by vasospasm, a reversible narrowing of subarachnoid arteries; usually occurs from third to fifth day up to 15th day after hemorrhage; peak at tenth day; in 70% of angiographic scans; causes symptoms in 20 to 30%; primarily describes findings of diagnostic studies; DCI should be used to describe hemiparesis, aphasia, and altered consciousness diagnosed by decrease of at least 2 points on Glasgow Coma scale

Pathophysiology of DCI: genetic factors: plasminogen activator inhibitor 1; main inhibitor of tissue plasminogen activator; inhibits conversion of plasminogen into active plasmin; 4G allele of plasminogen activator inhibitor 1 gene correlated

with higher levels of plasminogen activator inhibitor 1; associated with poor outcomes after subarachnoid hemorrhage, as it enhances microthrombosis; the endothelium nitric oxide synthase 27-VNTR, particularly 4E allele, significantly associated with aneurysmal subarachnoid hemorrhage; C allele significantly associated with cerebral vasospasm

Microemboli: induced by platelet aggregates in parenchymal microvessels in subarachnoid hemorrhage; one of main culprits in DCI; platelet activation associated with release of matrix metalloproteinase 9, which digests collagen 4 in cerebral blood vessel lamina; constriction of cortical or intraparenchymal artery precedes thrombus formation; can be at time of or delayed days after subarachnoid hemorrhage

Large artery angiographic vasospasm: induces endothelium injury that enhances platelet aggregation and microemboli formation; activation of clotting process in subarachnoid hemorrhage, which contributes to cessation of hemorrhage, can generate more emboli in distal circulation; systemic hypocoagulable response to subarachnoid hemorrhage enhances formation of microemboli of cerebral circulation; after subarachnoid hemorrhage, free hemoglobin in subarachnoid space induces expression of cell adhesion molecules in endothelial cells; facilitates migration of leukocytes to subarachnoid space, inducing inflammation and scavenging of nitric oxide, leading to impaired nitric oxide vasodilation; treat by giving calcium channel blocker nimodipine

Nimodipine: voltage-gated calcium channel antagonist; inhibits calcium entry into small muscle cells and neurons; prophylactic use diminishes risk of delayed cerebral ischemia; recommended by latest American Heart Association and American Stroke Association guidelines; class 1 level of evidence A; nimodipine improves functional outcome in subarachnoid hemorrhage, but has no effect in reducing angiographic vasospasm; attenuates neuronal calcium increase after cellular ischemia; prevents cortical spreading ischemia and cell death; increases fibrinolytic activity by decreasing plasminogen activator inhibitor type 1 levels in plasma; inhibits platelet function; diminishes release of thromboxane B2; 60 mg orally every 4 hours for 20 days from admission to ICU

Treatment: triple H therapy includes hypervolemia, hemodilution, and hypertension; most important is hyper blood pressure or perfusion pressure of brain, assuming normovolemia and maintaining hematocrit 30% or 32%

Takotsubo cardiomyopathy: another complication of subarachnoid hemorrhage; stress cardiomyopathy; described in early 1990s in Japan; name derived from appearance of left ventricle during diagnostic coronary angiogram for evaluation of acute coronary syndrome; classic left ventricular shape had round bottom and narrow neck due to stunning of apical ventricular segment; transient apical ballooning syndrome resembling Japanese octopus trap; pathophysiology may involve excessive release of catecholamines by myocardial sympathetic nerve terminals after subarachnoid hemorrhage, inducing hypothalamic injury; incidence 1% to 6%; predominantly postmenopausal women; associated with cardiac enzyme elevation and ST segment deviation, infrequently including elevation and T wave inversion; nonobstructive coronary artery disease in coronary angiogram and subarachnoid hemorrhage-induced left ventricular impairment; usually resolves within 2 to 4 weeks; no adverse sequelae; supportive management; inotropic support, intraaortic balloon counterpulsation, and aggressive diuresis; severe cases may be complicated by left ventricular apical thrombus formation; may need anticoagulation in context of subarachnoid hemorrhage

Complications of severe subarachnoid hemorrhage: hyponatremia; cerebral wasting syndrome and syndrome of inappropriate antidiuretic hormone secretion (SIADH); cerebral wasting syndrome involves renal salt loss and natriuresis by increased circulating natriuretic peptide, leading to negative sodium balance, hyponatremia, and intravascular depletion; SIADH involves increased antidiuretic hormone secretion with resulting inability to appropriately excrete free water, resulting in euvolemia or hypovolemia; both disorders associated with inappropriately elevated urine osmolality and urine sodium concentration; distinguish by volume status and urine output; do not correct hyponatremia faster than 12 to 24 millimolar per L in 24 hours to avoid central pontine myelinolysis; maintain euvolemia during hyponatremia management to avoid delayed cerebral ischemia; use caution with fluid restriction

Arteriovenous Malformation (AVM)

Overview: important to maintain normotension, avoid hypertension during resection of arteriovenous malformation; if using coiling, do not allow systolic to increase above 90 mm Hg to allow embolizing material (Onyx) to fix properly

Normal perfusion pressure breakthrough: can produce brain edema and brain hemorrhage after AVM correction, sudden obliteration of large arterial-venous shunts during embolization or resection; proposed pathophysiology — high blood flow through arteriovenous fistula creates region of chronic cerebral hypoperfusion; chronic cerebral hypotension leads to near maximum vasodilation and vasoparalysis; impairs vessel's ability to constrict or dilate; excision of lower resistance AVM shunt restores perfusion in formerly hypotensive regions of brain, leading to brain hyperemia

Management: diagnosis of exclusion; rule out common causes of cerebral edema and hemorrhage; maintaining normal blood pressure is crucial; treatment of cerebral edema and hemorrhage requires careful management of fluid and electrolyte balance, use of osmotic and loop diuretics; give attention to cerebral perfusion pressure

Awake Craniotomy

Overview: very challenging for anesthesiologist; performed in early 20th century by neurosurgeons Cushing and de Martel; use has increased recently as it is preferred setting for functional neurosurgery, including deep brain stimulation (DBS) for treatment of Parkinson disease and more recently for other conditions, including obesity, depression, and obsessive-compulsive disorders; may be indicated when intraoperative speech mapping is desired to avoid postoperative language disturbance following resection of epileptogenic foci in dominant hemisphere; used during surgery for tumor resection near or in the

Broca and Wernicke speech areas, awake craniotomy while maintaining verbal contact with patient optimizes neurological outcome; aim of anesthetic management is to ensure comfort, sedation, anesthesia, and hemodynamic control without interfering with patient cooperation and electrophysiologic monitoring; important to maintain adequate ventilation and patent airway; used to alternate asleep, awake, asleep; patients were fully anesthetized during major part of craniotomy, usually during cranium opening, awakened during stimulation, and anesthetized after resection; airway management by nasoendotracheal or laryngeal mask airway; alternative is sedation with infiltrative anesthesia of scalp

Drugs: propofol, fentanyl, remifentanil, midazolam, and dexmedetomidine commonly used; during sedation, block of auriculotemporal, zygomaticotemporal, supraorbital, supratrochlear, occipital, and greater occipital nerves allows for minimal discomfort during incision; doses up to 4.5 mg/kg of bupivacaine appear safe; propofol has a rapid onset of action and fast clearance from plasma by redistribution and metabolism, so level of sedation can be easily titrated; prolonged use can adversely affect mitochondrial function

Dexmedetomidine: offers cooperative sedation, anxiolysis, and analgesia without respiratory depression; valuable when eloquent areas of brain are stimulated; patient can do neurocognitive tasks; produces cerebral vasoconstriction by stimulating alpha 2B receptors in cerebral blood vessels; inhibits cerebral vasodilatation induced by hypercapnia, avoiding increased intracranial pressure and brain bulging; anticonvulsant effects

Recommendations: preferred technique is combination of dexmedetomidine and propofol infusion during patient positioning, application of head pin, and cranium opening; during resection period when patient is awake, stop propofol while reducing dexmedetomidine infusion; minimal doses of benzodiazepines during procedure to avoid respiratory depression and allow patient to perform neurocognitive tests

Complications: average 9.5% seizure during awake craniotomy (range 0% to 24%); most seizures can be resolved by irrigation of surgical field with cold saline or administration of propofol; prophylaxis with antiepileptic drugs is helpful to prevent intraoperative seizures

Intraoperative hypertension and tachycardia: usually encountered during painful phases and emergence; managed by short-acting beta blockers esmolol and labetalol

Deep Brain Stimulation

Overview: DBS; electrical stimulation; same surgical lesioning of basal ganglia for treatment of Parkinson disease as surgery; targets subthalamic nucleus and globus pallidus interior; improves intractable epilepsy, restless leg syndrome, multiple sclerosis, major depressive disorder, obsessive compulsive disorder, and essential disorders

Anesthetic management: neuronal circuity between striatum and globus pallidus and subthalamic nucleus contains dopaminergic pathways involved in Parkinson disease; avoidance of gabaminergic drugs like benzodiazepines and opioids crucial for electrode insertion; drugs for Parkinson disease should be stopped in perioperative period for proper target identification, called "off period;" causes depression, delirium, rigidity, tremors, and laryngospasm that can cause airway obstruction; patients with Parkinson disease may have dysarthria and impaired vocal cord function; prone to aspiration; head usually fixed in frame; sedation administered until burr hole is made; at this point, sedation is stopped to decrease or allow for target identification; keep systolic blood pressure less than or equal to 140 mm Hg to minimize intracerebral hemorrhage (ICH); dexmedetomidine used to provide sedation and anxiolysis with minimal effect on respiration; sympathicolytic effect of dexmedetomidine helps control blood pressure

Complications: recent analysis of 258 DBS cases found 11.6% complication rate; includes airway, respiratory, neurologic, and psychological problems; age above 64 independent risk factor for anesthetic complications; 3.6% intracerebral hemorrhage and seizures; 1.6% aspiration; 1.2% propofol potential cause of sudden sneezing

Interventional Neuroradiology (INR)

Overview: for endovascular surgery; has emerged as distinct specialty; treatment by endovascular access for purpose of delivering therapeutic drugs and devices; procedures classified based on aim; closing or occluding procedures include embolization of aneurysmal AVMs and fistula; also preoperative embolization of vascular tumors such as meningiomas; opening procedures include treatment of cerebral vasospasm or stenosis by angioplasty and stenting and chemical and mechanical thrombolysis in stroke

Radiation: digital subtraction angiography delivers more radiation than fluoroscopy; ionizing radiation follows inverse square law; radiation exposure drops off proportionally to square of distance from source; minimize activity near head; use extension tubing for infusion and monitoring

Uses: cerebral aneurysm clip coiling and management of AVM; small AVM can be cured by embolization; embolization of large AVMs can help to shrink size, thus reducing bleeding during subsequent surgery; 1% to 1.6% mortality after AVM embolization; 5% to 7% morbidity; embolization with glue into draining vein may result in venous obstruction and pulmonary embolization; general anesthesia often preferred during procedure to facilitate visualization of obstructions and prevent patient movement; controlled hypotension may be required to reduce flow across AVM; can worsen intracerebral steal adjacent to AVM; after embolization, monitor for perfusion pressure breakthrough; restoration of normal systemic pressure to a chronically hypotensive vascular bed may overwhelm autoregulation and result in hemorrhage or edema; maintain arterial pressure 15% to 20% below normal after procedure

Endovascular coiling: alternative to clipping; introduced in 1990s; number of procedures has greatly increased over past 2 decades; involves access to aneurysm with microcatheter and deployment of platinum coils to occlude aneurysm; adjuncts include balloon- and stent-assisted techniques, which can prevent coil prolapse and decrease risk of recurrence

Flow diverting stents: recently emerged as useful tool for treatment of aneurysms that were difficult to treat with clipping or coiling; lower porosity than other intracranial stents, which causes stasis of blood flow within aneurysm; leads to thrombosis and eventually occlusion while permitting patency of covered branch vessels

Choosing treatment modality: depends on aneurysm location and shape, patient clinical status and comorbidities, and preferences of patient and surgeon; randomized studies insufficient for strong conclusions; International Subarachnoid Aneurysm Trial (ISAT) found lower rate of death or dependency with coiling, 11%, versus clipping, 14%, but only 22% of eligible patients randomized; follow-up study of deaths, and clinical outcomes in 1644 patients showed that patients in coiling group were more likely to be alive and independent at 10 years than patients in clipping group; Barrow Ruptured Aneurysm Trial (BRAT) found better outcomes for coiling versus clipping for patients with posterior circulation aneurysms; no difference for anterior circulation; aneurysm morphology important; narrow neck favorable for coiling; older age, medical comorbidities, and poor clinical grade may favor endovascular therapy, as these patients may be at higher risk for adverse events; although trials flawed by selection bias and crossover, coiling has more favorable outcomes for rupture and posterior circulation aneurysm; decision-making continues to rely on operator experience

Anesthetic techniques for INR: usually general anesthesia; has advantage of immobile patient with improved image quality, patient comfort, and better control of respiratory and hemodynamic profile; disadvantage — inability to perform neurologic assessment; adverse hemodynamic and physiological consequences of endotracheal intubation and extubation include hypertension, coughing, or straining that can lead to increased ICP

Dexmedetomidine: ideal agent for sedation; patients are arousable and cooperative when stimulated; no respiratory depressant effect; used extensively in endovascular embolization

Sedation: employ standardized techniques tailored to optimize condition for serial neurological exams; standardized sedation avoids hemodynamic changes associated with intubation and emergence; monitored anesthesia care associated with better outcomes and improved mortality compared to general anesthesia during intraarterial therapy for acute ischemic stroke procedures; disadvantages include unprotected airway with risk of aspiration and potential hypoxia, hypercapnia, and sudden patient movement; delays in managing neurological emergency can occur

Blood pressure considerations: hypertension may be needed for procedures for cerebral vessel occlusion or vasospasm; hypotension may be needed to slow blood flow in feeding artery of AVM before glue injection; significant volume of heparinized flush solution and radiographic contrast often used; may need diuretics such as mannitol and furosemide; hypothermia can occur; keep temperature near normal

Postoperative care: maintain modest hypotension post-AVM embolization to prevent cerebral edema and hemorrhage; keep MAP 5% to 20% below baseline for 24 hours; MAP of 22 to 30 above baseline may be required to maintain cerebral perfusion with occlusive lesions or vasospasm; use phenylephrine or norepinephrine infusion; nausea and vomiting can occur as side effects of contrast or anesthetic

Intracranial Endoscopic Procedures

Overview: first performed in 1910; in 1970s, advances in fiber optics led to steerable neuroendoscopes; complex surgery within ventricular space in adults, children, and neonates; hydrocephalus patients with noncommunicating hydrocephalus due to aqueductal stenosis or space-occupying lesions of midbrain or posterior fossa can have CSF flow internally corrected through creation of opening of third ventricle; common complication of traditionally placed shunt system is obstruction of ventricular catheter tip from adjacent tissue; rigid fiber optic endoscope has been found to be safe and efficient for inserting ventricular catheter with improved accuracy over conventional method

Contraindications: patients with normal ventricular anatomy and those with an intraventricular hemorrhage or history of meningitis; damage to walls of third ventricle may occur in patients with smaller ventricular size

Technique: optimal position for endoscopic entry into third ventricle is usually supine with slight flexion of neck or with head tilted between 45 and 90 degrees; cranium may need to be fixed in head frame; endoscope introduced into skull through coronal burr hole; ventricular system entered via frontal horn and endoscope advanced into third ventricle, where mammillary bodies (an important landmark) can be visualized; tuber cinereum is immediately beyond; beneath this membrane are basilar artery and basal cistern; in patient with aqueductal stenosis, fenestration of this membrane creates opening through which CSF can be drained by passing through aqueduct of Sylvius; operating in fluid-filled cavities requires intermittent or continuous warm irrigant fluid; lactated Ringer's or normal saline used to maintain adequate ventricular pressure and visibility; fluid usually infused under pressure or gravity feed; allowed to egress passively through open port of endoscope; inadequate venting of irrigant fluid leads to marked increase in ICP, detected by increased blood pressure, bradycardia, and Cushing reflex

Toxic reactions: high fever and headaches due to meningeal irritation; can occur with large volumes of saline irrigation; artificial CSF has been used to reduce these reactions

Surgical complications: acute increase in intratranscranial pressure and injury to brain structures, including basilar artery, and hemorrhage; intracranial bleeding secondary to instrumentation can be catastrophic; intracranial hypotension can occur; usually follows sudden ventricular decompression, removal of CSF, causing pressure changes at level of midbrain and hypothalamus; can lead to sudden alteration of heart rate and blood pressure; hypothermia can occur, especially with large volume of irrigation fluid; cardiac arrhythmias in form of bradycardia and asystole can occur during stimulation of floor of third ventricle due to its proximity to vasomotor center or as result of inadequate venting of irrigant fluid; injury to intracranial structures may result in short-term memory loss, injury to fornix, SIADH, injury to hypothalamus, bleeding of pseudoaneurysm formation, injury to basilar artery; postoperative complications including transient confusion, headaches, and unresponsiveness have been described; patients with hydrocephalus may have hypovolemia due to vomiting, fluid restriction, contrast agents, or osmotic diuresis; adequate volume placement necessary prior to induction; general anesthesia with endotracheal intubation and controlled ventilation essential for immobility and because sudden increase in ICP may lead to vomiting; nitrous oxide avoided to prevent diffusion into air trapped in ventricles and subdural space following decompression, resulting in tension pneumocephalus

Anesthesia: can be maintained with sevoflurane or propofol with remifentanil infusion; intra-arterial monitoring recommended in view of hemodynamic variability and need for arterial blood sampling

Diabetes Insipidus

Overview: antidiuretic hormone synthesized in supraoptic nuclei of hypothalamus; transported down supraoptic hypophyseal tract to posterior loop of pituitary gland; diabetes insipidus rarely occurs intraoperatively, usually occurs 4 to 12 hours postoperatively

Clinical picture: polyuria in association with rising serum osmolality; diagnosis made by comparison of osmolalities of urine and serum; hypoosmolar urine with elevated and rising serum osmolality strongly supports diagnosis

Treatment: half-normal saline and 5% dextrose in water are commonly used as replacement fluids; be aware of hyperglycemia when large volume of 5% dextrose in water are used; unacceptable fluid regimen formerly used calls for maintenance of fluids plus previous hour's urine output; puts both patient and anesthesiologist in "chasing your tail" situation; precludes patient who becomes iatrogenically fluid overloaded from returning to isovolemia; guarantees that the patient will become increasingly hypervolemic; if hourly requirement exceeds 350 to 400 mL, desmopressin acetate is often administered

Suggested Reading

Chen GZ et al: Digital subtraction CT angiography for the detection of posterior inferior cerebellar artery aneurysms: Comparison with digital subtraction angiography. *Eur Radiol* 2017 Sep;27(9):3744-51; **Dabus G et al:** Current options for the management of aneurysmal subarachnoid hemorrhage-induced cerebral vasospasm: A comprehensive review of the literature. *Interv Neurol* 2013 Oct 2;2(1):30-51; **Ellis JA et al:** Intracranial aneurysm: Diagnostic monitoring, current interventional practices, and advances. *Curr Treat Options Cardiovasc Med* 2018 Oct 24; 0(12):94; **Morris NA et al:** Transcranial Doppler waveforms during intra-aortic balloon pump counterpulsation for vasospasm detection after subarachnoid hemorrhage. *Neurosurgery* 2018 Sep 1;83(3):416-21; **Rangel-Castilla L et al:** Normal perfusion pressure breakthrough theory: A reappraisal after 35 years. *Neurosurg Rev* 2015 Jul;38(3):399-404; **Shetty RM et al:** BIS monitoring versus clinical assessment for sedation in mechanically ventilated adults in the intensive care unit and its impact on clinical outcomes and resource utilization. *Cochrane Database Syst Rev* 2018 Feb 21;2:CD011240.

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Neurological Trauma

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Overview: neurologic trauma includes peripheral nerve injuries, spinal cord injuries, brain injuries caused by neurotoxic substances, and traumatic brain injury (TBI); lecture focuses on different types of TBI, Glasgow Coma Scale (GCS), brain herniation and sites and symptoms, Brain Trauma Foundation guidelines for TBI, thresholds for pressure levels, treatment options and recommendations, suggested monitoring modalities, airway management in patients with TBI

Types of TBI: different forms include subdural hematoma, epidural hematoma, subarachnoid hemorrhage, contusion and intraparenchymal hemorrhage, or diffuse axonal injury (DAI)

- Subdural hematoma: usually occurs from trauma to the head, tearing of the bridging veins; concave shape, resembling crescent; contusion often underlying area of hematoma; surgical indications include GCS ≤8, hematoma >10 mm wide, or midline shift >5 mm
- Epidural hematoma: usually occurs as result of skull fracture; most often tear in middle meningeal artery leading to bleed, but can also be from medial meningeal vein or from other veins; location usually temporal, but can be parietal, frontal, or occipital; convex shape, resembling lentil; surgical indications include GCS ≤8, hematoma >15 mm wide, volume >30 mm, or midline shift >5 mm
- Subarachnoid hemorrhage: bleeding into area between arachnoid membrane and pia mater (arachnoid space); blood spreads into sulci of brain (can be followed on CT imaging); usually no mass effect from bleeding itself; surgical treatment for nontraumatic cases of spontaneous rupture of cerebral aneurysm with either open aneurysm clipping or neurointerventional coiling; patients with subarachnoid hemorrhage at high risk of vasospasm leading to cerebral ischemia
- Contusion or intraparenchymal hemorrhage: result of blow to head with underlying bleeding into parenchyma; often lesion on one side of direct impact (coup) and lesion on the other side of impact (contrecoup lesion); most commonly frontal or temporobasal because of irregular bone structure in these areas of skull; may evolve over time; may not be visible at beginning, so often not visible on initial CT scan; surgical indications include increasing intracranial pressure (ICP) of herniation sites despite maximum medical management, volume >20 mL if GCS between 6 and 8 or volume >50 mm in any kind of injury irrespective of ICP, and midline shift >5 mm
- DAIs: most devastating types of injury; occur in white matter tracts in brain; result from shear injuries to axons and myelin sheath; not visible on CT but can show as punctate lesions on MRI scan; surgical indications only for uncontrolled ICP

Surgical indicators: *GCS* — first described by Teasdale and Jennett (1974); communicates level of consciousness of patients with an acute brain injury; provides practical method for assessment of conscious level impairment in response to certain defined stimuli; used to define TBI severity and predict outcome; Brain Trauma Foundation guidelines include GCS as part of indications for ICP monitoring in patients with TBI; Advanced Trauma Life Support (ATLS) uses it for decision making in airway management; GCS 8 = intubate; the international classification of severity of TBI based on GCS, with highest score of 15, the lowest score of 3, no 0 score; TBI classified as mild, moderate, or severe; GCS of 13 to 15 defines mild TBI, moderate TBI has GCS between 9 and 12, everything ≤8 is severe TBI; GCS determined by structured assessment that includes check, observe, stimulate, and rate; *check* — to identify factors that might interfere with the assessment; *observe* — for spontaneous behaviors in any of 3 GCS components; *stimulate* — verbal and physical stimuli needed in patients without spontaneous behaviors; *rate* — judge observed response against presence or absence of defined criteria

- Eye opening: 4 points for opening before any stimulus; 3 points after spoken or shouted request; 2 points after fingertip stimulus; 1 point for not opening eye at all)
- Verbal response: 5 points maximum if patient oriented (*ie*, can correctly give name, place, and date); 4 points for confused patient (not oriented but communicating coherently); 3 points for intelligible single words only; 2 points if patient only makes sounds, moans and groans; 1 point for no verbal response at all
- Motor response: total of 6 points if patient obeys commands; 5 points for localizing (*eg*, patient brings hand above clavicle for stimulus on head or neck); 4 points for normal flexion responses (patient bends arm at elbow rapidly); 3 points for abnormal flexion; 2 points for extension response (*ie*, either extension of arm at elbow or legs); 1 point for no response at all; recommended sites for physical stimulation include fingertips (pressing), trapezius muscle (pinching), or supraorbital notch (pressing)

Herniation sites and herniation symptoms: can occur at different areas of brain, including underneath falx cerebri (cingulate herniation), through tentorium cerebelli (tentorial or uncal herniation if unilateral, or central herniation if bilateral, tonsillar herniation if through

foramen magnum); general symptoms include eye abnormalities, autonomic dysfunctions (*eg*, Cushing response with hypertension and bradycardia), motor dysfunction, other symptoms like nausea, vomiting, altered level of consciousness, etc

Cingulate herniation: trapping of one or both anterior cerebral arteries causes paramedian cortex infarction, leading to paralysis of lower extremities; with expansion of infarcted area, edema develops and leads to increased ICP, putting patient at increased risk of transtentorial herniation, central herniation, or both

Transtentorial herniation: unilateral herniation of temporal lobe causes compression of different structures; compression of ipsilateral third cranial nerve leads to unilateral dilated, fixed pupils and oculomotor paresis; compression of the posterior cerebral artery leads to contralateral homonymous hemianopia and absence of blinking reflex; compression of contralateral third cranial nerve and cerebral peduncle leads to contralateral dilated pupils and oculomotor paresis, as well as ipsilateral hemiparesis; ipsilateral cerebral peduncle compression leads to contralateral hemiparesis and compression of upper brainstem, and area in and around thalamus will lead to impaired consciousness, abnormal breathing patterns, and fixed and unequal pupils; further compromise of brainstem leads to loss of oculocephalic, oculovestibular, and corneal reflexes, and eventually to decerebrate posturing

Central herniation: symptoms occur when both temporal lobes herniate because of bilateral masses or diffuse brain edema; causes bilateral damage to midbrain with symptoms such as fixed pupils in midposition and decerebrate posturing; symptoms in addition to same symptoms as transtentorial herniation; further compromise of brain stem leads to loss of all brainstem reflexes, disappearance of decerebrate posturing, respiration cessation, and eventually brain death

Tonsillar herniation: symptoms result from brainstem compression and obstruction of CSF flow; will initially lead to acute hydrocephalus with impaired consciousness, headache, vomiting, and meningismus; with cerebellar tonsil herniation, disconjugate eye movements; eventually, tonsillar herniation can lead to respiratory and cardiac arrest

2016 Brain Trauma Foundation TBI guidelines (4th edition): refers to threshold guidelines for blood pressure (BP), ICP, and cerebral perfusion pressure (CPP); refers to specific treatments of TBI and recommends when to use certain monitors; recommendation levels based on different qualities of evidence; Level I based on high-quality body of evidence; Level IIA based on moderate-quality body of evidence; Levels IIB and III based on low-quality body of evidence

Penumbra: areas of brain damaged but not yet dead, offering promise to rescue brain tissue with appropriate therapies; penumbra region typically occurs when blood flow drops <20 mL per 100 g of brain tissue per min; at this point, electrical communication between neurons fails, cells in these regions alive but metabolism inhibited; neurons may eventually begin to depolarize again; areas of brain generally do not become infarcted until blood flow to region drops <10 mL to 12 mL per 100 g per minute; at this point, glutamate release becomes unregulated, ion pumps inhibited, and adenosine triphosphate synthesis stops, ultimately causing intracellular processes disruption and neuronal death

BP: plays a critical role; maintaining systolic BP important to prevent secondary injury cascade after severe TBI; evidence shows mortality of 35% in patients admitted with systolic BP <85 mm Hg compared with only 6% of patients with high systolic BP; also, hypertension shown to correlate with diffuse brain swelling, leading to increased ICP; several underlying pathophysiologic mechanisms; if autoregulation remains intact, drop systolic BP triggers autoregulatory vasodilation in attempt to maintain adequate brain perfusion, resulting in increased cerebral blood volume, in turn elevating ICP; if autoregulation not intact, dependency on systolic BP to prevent cerebral ischemia (single most important secondary insult)

Hypertension: defined as systolic BP <90 mm Hg but evidence now supports higher level that varies by age; *Level III recommendation* — maintain systolic BP ≥100 mm Hg for patients aged 50 to 69 yrs, higher for younger and older patients (≥110 mm Hg for patients aged 15 to 49 yrs or >70 years)

ICP: pressure inside cranial vault, affected by intracranial contents (primarily brain, blood, and CSF); *Monro–Kellie hypothesis* — under normal conditions, fixed volumes for intracranial compartment space, cerebral blood volume, and volume inside cranium, if any component volume increases, compensation must occur to maintain ICP within normal range; these compensatory mechanisms include displacement of CSF and venous blood downward into the spinal spaces and decrease in blood volume; compensatory measures allow for maintenance of ICP within normal range of 0 mm Hg to 10 mm Hg; as mass lesions occupy more volume, intracranial compliance decreases and elastance increases; critical threshold reached when space-occupying lesions can no longer expand without neuronal injury, herniation, or brain death; *ICP Level IIB recommendation* — treating ICP >22 mm Hg recommended because values above this level associated with increased mortality

CPP: difference between mean arterial BP and ICP; can only be calculated when ICP known, should be factored into decision whether to place ICP monitor; valuable measure to optimize care of patients with TBI, as surrogate measure for delivery of nutrients to brain; BP metric to which brain autoregulatory mechanisms respond; literature suggests ICP elevation can be tolerated as long as acceptable CPP values maintained; study shows that the CPP values >70 mm Hg associated with elevated risk for respiratory complications and poorer outcome; patients with intact autoregulation best served by higher CPP values, pressure-passive patients with dysfunctional pressure autoregulation do better with lower CPP values; suggested that optimal CPP value may need to be tailored to individual patients; CPP levels of recommendation IIB and III; *Level IIB recommendation* — target through perfusion pressure value for survival and favorable outcomes 60 mm Hg to 70 mm Hg, whether 60 mm Hg or 70 mm Hg minimum optimal CPP threshold unclear and may depend on patient's autoregulatory status; *Level III recommendation* — avoid aggressive attempts to maintain CPP >70 mm Hg with fluids and vasopressors;

may be considered because of risk of adult respiratory failure, (shown to occur more often in patients in whom aggressive attempts have been made to increase CPP >70 mm Hg)

2016 Brain Trauma Foundation TBI treatment recommendation guidelines: recommendations for several different treatment modalities include

Decompressive craniectomy: surgical removal of portion of skull; cerebral edema can result from combination of several pathologic mechanisms associated with primary and secondary injury patterns and TBI; as pressure within skull increases, brain tissue displacement can lead to cerebral herniation, resulting in disability or death; decompressive craniectomy performed for purpose of relieving elevated ICP with outcome improvement in specific TBI patients; *Level IIA recommendation for decompressive craniectomy* — bifrontal decompressive craniectomy not recommended to improve outcomes as measured by GCS at 6 months postinjury in severe TBI patients with diffuse injury without mass lesions, and with ICP elevation >20 mm Hg for>15 mins within 1-hr period, refractory to first-tier therapies; however, this procedure demonstrated to reduce ICP and to minimize days in intensive care unit; large frontotemporoparietal decompressive craniectomy (not <12 by 15 cm or 15 cm in diameter) recommended over small frontotemporoparietal decompressive craniectomy for reduced mortality and improved neurologic outcomes in patients with severe TBI

Prophylactic hypothermia: well recognized to preserve cells and tissue; evidence supports administration of hypothermia as standard of care for neuroprotection after cardiac arrest from acute coronary syndromes; longstanding interest in applying hypothermia to reduce tissue damage associated with cerebral nervous system trauma; however, benefit cannot be presumed; hypothermia well known for ability to reduce ICP, but risks include coagulopathy and immunosuppression; profound hypothermia carries additional risk of cardiac dysrhythmia and death; hypothermia can be administered either early after injury or prior to ICP elevation (prophylactic) or as treatment for refractory ICP elevation (therapeutic); *Level IIB recommendation* — early (within 2 hrs), short-term (48 hrs post injury) prophylactic hypothermia not recommended to improve outcomes in patients with diffuse injury

Hyperosmolar therapy: mannitol and hypertonic saline routinely used hyperosmolar agents; choice determined by specific circumstances; hypertonic saline administration may be hazardous for hyponatremic patients; although mannitol can be used as resuscitation fluid, eventual diuretic effect undesirable in hypotensive patients and attention needs to be paid to replacing intravascular volume losses; while mannitol previously thought to reduce ICP through simple brain dehydration, both mannitol and hypertonic saline work to reduce ICP, at least in part, through reducing blood viscosity, leading to improved microcirculatory flow and blood constituents and consequent vasoconstrictions of pial arterioles, resulting in decreased cerebral blood volume and ICP; *Level I, II, and III recommendations* — insufficient evidence about effects on clinical outcomes to support specific recommendation, or to support use of any specific agent, for patients with severe TBI; recommendations from the prior (3rd) edition, did not support evidence meeting current standards; mannitol effective for control of raised ICP at doses of 0.25 gm/kg to 1 gm/kg of body weight; avoid arterial hypotension (systolic BP <90); restrict mannitol use before ICP monitoring of patients with signs of transtentorial herniation or progressive neurologic deterioration not attributable to extracranial causes

CSF drainage: management of external ventricular drainage (EVD) systems in patients with severe TBI remains controversial; EVD in closed position allows for ICP monitoring, while in open position spinal fluid drainage can occur; *Level III recommendation* — EVD system zeroed at the midbrain with continuous drainage of CSF may be considered to lower ICP burden more effectively than intermittent use; use of CSF drainage to lower ICP in patients with initial GCS <6 during the first 12 hrs after injury may be considered

Ventilation therapies: patients with severe TBI require definitive airway protection because risk of pulmonary aspiration or compromised respiratory drive and function; may also require transient hyperventilation to treat cerebral herniation; normal ventilation current goal for patients with severe TBI in absence of cerebral herniation; normal partial pressure of CO_2 in arterial blood ($PaCO_2$) ranges from 35 mm Hg to 45 mm Hg; $PaCO_2$ measure of arterial levels of CO_2, heavily depends on metabolic rate; $PaCO_2$ exhalation results in removal of metabolic waste; during times of high metabolism, respiratory rate normally increases to lower $PaCO_2$ levels; under normal conditions, $PaCO_2$ most powerful determinant of cerebral blood flow (CBF) and, between 20 mm Hg and 80 mm Hg, CBF linearly responsive to $PaCO_2$, important to meet brain's metabolic demands; low $PaCO_2$ thus results in low CBF and may result in cerebral ischemia, while high $PaCO_2$ levels can result in cerebral hyperemia and high ICP; therefore, providing optimal CBF important under all conditions; *Level IIB recommendation for ventilation therapies* — prolonged prophylactic hyperventilation with $PaCO_2$ in arterial blood of ≤25 mm Hg not recommended); recommendations from prior edition not supported by evidence meeting current standard; hyperventilation recommended as temporizing measure for reduction of elevated ICP; avoid hyperventilation during first 24 hrs after injury when CBF often critically reduced; if hyperventilation used, jugular venous O_2 saturation or brain tissue O_2 partial pressure (PaO_2) measurements recommended to monitor O_2 delivery

Anesthetics, analgesics, and sedatives: important, commonly used therapies in acute TBI for several reasons including prophylaxis or control of intracranial hypertension and seizures; barbiturates have long history of being used to control ICP by preventing unnecessary movement, coughing, and straining against endotracheal tubes as well as suppression of metabolism and alteration of cerebral vascular tone; decreased cerebral metabolism and O_2 consumption may be neuroprotective in some patients; anesthetics and sedatives, such as barbiturates, may also improve coupling of regional blood flow to metabolic demands, resulting in higher brain oxygenation with lower CBF, and decreased ICP from decreased cerebral blood volume; other brain-protective mechanisms include inhibition of O_2 radical–mediated

lipid peroxidation; *side effects* — hypotension, decreased cardiac output, increased intrapulmonary shunting that may lead to hypoxia; may give rise to paradoxical decrease in CPP, which may negate benefits of decreased ICP; anesthetics such as propofol associated with hyperkalemia, metabolic acidosis, myocardial failure, rhabdomyolysis, death; *Level IIB recommendation* — administer barbiturates to induce burst suppression measured by electroencephalography (EEG), as prophylaxis against development of ICP not recommended; high-dose barbiturate administration recommended to control elevated ICP refractory to maximum standard medical and surgical treatment; hemodynamic stability essential before and during barbiturate therapy; propofol recommended for ICP control but not for improvement in mortality or 6-month outcomes; caution required, as high-dose propofol can produce significant morbidity

Steroids: based on experience with patients with brain tumors, glucocorticoids became commonly administered to patients undergoing variety of neurosurgical procedures and became commonplace in treatment of severe TBI; however, studies in severe TBI patients failed to find benefit; the Corticosteroid Randomization After Significant Head Injury (CRASH) trial was designed to provide high-quality evidence on impact of steroids on patients with TBI; *Level I recommendation* — steroids not recommended for improving outcome or reducing ICP; in patients with severe TBI, high-dose methylprednisolone associated with increased mortality, contraindicated

Nutrition: Level IIA and IIB recommendations; *Level IIA recommendation* — feeding patients to attain basal caloric replacement at least by 5th day and, at most, by 7th day postinjury recommended to decrease mortality; *Level IIB recommendation* — transgastric jejunal feeding recommended to reduce incidence of ventilator-associated pneumonia (VAP)

Infection prophylaxis: severe TBI can increase susceptibility to infection because of necessary mechanical ventilation to prevent airway obstruction, aspiration, and consequential hypoxia, in addition to invasive monitoring; infection risks such as VAP and central line-associated bacteremia increased in all critically ill patients; patients undergoing ICP monitoring reported to have related infection rates as high as 27%; *Level IIA recommendation* — early tracheostomy recommended to reduce mechanical ventilation days when overall benefit felt to outweigh complications associated with such procedure; however, no evidence that early tracheostomy reduces mortality or rate of nosocomial pneumonia; use of povidone-iodine oral care not recommended to reduce VAP and may cause increased risk of acute respiratory distress syndrome; *Level III recommendation for infection prophylaxis* — antimicrobial-impregnated catheters may be considered to prevent catheter-related infections during EVD

Deep vein thrombosis (DVT) prophylaxis: patients with severe TBI can be at significant risk for venous thromboembolism due to hypercoagulability resulting from primary brain injury, prolonged periods of immobilization, and focal motor deficits; if untreated, DVT can result in potentially debilitating or fatal pulmonary embolism; particular concern, initiation of pharmacologic VTE prophylaxis, which, in conjunction with mechanical compression boots, has increased effectiveness over mechanical prophylaxis alone; however, such drugs constitute low-dose anticoagulation with potential to result in clinically significant intracranial hemorrhage (ICH) expansion; *Level III recommendation for DVT prophylaxis* — low-molecular-weight heparin or low-dose unfractionated heparin may be used in combination with mechanical prophylaxis; increased risk for ICH expansion; in addition to compression stockings, pharmacologic prophylaxis may be considered if brain injury stable and benefit considered to outweigh the risk of increased ICH; insufficient evidence to support recommendations regarding preferred agent, dose, or timing of pharmacologic prophylaxis for DVT

Seizure prophylaxis: acute symptomatic seizures may occur as result of severe TBI; such posttraumatic seizures classified as early when occur within 7 days of injury or late when they occur after 7 days post injury; posttraumatic epilepsy defined as recurrent seizures >7 days following injury; in patients with severe TBI, rate of clinical posttraumatic seizures may be as high as 12%, while that of subclinical seizures detected on EEG may be as high as 20% to 25%; risk factors for early posttraumatic seizures include GCS ≤10, immediate seizures; posttraumatic amnesia for <30 mins; linear or depressed skull fracture; penetrating head injury; subdural, epidural, or intracerebral hematoma; cortical contusion; aged ≤65 yrs; chronic alcoholism; *Level IIA recommendation for seizure prophylaxis* — prophylactic use of phenytoin or valproate not recommended for preventing late posttraumatic seizures; phenytoin recommended to decrease incidence of early posttraumatic seizures (within 7 days of injury), when overall benefit felt to outweigh complications associated with such treatment; however, early posttraumatic seizures have not been associated with worse outcomes; insufficient evidence to recommend levetiracetam (Keppra, Roweepra, Spritam) over phenytoin regarding efficacy in preventing early posttraumatic seizures and toxicity

Summary for anesthesiologist working with 2016 Brain Trauma Foundation TBI guidelines: maintain adequate systolic BP (either 100 mm Hg or 110 mm Hg, depending on age of patient); maintain adequate CPPs; treat increased ICPs; modalities include ventilation therapies (hypoventilation not <25 mm Hg only for short term to prevent herniation, hyperosmolar therapy with either hypertonic saline or mannitol, or anesthesia using anesthetics, analgesics, and sedatives such as propofol)

Airway management in patients with TBI: patients diagnosed with severe TBI as primary injury have a 7% to 8% risk of concomitant cervical spine injury, may not be obvious; spinal cord injury without radiographic abnormality (SCIWORA) denotes objective clinical signs of posttraumatic spinal cord injury without evidence of fracture or malalignment on plain radiographs or CT scans; most commonly seen in children but can also be seen in adults and, in rare cases, thoracolumbar spinal cord can be affected; MRIs have become valuable diagnostic tool in patients with SCIWORA because of superior ability to identify soft tissue lesions such as cord edema, hematomas, transections, and discoligamentous injuries that may not

be visualized on plain radiographs and CT scans; Farag (2016) states to keep the neck in neutral position with minimal movement during intubation for patients with TBI due to possible cervical spine injury; direct laryngoscopy may not be suitable in cases of cervical myelopathy and instability; manual inline stabilization can impair glottic view and increase subluxation; cervical spine movements during video laryngoscopy may be less than with direct laryngoscopy; fiberoptic intubation allows minimal neck movement, may be preferable for airway management during cervical spine injury; according to American Society of Anesthesiologists closed-claims analysis (2011), majority of cervical spinal cord injuries do not occur in cases with trauma, cervical spine instability, or airway management problems, but rather in injuries associated with cervical spine surgery, sitting procedures, or cervical spondylosis

Endotracheal intubation in patients with elevated ICP — caution: head should be elevated immediately after intubation; if possible, intubate in reverse Trendelenburg position; use adequate sedative, analgesics, and muscle relaxants to prevent reflex sympathetic response during intubation, as well as coughing; avoid aspiration; avoid hypoventilation (may increase ICP); avoid hyperventilation (cerebral vasoconstriction increases injury to ischemic area); avoid hypoxia (may exacerbate cerebral injury); maintain moderate hyperoxemia with PaO_2 between 110 mm Hg and 300 mm Hg; maintain CPPs >60 mm Hg

Suggested Reading

Carney N et al: Guidelines for the management of severe traumatic brain injury. Fourth edition. *Neurosurgery*. 2017;80(1):6-15; **Farag E et al:** Airway management for cervical spine surgery. *Best Pract Res Clin Anaesthesiol*. 2016;30(1):13-25; **Hindman BJ et al:** Cervical spinal cord, root, and bony spine injuries. A closed claim analysis. *Anesthesiology*. 2011;114(4):792-5; **Teasdale G et al:** Assessment of coma and impaired consciousness. A practical scale. *Lancet*. 1974;2(7872):81-4.

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Acute and Chronic Respiratory Problems

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Lung disease: categorized into restrictive and obstructive; clinical symptoms include chronic cough, dyspnea, and increased mucus secretions; differentiating between restrictive and obstructive lung disease requires physical examination and laboratory assessment

Restrictive lung disease: characterized by ability of lung to expand on inspiration; defined as reduction in both forced expiratory volume (FEV) and forced vital capacity (FVC); in restrictive lung disease, FEV declines less than FVC, leading to increased FEV/FVC ratio; patients with restrictive pattern can have either normal or higher FEV/FVC ratio (~70% in people without lung pathology)

Etiologies of restrictive lung disease:

Parenchymal: either acute or chronic; acute parenchymal etiologies include adult respiratory distress syndrome and neonatal respiratory distress syndrome; chronic parenchymal disease includes sarcoidosis, Wegener granulomatosis and Goodpasture syndrome

Pleural: include mechanical issues (*eg*, pneumothorax, pleural effusion), chest wall compliance (*eg*, ankylosing spondylitis and scoliosis create physical barrier to lung actually inflating, causing physical restriction), and neuromuscular diseases (*eg*, Guillain-Barre and amyotrophic lateral sclerosis)

Obstructive lung disease: characterized by airflow resistance; in contrast to restrictive lung disease, patients have difficulty exhaling; increased chest wall and lung compliance; patients can inhale large volume but narrowing of airways make it difficult; disease process reduces FEV and FVC in approximately equal amounts, therefore maintaining or slightly decreasing ratio to <70%; typical follow-up after diagnosis includes administering bronchodilator challenge and then repeating pulmonary function tests (PFTs) to determine if patient had response to bronchodilator (bronchodilator-receptive patients)

Etiology of obstructive lung disease: asthma, chronic obstructive pulmonary disease (COPD), and bronchiectasis

Anesthesia in Patients with Lung Disease

Patient population: provides unique challenges in perioperative period; to avoid common complications, need to formulate and follow well-thought-out preanesthetic plan and history

Preoperative anesthetic planning: should include focused history and physical**,** perioperative risk factors discussed with family

History: family history and pertinent risk factors such as age, status of chronic lung disease, smoking history, chronic heart disease, American Society of Anesthesiologists (ASA) classification, obesity, asthma, obstructive sleep apnea; should also include list of any medications such as amiodarone or bleomycin known to cause respiratory compromise in chronic setting, or any environmental exposure such as asbestos, coal, or beryllium dust; *physical exam* — should include auscultating for rales, rhonchi, or wheezing; note respiratory rate and inspect chest for use of accessory muscles or retractions during respiration; note pulse oximetry (SpO_2) at baseline, either on room air or their normal baseline O_2 requirement if on home O_2; for those with suspected or known pulmonary disease undergoing cardiac or pulmonary procedures, obtain routine chest x-ray and current CT scan; asymptomatic patients with lung disease should not routinely receive imaging; symptomatic patients should be examined and receive appropriate imaging to assess for any consolidations, pleural effusions, overall size of lung fields, and any possible mass effect on airways

Specific laboratory tests: should include arterial blood gas (ABG); for those with known pulmonary disease undergoing pulmonary, cardiac, or large abdominal procedures, obtain baseline ABG to help establish set point for O_2 and CO_2 concentration and current blood pH; can also give anesthesiologist idea of whether current situation acute or chronic; chronic lung disease patients retain bicarbonate to buffer pH and maintain normal pH; to facilitate extubation at end of surgery, also helpful to determine safe level or baseline for what their CO_2, PO_2, and pH when patient actually functional and at baseline

PFTs (spirometry): used to assess preoperative patient and make decisions based on pulmonary procedures; these values can be subjective depending on experience of practitioner providing test and patient's effort (whether pain or lack of compliance with tests); false numbers can lead to inadequate conclusions and make test worthless; particularly important with thoracic or lung-reduction surgeries; many variables for PFTs correlated with poor outcomes; *values predicting increased postoperative complications following pulmonary resection* — FEV over 1 sec (FEV_1) <40% predicted, diffusion lung capacity <40% predicted, and maximal O_2 consumption (VO_2 max) <15 mL/kg/min

Scoring systems: many systems try to take into account PFTs, labs, and patient's functional status; no current consensus on which scoring system should be used but strongest correlates with patient's functional status (*ie,* nutritional condition, any infectious or comorbid conditions, type of pulmonary dysfunction, and specific surgery)

Thorough preoperative preparation and planning: includes preoperative respiratory therapy techniques (*eg*, lung-expansion therapy, deep-breathing exercises, incentive spirometry, percussive therapy, continuous positive airway pressure [CPAP], baseline home O_2 prior to surgery) to optimize patient; no particular modality proven superior to others; maximize drug therapy by initiating antibiotics for potential infectious etiology; patients should continue current bronchodilator regimen if on one already; add rescue bronchodilators preoperatively if patient shown to be responsive; if patient on chronic steroids or having urgent procedure where preoperative optimization impractical, consider pulse-dose steroids to reduce swelling and maximize respiratory response; *smoking cessation* — optimal timing of cessation debatable; while some studies say ≥4 wks prior to planned procedures best, others show as little as ≥2 days prior will prevent some complications; while cessation does increase other complications (*eg*, sloughing and mucolytic clearance), risks considered worth benefit; smoking cessation >4 wks advantageous; nutritional status (albumin ≥3.5 mg/dL) proven to reduce postoperative risk; absent current infection or exacerbation, if possible hold off elective procedures until after treatment; >3 max optimal, better outcomes, but not always practical in patients with chronic lung disease

Intraoperative strategy: current studies inconclusive, but data suggest avoiding airway manipulation reduces postoperative morbidity; if possible, avoid general anesthesia; use regional neuraxial techniques if possible; regional anesthesia should be utilized for postoperative pain management to minimize complications and maximize pain relief without use of narcotics; minimize use of long-acting neuromuscular blocking agents; avoid use of long-acting narcotics; use lung-sparing ventilation of 6 mL/kg to 8 mL/kg of ideal body weight (can cause atelectasis but minimizes volutrauma); add positive end-expiratory pressure (PEEP) ≥5 to decrease atelectasis; minimize work of breathing; nasogastric tube to decompress stomach for abdominal procedures will reduce intraabdominal pressure and allow diaphragm to have full excursion

Postoperative strategy: pain treatment should include nonsteroidal drugs and regional adjuncts to minimize use of narcotics while decreasing pain; will help patient achieve adequate pulmonary toilet; patients will not cough and deep breathe if it hurts; try to extubate patient on completion of case (increased prolonged mechanical inhalation associated with worse outcomes); sometimes not practical to extubate after surgery; preoperatively discuss with family and patient possibility of going to intensive care unit (ICU) intubated and waking up over next day or 2; if patient unable to liberate from mechanical ventilation, chest percussive or oscillatory breathing treatments should be used to facilitate mucociliary clearance; schedule bronchodilator therapy and consider steroids early if patient in respiratory failure; titrate O_2 as low as possible to minimize free radicals and maintain PO_2 of 60 mm Hg to 100 mm Hg; permissive hypercapnia acceptable in this patient population in absence of head trauma; initiate enteral feeding within first 24 hours in patients with prolonged intubation; intubated patients should receive minimal sedation per local protocol; titrate to sedation score in which patient arousable and comfortable (generally, Riker score of 3 or 4); oversedation can lead to complications and increased length of mechanical ventilation; use daily sedation and wake-up protocol in absence of contraindications; assess patient daily for extubation

Weaning goals: should be set by institution; generally this patient population should be able oxygenate and ventilate adequately on inspired O_2 concentration of 40%, pressure support of 10 cm H_2O, and PEEP of 5 cm H_2O; this population may or may not have baseline dysfunction and O_2 requirements, so may need modification; extubate to increased FiO_2 ratio or extubate to noninvasive positive pressure ventilation or CPAP if required

Postoperative complications

Common complications: pneumonia, prolonged intubation, delirium, atelectasis, pulmonary embolism, acute respiratory distress syndrome (ARDS)

ARDS: not unique to this patient population, but high risk; first described in case series of ICU patients who shared common features of unusually persistent tachypnea and hypoxemia accompanied by opacification on chest x-ray and associated poor lung compliance despite different underlying causes; Berlin definition**,** acute diffuse inflammatory lung injury leading to increased pulmonary vascular permeability, increased lung weight, and loss of aerated tissue**,** with hypoxemia and bilateral radiographic opacities and associated with increased venous admixture, increased physiologic dead space, and decreased lung compliance; *3 categories* — mild, PaO_2/FiO_2 ratio 200 to 300, ~27% mortality rate; moderate, PaO_2/FiO_2 ratio 100 to 200, ~32% mortality rate; severe, PaO_2/FiO_2 <100, ~45% mortality rate; these numbers must be on PEEP of ≥5 cm H_2O

Treatment: mechanical ventilation almost always required; ARDS by definition severely hypoxemic, but mechanical ventilation itself can actually damage lungs; ventilator-induced lung injury known as barotrauma or volutrauma; central goal of mechanical ventilation in ARDS to minimize additional damage from ventilator while maintaining adequate gas exchange; *current ARDS protocol for mechanical ventilation* — can start in any ventilator mode; initial tidal volumes should be 8 mL/kg of ideal body weight (ideal body weight must be calculated, so need patient's height); lungs do not increase with size of patient; set respiratory rate up to 35 breaths per minute to deliver expected minute ventilation requirement (generally ~7-9 L/min); set PEEP to ≥5 cm H_2O (generally patients will require much higher); tune FiO_2 to maintain an arterial O_2 saturation of 88% to 95%, which should correlate with PaO_2 of ~55 mm Hg to 80 mm Hg; titrate FiO_2 to <60%, if possible, to minimize free radicals; after setting initial ventilator strategy, start reducing tidal volumes to 7 mL/kg, then to 6 mL/kg, over a period of <4 hrs; primary goal while adjusting ventilator, to keep plateau pressurePlateau pressure: surrogate number for distention pressure of alveoli; measured during inspiratory hold of 0.5 secs to <30 cm H_2O (preferably lower, if possible) while maintaining decent blood gas parameters; may not be same as in average patient, as baseline PO_2 and CO_2 numbers may be lower in lung patient; higher plateau pressures vastly elevate risk for harmful

alveolar distention (ventilator-associated lung injury or volutrauma); if plateau pressures remain elevated, can reduce tidal volumes even farther, going as low as 4 mL/kg of ideal body weight; sedate patient more to decrease dyssynchrony; consider muscle relaxation if patient severely hypoxemic at end of ventilator adjustments; after sedation and muscle relaxation, consider adjuncts or other mechanisms for increased plateau pressures; rule out pneumothorax (chronic lung patients sometimes have blebs that will pop with high airway pressures and complicate things)

Permissive hypercapnia: can minimize plateau pressures; lower tidal volumes so low it results in hypoventilation; will increase PCO_2 and cause respiratory acidemia; paradigm shift from previous eras when achieving normal blood gas values was main goal of mechanical ventilation; now believed safe to allow pH to fall to ≥7.2; actual PCO_2 of little importance; when pH does fall <7.2, many physicians choose to administer sodium bicarbonate to maintain blood pH between 7.15 and 7.2; unknown if helpful, harmful, or neither; evidence lacking for any of these hypotheses but permissive hypercapnia does permit running lower tidal volumes, therefore running lower plateau pressures

Obese patients: lung size same in all patients but chest wall compliance changes depending on thickness and compliance of tissue; some studies say indicate underutilizing plateau pressure in ARDS on obese patients; obese ARDS patient may run higher plateau pressures at baseline than nonobese patients; titrating tidal volumes to plateau pressures of <30 cm H_2O may be inadequate to ventilate these patients and may result in worse outcomes; no current recommendations on how to treat obese patients with ARDS differently from nonobese; studies suggest considering allowing higher plateau pressures

Proning: consider if unable to oxygenate and ventilate patient adequately after following ARDSNet guidelines; improves ventilation-perfusing matching by transferring delivered O_2 into bloodstream more efficiently; helps keep alveolar units open and evenly distributed in end expiration; decreases or prevents ventilator-induced lung injury by rotating which lung fields actually being applied with force; through 1 or more of these mechanisms, proning believed to improve survival for patients with ARDS; in 2017, strong recommendation by major critical care societies for early proning of ARDS patients; PROSEVA trial (2013) demonstrated ~50% relative risk reduction and 17% absolute risk reduction for mortality; patients kept in prone position for 16 hrs/day (27 European centers experienced with prone positioning in ARDS); benefits of prone positioning not yet replicated in large US trial, but meta-analysis of 6 trials also concluded that prone positioning saves lives in ARDS when added to lung-protective ventilator strategy; safety concern when proning patients with inexperienced staff (patients have lines, sedation, and endotracheal tubes, and injuries possible with proning including falls and pressure ulcers on face); should be used with caution and only with right equipment and personnel

Alternative strategies: known as alternative or salvage or rescue ventilator strategies; include extracorporeal membrane oxygenation(ECMO), cardiac bypass, or high-frequency oscillatory ventilation (APRV, airway pressure-release ventilation, or bilevel); commonly used when everything else has failed and patient rapidly deteriorating; APRV most commonly used; studies have shown APRV not appropriate as first-line treatment for ARDS; some studies suggest ECMO good modality for ARDS, but difficult to compare ECMO with ventilatory strategies (no way to do randomized controlled trial); patient either receives ECMO or they do not, therefore, tends to be bias as organizations that do early ECMO tend to have good outcomes (some patients may have been fine without ECMO); insufficient evidence to suggest steroids in ARDS; however, patients with chronic lung disease may benefit from steroids, which should be considered in ARDS; practitioners have utilized nitric oxide (NO) in ARDS to dilate pulmonary vasculature and decrease airway pressures; studies say giving inhaled NO to patients with ARDS improves oxygenation but has not been demonstrated to improve survival; some studies suggest NO works well in children but studies have not carried over to adult population; improves lab values but not outcomes

Atelectasis: reversible collapse of lung tissue with loss of volume; common complication of mechanical ventilation; using lung-protective strategy will underventilate certain areas of the lung and cause atelectasis; along with supine positioning and general anesthesia, leads to increased risk of atelectasis; common causes include intrinsic or extrinsic airway compression, hypoventilation, or malpositioned endotracheal tube; large areas of atelectasis can cause symptomatic hypoxemia, but other symptoms (*eg*, increased white blood cells, fever) should be attributed to superimposed pneumonia rather than atelectasis; if patient has increased white count and fever, examine for underlying infection; diagnosis commonly made by chest x-ray, but if not clinically apparent, bronchoscopy or chest CT should be performed; treatment involves PEEP; maximize coughing and use incentive spirometry if patient able; if not intubated, patient should be walking (movement and walking increase lung mechanics)

Pneumothorax: patients with chronic lung disease on mechanical ventilation have higher incidence of pneumothorax; classified as simple, iatrogenic, or tension; *tension pneumothorax* — life-threatening condition characterized by hypotension, dyspnea, and increased PEEP pressures (if patient intubated)**, possibly** tracheal deviation; treatment involves emergent decompression**,** either with needle in second midclavicular intercostal space or tube thoracostomy, typically in fourth to fifth midaxillary intercostal space

Pulmonary embolism (PE): from asymptomatic to life-threatening catastrophe; typically occurs when deep vein thrombosis migrates to pulmonary arterial tree; *massive PE* — acute pulmonary embolus with obstructive shock pattern or systolic blood pressure of <90 mm Hg; *submassive PE* — acute PE without systemic hypotension but can have right ventricular dysfunction on echocardiogram or right heart strain on ECG or myocardial necrosis; *nonmassive or low-risk PE* — in patients with none of above severe features; effects of PEs proportional to speed of propagation of clot and degree of obstruction (increased pulmonary vascular resistance leads to right ventricular failure, which leads to obstructive shock); increasing alveolar dead space and ventilation/perfusion mismatch causes pulmonary

vasoconstriction to optimize gas exchange, leading to pulmonary infarction; patients can develop chronic pulmonary hypertension after obstructive event

Risk factors: lack of mobility, smoking, recent surgery, cancer, pregnancy; high risk in patient with lung disease; PE should be high on differential diagnosis

Treatment: if patient hemodynamically unstable and has significant right heart strain on echocardiogram, emergency thrombectomy should be attempted surgically (open procedure), endovascular retrieval method, or tPA administration; if patient not acutely decompensating, supportive treatment, along with therapeutic anticoagulation; most PEs discovered after they occurred

Suggested Reading

Brochard L et al: Mechanical ventilation to minimize progression of lung injury in acute respiratory failure. *Am J Respir Crit Care Med*. 2017;195(4):438-42; **Prabhu M et al:** Pre-anaesthetic evaluation of the patient with end-stage lung disease. *Best Pract Res Clin Anaesthesiol*. 2017;31(2):249-60; **Scholten EL et al:** Treatment of ARDS with prone positioning. *Chest*. 2017;151(1):215-24.

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Asthma, Allergy, and Anesthesia

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Asthma: disease of chronic inflammation with increasing prevalence in developing world; characterized by reversible expiratory airflow obstruction occurring in response to various stimuli with resultant bronchial hyperreactivity; American Academy of Allergy, Asthma & Immunology estimates that 300 million people worldwide have asthma, with ~250,000 deaths each year attributed to asthma; Centers for Disease Control and Prevention (CDC) estimates that 3396 adults in US died from asthma in 2015; asthma causes episodic acute attacks mingled with symptom-free periods; episodic attacks consist of wheezing, cough, breathlessness, and chest tightness, particularly at night and early morning; symptoms usually associated with widespread bronchoconstriction and airflow limitation at least partially reversible, either spontaneously or with treatment; patients may also demonstrate varying degrees of bronchial wall inflammation and increased mucus secretion; most attacks short-lived, but some patients experience daily airway obstruction

- Pathophysiology: atopic and nonatopic types; mechanisms such as respiratory infections, environmental irritants (*eg*, smoke, fumes, cold air), emotional distress, exercise, pharmacologic agents, and foods can produce varying degrees of bronchospasm
  - Atopic asthma: most common type; usually begins in childhood; skin testing usually results in immediate wheal-and-flare reaction to offending antigens; usually family history of allergy, urticaria, and eczema; genetic predisposition to type 1 hypersensitivity on exposure to environmental triggers; in airways, reaction set by sensitization to inhaled allergens, which stimulate induction of cells to secrete cytokines that promote allergic inflammation and stimulate B cells to produce immunoglobulin E (IgE) and other antibodies; these products induce early-phase reaction dominated by bronchoconstriction, increased mucus production, and increased vascular permeability; late-phase reaction involves inflammation, which in turn causes epithelial damage; other mediators include leukotrienes, acetylcholine, histamine, and prostaglandin D2
  - Nonatopic asthma: no evidence of allergic sensitization, skin testing usually negative; viral respiratory infections common mediators, with hypersensitivity of bronchial tree underlying asthma; virus-induced inflammation of respiratory mucosa believed to cause bronchospasm
- Effects on mechanics of ventilation and gas exchange: in asthma, airway resistance comprises most (>70%) of total lung resistance at normal breathing frequencies; relative contribution of airway resistance and lung tissue resistance appear to be independent of degree of smooth-muscle contraction; airway closure occurs at higher lung volumes in patients with asthma; secretions, edema, and spasm reduce airway lumen; these processes affect gas exchange distribution, as do decreasing or eliminating ventilation in areas affected by airway obstruction and by increasing exchange in other, less obstructed, areas
  - Gas exchange disturbances: expected in asthma, based on alveolar ventilation-perfusion inequalities; considerable range of local airway obstruction occurs leading to reduced ventilation; large variation in alveolar ventilation-perfusion ratios can be seen in single patient; causes increase in "physiologic dead space"; therefore, patient can simultaneously suffer from alveolar ventilation-perfusion, which causes hypoxemia and high alveolar ventilation-perfusion, mimicking dead-space inhalation and impeding CO_2 elimination; ongoing degrees of alveolar ventilation-perfusion mismatch exist in all asthmatic patients and can explain all hypoxemia; CO_2 elimination even more limited by alveolar ventilation-perfusion mismatch than O_2 transfer; rare to see hypercapnia, because increased CO_2 tension stimulates increased ventilation to bring $PaCO_2$ back toward normal; repeated bouts result in airway remodeling caused by structural changes in bronchial wall (*eg*, hypertrophy and hyperplasia of bronchial smooth muscle, epithelial injury, increased airway vascularity, increased subepithelial mucous gland hypertrophy or hyperplasia, and deposition of subepithelial collagen); infections with common respiratory pathogens (*eg*, respiratory syncytial virus and influenza) exacerbate chronic changes and cause serious exacerbation of disease
  - Gas trapping and hyperventilation from airway remodeling: in patients with airways obstructed from these processes, exhalation prolonged; in severe airway obstruction, exhalation not complete before next inhalation, resulting in dynamic hyperinflation; trapped gas in distal air spaces creates positive end-expiratory pressure (PEEP), also called intrinsic or auto-PEEP; in presence of auto-PEEP, breathing occurs on flatter portion of pressure-volume curve, meaning respiratory muscles must generate higher transpulmonary pressure to pull normal volume of air into lungs; creates increased work of breathing, with possible respiratory fatigue or even failure resulting in hypercapnia

Perioperative Management of Adult Patient with Asthma

Evaluation and preparation: patients with asthma should be assessed ≥1 wk before elective surgery to allow for additional testing that may be required after physical examination and for modifications or treatment, if necessary; especially important in patients undergoing thoracic surgery, open abdominal aortic aneurysm surgery, neurosurgery, upper abdominal surgery, and head and neck surgery; postoperative pulmonary complications most common in these patients; goal of preoperative assessment to reduce risk of perioperative pulmonary complications by continuing or optimizing patient's current therapy

History and clinical examination: patients with asthma usually very well attuned to level of control and can detect when not normal; information that helps determine likelihood of perioperative bronchospasm includes asthma severity, historical information (*eg*, food and drugs allergies, other known triggering irritants, use frequency of short-acting beta-2 agonist, hospitalizations, emergency room visits, critical care unit admissions, intubation history, current upper respiratory infection, oral glucocorticoid use, and, if known, forced expiratory volume in 1 sec [FEV1]/forced vital capacity [FVC] data); limited data to support the impact of any of these findings, but retrospective studies show patients who take asthma medications, noticed asthma symptoms, or visited medical facility, particularly in past 30 days, more likely to have perioperative bronchospasm and/or laryngospasm; physical examination should focus on presence or absence of wheezing, signs of lung infection, use of accessory muscles of respiration, and ease or difficulty of air movement

Perioperative testing: non–steroid-dependent, well-controlled patients with asthma generally don't require additional testing beyond what would be performed on nonasthmatic patient; baseline pulse oximetry data should be noted; for patients with moderate to severe asthma, pulmonary function testing (PFT) considered; spirometry most common PFT method, can be accomplished in preanesthetic visit as needed; FEV_1 and FVC most commonly performed tests; patients with FEV_1 of >60% but <80% predicted, and those with <60% predicted, should be referred to primary asthma physician for optimization before any elective procedure; laboratory testing requirements similar to nonasthmatic patients except for those taking high-dose beta-2 adrenergic agonists or with hypokalemia, hyperglycemia, and hypomagnesemia not uncommon and should be evaluated

Hypothalamic-pituitary axis (HPA) suppression: risk absent in patients taking glucocorticoids at any dose <3 weeks (*eg*, prednisone 5 mg/day for any duration or 10 mg every other day); stress dose of glucocorticoid before anesthesia induction should be given to patients taking either prednisone >20 mg/day for ≥3 weeks, or with cushingoid appearance; patients who have taken prolonged course or high dose of inhaled glucocorticoid may be at risk for subclinical HPA suppression from systemic absorption of medication, but little risk of symptomatic adrenal suppression or acute crisis

Other evaluations: arterial blood gas evaluation not routinely indicated; during attack of severe, persistent disease, may be helpful in guiding therapy; electrocardiography (ECG) should be ordered in accordance with current guidelines of American Heart Association and American College of Cardiology; no particular ECG changes associated with asthma

Chest radiographs: should be obtained only if underlying infection suspected; signs of hyperinflated lungs such flattened diaphragm common and provide no further diagnostic or treatment guidelines; overall, patient should continue baseline medications, including inhalers, up to day of surgery; theophylline should be discontinued night prior to surgery

Premedication: most patients with asthma may benefit from anxiolytic (*eg*, midazolam) before anesthesia, as anxiety known to trigger attack in some patients; anticholinergic drugs (*eg*, glycopyrrolate and atropine) dry secretions and decrease vagal airway responses, but resulting tachycardia not well tolerated in some patients; dexmedetomidine (alpha-2 agonist) provides anxiolytic effect, sympatholytic properties, and drawing of secretions without respiratory suppression; close monitoring of vital signs required since this drug may cause significant bradycardia and hypotension

Optimal Anesthesia Drugs and Techniques

Induction: bronchospasm can occur with any type of anesthesia; need to be prepared when anesthetizing patient with asthma; general anesthesia may be associated with increased risk of bronchospasm secondary to mechanical stimulation of airway; additional stimulation from airway suctioning, aspiration of gastric or pharyngeal contents, inhalation of cold anesthetic gases, and medication side effects can also cause bronchospasm; peritoneal insufflation during laparoscopy, as well as visceral manipulation, vagally stimulating events that can increase airway tone; anesthesia induction should achieve sufficient depth to block all these responses; propofol intravenous (IV) drug of choice for hemodynamically stable patient; ketamine has sympathomimetic bronchodilator properties (but not as pronounced as with propofol), making it useful for hemodynamically unstable patients; etomidate can be used safely, but lacks bronchodilatory effects and results in transient acute adrenal insufficiency; methohexital can be used as alternative to propofol but may cause more bronchoconstriction than other agents

Opioids (*eg*, fentanyl): can be administered during induction to supplement sedation and suppress airway reflexes; synthetic opioids (*eg*, fentanyl, remifentanil, sufentanil, and hydromorphone) release very little histamine and have been used safely in asthmatic patients; lidocaine IV can be given to suppress cough reflex during laryngoscopy and intubation; inhaled lidocaine should be avoided (airway irritant)

Airway management: goal of anesthetic induction to minimize risk of bronchospasm from various sources of stimulation by providing deep level of anesthesia during induction; while risk of bronchospasm lower with laryngeal mask airway (LMA), or even masked ventilation, compared with endotracheal intubation, decisions about placement of either of these airway-control devices should

be similar to that in nonasthmatic patients; according to randomized study, endotracheal intubation caused increased airway resistance but placement of LMA did not; however, after 10 mins of inhaled isoflurane, no difference in airway resistance between groups

Maintenance: isoflurane and sevoflurane (potent inhalational agents) bronchodilators, decrease airway responsiveness, and attenuate bronchospasm; bronchodilatory action may result from beta-2 receptor stimulation, causing increased intracellular cyclic adenosine monophosphate (cAMP) and relaxation of bronchial smooth muscle; sevoflurane preferred because more pronounced bronchodilatory properties and less irritating; desflurane extremely pungent and can cause increased airway resistance, secretions, coughing, laryngospasm, and bronchospasm; *nitrous oxide* — often used in conjunction with potent inhalational agent to help maintain anesthesia; *IV anesthetics* — may be used as either bolus or infusion, as part of total IV anesthetic (TIVA); various combinations of propofol, ketamine, lidocaine, and dexmedetomidine, as well as different opioids, can be used in this manner; *beta blockers* — commonly used during anesthesia to help control heart rate and blood pressure; nonselective beta blockers can cause bronchospasm; beta-1 selective drugs (*eg*, esmolol and metoprolol) less likely to cause bronchospasm; however, at high doses, this may diminish; labetalol (combined beta and alpha blocker) less likely to cause bronchospasm

Nondepolarizing muscle-blocking agents (NMBAs): most common cause of intraoperative allergic reactions; NMBAs such as rocuronium, cisatracurium, and vecuronium don't release appreciable amounts of histamine, thus preferred NMBAs for asthmatics

Regional anesthesia: good choice for peripheral procedures that can be completed with low-level neuraxial (epidural or spinal) anesthetic; caution required with neuraxial anesthesia (midthoracic or higher level can result in paralysis of accessory muscles of respiration); asthmatics may depend on this musculature to create active exhalation for adequate gas exchange; brachial plexus block may paralyze diaphragm by blocking phrenic nerve and not well tolerated by patients with baseline respiratory compromise

Ventilation during anesthesia: should prevent air trapping during controlled ventilation, thereby preventing stack breaths resulting in hyperinflation and, in extreme, barotrauma; reduction of inspiratory-expiratory ratio important strategy, but most effective means reduction of miniventilation by reducing both rate and tidal volume; *lung protective ventilation* — for severe asthmatics, should include controlled ventilation with reduced tidal volumes, reduced respiratory rate to allow for total exhalation, reduced inspiratory time, cautious use of PEEP, administration of inhaled bronchodilators as needed to reduce resistance to expiratory flow; PEEP use in asthmatics controversial (extrinsic PEEP can worsen air trapping, causing or exacerbating hyperinflation); PEEP, however, can prevent airway collapse by stenting airways open and decreasing air trapping; use requires constant monitoring for hyperinflation

Intraoperative bronchospasm: several issues that can mimic severe intraoperative bronchospasm must be ruled out quickly; these include absence of breath sounds (usually on left, secondary to mainstem endobronchial intubation), pneumothorax with decreased breath sounds bilaterally or singularly on one side and asymmetric inspiratory chest expansion (associated with high peak inspiratory pressures), pulmonary edema with frothy endotracheal tube secretions, and kinked or otherwise blocked endotracheal tube); severe bronchospasm can also be associated with anaphylactic reaction, usually accompanied by hypotension, tachycardia, and rash; severe intraoperative bronchospasm secondary to asthma while under anesthesia can present in many ways (*eg*, wheezing on chest auscultation, change in end-tidal CO_2 concentration with upsloping, decrease, or even absent end-tidal CO_2 waveform, decreased tidal volumes, high inspiratory pressures, decreasing O_2 saturation)

Initial management: administer 100% O_2 and hand ventilation to assess compliance; mild bronchospasm can be treated by increasing concentration of potent inhalational agent or by IV bolus of propofol or ketamine; if bronchospasm persists, rapidly acting beta-2 agonist (*eg*, albuterol) should be administered by inline nebulizer; additional pharmacologic agents such as anticholinergics, epinephrine, magnesium sulfate, and glucocorticoids can be given; unusual approaches include nitroglycerin, which causes direct smooth-muscle relaxation, and heliox, mixture of helium and O_2, which acts as temporizing agent while bronchospasm treated; extracorporeal membrane oxygenation (ECMO) reserved for most severe bronchospasm refractory to maximum medical and mechanical ventilatory therapy

Emergence from neuromuscular blockers and anesthesia: can be accompanied by bronchospasm as anesthetic levels reduced; short-acting beta-2 agonists should be administered before emergence; IV lidocaine may attenuate airway reactivity and help control coughing; deep extubation before emergence can be considered but has significant risk; emerging from anesthesia without protected airway exposes patient to possibility of aspirated gastric contents and bronchospasm

Postoperative management: if intraoperative course uneventful, postoperative management similar to that of nonasthmatic patient; if intraoperative severe bronchospasm has occurred, postoperative ventilation may be considered to allow time for maximum treatment, return of airway function, and extra time for NMBA reversal with or without reversal agents; other considerations include adequate pain control, bronchodilator therapy, incentive spirometry, deep breathing, and early mobilization; postoperative epidural anesthesia may be considered to reduce splinting, atelectasis, and provide superior pain control

Pharmacology of Bronchodilators

Beta agonists: inhaled beta-2 agonists rapidly absorbed through respiratory epithelium and reach airway smooth muscle within few mins; therapeutic effect depends on local tissue concentrations not reflected in plasma drug concentrations; ~10% of inhaled dose reaches peripheral airways; mean time for 15% increase in FEV_1 6 mins following 3 albuterol inhalations, with peak effect at 55 mins and duration of 26 hrs; beta-2 agonists can potentiate hypokalemic effect of non–potassium-sparing diuretics and serum levels of digoxin reduced with oral or IV albuterol

Anticholinergics: promote airway relaxation by inhibiting M2 and M3 muscarinic receptors on airway smooth muscle; slower action of onset compared with beta-2 agonists make them unacceptable as rescue therapy for acute exacerbations; dry mouth common from inhibition of mucosal secretions; inhaled anticholinergics increase risk of urinary retention >4-fold in men with benign prostatic hypertrophy because of effects of parasympathetic interaction of detrusor muscle of bladder; may worsen acute narrow-angle glaucoma because of parasympathetic effects; inhaled ipratropium has initial onset of 15 mins with peak effect at 1 to 2 hrs and duration of 3 to 4 hrs; only 7% of inhaled drug bioavailable and elimination half-life 3.5 hours by all routes of elimination

Anti-inflammatory medications:

Inhaled corticosteroids: interact with intracellular steroid receptors that translate to nucleus and interact with transcription factor complex to regulate inflammatory protein synthesis; repression of transcription factors responsible for anti-inflammatory effects; 40% to 90% of inhaled corticosteroid swallowed, therefore available for systemic absorption and potential systemic side effects; most of drug deposited in lung absorbed systemically and not subjected to first-pass hepatic metabolism; deposition, thus absorption from lung, more related to efficiency of delivery device than drug itself; when delivered by metered-dose inhaler, systemic bioavailability as much as 25% greater than when given orally; ~70% of inhaled corticosteroids bound to plasma proteins and have half-lives of 3 to 8 hrs

Methylxanthines and phosphodiesterase (PDE) inhibitors: methylxanthines have several possible mechanisms of action to relieve bronchospasm; theophylline one-time mainstay of this group, thought to inhibit PDEs that metabolize cAMP, thereby increasing intracellular cAMP and causing bronchodilation; this occurs in vitro but not at therapeutic levels of theophylline; release of catecholamines from the adrenal glands another mechanism, and as nonselective adenosine receptor antagonist; other beneficial mechanisms include modulation of intracellular calcium ion flux through ryanodine receptors; once mainstay of chronic asthma therapy, methylxanthines have been eclipsed by inhaled corticosteroids

Roflumilast: represents new class of drugs released in 2011; type-4 PDE inhibitor that inhibits degradation of cAMP in cells of airway smooth muscle, epithelium, inflammatory cells, and elsewhere that express the type 4 isoenzyme; inactive against PDE isoforms 1, 2, 3, 5, and 7, suggesting that it produces fewer side effects than nonselective inhibition of theophylline; because extensively metabolized by the liver, liver disease can adversely affect concentrations

Leukotriene receptor and 5-lipoxygenase inhibitors: commonly used as additional therapy in asthma; leukotrienes synthesized from arachidonic acid by 5-lipoxygenase; cysteinyl leukotrienes increase smooth muscle contraction, microvascular permeability, and airway mucus secretion; montelukast and zafirlukast antagonists of cysteinyl leukotriene receptors; zileuton only 5-lipoxygenase inhibitor approved for asthma; leukotriene receptor antagonists may allow for reduction in steroid use

Monoclonal antibodies: omalizumab (recombinant human monoclonal antibody) selectively binds to human IgE and effective as adjunct therapy in adults with moderate to severe asthma; specifically impairs moderator release from mast cells, basophils, B lymphocytes, dendritic cells, and macrophages; effective adjunct therapy in patients with allergic or atopic asthma with high concentration of IgE; omalizumab administered subcutaneously every 2 to 4 wks based on serum IgE levels and body weight; absorption slow after injection, but serum-free IgE levels reduced within 1 hr of initial dose; also reduces expression on high-affinity IgE receptors on inflammatory cells and reduces circulating number of eosinophils

Magnesium: acts as calcium ion channel antagonist, stimulates production of vasodilator prostaglandins and nitric oxide, alters response of vascular endothelium to vasoactive drugs

Mast cell stabilizers: chromone medications for preventing or controlling certain allergic reactions; block mast cell degranulation, stabilizing cells, thereby preventing release of histamine and related moderators; attenuate bronchospasm induced by exercise, aspirin, cold air, and environmental irritants; used in management of childhood and exercise-induced asthma; in past, cromolyn proposed as firstline therapy in children to be used even before inhaled steroids because of concerns about effects of long-term inhaled steroids on skeletal development; despite these beneficial findings, efficacy of cromolyn has been questioned

Status asthmaticus: bronchospasm that does not resolve despite treatment; considered life threatening; emergency treatment includes intermittent or continuous administration of beta-2 agonist by inhaler or nebulizer, IV corticosteroids started early (may take several hours to achieve effects), supplemental O_2 administered to maintain O_2 saturation >90%; magnesium sulfate and leukotriene inhibitors can also be used; PFTs can guide therapy; patients with an FEV_1 or peak expiratory flow rate decreased to 25% of normal at risk for hypercapnia

Hypercapnia: indicative of respiratory fatigue that may lead to respiratory failure and need endotracheal intubation; mechanical ventilation of these patients same as for intraoperative ventilatory care; as last resort, potent inhalational agent may be required to break bronchospasm

Allergies and Anesthesia

Drug sensitivity: historically responsible for 3.4% to 4.3% of anesthesia-related deaths; while impossible to predict who will have anaphylactic reaction to administered drug, patients with history of allergy have increased incidence; patients allergic to penicillin have a 3- to 4-fold greater risk of allergic reaction to any drug; detailed history of drug allergies helpful but doesn't eliminate possibility of anaphylactic reaction to any administered drug; most drug-induced allergic reactions occur within 5 to 10 mins of drug administration, with exception of latex (can take ≥30 minutes to manifest)

Muscle relaxants: responsible for ~60% of perioperative drug-induced allergic reactions; reactions IgE-mediated and cross-sensitivity to other muscle relaxants likely; antibodies that develop against muscle relaxants remain for decades, so patient with history of anaphylaxis to any

muscle relaxant should be skin-tested preoperatively for all drugs in future anesthetic management; nonimmune reactions to muscle relaxants like D-tubocurarine, metocurine, atracurium, and mivacurium include direct mast cell degranulation that causes release of histamine and other mediators; no mast cell degranulation with aminosteroid relaxants like vecuronium, pancuronium, and rocuronium

Induction drugs: hypnotic induction drugs responsible for 5% of perioperative anaphylactic events; rates higher for barbiturates than for nonbarbiturates; first and repeated exposures of propofol implicated in allergic reactions; allergic reaction to midazolam, etomidate, and ketamine rare

Local anesthetics: true allergy rare; allergic reactions to ester-type local anesthetics more common than with amide-type anesthetics; preservatives used in local anesthetics also produce allergic reactions

Opioids: anaphylaxis to opioids rare; morphine, codeine, and meperidine may directly evoke release of histamine from mast cells and basophils, which mimic allergic reactions; fentanyl unique in that it does not stimulate mast cell degranulation

Volatile anesthetics: halothane-induced hepatitis suggests drug-induced allergic reaction; patients with this condition have antibodies that react with halothane-induced liver antigens; similar metabolites produced after exposure to enflurane, isoflurane, and desflurane, indicating possibility of cross-sensitivity to volatile anesthetics in susceptible patients; based on degree of metabolism, chance of anesthetic-induced allergic hepatitis greatest for halothane, intermediate for enflurane, minimal for isoflurane, and remote for desflurane; sevoflurane does not produce these metabolites and therefore no cross-sensitivity

IV radiocontrast media: cause allergic reaction in 3% of patients; history of asthma or allergies to other drugs or foods increases risk; nonimmune reaction, so pretreatment with corticosteroids and histamine antagonist usually effective; severe progressive nephrogenic fibrosis reported in patients exposed to gadolinium-based contrast agents; delayed gadolinium excretion from preexisting renal failure important predisposing factor

Latex: latex allergy IgE-mediated response that can lead to cardiovascular collapse during anesthesia and surgery; delayed onset (as long as 30 mins after exposure); operating room personnel and patients with spina bifida have increased incidence of latex allergy; may exceed 15% in anesthesiologists; intraoperative management includes strict maintenance of latex-free environment; medications should not be drawn up through latex container caps or injected through latex ports on IV-delivery tubing

Protamine: reaction to protamine not allergic, but predictable response directly related to rate of injection; can cause release of histamine from mast cells, activating the complement pathway to produce thromboxane, which causes bronchoconstriction, pulmonary artery hypertension, and systemic hypotension; protamine derived from salmon sperm and protamine allergy more likely to occur in patients allergic to seafood; after vasectomy, men may be at higher risk of allergic reactions to protamine because of existing or developing circulating antibodies to spermatozoa; patients with diabetes treated with protamine-containing insulin products such as neutral protamine Hagedorn also at increased risk

Antibiotics: second most common cause of anaphylaxis in perioperative period, accounting for 10% to 15% of all episodes; penicillin allergy most common, accounting for most fatal anaphylactic drug reactions; sulfonamide antibiotics allergy second most common reported antibiotic allergy (reactions manifest as cutaneous rashes; most common cause of Stevens-Johnson syndrome); vancomycin allergy non–IgE-mediated response involving direct histamine release from mast cells and basophils, directly related to rate of drug infusion

Blood products and synthetic volume expanders: 1% to 3% of patients may have minor urticaria reaction to properly cross-matched blood products, possibly involving soluble antigens in donor unit to which recipient previously sensitized; anaphylactic reactions rare; transfusion-related acute lung injury (TRALI) leading cause of transfusion-related morbidity and mortality; TRALI appears to be activation of neutrophils on pulmonary vascular endothelium as result of donor leukocyte antibodies, particularly anti-HLA and antineutrophil antibodies in plasma component of transfused blood products, especially fresh frozen plasma and platelets; supportive treatment, patients recover in few days; plasma volume expanders implicated, but reactions more common with dextrans and gelatins than with albumin and hydroxyethyl starches; immune- and nonimmune-mediated mechanisms implicated; manifestations range from rash and modest hypertension to bronchoconstriction and shock

Suggested Reading

Di Leo E et al: Focus on the agents most frequently responsible for perioperative anaphylaxis. *Clin Mol Allergy*. 2018;16:16; **Patel O et al:** Asthma mortality among persons aged 15-64 years, by industry and occupation — United States, 1999-2016. MMWR Morb Mortal Wkly Rep. 2018;67(2):60-5; **Woods BD, Sladen RN:** Perioperative considerations for the patient with asthma and bronchospasm. Br J Anaesth. 2009;103(suppl 1):i57-65.

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Anesthesia for Thoracic and Thoracoscopic Surgery

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Preoperative Assessment for Pulmonary Resection

Case: 75-year-old man with carcinoma of right middle and lower lobes; being considered for bilobectomy or pneumonectomy

- Respiratory risk assessment: disjointed; assessment at first contact; final assessment usually on day of surgery; assessments often performed by different members of anesthesia department, so all team members must be coordinated with respect to assessment; assessment begins with understanding risks for patient; ~21% of patients at risk for respiratory complications (*eg*, pneumonia, atelectasis, empyema); ~15% of patients have cardiac complications
- Need to check lung mechanics for extracellular respiration; 3 steps:
  - Delivery of O_2 to alveoli: best measure forced expiratory volume in 1 sec (FEV_1), as percent of normal for patient age, sex, and height; calculate predicted postoperative FEV_1 using amount of lung to be resected; determine number of lung subsegments to be resected; right lung contains 6, 4, and 12 subsegments in upper, middle, and lower lobes; left lung contains 10 subsegments each in upper and 10 lower lobe; if patient has preoperative FEV_1 70% of normal and will undergo right-lower lobectomy, patient will lose 12/42 of functioning lung tissue and be left with ~30%; if 70% FEV_1 and lose 30% of that, will be left with ~50%; likelihood of respiratory complications dependent on predicted postoperative FEV_1; if >40% predicted, no increased risk expected, but threshold for risk 40%, high risk at 30% (as validated by multiple recent studies)
  - Lung parenchymal function (getting oxygen into blood): use pulmonary function test to get diffusing capacity of lung for CO (DLCO), measure of surface area of alveolar capillary membrane; preoperative assessment percentage of normal based on age, sex, and height; can predict postoperative DLCO; risk threshold, <40% increased risk
  - Cardiopulmonary reserve (how well O_2 delivered to tissues): cardiopulmonary interaction, exercise tolerance; gold standard measuring exercise capacity with maximal oxygen consumption (VO_2 max); >20 mL/kg/min), no increased risk; <20 mL/kg/min) increased risk; <15 mL/kg/min), high risk; formal exercise testing too expensive and time consuming; most useful test 6-minute walk test (distance [m] walked as fast as possible in 6 min, divided by 30; *eg*, if patient walks 450 meters, divide by 30; estimated VO_2 max is 15 mL/kg/min); stair climbing less objective than VO_2 max or 6-minute walk distance
- Respiratory risk stratification: can use to determine management if procedure changes intraoperatively; if patient at low risk, should be able to extubate in operating room at end of case if patient alert, warm, and comfortable; if patient at 30% to 40% level and all other factors favorable, should be able to extubate; if <30%, evaluate individual case; for patients at extremely high risk, may be better to wean gradually to see how respiratory system deals with increased work of spontaneous respiration; for extremely high-risk group, thoracic epidural for open surgery quite beneficial and may allow extubation of patient in operating room; in minimally invasive (video assisted or robotic), *eg*, lobectomies and wedge resections, complication risk threshold for FEV_1 shifted downward from 40% to 30% but threshold for DLCO does not change (still 40%)
- Cardiac risk assessment: American College of Cardiology (ACC) gives good guidelines; thoracic surgery intermediate-risk surgery; if patient has intermediate predictors of cardiac risk (*eg*, stable coronary artery disease, stable treated congestive heart failure, or diabetes) and good functional capacity, no further cardiovascular workup needed; if patient has poor functional capacity, need noninvasive assessment of myocardial performance
- Elderly patients (aged ≥70 yrs): ACC guidelines do not consider patients aged ≥70 yrs; elderly patients have double respiratory complication risk and triple cardiac complication risk compared with younger patients; risk increased probably because right ventricle not designed for sudden increase in afterload that occurs after portion of functioning pulmonary vascular bed removed during surgery; ability of right ventricle to deal with sudden increase in afterload decreases with age; exercise capacity most important method to assess elderly patients for both respiratory and cardiac risk after thoracic surgery; thoracic surgery high risk for cardiac complications in elderly patients, who should have at least transthoracic echocardiogram preoperatively; elderly patients do not tolerate pneumonectomies if raised right-sided cardiac pressures; if risk factors for coronary artery disease present, should have noninvasive testing of myocardial performance
- Lung cancer assessment (4 "M"s): mass effect, metabolic effect, metastases, and medications should be considered
  - Mass effect: is tumor compressing intrathoracic structure like recurrent laryngeal nerve or superior vena cava?

Metabolic effect: asymptomatic hyponatremia or hypercalcemia (common), myasthenic or Eaton-Lambert syndrome (rare) patients poorly tolerant of standard nondepolarizing muscle relaxants

Metastases: to bone, brain, liver, adrenal gland; consider complaints related to these systems

Medications: preoperative chemotherapy; cisplatinum mildly nephrotoxic, avoid nonsteroidal anti-inflammatories in these patients; bleomycin rarely except in patients with germ cell tumors from metastases resections, for whom caution needed to recognize pulmonary O_2 toxicity with high inspired O_2 concentration

Smoking: all patients should stop smoking; patients who stop smoking ≥4 wks before surgery have decreased postoperative respiratory complications

Physiotherapy for patients with COPD before and after surgery important

Patient considerations: will patient in this case tolerate pneumonectomy?; FEV_1 50% of predicted, so if he loses right lung, will be ≤25%; DLCO 45%, so will be in low 20%s; exercise capacity good because can walk 450 m; VO_2 max probably 15 mL/kg/min); ventilation perfusion scan shows 60% of ventilation perfusion to left lung; that means postoperative FEV_1 and DLCO probably slightly higher, maybe in upper 20%s; echocardiogram shows right ventricular systolic pressure of 45; chance poor that he will tolerate right pneumonectomy; other options should be discussed with surgeon; could surgery be bilobectomy or sleeve resection to preserve lobe?; although wedge resection of involved segment may not be best cancer operation, may improve survival and get him through perioperative period; smaller surgeries may be performed minimally invasively; discuss with surgeon prior to induction of anesthesia

Final anesthetic assessment (just before induction): review initial assessment and test results; examine chest imaging (x-ray and CT scan); consider risk of patient desaturating during 1-lung ventilation based on initial assessment and plan for preventive and therapeutic measures

Intraoperative management: during thoracic surgery, 2 things different in anesthesia; separate lungs and ventilate patient during period of 1 lung; manage patient during period of 1-lung ventilation

Lung Isolation in Patient with Difficult Airway

Case: 62-year-old male scheduled for left-lower lobe resection for cancer using VATS thoracoscopic surgery; during elective surgery 15 yrs ago for cholecystectomy, patient had failed intubation; required waking patient up and doing fiberoptic oral intubation; on exam, patient has 4-cm mouth opening with full, normal dentition; Mallampati 2; severely decreased mobility of cervical spine due to osteoarthritis; not obese; does not appear to be difficult for bagged, masked ventilation

Methods for achieving lung isolation: *single-lumen tube advanced as endobronchial tube* — rarely used; sometimes appropriate in emergency; when used in right side for left-lung surgery, almost certain to block right upper lobe; this causes 2-lobe ventilation instead of 1-lung ventilation; sometimes use single-lumen tube for carinal surgery; *double-lumen tube* — most anesthesiologists' first choice for lung isolation; greatly improved since original of 1940s; now have disposable PVC tubes with larger lumens, not significantly higher flow resistance compared with standard single-lumen endotracheal tubes; specific tubes available for right-sided and left-sided surgery; *bronchial blockers* — can be placed intraluminally with endotracheal tube placed after tracheostomy device removed, or extraluminally (passed outside (passed outside single-lumen tube through trachea)

Fuji Univent tube: first disposable bronchial blocker; introduced in North America in 1980s; disposable, single-lumen tube with inside channel for bronchial blocker extension and retraction; fairly stiff and not user friendly, especially in difficult airways

Arndt endotracheal blocker: introduced in 1990s in North America; has loop to place over bronchoscope to deliver blocker to left lung, right lung, or lobe

Fuji Uniblocker: more recent; not same as Univent tube; single, disposable bronchial blocker designed for use through standard single-lumen tube; fixed, hockey-stick shape on the end; rotate left or right under direct visualization with bronchoscope in place behind blocker; useful with abnormal lower-airway anatomy because blocker visualized; useful in patients with tracheostomies

Other blockers available

Challenges with bronchial blockers:

Lung does not collapse as well as with double-lumen tube: not true; few tricks help lung collapse efficiently

1. Denitrogenate lung before collapse; ventilate both lungs with 100% oxygen for 3 min to 5 min to get rid of all nitrogen; once blocker inflated, distally trapped gas needs to be absorbed; nitrogen absorbed much more slowly than O_2, so lung collapse delayed
2. Inflate blocker under direct visualization; disconnect anesthetic circuit to give patient 20-to 30-sec period of apnea to breathe out completely before inflating blocker; when ventilation initiated, atelectasis will have developed in ventilated lung, so need to do recruitment maneuver
3. New blockers have suction channels; always put suction (-20 cm) on blocker until lung fully collapsed
4. Use pressure-controlled ventilation with blocker; if patient coughs or surgeon manipulates carina and airway pressure increases while using volume-controlled ventilation, high airway pressure can force air or gas around blocker to reinflate lung, but blocker does not let lung deflate; if using pressure-controlled ventilation, sudden change in compliance due to patient coughing or surgical manipulation will only decrease tidal volume

Bronchial blockers unstable: more likely to become misplaced during surgery so lung reinflates, and bronchoscopy required to reposition device; occurs with all bronchial blockers; less than one-third of time but more common than with double-lumen tubes, which rarely move; if patient has blood or pus, double-lumen tube recommended to ensure adequate lung isolation

Bronchial blockers for lung deflation: can work very well but need to be vigilant; watch surgical field; at first indication of lung reinflation, get bronchoscope, stop ventilation, check blocker position; EZ-Blocker, new to North America; has 2 blockers in Y-configuration; sits on carina; 1 limb into each mainstem bronchus; inflate

whichever blocker needed for whichever lung needs to be blocked; good alternative to double-lumen tubes

Patients with tracheostomies: blockers not first choice for lung isolation in patients with tracheostomies or laryngectomies; specially designed double-lumen tubes available for patients with tracheostomies, but not widely available; standard double-lumen tubes often cannot be placed; bronchial blocker can be placed intraluminally followed by tracheostomy device removal and endotracheal tube placement, or can be used extraluminally; bronchial blockers can be passed outside the single-lumen tube, through the tracheal stoma, then positioned using the bronchoscope, which is passed through the endo-tracheal tube

ABCs of lung isolation: A, know your anatomy; B, use bronchoscope; C, look at chest imaging (x-ray or CT scan) before induction

Anatomy: textbook never as good as real life

Bronchoscope: difficult, particularly for those in training, to get experience; online bronchoscopy simulator at thoracicanesthesia.com; free, noncommercial, teaching resource; interactive; drive bronchoscope through tracheobronchial tree under guidance of labeled map; 50 years ago, right-sided double-lumen tubes common for left-sided surgery; now out of favor because small safety margin, especially in ensuring right upper-lobe ventilation; increased use of pediatric-sized fiberoptic bronchoscope associated with increased interest in using right-sided double-lumen tubes for left-sided surgery and left-sided tubes for right-sided surgery

Chest imaging: if using right-sided tube or right-sided blocker, always measure length of the right mainstem bronchus on preoperative CT scan; if right mainstem bronchus ≥2 cm, right-sided tube or right-sided blocker works well; if right mainstem bronchus <1 cm, neither right-sided tube nor right-sided bronchial blocker works well; not enough safety margin to position tube or blocker; many patients have right mainstem bronchus between 1 cm and 2 cm long; distal distortions of tracheobronchial tree may cause problems with blind intubation when using double-lumen tube; if distortion present on imaging, use bronchoscope in bronchial lumen of double-lumen tube and do bronchial portion of intubation while passing carina under direct visualization to decrease risk bronchial injury from blind placement

Patient considerations:

Awake fiberoptic intubation with double-lumen tube: pediatric bronchoscopes not designed for this because barely long enough and too flexible; difficult; possible but may be awkward

Video laryngoscope: big advance for patients with difficult airways

Approach: place single-lumen tube awake or after induction with fiberoptic or video laryngoscope; induce anesthesia if not yet done; use video laryngoscope to get glottic view; if very poor, use single-lumen tube with ≥7.5 mm internal diameter with bronchial blocker through the single-lumen tube; if view with video laryngoscope very good, replace single-lumen tube with double-lumen tube under direct visualization with video laryngoscope; if intermediate view (part of arytenoids or part of cords), use tube-exchange technique; use double-lumen tube exchangers to remove single-lumen tube and slide double-lumen tube over it under direct visualization using video laryngoscope; Fuji designed Silbroncho double-lumen tube for this procedure; tube has elongated bevel and flexible distal tip; easier to place over tube exchange catheter than commercially available double-lumen tubes

Video laryngoscopes for difficult airways: several brands available; some work well in elective cases with easy airways

Management of 1-Lung Ventilation

Case: 60-year-old man with lung cancer (right upper-lobe tumor); excellent pulmonary function tests; no significant comorbidities; scheduled for right thoracoscopic lobectomy; anesthesia with left-sided double-lumen tube; 20 min into 1-lung ventilation; lung well collapsed, surgeon working, no change in heart rate, blood pressure, airway pressure; end-tidal CO_2 stable at 44; pulse oxymetric saturation falls over several mins from 99 to 95, to 90, to 88; no gold standard for acceptable O_2 saturation, but most anesthesiologists intervene when saturation falls below 90% intraoperatively

Gradual desaturation in stable patient during 1-lung ventilation for minimally invasive surgery: <5% of patients de-saturate significantly (to <90%) during 1-lung ventilation; 30 years ago, ~25% of patients desaturated

Who will desaturate: patient having right-sided surgery with good pulmonary function more likely than woman with severe emphysema having left-sided surgery; right lung bigger, so more likely to desaturate and lung mechanical function (elastic recoil) plays role; patients with low PaO_2 during 2-lung ventilation (bilateral severe pulmonary fibrosis) likely to desaturate during 1-lung ventilation; but not those with preoperative ventilation and perfusion scan showing that lung to be collapsed poorly ventilated and perfused

Prevention and treatment of hypoxemia: use high-inspired O_2 concentration during 1-lung ventilation; apply continuous positive airway pressure (CPAP) to nonventilated lung; apply positive end-expiratory pressure (PEEP) to ventilated lung

CPAP vs PEEP: 30 years ago, studies showed PEEP applied to ventilated lung associated with poorer oxygenation during 1-lung ventilation but CPAP improved oxygenation during 1-lung anesthesia; those studies conducted in patients with COPD having open thoracotomies, so surgeon could push slightly inflated portion of lung out of way; however, even small degree of reinflation of the nonventilated lung from CPAP during minimally invasive surgery with VATS or robotic surgery can interfere with procedure (can impede surgeon's access)

Volatile anesthetic choice: halothane worst choice because potent inhibitor of hypoxic pulmonary vasoconstriction (HPV), responsible for many desaturations in past; modern volatile anesthetics (isoflurane, desflurane, and sevoflurane) equivalent in equi-minimum alveolar concentration (MAC) doses but only mildly inhibit HPV; very little difference between oxygenation during anesthesia with 1 MAC of any of new volatiles and total intravenous (IV) anesthesia (does not interfere with HPV)

- Thoracic epidural: no direct effect on oxygenation, but side effects may affect oxygenation; may allow decreased dose of volatile anesthetic, which improves oxygenation; if thoracic epidural causes hypotension and decreased cardiac output, patients get decreased mixed venous saturation, gets shunted to arterial side to cause decreased saturation; thoracic epidural neither good nor bad for 1-lung ventilation; always maintain cardiac output
- Patient position: predicts desaturation; in lateral position, gravity increases pulmonary blood flow ~10% to dependent ventilated lung; in supine position (*eg*, during bilateral resections of metastases using bilateral VATS), patients desaturate much more
- COPD patients: more resistant to desaturation than patients with normal pulmonary function; tend to develop auto-PEEP; have decreased lung elastic recoil and cannot get entire tidal volume out through 1 side of double-lumen tube by end expiration; get breath stacking and develop auto-PEEP; normally, auto-PEEP considered bad because interferes with patient ventilation; however, in 1-lung anesthesia, small degree of auto-PEEP beneficial; once chest open, mediastinum collapses onto ventilated lung, which compresses ventilated lung below its functional residual capacity (FRC); pulmonary vascular resistance lowest when lung FRC, so want to keep lung at FRC during 1-lung ventilation; patients with COPD, because of auto-PEEP, often keep ventilated lung at normal FRC; in patients with normal lung elastic recoil, lung goes below FRC, so they benefit from PEEP during 1-lung ventilation; patients with COPD develop poor oxygenation when PEEP applied during 1-lung anesthesia because additive with auto-PEEP; unpredictable level, but expansion of lung above FRC from too much PEEP increases pulmonary vascular resistance and forces blood to nonventilated lung; goal during anesthesia maintaining ventilated lung as close to FRC as possible; patients with normal pulmonary function or with increased elastic recoil (*eg*, pulmonary fibrosis) benefit from PEEP during 1-lung anesthesia; patients with COPD have poorer oxygenation with PEEP during 1-lung anesthesia
- Tidal volume: used to think need same tidal volume for 2-lung ventilation as for 1-lung ventilation; very large tidal volumes (10 mL/kg to 14 mL/kg) during 1-lung anesthesia improved oxygenation; however, oxygenation and desaturation during 1-lung ventilation not much problem with modern anesthetics; very large tidal volumes cause lung injury; even 4 hrs of 1-lung ventilation with very large tidal volume (normal 2-lung tidal volume) given to 1 lung causes significant injury in nonoperated lung
- Oxygenation management: decrease tidal volume to 4 mL/kg to 5 mL/kg ideal body weight; do not let peak airway pressure exceed 35 cm of water; maintain plateau airway pressure <25 cm of water; PEEP for all patients except those with moderate or severe COPD; start PEEP at 5 cm and, if inadequate, do recruitment maneuver with 7 cm or 10 cm of PEEP to get best oxygenation and restore FRC; start 1-lung ventilation with 100% O_2 FiO_2, then decrease as tolerated to prevent atelectasis in dependent ventilated lung; because of slight increase in dead space during 1-lung anesthesia, increase respiratory rate slightly; mild hypercapnia not significantly harmful during 1-lung anesthesia; pressure-controlled ventilation slightly improves gas exchange in patients with COPD, but otherwise there very little reason to choose between that and volume-controlled ventilation
- Fluid management: important; lung injury exacerbated by fluid overdose; restrict fluids during surgery; noninvasive cardiac output guides not useful in open-chest surgery; guides to fluid therapy more useful
- Anesthetic technique: modern volatile anesthetics (isoflurane, desflurane, and sevoflurane) may decrease lung injury compared with total IV anesthesia
- Patient considerations: 60-year-old man with 1-lung ventilation, desaturating
  - Severe or acute: resume 2-lung ventilation; interrupt surgery and determine cause of desaturation
  - Gradual desaturation, other vital signs stable: ensure delivery of 100% O_2; check position of double-lumen tube or blocker using fiberoptic bronchoscopy to ensure no lobar obstruction in ventilated lung; optimize cardiac output and try to decrease volatile anesthetic dose to <1 MAC; apply recruitment maneuver to ventilated lung, which will transiently worsen hypoxemia as blood forced into nonventilated atelectatic lung; after recruitment maneuver, apply or increase PEEP
  - Other options: apneic oxygen insufflation to nonventilated lung; CPAP, which may partially reinflate lung in minimally invasive surgery; partial ventilation of nonventilated lung using intermittent ventilation, fiberoptic insufflation of O_2 into segments of nonventilated lung through bronchoscope, selective lobar collapse using bronchial blocker (placed at anesthetic induction) using very small tidal volumes to ventilated lung; mechanical restriction of blood flow to nonventilated lung by surgeon, who can clamp or compress pulmonary artery on side of nonventilated lung (desperation maneuver, only useful in open thoracotomies); veno-venous ECMO (rare in standard lung surgery but may be used in lung lavage or complex tracheal surgery)
  - Best treatment for patient: best treatment for hypoxemia in this patient, recruitment maneuver and PEEP

Summary

Discussion of anesthesia for thoracic and thoracoscopic surgery covered preoperative assessment, lung isolation, and management of 1-lung ventilation; during preoperative assessment, every patient requires assessment of lung mechanical function, lung parenchymal function, and cardiopulmonary interaction (exercise capacity); with respect to lung isolation, remember the ABCs (know anatomy, use bronchoscope, and look the chest imaging); for patients with difficult airways, video laryngoscopes useful; new bronchial blockers and improved double-lumen tubes also helpful in managing patients with difficult airways; in managing 1-lung ventilation, possible to predict, prevent, and treat hypoxemia in vast majority of patients; focus in thoracic anesthesia has shifted from hypoxemia towards lung injury; much more concerned about giving anesthetic that does not cause lung injury

Suggested Reading

Blank RS et al. Management of one-lung ventilation: impact of tidal volume on complications after thoracic surgery. *Anesthesiology*. 2016;124(6):1286-95; **Clayton-Smith A et al:** A comparison of the efficacy and adverse effects of double-lumen endobronchial tubes and bronchial blockers in thoracic surgery: a systematic review and meta-analysis of randomized controlled trials. *J Cardiothorac Vasc Anesth*. 2015;29(4):955-66; **Collins SR et al:** Lung isolation in the patient with a difficult airway. *Anesth Analg*. 2018;126(6):1968-78; **Lumb AB et al:** Hypoxic pulmonary vasoconstriction: physiology and anesthetic implications. *Anesthesiology*. 2015;122(4):932-46.

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Important Aspects of Critical Care

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Management of respiratory failure

Mechanical ventilation: improves pulmonary gas exchange in patients with hypoxemic or hypercapnic respiratory failure; useful adjunct in management of patients in shock; commonly used modes of mechanical ventilation include assist-control ventilation, synchronized intermittent mandatory ventilation (SIMV), and pressure support ventilation; these modes typically combined with positive end-expiratory pressure (PEEP)

- Assist-control ventilation (continuous mandatory ventilation): ventilator senses inspiratory effort and delivers preset tidal volume or pressure; control mode with backup rate set to prevent hypoventilation; work of breathing may be significantly decreased; however, if ventilator/patient not in synchrony or if flow rates not matched to patient demand, may lead to increased patient work
- SIMV: delivers preset machine breaths in conjunction with patient's inspiratory effort; breaths between mandatory breaths not assisted; volumes determined by the patient's strength, effort, and lung mechanics; pressure support may be added to augment breaths; ventilator-assisted breaths different from spontaneous breaths; assist-control ventilation and SIMV identical when no spontaneous breathing; SIMV allows exercise of respiratory muscles, but can lead to respiratory muscle fatigue, may thwart weaning efforts
- Pressure support ventilation: supports spontaneous respiratory efforts; with each effort, patient triggers ventilator, which maintains preset pressure level in circuit during inspiration; appropriate apnea alarms and backup ventilation essential; benefits include increased comfort and tolerance, reduced work of breathing
- Noninvasive positive-pressure ventilation (PPV): delivery of mechanically assisted or generated breaths without endotracheal tube or tracheostomy tube; delivered via nasal or face mask or helmet; uses 2 levels of positive airway pressure that combine modes of pressure support and continuous positive airway pressure (CPAP); pressure-support modality with noninvasive ventilation referred to as inspiratory positive airway pressure (IPAP), and CPAP modality referred to as expiratory positive airway pressure (EPAP); CPAP can also be applied alone but does not provide supportive ventilation; advantages of noninvasive PPV include avoiding risks relating to intubation, reduced need for sedation, and lower risk of nosocomial pneumonia; disadvantages include lack of airway protection against aspiration, less airway-pressure tolerance, and no access to airway for suctioning; best used in alert, cooperative patient expected to improve within 24 hrs to 48 hrs; patient should be hemodynamically stable, able to control airway secretions, and able to coordinate their breathing with ventilator; most beneficial for patients with COPD exacerbations and those with cardiogenic pulmonary edema

Mechanical ventilation monitoring: patients on mechanical ventilation require continuous monitoring; includes arterial blood-gas measurements, ventilation, and acid–base balance, especially in initial phases and if patient unstable; continuous pulse oximetry; capnography also useful; sophisticated alarms and monitors assist with patient management and detection of adverse events; low-volume alarm alerts for leak or ventilator disconnection; high-pressure alarm alerts for exceeding set maximum airway pressure; to avoid lung injury, inspiratory pressure should be maintained <30 cm H_2O

Complications of mechanical ventilation: lung injury from barotrauma (if abnormally high pressures) or volutrauma occurs, resulting in overdistention of alveoli; both barotrauma and volutrauma produce inflammation and increased alveolar-capillary membrane permeability; may lead to alveolar rupture during PPV, which can result in extravasation of air into mediastinum, pericardium, pleural space and subcutaneous tissue; excessive opening and closing of alveoli can result in atelectrauma; appropriate levels of PEEP may prevent atelectrauma; extended high concentrations of O_2 may cause lung damage and atelectasis; reduce inspired O_2 levels as tolerated if arterial oxygenation adequate; however, do not withhold appropriate levels of inspired O_2

- Patient-ventilator dyssynchrony: mismatch of patient's breaths to ventilator-assisted breaths and inability of ventilator's flow delivery to match patient's flow demand; can lead to hypoxemia, ineffective ventilation, increased respiratory muscle workload, cardiovascular compromise, and patient discomfort
- Hemodynamic instability: PPV increases intrathoracic pressure and decreases venous return, resulting in reduced right ventricular filling; when alveolar pressure exceeds pulmonary venous pressure, pulmonary vascular resistance increases, leading to increased right ventricular afterload, and right ventricular ejection fraction falls; left ventricular filling limited by reduced right ventricular output reducing cardiac output (CO); counteract with volume replacement; auto-PEEP may

also adversely affect hemodynamics; reduce auto-PEEP by allowing more exhalation time and decreasing respiratory rate, decreasing tidal volume, or increasing gas flow rate

Ventilator-associated pneumonia: occurs >48 hrs after initiation of mechanical ventilation; mortality rate ~20% to 50%; employ hand washing, bed head elevation, nonnasal intubation, proper nutrition, and minimizing duration of mechanical ventilation to reduce rates; avoid unnecessary antibiotics

Mechanical ventilation in acute lung injury and acute respiratory distress syndrome (ARDS): *lung-protective ventilation strategy (ARDSNet trial)* — low tidal volumes (≤6 mL/kg of ideal body weight [IBW]); maintain low plateau pressures (<30 cm H_2O); set PEEP at moderate levels according to specified (per ARDSNet) PEEP-to-FiO_2 algorithm; however, recent studies suggests high PEEP safe, improves oxygenation; also possible survival benefit in patients with more severe lung injury

Additional therapeutic management of ARDS:

Restrictive fluid management: if tenuous hemodynamic status, using albumin with furosemide may improve fluid balance and oxygenation

Neuromuscular blockade: improves oxygenation through patient-ventilator synchrony, decreased O_2 consumption, and decreased pulmonary inflammatory response; however, associated with intensive care unit (ICU)-acquired weakness and require deep sedation, minimized use recommended; recent study showed mortality benefit with cisatracurium

Prone ventilation: increase in arterial oxygenation in prone position; fades when supine; complications include loss of lines, tubes (including endotracheal tube), and monitoring devices; skin-pressure sores, nerve damage, and hemodynamic instability; considered high-risk maneuver in unstable patients

Inhaled NO: reduces pulmonary hypertension and increases arterial oxygenation; transient effect; often no appreciable change in ventilatory management; can be used as bridge to complex therapies such as extracorporeal membrane oxygenation (ECMO)

ECMO: temporary substitute for transpulmonary respiration to allow rest and recovery for severely injured lungs; confined to highly specialized centers, for limited indications

Corticosteroids: recent study failed to find survival benefit and indicated increased risk of mortality when treatment initiated >13 days after ARDS onset; routine use of corticosteroids for ARDS not recommended

Discontinuation of mechanical ventilation: attempt weaning patients as soon as possible; candidates for spontaneous breathing trial (SBT) include patients with stable vital signs, minimal secretions, and adequate gas exchange; adjust sedatives and coordinate with daily awakenings from sedation; SBT may be conducted using T-piece or low level of pressure-support ventilation (*eg*, 5 cm H_2O with 5 cm H_2O of PEEP); low-level CPAP may facilitate breath triggering in patients with auto-PEEP; SIMV also used for weaning; however, studies suggest SIMV weaning inferior to pressure-support ventilation; may prolong duration of ventilation

Duration of SBT: most commonly 30 mins to 120 mins; 30 mins as good as 120 mins; often no benefit of prolonged SBT (>120 mins); may cause fatigue and failure; closely monitor patient during SBT; restore ventilator support if failure

SBT failure: often same reasons for commencing mechanical ventilation; other causes include auto-PEEP, cardiac dysfunction, critical illness, polyneuropathy, myopathy; repeat SBT when reason for failure corrected; once-daily SBT usually enough

Success of SBT: maintenance of acceptable gas exchange, hemodynamic stability, and stable ventilatory pattern; subjective parameters include mental status, degree of discomfort, diaphoresis, signs of increased work of breathing

Ventilator weaning outcome parameters: common parameters include rapid shallow breathing index (RSBI) and maximum inspiratory force; RSBI >105 indicates need for continued ventilator dependence; maximum inspiratory pressure (MIP; also called negative inspiratory force), measure of respiratory muscle strength; MIP <-30 cm H_2O predicts successful ventilator liberation; SBT more predictive of patient's ability to breathe without ventilator than any other weaning parameter

Ventilator dependence: need for mechanical ventilation >24 hrs, or failure to respond to attempts to discontinue; often multifactorial; identifying all potential contributing causes important

Respiratory issues**:** respiratory muscle insufficiency, increased respiratory muscle load, or mismatch between these 2 factors

Metabolic factors**:** nutritional deficiency, electrolyte imbalances, and hormonal abnormalities

Neurologic diseases: brainstem stroke, central apnea, or occult seizures

Other: critical illness**,** polyneuropathy and myopathy (often first apparent when difficulty stopping ventilator)

Cardiac dysfunction: increased venous return when ceasing PPV may overload compromised heart, leading to congestive heart failure (CHF) in susceptible patients; increases in heart rate and blood pressure (BP), and arrhythmias during weaning can induce myocardial ischemia in coronary artery disease

Failure after successful SBT: consider if continued need for mechanical ventilation; patients with poor cough, large amounts of secretions, poor mental status, or significant neurologic deficits may have successful SBT but fail extubation; tracheostomy may be required prior to ventilator liberation; upper-airway edema can also lead to extubation failure, most commonly occurs in prolonged mechanical ventilation in patients with smaller airways (*ie*, women and children), and repeated or traumatic intubation; leak test with cuff of endotracheal tube deflated may identify risk for upper-airway obstruction; stridor after extubation treated with nebulized epinephrine and/or steroids; intravenous (IV) steroids 12 hrs prior to planned extubation may reduce extubation failure and need for reintubation; Heliox and mask CPAP can also be used

Extubation failure: reintubation increases risk of pneumonia and mortality; reintubation rate 5% to 10% likely reflects optimal balance between risks prolonged intubation and reintubation; selected patients (especially those with COPD) who fail SBT may be considered for extubation to noninvasive PPV; postextubation support with noninvasive PPV associated with decreased duration of mechanical ventilation, decreased incidence of

nosocomial pneumonia, and shorter ICU stay; noninvasive PPV should not be used as rescue for patients with respiratory failure following planned extubation, and may be harmful; tracheostomy may be needed for unsuccessful extubations; tracheostomies improve patient comfort, facilitate speaking, improve mouth care, and may decrease airway resistance, which may be helpful in promoting weaning from mechanical ventilation

Chest trauma

Chest-wall injuries: can involve any part of bony structure or soft tissue of thorax; rib fractures most common injury after chest trauma; multiple rib fractures leading to flail chest occur in 15 to 25% of patients with blunt chest trauma; first and second rib fractures indicate high energy mechanism of injury, associated with underlying pulmonary, neurologic, and vascular injuries; fractures of lower chest (ribs 8 to 12) should raise suspicion for diaphragmatic, hepatic, splenic, or renal injury

Flail chest: defined as fractures of ≥3 consecutive ribs or costal cartilages fractured in ≥2 places; free-floating portion of thorax; moves paradoxically throughout respiratory cycle (inward motion during inspiration, outward motion with exhalation); >90% of patients have associated intrathoracic injuries, often pulmonary contusions; often hemothorax, pneumothorax, or both; additional injuries likely, including head or intraabdominal injuries

Pulmonary contusion: most common intrathoracic injury, occurring in 40% to 60% of patients; bruise of lung with alveolar and interstitial hemorrhage and destruction of lung parenchyma; subsequent inflammation leads to edema, atelectasis, and poor airway mucus clearance, resulting in progressive ventilation/perfusion (VQ) mismatch and loss of pulmonary compliance; may manifest clinically as progressive respiratory failure, typically within 6 hrs to 24 hrs of injury; initial chest x-rays may be unremarkable, but if contusions visible, injury may be more severe; computed tomography (CT) scan more sensitive for diagnosis of pulmonary contusions; volume of lung parenchyma involved, as determined by CT scan, risk factor for development of ARDS; patients with contusion volumes >20% at highest risk

Chest trauma management: early intubation and mechanical ventilation if respiratory failure, shock, or other serious traumatic injuries; low tidal volume and pressure-limited approach, often employed with aim of reducing further ventilator injury; for stable patient with chest trauma, close monitoring of respiratory status, pain control, aggressive lung physiotherapy, early mobilization, and adequate nutrition; rib fractures cause intense pain; patients minimize chest wall motion by reducing tidal volume and coughing effort

Pain management: enables patient mobilization, deep breathing, secretion clearance, and reduced risk for pneumonia; narcotic medications effective but can cause oversedation (thus hypoventilation) and depress cough reflex (thus increased aspiration risk); alternative therapies of interest include epidural anesthesia, intrapleural blocks, intercostal blocks, and paravertebral blocks; spinal fractures or coagulopathy precludes use of epidural catheters

Fluid resuscitation: injured lung prone to fluid overload; pulmonary contusion leads to pulmonary edema, resulting in worsening of gas exchange; use of colloid solutions for pulmonary contusion advocated, with aim of maintaining plasma oncotic pressure; however, no randomized trials to demonstrate this; in unintubated patients with blunt chest trauma, lung expansion therapy using incentive spirometry, deep breathing, and coughing to prevent atelectasis, reduce secretions, and avoid need for intubation; in patients not achieving lung expansion with incentive spirometry, CPAP may be beneficial

Management of acute pulmonary edema

Two types of acute pulmonary edema: cardiogenic and noncardiogenic; although distinct causes, may be difficult to distinguish between them because of similar clinical manifestations; combination of cardiogenic and noncardiogenic mechanisms may coexist; knowledge of cause has important treatment implications (*eg*, cardiac pulmonary edema treated with preload and afterload reduction and possibly inotropes but noncardiogenic edema treated differently)

Medical evaluation: signs and symptoms of acute or chronic cardiac disease, as well as evidence of primary pulmonary process (*eg*, pneumonia) or nonpulmonary source of infection; electrocardiogram to rule out cardiac ischemia; chest radiograph for cardiogenic edema; measurement of brain natriuretic peptide (BNP; if low BNP, CHF unlikely); transthoracic echocardiogram to evaluate left ventricular systolic function as well as aortic and mitral valve function; acute pulmonary edema usually can be diagnosed noninvasively; specific causes of noncardiogenic acute pulmonary edema include anaphylaxis, neurogenic causes, ARDS, and negative pressure

Anaphylactic pulmonary edema: in perioperative setting, neuromuscular blocking agents, antibiotics, anesthetics, or latex may be triggers for anaphylactic reaction; sudden onset, typically accompanied by rash, urticaria and swelling; frequently presents with bronchospasm and hypotension; clinical picture, time course, severity, and occurrence after administration of allergen help to diagnose anaphylactic mechanism

Neurogenic pulmonary edema: typically, recent severe brain insult (*eg*, subarachnoid hemorrhage, stroke, status epilepticus, trauma, intracranial mass); typically accompanied by unregulated sympathetic discharge, leading to pulmonary hypertension, which induces stress failure of pulmonary capillaries and subsequent high-permeability pulmonary edema

Pulmonary edema from ARDS: represents heterogeneous group of severe hypoxic lung diseases, resulting from damage to pulmonary endothelium; can be caused by sepsis, systemic inflammation, aspiration, caustic ingestion, blood transfusions, or trauma; key elements to consider include severity of hypoxic respiratory failure, chest radiographic findings, absence of cardiogenic component, and time course

Negative-pressure pulmonary edema: occurs in response to upper airway obstruction; high negative intrathoracic pressure leads to increased pulmonary capillary pressures, disruption of alveolar cell junctions, and rapid fluid movement into interstitial and alveolar spaces; typical causes perioperatively include laryngospasm and

endotracheal tube occlusion by biting; younger patients at greatest risk; generally benign, with recovery in 12 hrs to 24 hrs with supportive treatment

Treatment of acute pulmonary edema: regardless of cause, supplemental O_2 and diuretic therapy may be initiated; treatment of cardiogenic pulmonary edema focuses on preload and afterload reduction, and sometimes inotropic support; benefits of noninvasive PPV in management of cardiogenic pulmonary edema; treatment of noncardiogenic pulmonary edema includes hemodynamic and respiratory support during diagnosis; if patient requires mechanical ventilation for acute pulmonary edema, lung-protective strategy of ventilation with low tidal volume recommended

Cardiovascular support of the critically ill patient

Shock: state of generalized inadequate tissue perfusion; classified physiologically according to 1 of 4 mechanisms

- Hypovolemic shock: depletion of effective intravascular volume; common causes include dehydration, acute hemorrhage, gastrointestinal and renal losses, and interstitial fluid redistribution; occurs in context of severe tissue trauma, burns, pancreatitis, and other injury; hemorrhage most common cause of shock in trauma patients; characterized by decreased CO, decreased filling pressures, and increased systemic vascular resistance (SVR)
- Cardiogenic shock: results from primary cardiac dysfunction occurring in context of adequate intravascular volume and adequate or elevated ventricular filling pressures; caused by changes in heart rate, rhythm, or contractility; occurs most commonly after myocardial ischemia or infarction, leading to left ventricular failure; acute or chronic cardiomyopathies, myocarditis, and myocardial contusion; characterized by decreased CO, increased filling pressures, and increased SVR
- Obstructive shock: obstruction to blood inflow or outflow to or from heart; common causes include tension pneumothorax, abdominal compartment syndrome, pulmonary embolism, pericardial tamponade, auto-PEEP, and dissecting aortic aneurysm; characterized by decreased CO, increased filling pressures, and increased SVR
- Distributive shock: tends to represent hyperdynamic state; normal or high CO and low SVR; etiologies include sepsis, neurogenic shock, anaphylaxis, adrenal insufficiency, hepatic failure, and arteriovenous fistulae

Monitoring shock: directed toward detecting tissue hypoperfusion, and assessing adequacy of resuscitation; *hemodynamic indices* — include measurement of systemic BP, often via arterial line (provides continuous BP measurement, allows frequent blood draws to track trends in arterial blood gases and serum lactate levels) and central venous catheter (monitors central filling pressures, large volume access, infuses vasoactive medications, and draws serial central blood samples); pulmonary artery catheter cardiac ultrasound may further assist in differential diagnosis if hemodynamic profile not clear, and assists in monitoring of responses to therapeutic interventions; several monitors available that allow for non- or less-invasive assessment of CO, stroke volume, and SVR; *metabolic indices* — serum pH, serum lactate, and mixed venous O_2 saturation or central venous O_2 saturation

Hemodynamic management: fluid resuscitation increases intravascular volume and CO; although inadequate fluid replacement may result in ongoing tissue hypoperfusion, aggressive resuscitation may cause cardiac failure and pulmonary and tissue edema, which further compromise tissue perfusion; fluids available for resuscitation include crystalloids, colloids, and blood products; optimal choice of fluid controversial; if fluid resuscitation insufficient to maintain adequate systemic O_2 delivery, pharmacologic therapy with inotropes and/or vasopressors required; *specific considerations for management* — for hypovolemic shock, typically involves rapid volume resuscitation; for hemorrhagic shock with ongoing blood loss, delayed and initially limited fluid resuscitation may be beneficial to reduce bleeding; for cardiogenic shock, management of abnormalities in rate, rhythm, contractility, and valvular mechanics may require specialized interventions including cardiac pacing, cardioversion, coronary angioplasty with stenting, open coronary revascularization, or mechanical support with intra-aortic blue pumps or ventricular assist devices; obstructive shock requires specific interventions targeted to cause of blood flow impairment; tension pneumothorax treated with needle decompression or tube thoracostomy; abdominal compartment syndrome treated with surgical decompression; pulmonary embolism treated with supportive care and possibly thrombolysis or surgical embolectomy; cardiac tamponade treated with pericardiocentesis; auto-PEEP requires temporary suspension of mechanical ventilation and adjustment of ventilatory parameters; in critical care setting, distributive shock most commonly caused by sepsis or systemic inflammatory response syndrome (SIRS)

Severe, uncontrolled hypertension: hypertensive emergency, BP >180/120 mm Hg with evidence of end-organ damage; requires immediate BP reduction (not necessarily to normal ranges); *neurologic signs and symptoms* — encephalopathy, headache, nausea, vomiting, visual disturbances, altered mental status, seizures, stroke; *cardiovascular signs and symptoms* — angina, acute coronary syndromes, acute aortic dissection; *respiratory signs and symptoms* — dyspnea, acute pulmonary edema, respiratory failure; *renal manifestations* — oliguria, acute kidney injury; *hematologic signs* — hemolytic anemia, coagulopathy; *obstetric signs* — preeclampsia, eclampsia, or **h**emolysis, **e**levated **l**iver enzymes, and **l**ow **p**latelet count (HELLP syndrome); general goal (not in recent ischemic stroke or acute aortic dissection) to reduce BP by ≤25% within 1 hr, then to 160/100 mm Hg over next 2 hrs to 6 hrs; if tolerated, further reductions over next 24 hrs to 48 hrs; if reduction too rapid, blood flow may be compromised, leading to end-organ ischemia; in acute ischemic stroke, higher pressures may be tolerated to improve perfusion of compromised tissues; for patients not eligible for thrombolytic therapy and lacking evidence of other end-organ involvement, American Stroke Association recommends pharmacologic treatment if systolic BP >220 mm Hg and/or diastolic BP >140 mm Hg, goal 10% to 15% reduction; patients eligible for thrombolytic therapy require treatment for systolic BP >185 mm Hg and diastolic BP >110 mm Hg; for patients with acute aortic dissections, systolic BP 100 mm Hg and 120 mm Hg recommended, provided no end-organ hypoperfusion; for acute aortic dissection goals to reduce rate of change of

BP and shear forces on aortic wall, without compromising organ function

Septic shock

Mortality rate: >30% in many studies; sepsis ranges from mild inflammatory response to multiple organ failure; early detection and treatment crucial to improve survival

SIRS: group of systemic manifestations from activation of innate immune response; infectious and noninfectious causes (*eg*, surgery, burns, trauma, pancreatitis); diagnosed with ≥2 of following criteria: temperature >38°C or <35°C, tachycardia (HR >90), tachypnea (respiratory rate >20), or arterial pCO_2 <30 mm Hg, leukocytosis (WBC >12,000/mcL), or leukopenia (white blood cell count <4,000/mcL, or with >10% bands)

Sepsis: SIRS plus evidence or strong suspicion of infection; severe sepsis=sepsis with evidence of organ dysfunction; septic shock=sepsis with persistent hypotension despite adequate volume resuscitation; multiple organ dysfunction syndrome (MODS)=dysfunction of ≥1 organ requiring intervention to achieve homeostasis; MODS common sequela of septic shock

Management of severe sepsis or septic shock: correct hypoxemia and hypotension; identify and treat causative agent; early optimization of resuscitation reduces mortality; target improvements in global and regional tissue perfusion; target mean arterial BP >65 mm Hg; initial target for central venous pressure (CVP) 8 mm Hg to 12 mm Hg in nonmechanically ventilated patients, and 12 mm Hg to 15 mm Hg in ventilated patients; urine output goal >0.5 mL/kg/hr, central venous O_2 saturation goal >70%, or mixed venous O_2 saturation goal >65%; serum lactate concentration and base deficits may also be used as indicators of global perfusion; resuscitation with large volumes of IV fluids may initially be required; no significant difference in choice of fluid (crystalloid or colloid); however, hydroxyethyl starch may increase risk of renal failure, so not recommended; fluid administration for resuscitation should target composite goals for CVP, central venous O_2 saturation, and urine output; if no improvement with fluid administration, decrease rate of administration and institute other therapies; consider transfusion of red blood cells

Vasopressors: often required; norepinephrine and dopamine common vasopressors; start vasopressors after hypovolemia corrected; however, often necessary to initiate early to avoid life-threatening hypotension; norepinephrine causes less tachycardia and more vasoconstriction than dopamine; epinephrine used second-line when poor response to norepinephrine; low-dose vasopressin (0.01-0.04 U/min) as adjunct; monitor patients closely

Dobutamine: often used for inotropic support when evidence of myocardial dysfunction; can cause tachyarrhythmias, but often preferred over milrinone (shorter half-life and easier titration); CO monitor often used in conjunction with venous saturations to titrate

Corticosteroids: role of exogenous steroids controversial; conflicting data exist; adverse effects of corticosteroids include increased risk of infection and myopathy; IV hydrocortisone considered if BP nonresponsive to fluid therapy and high or escalating doses of vasopressors; IV hydrocortisone 50 mg every 6 hrs recommended; higher doses may be harmful and not recommended in septic shock; duration ≤7 days; discontinue when vasopressors ceased; ACTH stimulation testing not recommended

Treatment of causative antimicrobial agent: obtain cultures via 2 sets of peripheral blood cultures; urine, sputum, cerebral spinal fluid, or other body fluids also cultured depending on clinical situation; start broad-spectrum IV antibiotics as soon as blood cultures obtained, ideally within 1 hr of sepsis diagnosis; however, do not delay antibiotic if delay in obtaining cultures, since mortality from sepsis increases with each hr of treatment delay; antibiotics should be tailored when culture and sensitivity results available within 24 hrs to 48 hrs; extended use of broad-spectrum antibiotics not recommended (may select for greater resistance); if source of infection identified by imaging studies or on physical examination, intervention generally necessary (*eg*, percutaneous drainage of abscess, surgical debridement of necrotizing fasciitis)

Prevention of nosocomial infection

Nosocomial infection: occurring ≥48 hours after hospital admission, or ≤30 days after discharge; many can be prevented; variety of multidrug-resistant microbes; 2 pathogens in particular, methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE)

MRSA/VRE: majority of MRSA and VRE transmissions occur via contaminated hands of health care workers, both endemic in most ICUs; cocolonization with MRSA and VRE common in ICU; global (for multiple pathogens) and targeted (for specific pathogens) strategies for control; hand hygiene important for infection prevention; understaffing associated with increased rates of transmission and infection; environmental cleaning and disinfection should occur at least daily, and at end of patient's stay

Chlorhexidine: topical antiseptic with wide spectrum of activity against bacteria, fungi and some viruses; component of MRSA decolonization; daily chlorhexidine bathing of ICU patients potentially reduces infections from skin flora (*eg*, central venous catheter–associated bloodstream infections) and to decrease cross-contamination of microbes; resistance to chlorhexidine not significant; however, resistance genes have been detected in MRSA

Prevention methods: multiple evidence-based interventions (bundled interventions) reduce rates of device-associated infections in ICU; MRSA and VRE frequent causes of such infections, MRSA/VRE infection will also decrease

Active surveillance: screening of asymptomatic patients for MRSA or VRE colonization by obtaining swab specimens mainstay of targeted infection control; anterior nares most frequently sampled for MRSA detection; rectal swab specimens most frequently collected for VRE detection; prevents misclassification of imported MRSA or VRE carriers as new cases; MRSA or VRE carriers generally placed in contact precautions to prevent patient-to-patient spread; for MRSA patients, decolonization; for VRE carriers, no decolonization option; patients in contact isolation at greater risk of noninfectious adverse events, anxiety and depression with less health care worker contacts

Suggested Reading

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Heart Diseases and Anesthesia: Part I

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Ischemic heart disease: reduced blood flow to cardiomyocytes from decreased lumen diameter or acute thrombosis; most due to atherosclerosis (chronic inflammation of arterial wall leading to endothelial dysfunction, local macrophage accumulation, intracellular lipid accumulation, atheroma formation, calcification, and thrombus formation [in unstable plaque]); swift diagnosis and treatment very important in order to avoid complications of acute heart failure, arrhythmia, cardiogenic shock, and sudden cardiac death

- Clinical presentation and risk factors: asymptomatic disease, stable or unstable angina, myocardial infarction, or sudden cardiac death; symptoms include chest tightness or pressure, pain radiating down left arm, to jaw, or epigastric region (can be mistaken for heartburn), shortness of breath, diaphoresis, and feeling of doom; sedated patients and those under general anesthesia cannot report symptoms; complete history and physical examination to exclude other life-threatening causes (aortic dissection or pulmonary embolism); evaluate pain onset, location, radiation, quality (sharp versus pressure), aggravating factors, and timing relative to activity; associated symptoms of nausea, dyspnea, palpitations, or syncope; prior diagnosis, workup, and comorbidities should be elicited; diagnostic value of risk factors relatively poor in acute setting (male sex, age over 55 years, family history, diabetes mellitus, hypercholesterolemia, hypertension, tobacco use, and coronary artery calcium score [independent predictor for cardiac events, cardiac mortality, and all-cause mortality])
- Anesthesia: have high index of suspicion; 12-lead electrocardiogram (ECG) most readily available test, but combination of findings needed
- Third Universal Definition of acute myocardial infarction (MI): rise or fall in biomarkers (cardiac troponin) plus 1 other finding: (1) symptoms of ischemia; (2) new ST changes or new left bundle branch block; (3) development of pathologic Q waves; (4) imaging showing loss of vital myocardium or new regional wall motion abnormalities; or (5) intra-coronary thrombosis on angiography or autopsy
- Two types of acute MI on ECG:
  - ST elevation myocardial infarction (STEMI): shows new ST elevations of at least 0.1 mV in at least 2 anatomically contiguous leads (all leads other than V2 and V3, which have higher threshold depending on gender and age)
  - Non–ST elevation myocardial infarction (NSTEMI): shows new horizontal or down-sloping ST depressions (at least 0.05 mV) in at least 2 anatomically contiguous leads with T wave inversion (at least 0.1 mV) in at least 2 anatomically contiguous leads plus prominent R wave
- Anatomy and ECG: right coronary artery supplies left ventricle (LV) inferior wall, usually the AV node, and whole right ventricle (RV); changes are seen in leads II, III, and aVF; left circumflex coronary artery supplies lateral wall of LV; changes seen in leads I and aVL; left anterior descending (LAD) supplies LV anterior and septal walls (leads V1 to V6); arrhythmia not diagnostically specific but suggestive
- Cardiac biomarkers: troponin I highly sensitive; routinely used in patients with chest pain to diagnose acute MI; has replaced other troponins and creatinine kinases (such as CK-MB); troponin I rises within 3h, peaks at 12 h, remains elevated up to 10 days
- Chest X ray: can be used to evaluate for other potentially life-threatening causes of chest pain (eg, acute aortic dissection) but inconclusive in acute coronary syndrome
- Stress testing: commonly performed if acute coronary syndrome suspected, but patient has negative ECG and cardiac troponins
- Bedside echocardiography: increasingly being used to diagnose cardiac involvement and rule out other causes of chest pain in cases of suspected acute coronary syndrome
- Transesophageal intraoperative echocardiography (TIE): rapid method; regional wall motion abnormalities present before ST changes; trans-gastric mid-papillary views allow visualization of all coronary artery supply territories of LV in single view; LAD territory seen in far field, the circumflex territory on the LV lateral wall; right coronary territory supplying inferior wall and parts of septum; view allows diagnosis or exclusion of right and left heart failure, valvular disease, pulmonary arterial hypertension, aortic dissection, pericardial tamponade, and possibly pulmonary embolism
- Classification of acute coronary syndrome
  - STEMI: change in cardiac biomarkers plus ST elevations; pathophysiology is transmural ischemia, often with acute or sub-acute coronary occlusion from embolism related to atherosclerotic plaque rupture
  - NSTEMI: change in cardiac biomarkers plus clinical or imaging signs and symptoms; no ST elevations; pathophysiology is demand ischemia distal to coronary artery narrowing, often subendocardial

Unstable angina: most common; chest pain without ST elevations or cardiac enzyme elevation

Classification of MI according to Third Universal Definition:

Type 1 myocardial infarction: related to atherosclerotic plaque rupture, ulceration, fissuring, erosion, or dissection with thrombus occluding distal blood flow

Type 2 myocardial infarction: caused by ischemic imbalance other than coronary artery disease; includes supply and demand imbalance; frequently encountered in anesthesia

Type 3 myocardial infarction: patients with presumed cardiac death; biomarkers not obtained

Type 4 and 5 myocardial infarctions: associated with revascularization procedures

Determinants of myocardial oxygen supply: 4 factors, first 3 of which can be manipulated by provider

1. Coronary blood flow: high pressure inside left ventricle (LV) during contraction impedes subendocardial blood flow; coronary blood flow to LV occurs mainly during diastole; linked to heart rate — the slower the heart rate, the more time for LV perfusion; RV perfused during systole and diastole, depends both on time in diastole and on coronary perfusion pressure (diastolic blood pressure in aortic root minus left ventricular end-diastolic pressure [LVEDP]); higher gradient supplies blood more readily to LV; coronary blood flow depends on coronary artery stenosis and/or collateral blood flow; Management: critical to maintain perfusion pressure by maintaining or raising diastolic blood pressure in aortic root using vasopressor or by minimizing LVEDP and thereby ventricular preload with, eg, nitroglycerin; nitroglycerin metabolized to nitric oxide inside vascular smooth muscle cells, good for myocardial ischemia as preferentially dilates veins but has less effect on arterial resistance vessels; leads to peripheral blood pooling, decreased heart size, decreased wall stress; avoid hypotension (compromises myocardial oxygen supply); beta blockers (preferentially short acting and cardioselective) lower heart rate, increase time in diastole, and improve perfusion of LV; have beneficial effects on myocardial oxygen demand by reducing heart rate and conductility

   Collateral blood flow and degree of coronary artery stenosis: less amenable to treatment by anesthesiologist than other factors contributing to coronary blood flow; treated with aspirin (with or without heparin drip); ultimately, need interventional treatment by cardiologist or cardiac surgeon; consult early; percutaneous coronary intervention may reopen blocked arteries using balloon angioplasty and bare-metal or drug-eluting stent; important consequences in perioperative period as both require anticoagulation with aspirin and antiplatelet medication for at least 1 month (bare metal stent) or 1 year (drug-eluting stent)

2. Oxygen content of blood: depends on hemoglobin concentration, oxygen saturation, and partial pressure of oxygen; product of 1.34 times hemoglobin times oxygen saturation plus product of 0.003 and PaO_2; 1.34 is oxygen binding capacity of hemoglobin (1 g hemoglobin binds 1.34 mL oxygen), 0.003 is amount dissolved oxygen in blood (for every 1 mm Hg oxygen tension, 0.003 mL oxygen dissolved in 100 mL blood)

   Management: provide patient with 100% FIO2, optimize ventilation

3. Oxygen dissociation curve: ease with which oxygen delivered to tissues; avoid left shifts (minor compared to other factors)

   Management: not all patients need transfusion, but acute surgical blood loss should be considered as well as changing transfusion threshold

4. Oxygen extraction: theoretical concern; nearly maximum at baseline; cannot increase significantly to improve myocardial oxygen supply

Determinants of myocardial oxygen demand: all can be influenced by anesthesiologist

1. Wall stress: product of pressure times radius, divided by twice the wall thickness; thus, wall stress depends on preload (radius) and afterload (pressure); ventricular hypertrophy temporarily mitigates wall stress by increasing wall thickness

   Management: wall stress ameliorated by decreasing preload using nitroglycerin

2. Heart rate: influences both wall stress and contractility; increased heart rate increases myocardial oxygen demand directly (more beats per minute) and indirectly (increasing contractility; Treppe phenomenon); increased rate decreases LV end diastolic volume and thus preload thereby decreasing wall stress; demand and supply are affected

   Management: control rate with short-acting, cardio-selective beta blockers

3. Myocardial contractility: control with beta blockers
4. Basal myocardial cellular oxygen demand: decrease by treating anxiety and pain to lower catecholamine levels; for patient under anesthesia, deepen anesthesia; cool patients after cardiac arrest or during coronary artery bypass graft (CABG)

   Afterload: only factor with opposing goals; supply: goal to increase diastolic blood pressure in aortic root; demand: goal to decrease afterload to minimize wall stress; choose blood pressure high enough to ensure LV perfusion, but not too high to impede LV output

Intra-aortic balloon pump: consider for patients with persistent chest pain or other symptoms; place percutaneously via femoral artery and advance into descending thoracic aorta until tip rests just distal to left subclavian artery; inflate during diastole under ECG or pressure triggering guidance; increases diastolic blood pressure in aortic root and coronary artery perfusion pressure; deflation during systole decreases LV afterload (less important to cardiac function than coronary perfusion); contraindicated in aortic valve insufficiency, aortic dissection, aneurysms, or severe peripheral vascular disease that would impede placement

Cardiac management during elective, non-cardiac surgery: purpose of pre-operative cardiovascular evaluation to identify patients with heart disease at risk of perioperative cardiac complications (ischemia, heart failure, arrhythmia, death); goals: determine risk, determine who will benefit from further testing, form appropriate anesthetic plan, possibly initiate beta blockade, and recommend interventional therapy or cardiac surgery prior to non-cardiac procedure

American College of Cardiology/American Heart Association (ACC/AHA) 2014 joint guidelines

on perioperative cardiovascular evaluation and management for non-cardiac surgery

1. Determine if patient has any active cardiac conditions (myocardial infarction within 30 days, unstable angina); patients at highest perioperative risk; need evaluation and treatment prior to and independent of surgical procedure
2. Use established and validated risk prediction tool to estimate risk of major adverse cardiac events (myocardial infarction, pulmonary edema, ventricular fibrillation, primary cardiac arrest, and complete heart block); revised Goldman cardiac risk index simple, validated, and widely used to predict major complications; 6 factors scored as 0 or 1 point are summed; 2 or more points predicts increased cardiovascular risk; revised cardiac risk index assesses (1) type of surgery (supra-inguinal, vascular, intraperitoneal, or intrathoracic); (2) history of ischemic heart disease; (3) history of congestive heart failure; (4) history of cerebral vascular disease; (5) preoperative insulin treatment; and (6) preoperative serum creatinine higher than 2.0 mg/dL; American College of Surgeons National Surgical Quality Improvement Program (NSQIP) surgical risk calculator online; 21 variables (age, sex, body mass index, dyspnea, previous MI, functional status); calculates percentage risk for major adverse cardiac events, death, and 8 other outcomes; Gupta score risk index estimates probability for perioperative major cardiovascular events using age, functional status, American Society of Anesthesiologists (ASA) class, creatinine, and procedure type
3. Evaluate exercise tolerance: can patient perform at least 4 metabolic equivalents (METs)? One MET is resting basal oxygen consumption of 40-year-old, normal weight male; 4 to 6 METs (climb single flight of stairs, walk up a hill, walk on level ground at 4 mph, or perform heavy house work) moderate

Predict patient risk, guide perioperative testing, and modify and mitigate risk: coronary revascularization before elective non-cardiac surgery is ultimate risk modifier; especially true for patients undergoing elective intermediate or high-risk non-cardiac surgery with high-risk coronary anatomy and long-term outlook that would be improved by CABG or percutaneous coronary intervention; indications for CABG surgery or percutaneous transluminal coronary angioplasty independent of non-cardiac surgery; patient should undergo procedure if criteria fulfilled; consider cumulative mortality and morbidity of coronary revascularization and non-cardiac surgery, overall health, functional status, prognosis, and urgency; coronary angioplasty and stenting require post-intervention anticoagulation for up to 1 year or more (may impact timing of non-cardiac surgery and urgent intervention like cancer surgery); role and importance of percutaneous coronary angioplasty uncertain; elective surgery should be postponed 30 days for bare metal stents and at least 1 year for drug-eluting stents; after CABG, uncertain how long to wait before non-cardiac surgery; not indicated solely to reduce perioperative cardiac events

CABG indications (per ACC/AHA 2014 guidelines): (1) unprotected left main coronary artery disease (no patent graft distal to left main); (2) 3-vessel disease with or without proximal LAD disease; (3) 2-vessel disease with proximal LAD disease; whether or not to use cardiopulmonary bypass hotly debated; enthusiasm for off-pump techniques decreased as anticipated improved neurologic outcomes not demonstrated consistently in large trials; trend to revascularize fewer vessels with off-pump than on-pump surgery; on-pump CABG routinely performed with low mortality and morbidity and excellent results by many surgeons; cardiopulmonary bypass surgery and ventricular assist devices will be discussed elsewhere

Non-invasive perioperative treatment

Beta blockers: previous enthusiasm to start almost everybody on beta blockers tempered by POISE trial that showed extended-release metoprolol reduced non-fatal myocardial infarction risk, but increased stroke and overall mortality compared with placebo

Guidelines: continue in patients already taking them; reasonable for postoperative management, as clinically indicated for patients (high level evidence); patients at intermediate or high risk (3 or more risk factors for myocardial ischemia in revised cardiac index) may benefit from perioperative beta blockers (lower level evidence); timing unclear, but do not start on day of surgery

Statins: consider initiation if clinically indicated in patients undergoing high-risk surgery; reasonable in patients undergoing vascular surgery

Insufficient evidence to recommend routinely starting other drugs (aspirin) perioperatively to mitigate cardiovascular risk in non-cardiac or non-carotid surgery

Intraoperative diagnosis: hypotension and rhythm changes common, non-specific; use patient history and ECG changes; interpreting subtle ECG changes on monitor can be difficult; automatic ST tracing helpful; V5 lead will detect the most ST changes, followed by V4; lead II monitors different coronary artery distribution; good for monitoring rhythm changes because of good P wave visibility; ST changes, hypotension, and arrhythmia (bradycardia) often only indicators available for diagnosing cardiac ischemia; 40% of acute coronary syndromes present as unstable angina (no ST or enzyme changes); anesthesiologists at significant disadvantage in diagnosing cardiac ischemia intraoperatively

Transesophageal echocardiography (TEE): used in cardiac anesthesia; increasingly used in vascular surgery and for patients with high cardiac risk; direct, real-time view of heart for quick diagnosis of myocardial ischemia presenting with regional wall motion abnormalities before ST changes; can diagnose or exclude several problems that may cause ECG changes or mimic myocardial infarction; can evaluate right and left heart function, valvular heart disease, pulmonary artery pressure, possible aortic dissection, pericardial tamponade, and pulmonary embolism

Intraoperative treatment: hemodynamic goal to have a slow, small, and well-perfused heart; consider preload, afterload, contractility, rate, and rhythm; preload –

- need small heart, as small diameter decreases wall tension and improves LVEDP and coronary perfusion pressure; afterload — maintain blood pressure for

adequate coronary perfusion pressure, no dramatic blood pressure changes; keep contractility low (may use beta blocker) without inotropes unless needed to maintain coronary perfusion; slow heart rate to maximize time in diastole to improve coronary perfusion; maintain sinus rhythm; inform whole team about emergencies and call for help early;

- Treatment: diagnose while treating to optimize myocardial oxygen supply and minimize demand; supply 100% oxygen, optimize ventilation and anesthetic depth to improve blood oxygen content; to improve coronary blood flow, increase coronary perfusion pressure by increasing diastolic blood pressure in aortic root (phenylephrine) while decreasing LVEDP (nitroglycerin); this lowers oxygen demand by decreasing preload and wall tension; verify blood loss, check hemoglobin level, and consider transfusing; use beta blockers to decrease heart rate, improve LV perfusion time, and lower myocardial oxygen demand (lowered heart rate and contractility); discuss feasibility of anticoagulation (aspirin) with surgeon; take time to stabilize patient if feasible; use 12-lead ECG and cardiac enzymes for firm diagnosis; use TEE if equipment and expertise available (especially for refractory cases); consult cardiologist; intra-aortic balloon pump may be needed

Valvular heart disease: regurgitant or stenotic valves cause pathophysiologic changes due to volume or pressure overload and chamber dilation or hypertrophy; adjust anesthetic goals and patient management; common for valvular lesions to remain asymptomatic for long time until discovered during diagnostic testing or evaluation of heart murmur; a murmur does not always indicate underlying valvular disease or require advanced diagnostic workup; most systolic murmurs benign, especially in healthy patients; increased flow velocity causes flow murmur; murmur plus cardio-respiratory symptoms require further testing, which may include auscultation, fluoroscopy with dye injection, or cardiac MRI; most patients undergo echocardiography, which is non-invasive (trans-thoracic) and provides reliable results in real time; echocardiogram allows visualization of lesion type and severity and underlying pathology and associated cardiac problems

Aortic stenosis (AS): "patients with aortic stenosis are SAD" — S-Syncope; A-Angina; and D-dyspnea;" symptoms often experienced when a patient's rhythm converts to atrial fibrillation and atrial kick lost; syncope suggests progressive disease requiring immediate attention; more often symptoms non-specific (dyspnea, decreased exercise tolerance, fatigue)

Severity: normal aortic valve area, 3 to 4 cm^2; mild, less than 2 cm^2; severe disease, less than 1 cm^2; with echocardiogram can categorize based on aortic jet velocity (more than 4 m/s, severe) and median pressure gradient (more than 40 mm Hg, severe)

Underlying pathologies: sub-valvular and supra-valvular mainly congenital, encountered uncommonly; most common cause in developed countries is aging-associated atherosclerotic calcification of thin epithelial layer overlying aortic valve leaflets; rheumatic disease and bicuspid valves less common; bicuspid valve should be considered in patients in 40s or 50s with advanced disease (may have aortic root or ascending aortic dilation)

Morphologic and functional changes: chronic pressure overload in ventricle increases wall stress (pressure times radius, divided by twice the wall thickness); increases in wall thickness compensate for increased pressures in LV (to a point); in concentric LV hypertrophy, thicker ventricle impairs LV compliance, relaxation, and diastolic filling; LV more dependent on atrial kick; LV initially compensates for high afterload better than RV; advanced, severe disease with LV failure known as low-grade AS (despite very narrow aortic valve area, LV cannot mount high enough intraventricular pressure to overcome stenosis, cardiac output low); tight hemodynamic management required; even brief hypotension (decreased diastolic pressure in aortic root) lowers coronary perfusion pressure (already low because LVEDP increased); decreased myocardial oxygen supply (especially in subendocardium of thickened ventricle) causes ischemia and hypotension to further decrease coronary perfusion pressure; can increase heart rate to raise cardiac output, but this increases myocardial oxygen demand and decreases time in diastole, which LV needs for perfusion; difficult to resuscitate patient with fixed stenotic lesion

Anesthetic goals: maintain adequate ventricular volume, coronary perfusion pressure, heart rate, and stroke volume; preload adequate or full; afterload maintained; avoid hypotension; hypertension usually not a problem, given fixed stenosis and adaptive LV; avoid tachycardia (increases demand, reduces supply); maintain heart rate because slowing rate in stiff ventricle to increase diastolic time will not necessarily increase stroke volume; does improve diastolic perfusion time of LV; avoid bradycardia (decreases cardiac output and oxygen delivery, causing ischemia); maintain or slightly increase contractility (increases LV oxygen demand but ensures forward flow); in patients with hypertrophic obstructive cardiomyopathy, goal to decrease contractility (unlike in valvular stenosis); sinus rhythm important, given dependence on atrial kick for ventricular filling; [drug name?] (43:42) very useful; propofol not first-line; consider etomidate, ketamine (especially in beta-blocked patient), or midazolam-fentanyl technique; no evidence-based preferred anesthetic technique

Monitoring: low threshold to place arterial line in awake patient with severe aortic stenosis certainly for cardiac surgery, but also for other procedures; invasive monitoring indications (TEE, central line, or pulmonary artery catheter) depend on comorbidities and surgical procedure; patients undergoing valve replacement separate easily from cardiopulmonary bypass if not in heart failure and time on bypass relatively short; after removing fixed aortic obstruction, LV wall ejects against lower afterload, despite peripheral vasoconstriction to maintain perfusion; after stenosis corrected, patients often need vasodilator to treat hypertension

Aortic insufficiency (AI): idiopathic aortic root dilation is most common cause of chronic AI in developed countries; other causes related to underlying hypertension, arthritis, aging, bicuspid

valve, endocarditis; rheumatic heart disease very rare in developed world, but common in developing world; acute AI mostly due to trauma, dissection, or endocarditis; AI causes LV volume overload and eventual increased LV diastolic volumes; an increased radius increases wall stress (pressure times radius divided by twice the wall thickness) and oxygen consumption; end diastolic pressures severely elevated in acute AI, mildly elevated in chronic AI

Severity: AI quantified by echocardiography with or without color Doppler into mild, moderate, severe; criteria for classification include (1) vena contracta (width of regurgitation jet at narrowest point; (2) ratio of jet width relative to LV outflow tract; (3) flow reversal in descending aorta; (4) regurgitant volume; or (5) regurgitant fraction; hemodynamically, want to minimize increases in LV wall stress by keeping preload normal and decreasing afterload to favor forward flow; higher heart rate minimizes time in diastole (not ideal for coronary perfusion but not usually a problem, given lack of increased muscle mass and absence of severe coronary stenosis) and time for blood regurgitation into LV; produces net increase in forward flow and cardiac output; maintain normal contractility and sinus rhythm; no evidence-based preferred anesthetic technique or medication

Monitoring: use of arterial line, central venous line, TEE determined by patient comorbidities and proposed surgery; for cardiac surgery, many practitioners elect to place arterial line after induction, just before central vein cannulation and after TEE probe placement; weaning off cardiopulmonary bypass after valve replacement requires high preload to fill dilated LV; ample adrenergic support usually needed as ventricle is adjusted to pumping against artificially low resistance, given the low pressure pop-off into left atrium

Mitral stenosis (MS): usually caused by rheumatic fever, less commonly from mitral valve calcification; rarely from congenital MS, infective endocarditis, or rheumatoid arthritis; non-specific presentation (syncope, fatigue); long interval between disease onset and symptoms; normal valve area, 4 to 6 cm^2; moderate MS, less than 1.5 cm^2; severe MS, less than 1 cm^2; classified using echocardiography with Doppler to determine mean mitral valve pressure gradients: mild, less than 5 mm Hg; severe, more than 10 mm Hg; LV relatively empty in MS; patients have low LVEDP, LV volume, stroke volume, blood pressure, and contractility, all due to LV underfilling

Pathologic changes: due to increased left atrial and pulmonary pressures and left atrial dilation; often unmasked by increased volume during pregnancy and delivery; increased left atrial diameters predispose to atrial arrhythmias, especially atrial fibrillation, which abolishes atrial kick (LV depends on it in MS)

Anesthetic goals: avoid tachycardia; maintain pulmonary artery pressure; maintain preload using high atrial pressures, as hypovolemia impairs LV filling; afterload of left heart not usually a concern; minimize pulmonary pressures and right heart strain; contractility often low on LV side, but frequently adequate at baseline; inotropic support may be needed for afterload-insensitive RV; keep heart rate low to allow time for LV filling; avoid tachycardia; maintain sinus rhythm; cardiovert quickly if lose sinus rhythm; in long-standing MS, severely enlarged LA causes atrial fibrillation; low ventricular response should be targeted; treat non-cardiac surgery patients similar to those with pulmonary hypertension or right heart failure; improve oxygenation and ventilation, as hypoxia and hypercarbia poorly tolerated; pre-medicate cautiously; avoid nitrous oxide; if patient anxious or inadequately anesthetized, increased catecholamines increase pulmonary pressures; minimize acidosis, hyperthermia, and positive pressure ventilation; treat with inotropes or inodilators (milrinone or dobutamine); minimize vasoconstrictor use (phenylephrine)

Monitoring: similar to AS; low threshold for arterial line; depends on disease severity and planned surgery

Mitral regurgitation/insufficiency (MR): structural causes(rheumatic heart disease, mitral valve prolapse, congenital, endocarditis, papillary muscle rupture) or functional causes (annular dilation or LV ischemia); physiologic changes and presenting symptoms classified by acuity; chronic MR causes atrial fibrillation and low atrial pressures with significantly enlarged left atrium and normal ejection fraction (EF); acute MR presents with pulmonary edema, increased left atrial pressures, and decreased stroke volume, as left atrium and LV have not had time to remodel to adapt to increased load

Severity: classified by echocardiography; about a dozen parameters can be measured; most commonly evaluated are vena contracta (more than 7 mm, severe) left atrial size, regurgitant volume (more than 60 mL, severe), and regurgitant fraction (more than 50%, severe); in evaluating severity of systolic heart failure, note that EF frequently may seem normal or high on echocardiogram, but this is misleading, because EF calculated using LV short axis and diastolic and systolic area changes; calculated this way, EF tells fraction of blood ejected per cardiac cycle but does not indicate direction of flow; in MR, blood follows path of least resistance, often towards left atrium; forward stroke volume (effective cardiac output) low despite normal or high EF, especially in chronic MR, where LV and left atrium severely volume-overloaded, but LVEDP is relatively normal

Anesthetic goals: promote vasodilation and mild tachycardia; keep preload and afterload low to minimize regurgitant flow; maintain or support contractility; mild tachycardia to decrease time in diastole; sinus rhythm preferred; no preferred drug regimen; patients undergoing cardiac surgery difficult to separate from cardiopulmonary bypass; chronically volume-overloaded ventricle with low contractility has pressure pop-up toward left atrium but has to pump against high-afterload systemic circulation when coming off-pump; high doses of inotropes or temporary balloon pump may be needed

Infective endocarditis: important and often deadly, with in-hospital mortality of 15% to 20%, 1-year mortality, nearly 40%; in developing countries most often related to rheumatic heart disease; in developed countries associated with prosthetic heart valves, immunosuppression, and IV drug abuse; more frequent on right side; left side disease prompts search for right to

left shunt; early surgical intervention and anti-bacterial therapy mainstays of therapy; surgical intervention and timing depend on tissue destruction and valve dysfunction and should be made by multidisciplinary team; antibiotic use guided by susceptibility profile from 2 blood cultures drawn before antibiotic initiation

Echocardiogram: trans-thoracic echocardiogram (TTE) used to assess vegetation, hemodynamic severity, ventricular function, pulmonary pressure, and other complications; TEE recommended if TTE non-diagnostic and patient undergoing valve surgery for infective endocarditis

Prophylaxis: lack of evidence for antibiotic prophylaxis for prevention; limit to those at highest risk of developing endocarditis and highest risk of adverse outcome; recommended before dental procedures (especially manipulation of gingival tissue or periapical areas of teeth, or perforation of oral mucosa) in patients (1) with prosthetic heart valves; (2) with a history of infective endocarditis; (3) after heart transplant with valvular regurgitation due to structural defect; and (4) with certain forms of congenital heart disease (unrepaired cyanotic heart disease, completely repaired defect with prosthetic material within past 6 months, repaired defects with residual defects near site of repair); amoxicillin is first-line therapy

Suggested Reading

American College of Surgeons: NSQIP Surgical Risk Calculator. ACS Risk Calculator Web site. https://riskcalculator.facs.org/RiskCalculator/. Accessed October 29, 2018; **Fleisher LA et al:** 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014;130:2215-45; **Goldman L:** Revised Cardiac Risk Index for Pre-operative Risk MDCalc Web site. https://www.mdcalc.com/revised-cardiac-risk-index-pre-operative-risk. Accessed October 30, 2018; **Gupta PK et al:** Development and validation of a risk calculator for prediction of cardiac risk after surgery. *Circulation* 2011 Jul 26;124(4):381-7.

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Heart Diseases and Anesthesia: Part 2

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Rhythm Disorders and Conduction Defects

Rhythm disorders: subdivided into bradycardia, tachycardia, and dysrhythmias; the more unspecific dysrhythmias actually are the more frequent arrhythmias and are due to ectopic beats, either premature atrial or ventricular contractions; premature atrial contractions have a origin in the atrium and are conducted by the atrioventricular (AV) node, resulting in a narrow ECG complex; premature ventricular contractions originate in Purkinje fibers of the ventricles and show up as broad, often misshapen QRS complexes; can be benign, but can be a sign of an underlying pathology such as ischemia, hypoxia, hypercarbia, catecholamine release, electrolyte abnormalities, and thyroid storm

Rhythm treatment: aims at correcting the underlying cause and controlling heart rate; tachycardia is a heart rate above 100 beats per minute; the differential diagnosis is broad, as tachycardia can come from an intrinsic cardiac problem or as a response to an extracardiac stimulus; tachycardia can be classified by its appearance on the ECG as either narrow or wide complex

Narrow complex tachycardia: can be subdivided as regular or irregular; cause of regular narrow complex tachycardia can be sinus tachycardia due to catecholamine release in response to pain or anxiety; irregular narrow complex tachycardia can be a reflex tachycardia; other causes of narrow complex tachycardia are atrial fibrillation, irregular atrial flutter, AV node reentry tachycardia, junctional tachycardia, or multifocal atrial tachycardia

Wide complex tachycardia: is considered ventricular tachycardia (VT) until proven otherwise, but can be a combination of the narrow complex tachycardias with aberrancy or a pacemaker-mediated tachycardia; blind treatment with a beta-blocker is rarely indicated; should try to define underlying problem

Bradycardia: defined as a heart rate below 60 beats per minute; broad differential diagnosis; one specific cause of bradycardia is AV block; 3 types; a first-degree AV block is a prolonged PR interval on the ECG above 0.2 seconds; often seen in lead II; often asymptomatic; a second-degree AV block can be further subdivided into Mobitz type 1, a Wenckebach block, and a Mobitz type 2 block; the Mobitz type 1 results from a block inside the AV node and is diagnosed by an increasingly longer PR interval until a QRS complex is skipped and a P-wave is not conducted; the following conducted P-wave then starts out with a shorter PR interval; the Mobitz type 2 block results from a block just below the AV node and leads to non-conducted P-waves without prior prolongation of the PR interval; a third-degree AV block, or complete heart block, occurs either at the level of the AV node, or just below it; it results in complete atrioventricular disassociation; no P-waves are conducted; the ventricular response is usually a slow, broad escape rhythm; the underling pathology for an AV block can be either extrinsic, such as medications, hypoxia, hypothyroidism, or increased vagal tone, or intrinsic causes such as coronary artery disease, ischemia, myocarditis, or surgery; treatment depends on symptoms and severity, and can be medically managed with atropine or glycopyrrolate, or with electrical pacing, either internal or external

Cardiac rhythm management devices: pacemakers and automatic cardiac defibrillators are referred to as cardiac rhythm management devices (CRMDs}; pacing can be done either by permanent implantable pacemakers, transvenous, subcutaneous, or epicardial, or temporary pacemakers, either transvenous or transcutaneous; permanent transvenous pacemakers consist of an impulse generator and leads which can have unipolar, bipolar, or multipolar electrodes with connections in different chambers; to describe pacemaker function we use the 5-letter coding system of the North American Society of Pacing and Electrophysiology and the British Pacing and Electrophysiology Group; the first letter codes the chamber paced — none, atrium, ventricle, or dual; the second codes the chamber sensed — none, atrium, ventricle, or dual; the third codes the motor response, — triggered, inhibited, or dual; the fourth codes programmability — none, simple, multiprogrammable, or rate responsive; the fifth codes anti-tachycardia functions — none, pacing, shock, or dual; often use only 3 letters, eg, VOO pacer is pacing the ventricle without sensing the mode of response (asynchronous pacing); seldom seen in outpatients; used in operating room (OR) in setting of electrocautery and artifacts; most common mode of pacing today is DDD; pacers can be used in all patients with symptomatic bradycardia not responsive to medical treatment; indications for permanent pacemaker implantation include sinus node disease, high grade AV block, long QT syndrome, hypertrophic obstructive cardiomyopathy, and dilated cardiomyopathy

Automatic implantable cardioverter defibrillator (AICD): coding system used for AICDs the first letter codes the chamber shocked, the second codes chamber for anti-tachycardia pacing, the third codes mode of tachycardia detection — ECG vs. hemodynamics, and the fourth letter codes position; in addition to pacing a slow heart rate AICDs can also initiate anti-tachycardia pacing or shock in case of VT or ventricular fibrillation

(V-fib); other indications include hypertrophic obstructive cardiomyopathy HOCM), pre-heart transplant, long QT syndrome, arrhythmogenic RV dysplasia or Brugada syndrome; they are indicated in patients with decreased ejection fraction for biventricular pacing and resynchronization of the right and left heart

CRMD implantation: can be done with sedation using monitored anesthesia care in spontaneously breathing patients

CRMDs in the OR: caution on use of magnets with CRMDs; have ***not*** been designed as an emergency treatment or to protect a patient from falsely sensing electrocautery; were designed to interrogate the device about battery life and pacing thresholds; placing a magnet over a pacemaker may or may not switch it into asynchronous mode; effect many-factorial and device-dependent; placing a magnet over an AICD does not simply prevent antitachycardia function; critical to know what the magnet response of the device is before bringing patient to OR; look up manufacturer and model number and interrogate device before surgery; tells you if battery nearing end of life (could replace it during surgery) and what patient's underlying rhythm and pacemaker dependency is; lecturer's institution does not routinely reprogram pacemaker if patient not pacemaker dependent or reprogram CRMDs if surgery is below umbilicus or in upper extremity distal to elbow; if patient pacemaker dependent or has AICD and surgery is above umbilicus and not distal to elbow, do reprogram pacemaker to asynchronous pacing mode, disabling all tachycardia therapies as well as rate enhancements on day of surgery; can also consider increasing the baseline pacing rate to optimize oxygen delivery in patients undergoing major surgery; no special monitoring for every patient with CRMD; cardiac rhythm should be assessed continuously using ECG, pulse oximetry, or electrical waveform; the artifact filter on the ECG should be turned off to visualize patient spikes; some monitors will allow one to do the opposite and enhance pacer spikes with colored markings; the use of monopolar electrocautery should be minimized or avoided altogether in favor or bipolar cautery, and the current return pad, often erroneously called the grounding pad, should be placed in such a way that the electricity is not crossing the generator hard circuit; after procedure the device should be reprogrammed to its presurgical settings before discharging the patient; besides the implantation of CRMDs, some syndromes like intermittent VT, reentry tachycardia, or atrial fibrillation can be treated by interventional cardiology using ablation procedures where the focus of the arrhythmia is isolated and destroyed

Intraoperative evaluation of patient with new-onset arrythmia: want to diagnose and treat at the same time, verifying the arrhythmia, either by palpating a pulse or inspecting the ECG; quickly check all the other monitors, blood pressure, oxygen saturation, ventilation, volume status, to make sure the patient is hemodynamically stable, then make diagnosis and treat; with tachycardia, the differential diagnosis includes iatrogenic (drug effect, electrocautery), CNS (light anesthesia, pain, anxiety, stroke), cardiac (narrow or wide complex), respiratory (hypoxia, hypercarbia), metabolic (malignant hyperthermia, hyperglycemia, sepsis, fever) and endocrine (pheochromocytoma, thyroid storm, carcinoid)

Cardiac causes: could be hypotension leading to a reflex tachycardia, treated with restoring blood pressure first; supraventricular tachycardia (SVT), if regular, could be reentry tachycardia, in which case a vagal maneuver followed by cardioversion may be indicated; irregular SVT could be due to atrial fibrillation, or be ventricular tachycardia which either needs immediate conversion if the patient is unstable or, if the patient is stable, could be treated with amiodarone, for example; the list for cardiac causes is not exhaustive and other diagnoses like pulmonary embolus, multifactorial atrial tachycardia, or myocardial infarction are all possibilities; the same is true for perioperative bradycardia with a similarly long list of different diagnoses like: iatrogenic (drug effect, electrocautery), CNS (increased intracranial pressure (ICP), vagal stimulation) cardiac (MI, AV block, sinus node, pacemaker malfunction),respiratory (hypoxia, hypercarbia), metabolic (hypothermia, acidosis) and endocrine (hypothyroid, adrenal insufficiency)

Hypertension

Hypertension background: prevalent disease with ~1 billion worldwide; hypertension can be classified as primary hypertension, the vast majority of cases, or secondary hypertension, due to defined underlying cause such as pheochromocytoma or renal artery stenosis among others

Primary hypertension: systolic blood pressure of ≥120 mm Hg is considered elevated, systolic blood pressure >130 mm Hg and diastolic blood pressure >80 mm Hg are stage 1 hypertension; age distribution; isolated diastolic hypertension or combined systolic-diastolic hypertension is more prevalent among younger adults; older adults almost exclusively have isolated systolic hypertension and an increased pulse pressure

Hypertension mechanisms: the leading causes are narrowing of the small arteries, increased vascular stiffness (especially for systolic hypertension in the elderly), and the activation of the renin angiotensin system; vascular stiffness is a disease of the whole vessel wall, including endothelial dysfunction, changes in the redux milieu of cells, changes in smooth muscle cell contractility, accumulation of advanced medication end-products, changes in extracellular matrix composition due to accumulation of collagen and breakdown of elastin; these result in increased vascular stiffness which can be seen clinically as an elevated pulse pressure that is an increasing systolic blood pressure with a normal or even decreased diastolic blood pressure; increased vascular stiffness can be demonstrated before changes in blood pressure occur, pointing towards a fundamental element in the development of hypertension and resulting in end-organ damage; hypertension can be present for a long time without being recognized, increasing the risk of ischemic heart disease, heart failure, renal disease, and cerebrovascular disease

Hypertension treatment: treatment should be instituted longitudinally unless the patient has a hypertensive emergency (elevated blood pressure with active or acute signs of end-organ impairment) or another disease that requires urgent blood pressure control (eg, aortic dissection, cerebral bleed); severely elevated preoperative blood pressure results in increased perioperative risk and

should be investigated; lasting treatment includes lifestyle modifications, and in refractory cases, medications

Drugs for treating hypertension: medications include diuretics, calcium channel blockers, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), beta-blockers, and alpha blockers, all of which can interact with the intended anesthetic; diuretics can lead to electrolyte abnormalities, especially of potassium, and volume depletion; often held morning of surgery unless they are taken for heart failure or pulmonary hypertension; ACE inhibitors and ARBs can potentially lead to refractory hypotension after induction of anesthesia; debate about whether to hold them the day before surgery; beta-blockers and calcium channel blockers, while associated with bradycardia, should be continued on the day of surgery, especially in patients with coronary artery disease; patients with hypertension are more sensitive to the negative inotropic effect of some anesthetics and also to the vasodilating effects of anesthetic agents because of relative volume depletion, which is compensated for by increased afterload and vasoconstrictive state, often exaggerated by medical treatment

Perioperative mortality assessment: simply having hypertension is not a good predictor of increased perioperative mortality in several risk scores; the revised cardiac risk index and the Gupta score do not include hypertension; the National Surgical Quality Improvement Program (NYSQUIP) surgical risk calculator does include hypertension requiring medication

Hypertension management in surgical setting: it is recommended that patients undergoing elective surgery who have hypertension and other cardiac risk factors should be treated well before surgery, not started the day after procedure; with regard to patients hypertensive the morning of procedure — on the one hand, many have skipped last one or 2 doses of medication; can just give one dose; many just anxious; at the other extreme, patients with hypertensive crisis with end-organ damage require immediate treatment; for cases in between, as long as the blood pressure is less than 160 or 180 systolic and/or is 110 or less diastolic, generally thought all right to proceed; however, these recommendations are not backed up by solid data and ultimately need to individualize this decision for each patient; some factors influencing the decision include the effect of the potent vasodilators used for anesthetic purposes, like vapor anesthetics or propofol; especially risky in uncontrolled and volume-contracted hypertensives, especially if elderly and dehydrated from fasting; the urgency of surgery and the patient's medical optimization need to be considered before treating blood pressure acutely or postponing a case

Intra- or postoperative hypertension: has broad differential diagnosis; start with an evaluation common for all types of hypertension; recheck blood pressure, check arterial line placement, check all monitors — ECG, oxygen saturation, ventilation, temperature, volume status; ensure patient hemodynamically stable and anesthesia adequate; it is rarely indicated to treat patients with vasodilators, like sodium nitroprusside, nitroglycerin, hydralazine, calcium channel blockers, alpha or beta blockers, without taking time to consider several differential possibilities for the current episode of hypertension

Hypertension diagnosis: according to organ systems, the differential diagnosis for hypertension includes: iatrogenic (drug side effects (drugs given or drugs withheld), transducer malposition, or wrong cuff size), CNS (light anesthesia, pain, anxiety, increased ICP, or autonomic hyperreflexia), cardiac (baseline hypertension, ischemia, preeclampsia, increased afterload, or hypervolemia), respiratory (hypoxia or hypercarbia), metabolic (malignant hyperthermia, hyperglycemia, or fever), and endocrine (pheochromocytoma, thyroid storm, carcinoid, or Cushing)

Heart Failure and Cardiomyopathies

Heart failure: estimated to be about 1 in 100 individuals over the age of 65 with almost 6 million patients in the United States; 80% of men and 70% of women under [?] 65 who have heart failure will die within 8 years of diagnosis; heart failure is characterized by systemic perfusion that is inadequate to meet body's metabolic demands due to impaired cardiac function; this can be subdivided into left or right heart failure and also into systolic heart failure, which is reduced myocardial contractility, and diastolic heart failure, which is impaired cardiac relaxation and abnormal ventricular filling

Heart failure causes: it is important to differentiate between heart failure and the underlying causes of heart failure, such as coronary artery disease, hypertension, or cardiomyopathy; cardiomyopathies can be due to coronary artery disease, viral infections, or septal hypertrophy; cardiomyopathies are a diverse group of cardiac pathologies, often of unknown origin, that result in hypertrophy, dilation, or increased stiffness of the myocardium, leading to heart failure or an increased arrhythmia burden; the main types of cardiomyopathy in adults include: dilated cardiomyopathy, due to coronary artery disease, myocardial infarctions, or alcohol abuse; hypertrophic cardiomyopathy, familial with a strong genetic predisposition; restrictive cardiomyopathy, idiopathic or secondary to a systemic disease such as amyloidosis; arrhythmogenic cardiomyopathy, due to genetic mutations; and unclassified cardiomyopathies; in addition, stress cardiomyopathies, such as Takotsubo cardiomyopathy or inflammatory cardiomyopathies (secondary to myocarditis, sarcoidosis, or Chagas disease), are considered separate entities; symptoms tend to be nonspecific and include dyspnea, fatigue, dizziness, lightheadedness, irregular heartbeat, edema, and venous distention

Cardiomyopathy treatment: depends on the type of cardiomyopathy and the severity of symptoms; includes lifestyle modifications (diet, exercise), medications (diuretics, ACE inhibitors), cardiac rhythm management devices (pacemakers, defibrillators), ventricular assist devices (LVADs), interventions such as arrhythmia ablation, and heart transplant

Heart failure diagnosis: supported by several findings with different tests including physical exam, chest x-ray, or laboratory data; there are several algorithms available to derive the diagnosis of heart failure, eg, Framingham criteria; the echocardiogram aids in a subclassification of systolic versus diastolic heart failure; this can be differentiated by looking at the ejection fraction; systolic heart failure tends to be associated with a reduced ejection fraction while diastolic heart failure usually shows a normal ejection fraction (HFWPEF, heart failure with preserved ejection fraction); this is a simplification, as diastolic heart failure has several abnormal indices of diastolic function, such as abnormal E/A ratio

Heart failure classification: clinically, heart failure can be classified either by the New York Heart Association class which focuses on symptoms, or the ACC/AHA classification which focuses on early stages of heart failure and the underlying pathology

New York Heart Association classification: Class I, no symptoms with ordinary activity; Class II, symptoms limited to ordinary activities, Class III, exercise limited by symptoms, and Class IV, symptoms at rest

ACC/AHA classification: Class A, high risk for developing heart failure; Class B asymptomatic heart failure; Class C, symptomatic heart failure; Class D, refractory, end-stage heart failure

Heart failure diagnosis and treatment: preoperatively, go by physical signs of heart failure, cardiac dysfunction on echocardiography, pulmonary congestion, or an elevated B-type natriuretic peptide (BNP); treatment is done according to the ACC/AHA classification; patients with ACC/AHA classification class A heart failure should be treated by modifying risk factors with lifestyle modifications; in class B heart failure should add a beta-blocker or ACE inhibitor; class C add diuretics, or digitalis; class D heart failure needs the addition of inotropes, mechanical circulatory support, heart transplant, or hospice; ventricular assist devices have improved the prognosis for end-stage heart failure, and their expanded use means that more patients with such devices will be presenting for surgery; in the operating room or perioperatively often must deal with acute decompensated heart failure, in which adequate perfusion and oxygen delivery is critical to end organs; important to know what type of heart failure we encounter as it affects treatment beyond optimizing preload and volume status; left-sided systolic heart failure benefits from inotropic support, especially with the presence of low blood pressures; agents such as dopamine or epinephrine tend to work well; patients with diastolic heart failure and some with systolic heart failure might benefit from afterload reduction or the addition of milrinone or dobutamine; systolic right-sided heart failure tends to benefit from lowering pulmonary pressures and from inotropic support, eg, with dobutamine; pulmonary pressures can be affected by high PaO_2, low PCO_2, alkalosis, avoidance of hypothermia, lowering intrathoracic pressures, blunting catecholamine release, drugs like inhaled nitric oxide, milrinone, or prostaglandins

Medical Treatment of Pulmonary Edema, Pulmonary Hypertension, and Cardiogenic Shock

Pulmonary edema: accumulation of fluid in the lungs; can have multiple causes; in the acute situation, the anesthesiologist should differentiate between negative pressure pulmonary edema (a patient trying to inhale against a closed (?) breathing circuit), capillary leak syndrome (eg, eclampsia), or low end-cardiac pressures or anaphylaxis; other considerations include pulmonary embolus, myocardial infarction, heart failure, fluid overload and aspiration; try to determine and treat cause; patients usually present with dyspnea, frothy, pink sputum, hemoptysis, and anxiety; hypoxia and tachycardia also common in pulmonary edema; diagnosis is most commonly made with a chest x-ray demonstrating the accumulation of fluid in the lung parenchyma, interstitial space, and/or the presence of pleural effusions

Acute pulmonary edema: often requires immediate treatment of symptoms; oxygen by face mask may not be sufficient, and continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP) might be required; endotracheal intubation may be needed to administer 100% oxygen and to add positive end-expiratory pressure to the breathing circuit; these maneuvers may buy time to treat underlying problem

Pulmonary hypertension: pulmonary hypertension with right heart failure can have high mortality due to volume overload or right ventricular failure due to ischemia as a result of systemic hypotension; pulmonary hypertension is defined as a persistent increase in mean pulmonary artery pressures equal or higher than 25 mm Hg at rest; according to the World Health Organization (WHO), classification of pulmonary hypertension is divided into 5 groups: pulmonary arterial hypertension, pulmonary hypertension associated with left heart disease, pulmonary hypertension associated with lung disease, pulmonary hypertension due to chronic thrombotic disease, and miscellaneous cause pulmonary hypertension; often diagnose pulmonary hypertension on an echocardiogram when the right ventricular end systolic pressure is elevated as measured by using Doppler on the tricuspid regurgitation (TR) jet; the assumption is that right ventricular systolic pressure plus central venous pressure is equal to pulmonary artery pressure; accuracy of this assumption depends on presence of TR, the knowledge of central venous pressure (often only estimated), and lack of obstruction between right ventricle and pulmonary artery

Treatment: targets the underlying cause and tries to decrease pulmonary pressures by utilizing the 7 factors discussed earlier PaO_2, pCO_2, pH, temperatures, intrathoracic pressures, catecholamine release, and drug therapy such as milrinone or inhaled nitric oxide; all these factors tend to change in the wrong direction during the perioperative period; patients can experience periods of hypoventilation leading to hypoxia and hypercarbia, become acidotic due to malperfusion(?) and lactate production, and potentially experience hypothermia; additionally, positive pressure ventilation and PEEP increase intrathoracic pressures; the perioperative period has the potential for pain, anxiety, and light anesthesia, which lead to catecholamine release; lastly, some drugs directly increase pulmonary artery pressures, like phenylephrine

Three major pathways affecting pulmonary artery tone: the nitric oxide pathway, the endothelin pathway and prostacyclin pathway, all of which can be targeted by specific drugs; nitric oxide causes vasodilation and can be inhaled in the form of INO, provided intravenously in the form of nitroglycerine or sodium nitroprusside, or provided indirectly by blocking the breakdown of one of the second messengers activated by nitric oxide, using milrinone; prostacyclin leads to pulmonary vasodilation; can be given IV or by inhalation; the endothelin pathway is involved in vasoconstriction and endothelin receptor antagonists like bosentan can be administered

Patients presenting with elevated pulmonary pressures perioperatively while already on maximal and stable medical therapy: goals are 2-fold: 1) to minimize pulmonary pressures in order to support the right ventricle, which is not well equipped to conduct pressure work and tends to fail if exposed to increased afterload, and 2) to support or augment right ventricular contractility to aid the

right ventricle in overcoming high pulmonary pressures; the quick checklist is to maximize PO_2, decrease PCO_2, avoid acidosis and hypothermia, lower intrathoracic pressures, blunt catecholamine release, and institute appropriate medical management using inhaled nitric oxide, milrinone, or inhaled prostaglandins

Important considerations: whether to use general anesthesia, which avoids sympathetic surges and hypoventilation, but requires positive-pressure ventilation and use of myocardial depressants or to use sedation, which avoids mechanical ventilation, but might lead to hypercarbia; neuraxial technique also avoids mechanical ventilation and hypercarbia, but could result in anxiety and preload (? recording unclear) reduction of right ventricle; should surgery be open or laparoscopic? it is prudent to favor inotropic support, like milrinone or norepinephrine over pure vasopressor support, especially phenylephrine, which increases pulmonary artery pressures, and to avoid large fluid boluses, even worse with cold fluids; always have a contingency plan for pulmonary vasodilators like INO, right ventricular assist device, or even extracorporeal membrane oxygenation (ECMO)

Cardiogenic shock: an extreme form of inadequate end-organ perfusion that is cardiac in origin and leads to insufficient delivery of oxygen to tissue; results in low cardiac output, local tissue hypoxia, and nutrient starvation, leading to ischemia and cell death; cardiogenic shock presents with hypotension, low cardiac index and end-organ malperfusion, oliguria, cool extremities, weak pulses, altered mental status despite adequate intravascular volume and normal, or even high, cardiac filling pressures; given the high incidence of atherosclerosis and coronary artery disease, one of the causes of cardiogenic shock is left ventricular failure due to myocardial infarction, with patients presenting with ST elevation myocardial infarction having a 5 to 8% chance of deteriorating into cardiogenic shock; other causes include papillary muscle rupture, myopericarditis, Takotsubo cardiomyopathy, acute valvular insufficiency, aortic dissection, cardiac tamponade, pulmonary embolism, and cardiac arrhythmias

Cardiogenic shock diagnosis and treatment: diagnosis classically made with a pulmonary artery catheter or with echocardiography, both of which are useful for evaluating therapy; maintenance of an adequate volume status and pharmacological support constitute the mainstays of therapy; inotropic agents in doses as low as possible are essential in treatment given the underlying contractile failure of the myocardium, but they also increase oxygen consumption and ATP generation in a failing ventricle; consequently there is no inotrope that is preferred for cardiogenic shock; drugs to consider should have beta-1 receptor activity and include epinephrine, norepinephrine, and dobutamine; other adjunct therapy can include dopamine, vasopressin, and in Europe, the calcium sensitizer levosimendan; an intra-aortic balloon pump is sometimes needed to improve coronary perfusion pressure by augmenting diastolic blood pressure in the aortic root; last resort treatments include a ventricular assist device, ECMO or heart transplantation

Cardiac Transplantation

Background: cardiac transplantation remains the most effective treatment for heart failure refractory to medical or surgical therapy; risk factors for heart failure include hypertension, diabetes, coronary artery disease, and myocardial infractions; the leading etiology for which adult patients receive heart transplants is nonischemic cardiomyopathy followed by ischemic cardiomyopathy

Anesthesia for heart transplant: induction and surgery need to be carefully timed in order to minimize ischemia duration; due to low cardiac reserve, an arterial line is routinely placed prior to induction of general anesthesia; patients with end-stage heart failure have a low fixed stroke volume and are preload dependent; due to compromised cardiac function, even minor increase in afterload may decrease stroke volume and cardiac output; therefore, swiftly securing the airway in a patient who has not been NPO must be balanced with a smooth induction to guarantee hemodynamic stability; after obtaining central access and placement of a transesophageal echo probe, anesthesia is usually maintained with a balanced technique; surgical technique has shifted from bi-atrial approach, in which parts of the donor and recipient right atria are anastamosed, to an approach in which the recipient's right atrium is completely excised and the anastomosis performed between the 2 venae cavae; for most anesthesiologists, however, it is much more common to encounter a patient who has had a heart transplant in the past and is now presenting for non-cardiac surgery

Heart transplant considerations: these hearts are denervated and have no direct sensory, sympathetic, or parasympathetic connections; the lack of parasympathetic tone, which lowers heart rate at baseline, results in a higher-than-expected heart rate, around 90 to 100 beats per minute, in a heart-transplanted patient; stroke volume cannot increase due to direct sympathetic stimulation but depends on circulating catecholamines and an adequate preload to produce a satisfactory, yet delayed, stress response; management of the denervated heart is of particular interest in regards to pharmacological therapy; the transplanted heart will not be able to respond to medications that work by blocking the parasympathetic nervous system, such as anticholinergics, like atropine or glycopyrrolate, cholinesterase inhibitors, like neostygmine and some muscle relaxants, such as pancuronium; need to use drugs such as isoproterenol, epinephrine, or norepinephrine with a more direct effect on heart rate; external or internal electrical pacing can be performed; a transplanted heart is sluggish to respond to ephedrine, given the relatively depleted catecholamine stores at baseline, and direct acting agents like epinephrine are much more effective in reducing the side effects

Cardiac Tamponade and Constrictive Pericarditis

Background: both cardiac tamponade and constrictive pericarditis are pathological conditions that lead to impaired ventricular filling; cardiac tamponade is an emergency in which accumulation of pericardial fluid or blood leads to impaired ventricular filling and low cardiac output; constrictive pericarditis leads to impaired ventricular filling due to an inflammatory process of the pericardium that results in pericardial fibrosis without an emergent presentation; cardiac tamponade can be the result of many different causes that lead to fluid accumulation in the pericardial sac, such as trauma, dissection of the ascending aorta, cardiac surgery, MI leading to ventricular rupture, lung cancer, pericarditis, radiation therapy, or central line placement; because the pericardium is

comprised of fibrous tissue that is stretch resistant, fluid accumulation leads to increased intrapericardial pressures, impairing the low pressure chambers of the heart (right and left atria), which become compressed, leading to impaired ventricular filling; ventricles, especially RV, compromised, intraventricular septum pushed leftward, stroke volume is severely compromised, and cardiac arrest ensues; symptoms are nonspecific and include many that are associated with chest pain and its differential diagnosis

Cardiac tamponade diagnosis: Beck's triad, consisting of hypertension, jugular venous distention, and muffled heart sounds; another frequently tested clinical sign is pulsus paradoxus, which is not specific for cardiac tamponade and can occur without diseases like pericarditis, sleep apnea or COPD; physiologically, there is a small decrease in blood pressure with inspiration in a spontaneously breathing patient, due to more negative intrathoracic pressure, leading to increased venous return on the right side and more blood pooling in the lungs, resulting in lower left heart preload and consequently decreased stroke volume; in a patient with pulsus paradoxus this drop is larger than 10 mm Hg during inspiration due to increased right-sided heart pressures relative to normal that now approximate left heart pressures; the increased volume on the right side lead to bending of the septum, further compromising left ventricular filling and exaggerating the drop in stroke volume and blood pressure; other signs of pericardial tamponade are ST changes, arrhythmias, or low voltage of the ECG, as the heart is more insulated from the surface by the increased amount of fluid; imaging studies include chest X-ray and echocardiography; TEE in particular can be useful to visualize the amount of pericardial fluid around the heart, the atrioventricular compression, and the dynamic shift of the ventricular septum; invasive monitors include an arterial line demonstrating hypertension and pulsus paradoxus

Cardiac tamponade treatment: a pulmonary artery catheter is used which shows the equalization of pressures in the heart, meaning with progressing tamponade central venous pressure, pulmonary artery pressure, and wedge pressure will all converge on the same number, as flow across the heart diminishes and ultimately seizes; depending on severity, patients can undergo either subxiphoidal percutaneous drainage or a pericardial window; the goal is to maintain myocardial contractility and heart rate in these patients with a low and fixed stroke volume and to maintain afterload to keep the coronary artery perfusing both ventricles; keep in mind that subcutaneous drainage can be done using local anesthesia exclusively and can be augmented by some ketamine in a severely compromised patient; lecturer likes adjunct ketamine as it usually maintains contractility, heart rate, and afterload in all but most catecholamine-depleted patients

Constrictive pericarditis diagnosis: the causes of constrictive pericarditis can roughly be divided into infectious (tuberculosis, bacterial), inflammatory and autoimmune (postviral, post-MI), and miscellaneous types like radiation exposure or neoplastic infiltration; all of those causes lead to a thickened, calcified, and increasingly fibrosed pericardium, shrinking it and making it even less compliant, thereby preventing adequate cardiac expansion to fill the main chambers of the heart in diastole; constrictive pericarditis leads to ventricular filling impairment; presentation is gradual; symptoms are usually consistent with heart failure, such as dyspnea, fatigue, lower extremity edema; on physical examination, may find increased jugular venous pressures and hepatomegaly; cardiac catheterization can demonstrate an equalization of diastolic pressures; the mainstay of diagnosis consists of imaging modalities such as chest x-ray, which may demonstrate pericardial calcifications, and CT scan or echocardiography, which demonstrate dynamic septal movement, thickened pericardium, and impaired filling patterns of the ventricle

Constrictive pericarditis treatment: surgical pericardiectomy commonly performed by a median sternotomy to remove the entire pericardium; hemodynamic goals for this procedure, or any other constrictive pericarditis, include maintenance of heart rate, afterload, and myocardial contractility while maintaining an adequate preload; invasive monitors such as an arterial line and a central line are frequently placed to observe hemodynamics; benzodiazepines, opiates, and a volatile anesthetic are lecturer's preference for balanced approach

Suggested Reading

American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Rhythm Management Devices: Practice advisory for the perioperative management of patients with cardiac rhythm management devices: pacemakers and implantable cardioverter-defibrillators: a report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Rhythm Management Devices. *Anesthesiology* 2005 Jul;103(1):186-98; **Fleisher LA et al:** 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014 Dec;130(24):2215-45; **Ramsingh D et al:** Anesthesia for Heart Transplantation. *Anesthesiol Clin* 2017 Sep;35(3):453-71; **Varon J et al:** Perioperative hypertension management. *Vasc Health Risk Manag* 2008 Jun;4(3):615-27.

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Cardiac Anesthesiology: Part 1

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Background: goal of anesthesia to make patient compatible with surgical requirements, reduce surgical morbidity and mortality; components of anesthesiology include control of autonomic effects, anxiety, movement, memory, pain, consciousness, posttraumatic stress disorder (PTSD) in surgical/postoperative period

Anesthesia: cardiac anesthesia differs from regular anesthesia by halting breathing, stopping heart, eliminating coagulation system, then repairing coagulation system; every patient in cardiac anesthesia has issues including arrhythmias, hemodynamic issues, coagulopathies, heart disease; must safely anesthetize patients in whom risk factors would otherwise need procedure canceled; cardiac anesthesiologists reduce risk in high-risk procedures

Requirements for cardiac anesthesiologists: ability to provide anesthesia care to patients undergoing extracorporeal circulatory support (*eg*, cardiopulmonary bypass), patients having off-pump coronary artery bypass (CABG); handle one-lung ventilation (OLV); robotic cardiac surgery; handle emergency CABG after failed percutaneous coronary intervention (PCI) or PCI with tamponade; operate pacemaker, intra-aortic balloon pumps (IABPs); provide anesthesia care for heart transplants, left ventricular assist devices (LVADs), biventricular assist devices (BiVADs); use pharmacology to optimize hemodynamic performance; create, reverse, and treat coagulopathies, catastrophic bleeding; perform transesophageal echocardiography (TEE); identify anatomic problems; optimize hemodynamics; assist in intraoperative care; intravenous (IV) catheter/line placement; operate cell salvage (Cell Saver); understand and run perfusion system; be compatible with psychology of cardiac operating room (OR; higher intensity, more critical decision making); study of anesthesia "near misses" found that ~3% of regional anesthesia cases had "near miss" requiring salvage, ~50% of general anesthesia cases required salvage (*eg*, treating hypotension), ~80% combined regional and general anesthesia; 100% of cardiac anesthesia patients had episodes in which correction was necessary to avoid "near miss" (on average, 3 "near misses" per case)

Risk reduction: better monitoring in cardiac anesthesia; place arterial lines (a-lines) in all patients, pulmonary artery (PA) catheters, TEEs in many; place IV catheters, monitors prior to induction of anesthesia; *prophylactic therapy* — key to initiate therapies before problem rather than react to problem; quality anesthesia care, attention to detail can greatly enhance safety and outcome; ignoring details can lead to disaster

Basic Sequence for Cardiac Anesthesia for Adult CABG and Valve Procedures

History: pay attention to cardiac history; evaluate cardiac catheterization report, thallium stress test, echocardiogram, electrocardiogram (ECG); critical information includes left main disease or equivalent, poor distal targets in coronary artery, ejection fraction (EF), left ventricular end diastolic pressures, presence of aneurysms, pulmonary hypertension, valvular lesions, congenital lesions; note how patient manifests angina in order to understand verbal reports/symptoms (*eg*, shortness of breath, nausea, cough, restless sleep, heartburn) and link symptoms to possible myocardial ischemia; coughing or nausea on morning of surgery, rule out myocardial ischemia; past medical history such as chronic obstructive pulmonary disease (COPD), transient ischemic attack (TIA), stroke, cerebral vascular disease, chronic renal insufficiency, hepatic insufficiency; allergies; current medications (especially antianginal drugs); discontinuation of some medications may increase risk; do not withdraw on day of surgery

Physical examination: assess airway; auscult chest, note murmurs; note heart failure status; pneumonia, COPD present and managed; assess for ascites, obesity

Diagnostics: assess complete blood count (CBC), platelets, electrolytes, blood urea nitrogen (BUN), creatinine, glucose, coagulation factors; evaluate thoracic radiographs for cardiomegaly, tumors, pleural effusion; assess for left bundle branch block on ECG (if placing PA catheter, can develop third-degree block); assess for recent myocardial infarction (MI), resting ischemia, ST wave changes, and compare with previous ECG history; assess pulmonary function tests (PFTs), blood gases; if forced expiratory volume in 1 sec (FEV1) <600 L/min, difficult to extubate

Patient communication: inform patient of procedures (*eg*, a-line, PA catheter, postoperative ventilation) and what to expect during recovery (*eg*, intensive care unit [ICU] recovery, endotracheal tube [ETT] removal); get consent; *explain risks* — MI (6%), stroke (3%), neuropsychiatric effects (`95%), other neurologic events (3%), transfusion needed (40%-90%), pneumonia (10%), death (1%-10%, depending on procedure); document discussions

Premedications: patients often scared; can become ischemic with stress; limit premedications prior to going into operating OR, but recognize patient fears; if premedications given, start nasal O_2; 10 mg diazepam (Valium) can be helpful for anxiety

Antianginal medications: do not stop any concurrent antianginal medications; ensure administration morning of procedure; include in preoperative orders; withdrawal of antianginal medications during cardiac surgery increases

risk of death, MI, cerebrovascular accident (CVA), renal failure

PA catheters: use depends on local customs, surgical needs, patient risk, case type; in some facilities, 100% of patients get PA catheter and at others, few get them; limited evidence that PA catheters beneficial or reduce operative risk; if used, ensure reduced risks of line placement (*ie*, be skillful, avoid injury with placement); reduce risk via ultrasonic mapping prior to and during catheter placement by removing towels behind patient's head, position patient, taping head in place, sedation (*eg*, dexmedetomidine 0.7 mcg/kg/hr plus midazolam [Versed]); 2 approaches to using ultrasound for central lines; *prelocation* — draw out anatomy (*ie*, sternocleidomastoid, clavicles, carotid) with permanent marker (more lines the better), place blue line on echocardiogram (echo) machine in vessel center, place probe's blue dot to patient's right, probe perpendicular to bed (*ie*, horizontally, so as not to require accounting for probe angle); with 5-MHz probe, map out path to carotid and internal jugular (IJ; bigger, collapses under pressure); prep, drape, place central line using marks; *continuous echo approach* — position patient; echo neck to ensure IJ normal; prep, drape; place sterile echo probe cover on echo, remembering to put echo lube inside (latex used because polyethylene does not transmit as well), squeeze probe cover tip to remove air bubbles, inject local anesthetic, hold echo probe in one hand while placing needle in IJ with other; check guide wire placement; real-time/continuous ultrasound better than prelocation, but both techniques work

Anesthetic techniques: difficult to demonstrate one form of anesthesia better than any other; few exceptions; all anesthetic agents such as isoflurane (eg, Aerrane, Forane, Isorane), sevoflurane (Ultane), dexmedetomidine (Precedex), high- or low-dose narcotics, propofol (Diprivan)-based anesthetics roughly equivalent if hemodynamics controlled; exception desflurane (demonstrated to cause pulmonary hypertension and myocardial ischemia, not recommended for patients with known coronary artery disease); for high-dose spinal narcotics (*eg*, 1 mg subarachnoid) but limited safety data for this technique

Opiates: different dose ranges; sufentanil (Dsuvia, Sufenta) high dose 20 mcg/kg to 40 mcg/kg, low dose 1 mcg/kg to 2 mcg/kg; remifentanil (Ultiva) starts at 0.1 mcg/kg/min to 1 mcg/kg/min; midazolam can be added to avoid "drop-in awareness" (*ie*, anesthesia awareness), can cause delirium; fentanyl, 250 mcg to 1000 mcg for adult cardiac surgery; remifentanil has short half-life (5 mins to 10 mins), because of metabolism by nonspecific cholinesterase, allows for rapid emergence; expensive; additional narcotic needed prior to emergence; can reduce dosage with longer-acting, inexpensive narcotic such as fentanyl to occupy fraction of mu receptors, then use remifentanil to occupy smaller fraction; fentanyl works well in cardiac cases; remifentanil combined with dexmedetomidine infusions often used for transcatheter aortic valve replacement (TAVR) cases under monitored anesthesia care (MAC), provides slow heart rate, controlled infusion, metabolized quickly

Propofol: no real benefit of propofol infusions over other infusions for cardiac surgery; allows for quick emergence

Dexmedetomidine: alpha-2 adrenergic receptor agonist; 1500:1 alpha-2:alpha-1 ratio (clonidine 30:1 alpha-2:alpha-1 ratio); can be used as adjunct to anesthetic, reduction in MAC, or as postoperative sedative by infusion; study on cardiac anesthesia and postoperative sedation; group 1 received fentanyl-midazolam sedation, group 2 propofol sedation, group 3 dexmedetomidine sedation; postoperative day 1, 50% of groups 1 and 2 had delirium, 10% from group 3; at hospital discharge, 10% groups 1 and 2 had episodes of delirium, 5% from group 3

Planning for early extubation: key to early extubation, multiple minor changes in anesthetic technique combined with good candidate; difficulty lies in that many patients seem good candidates for early extubation but then not when they get to ICU (*eg*, bleeding, hemodynamic issues) while others do not appear to be good candidates but then have no issues; solution, treat all patients as candidates for early extubation, then see who qualifies; requires planning from start of case; successful candidates have reasonable cardiac and pulmonary function; anesthetic technique changes include limiting fluid administered, limiting total narcotic and benzodiazepine doses, relying on volatile agents (*eg*, sevoflurane), administering dexmedetomidine infusions during case, careful control of blood pressure (BP) with emergence, and remembering that some vasodilators (*eg*, nitroprusside [Nipride, Nitropress]) inhibit hypoxic pulmonary vasoconstriction, increase shunt, and make weaning of O_2 more difficult; rapid weaning of O_2 postoperatively critical; when oxygenation acceptable, alveolar-arterial O_2 (A-a) gradient reasonable, patient awake, hemodynamically stable, extubate; note that extubation time often controlled by nursing shifts and protocols; to extubate early, wean fraction of inspired O_2 (FiO_2) rapidly, awaken patient, and upon meeting extubation criteria, extubate, regardless of shift changes, etc; most common reason for delayed extubation ventilation/perfusion ratio (V/Q) mismatch caused by heparin-protamine complexes in lungs (not anesthetic issue; do not extubate yet; wean O_2 as tolerated)

OR setup: standard room set includes suction, machine checkout, airway equipment; drugs, including succinylcholine, propofol, nondepolarizing muscle relaxants, atropine, glycopyrrolate (*eg*, Cuvposa, Robinul, Seebri, ephedrine (Akovaz), phenylephrine (*eg*, Neo-Synephrine, Sudagest PE, Wal-Phed PE); both syringe and infusion), epinephrine (infusion ready), calcium chloride, heparin (≥30,000 U drawn up), and lidocaine; label every single infusion line, bag, and syringe to make finding what you need in emergency situation easier

Patient preparation: place at ≥1 large-bore IV catheter (*ie*, 14- or 16-gauge), 2 better; place a-line, ideally right radial artery (left side commonly occluded by retractor for left internal mammary artery [IMA]); place patient on O_2 (*ie*, preoxygenate), attach ECGs (5-lead for anesthesia machine, 3-lead for echo machine), cover leads with Tegaderm, place right IJ PA catheter, obtain baseline values

Intraoperative safety for anesthesiologists: cardiac surgery involves large quantities of blood at arterial and higher pressures, frequent splash; wear eye protection at all times in OR; eye splash common reason people exposed to viruses, other pathogens in OR

Communication among OR staff: perform each task correctly and stay focused; communicate with surgeons; ask questions, tell him or her what you are doing, inform him or her if issue arises; operations require team

approach; no place for emotion, anger, or hostility in OR (experiencing and exhibiting these emotions means mind not 100% on patient; diminishes safety); bear in mind that if surgeon yelling, likely upset, which usually means fear, not anger with the anesthesiologist; communication critical to safety

Hypotension: cardiac surgeons can cause profound hypotension with cardiac manipulation; if BP suddenly drops or acute ventricular premature contractions (VPCs) noted, assess surgical field first before treating, then communicate with the surgeon

Ventilating: surgeons may ask you to hand ventilate during procedure; ensure helping not hindering (*eg*, look at what surgeon doing and see if they can visualize what they need to see when you ventilate); if asked to turn off ventilator, leave your hand on switch to remember to turn it back on (easy to get distracted and forget); if on cardiopulmonary bypass, can turn off ventilator, but if pulsatility on PA catheter trace, ejecting from right ventricle, ventilator should be on

Hemodynamics: specific recommendations for valve repairs; aortic stenosis, consider preload, afterload, systemic vascular resistance (SVR), heart rate, and rhythm; aortic stenosis preload, ensure full; afterload, maintain SVR (do not allow decrease, mild increase acceptable); maintain heart rate 50 bpm to 80 bpm, normal sinus rhythm; easiest with large-bore IV catheters, able to give volume, be able to turn on phenylephrine infusion to maintain SVR; for aortic insufficiency, maintain preload; SVR can mildly decrease because forward flow improves; maintain heart rate 60 bpm to 80 bpm, normal sinus rhythm; for mitral stenosis, maintain preload (*ie*, large-bore IV catheters), maintain SVR for afterload; heart rate 50 bpm to 80 bpm, normal sinus rhythm; for mitral regurgitation, maintain preload, maintain afterload (SVR can decrease slightly); heart rate 50 bpm to 80 bpm, normal sinus rhythm

Cardiopulmonary bypass hemodynamics: prebypass, maintain BP within 20% of baseline pressures; heart rate 40 bpm to 80 bpm; postbypass, mean arterial pressure 60 mm Hg to 80 mm Hg; occasionally 40 mm Hg to 80 mm Hg during "cold period," 60 mm Hg to 80 mm Hg during "warm period" (*ie*, when cross-clamp off); if carotid vascular disease or chronic renal insufficiency, need higher BP (can achieve by infusing phenylephrine; coordinate with perfusionist); *postbypass hemodynamics* — systolic BP >80 mm Hg (100-120 mm Hg ideal); >120 mm Hg, patient likely hypertensive or having more bleeding; cardiac index >2.0; PA diastolic pressure <~20 mm Hg; central venous pressure <~15 mm Hg; if central venous pressure greater than PA diastolic pressure, either poor calibration of monitor or right ventricular failure; if PA systolic pressure exceeds systemic arterial pressure, patient may die; PA systolic pressures greater than systemic arterial pressures very bad sign; hypotension could be from surgical manipulation of heart if chest open or tamponade if closed (primary issue to rule out for hypotension in closed chest)

Preinduction hemodynamic measurement: record systemic arterial pressure, heart rate, central venous pressure, pulmonary artery pressure, partial pressure of O_2, and cardiac output prior to anesthetic induction; allows correction of problems prior to induction

Fluids: cardiac cases have potential to receive significant amounts of fluids intraoperatively (with little obvious benefit), thus requiring diuresis postoperatively, often resulting in electrolyte disturbances; postoperative extubation can frequently be delayed by intraoperative fluid administration; thus, attempt to limit fluid administration intraoperatively; *suggestions* — if using 2 large-bore IV catheters, keep one closed, use 500-mL fluid bag, attempt to administer <500 mL of crystalloid fluid prior to bypass and do not administer any fluids during bypass (expect for fluids for vasoactive drugs); do not use hydroxyethyl starches (can lead to renal injury and pruritis); if volume needed postbypass , use albumin 5%; use pumps on all drug infusions to prevent accidental high flows; use phenylephrine to support BP before administering large amounts of fluid prebypass; *tally fluids* — from crystalloids, colloids, blood, Cell Saver machine, pump blood, bypass prime volume, and total fluid given by perfusionist

Tallying blood loss: impossible to know; infuse based on hematocrit; set transfusion trigger (*eg*, 21%; risk increases >26%)

Ischemia: patients having cardiac surgery because of myocardial ischemia and 40% of patients undergoing CABG surgery used to have intraoperative episodes of myocardial ischemia; record 5-lead ECG prior to induction for baseline comparison; ask patient if experiencing chest pain; look at ECG continuously or at least every 60 secs; absolute attention to ECG will detect fraction of ischemia

Myocardial blood flow: if insufficient, myocardium immediately stops contracting within 5 secs to 10 secs; pH and NADH ratio changes follow; at 60 secs to 90 secs after ischemia, ECG starts to change; focal reduction in cardiac function can be detected by watching echocardiogram (best seen with short access midpapillary view)

Echocardiogram: view as adjunct care, not requirement; do not ignore patient

Induction and intubation: never induce patient without surgeon who can put patient on bypass available in room; never induce without perfusionist and pump; surgical team should be able to place patient on bypass in <5 mins if patient arrests on induction; avoid hypotension and hypoxia; limit amount of IV fluids to <1 L, <500 mL prior to bypass; limit BP drop upon induction by giving vasoactive substances; *2 approaches* — 1) induce patient, then respond to hypotension (in 95% of patients induced); 2) start phenylephrine infusion prior to induction in all patients and turn it off when not needed

TEE probes: need to be sterilized between cases; empty patient's stomach with orogastric tube, lubricate mouth, insert unlocked probe; always use bite block; probes expensive; should be adjunct to patient care, not substitute or requirement; do not ignore patient; useful for detecting air, atrial septal defects, ventricular septal defects, aortic stenosis, aortic regurgitation, mitral regurgitation, mitral stenosis, volume status, aortic plaques, microischemia, regional and global ventricular function, valvular anatomy, valvular function; TEE examination frequently causes modification in surgical plan (*eg*, unrecognized aortic plaque, shifts patients to off-pump CABGs, alters cannulation site, cancels case); perform early on; to remove, always unlock before removal, hold endotracheal tube when pulling out probe to avoid accidental extubation

Blood gas and activated clotting time (ACT): obtain after induction for baseline; multiple techniques for ACT (*eg*, Hemochron, HemoTec, i-STAT); important to understand different techniques for each system

Sternotomy: painful; occurs rapidly after induction; ensure patient adequately anesthetized; do not forget to turn ventilator back on afterward; when sternotomy repeated, often many adhesions, which may bring ventricle close to sternum; cutting right ventricle results in hemorrhage; have blood products available, another reason for large-bore IV catheters; may also cut through IMA graft or saphenous graft; prior to surgery, cardiac catheterization will have determined if grafts failed, ensure report read; if grafts failed and cut, little concern; if grafts viable and cut, severe instant myocardial ischemia with rapid deterioration

IMA dissection: surgeons may want table elevated and tilted to left, may want tidal volumes reduced and rate increased; difficult to obtain echocardiogram image during IMA dissection; ECG may also be abnormal

Heparinization: do not allow bypass without heparinization; if patient not heparinized when clamp from bypass machine opened, pump, oxygenator will clot, patient will most likely die; if surgeons placing cannula in artery, ask if they want heparin; always communicate when heparin given; always use central line to administer; aspirate blood from line before and after heparin dose to ensure proper administration; usually 300 U/kg to 400 U/kg; check ACT 1 min to 2 mins after dose; do not use same IV catheter or draw blood back from where heparin infused, draw from arterial line; check ACT quickly because needs to be >450 secs to go on bypass and takes 7.5 mins to reach >450; if patient on heparin preoperatively, give same dose; do not stop preoperative heparin; take care putting in IV catheters/lines; do not give antifibrinolytics (aminocaproic acid [Amicar], tranexamic acid [Lysteda]) until fully heparinized; if ACT not >450 secs after dose, give more heparin; if patient heparin resistant, administer fresh frozen plasma (FFP) or antithrombin III, rare; if patient arrests prior to bypass, give heparin so patient can be put on bypass for resuscitation

Antifibrinolytic drugs: all patients undergoing cardiac surgery using extracorporeal circulatory support likely need an antifibrinolytic; several choices; aprotinin (Trasylol) taken off market in United States due to secondary increased morbidity, mortality, and renal failure; raised risk of death 4-fold; no increase risk with aminocaproic acid or tranexamic acid; aminocaproic acid reduces postbypass bleeding; some clinical reports of problems include left ventricular thrombosis, arterial thrombi; 5 g to 10 g prior to bypass and 5 g to 10 g after bypass; adverse events similar to protamine

Suggested Reading

Chakravarthy M: Modifying risks to improve outcome in cardiac surgery: an anesthesiologist's perspective. *Ann Card Anaesth.* 2017;20(2):226-33; **Hensley FA et al:** *The practice of cardiac anesthesia*. Boston, MA: Little, Brown; 1990; **Nowak-Machen M:** [Impact of cardiac anaesthesia on patient outcome]. *Anasthesiol Intensivmed Notfallmed Schmerzther.* 2017;52(7-08):498-511; **Renner J et al:** [Cardiac anaesthesia: anaesthesiological management]. *Anasthesiol Intensivmed Notfallmed Schmerzther.* 2018;53(5):346-62.

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Cardiac Anesthesiology: Part 2

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Aprotinin: antifibrinolytic and platelet preserver; reduced bleeding and transfusion associated with coronary artery bypass graft (CABG) surgery, "redos" (repeated cardiac procedures), patients on aspirin; expensive; considered beneficial compared with risk of disease transmission from blood transfusion; however, increased risk of graft closure, renal failure, and death from clotting; study looked at United States (US), Canada, England, France, *etc*, showed mortality rate of ~3% in cardiac patients; in Germany, mortality rate 15%; whereas other countries gave aprotinin to 15% of patients, in Germany, 85% got aprotinin; of importance, that Bayer located in Germany, denied problem until "whistleblower" released data showing that Bayer had done study in 60,000 patients and knew about issue; randomized trial then conducted and confirmed epidemiology; aprotinin taken off US market; important to understand that companies have vested interest in selling drugs, may not disclose everything known about risks (*ie*, money can affect ethical behavior)

Operations: in 1990s, percentage of cardiac surgeries done using off-pump CABG compared with on-pump CABG techniques rose dramatically; invention of Medtronic Octopus tissue stabilizer and Medtronic Starfish cardiac positioner made off-pump CABG easier, safer, more practical; unfortunately, ROOBY trial, randomized on-pump/off-pump CABG trial, demonstrated no benefit in neurologic outcomes with off-pump CABG, decreased patency in lateral-wall grafts; anesthetic care fundamentally different for these 2 approaches; be flexible and prepare for either procedure in case change needed

On-pump CABG: when surgeons place cannulas, check twitch monitor; may need to administer additional nondepolarizing muscle relaxant prior to cannula placement; if patient takes deep breath with right atrium open, can have gas emboli, severe injury; do not allow surgeons to go on bypass without heparinization; arterial pressure at this point should be ~<120 mm Hg; small cannula in aorta (often has red tape) should not have bubbles: if bubble seen, inform surgeon immediately; when aortic cannula placed, often blood splash, so wear safety glasses; larger cannula (usually blue tape), venous cannula, drain line, may have bubbles; in surgery on mitral valve or atrial septal defect (ASD), will be 2 smaller drain lines into superior and inferior vena cava; if small cannula with balloon at 1 end placed in coronary sinus through purse string in right atrium, anesthesiologist needs to measure cannula pressure; hook this up to central venous pressure (CVP) transducer; may need to change scale; when flow in coronary sinus catheter 200 mL/min, pressure should be ~40 mm Hg; if pressure does not increase with coronary sinus flow (*ie*, appear as standard CVP), cannula not in coronary sinus; if this occurs during continuous warm cardioplegia, period of warm ischemia, can result in severe ventricular dysfunction and death; if cannula pressure very high, >100 mm Hg, with 200 mL/min, cannula against wall and should be repositioned to achieve adequate retrograde cardioplegia; surgeon may ask anesthesiologist to check echocardiogram (echo) of coronary sinus to demonstrate coronary sinus catheter; best image found between depth of short axis, and 4-chamber view; adjust level, will see catheter with metal spring in coronary sinus; afterward, left ventricular vent line may be placed through right superior pulmonary vein to decompress ventricle

Checklist for going on pump: "HAD to SUE" pneumonic (mnemonic; if performed incorrectly, "you may get sued"); *H*— heparin; always give heparin prior to bypass; *A*— always check activated clotting time (ACT) before going on bypass; must be >450 secs; *D*— drugs; what needs to be administered or discontinued (*eg*, nondepolarizing muscle relaxants needed, turn off inotropes); *S*— pull "Swan (Swan-Ganz, standard pulmonary artery [PA] catheter)" back slightly; *U*— check urine prior to bypass; *E*— emboli; ensure no air bubbles to cause arterial emboli

Perfusionist complications: mistakes made by perfusionist often called "clean kills"; *3 most common fatal mistakes*— no O_2 in oxygenator, no heparin, or reservoir runs empty; if power goes out on bypass machine, perfusionist uses hand crank, may ask for assistance by anesthesiologist; if line ruptures, anesthesiologist may be asked to help replace it; anesthesiologist should understand pump and other such equipment (occasionally may be needed to run pump); *air lock*— another complication of pump; blood removed from patient by siphon (venous drain line drains by siphon); air introduced into siphon system will cause it to stop working; if anesthesiologist or perfusionist notes bubbles in venous return line, inform operating room (OR) staff; check integrity of cordis, close all stopcocks, surgeon will check atrial purse string; if pump flow temporarily reduced, venous pressure will increase and air leak will diminish; if lines become empty, can refill with saline if air lock occurs; avoid air lock because requires coming off pump

Cardioplegia: *many types of cardioplegia*— cold, warm, warm induction, cold maintenance, warm reperfusion, hot shot, crystalloid, blood, antegrade, retrograde; best kind of cardioplegia, short cross-clamp time with skillful surgeon; record on-bypass time, off-bypass time, on-cross-clamp time, off-cross-clamp time; as cross-clamp time exceeds 1 hr, ventricular function deteriorates, worse

after 2 hrs; bypass not healthy for patients; lethal dose (LD_{50}) of cardiopulmonary bypass used to be ~240 mins (will experience more problems with coagulopathy, *etc*); cardioplegia helps during cross-clamp; cardioplegia solution can vary; always ask perfusionist what specifically being used to prime pump and contents of cardioplegia solution bag

Deairing maneuvers: do not pump air into patient; difficult to remove air from bypass machine; can fill with CO_2 prior to priming; fill carefully to prevent bubbles; regardless, Doppler studies on middle cerebral artery during bypass have demonstrated 50 to 2000 emboli per case; difficult to determine if air or atherosclerotic plaque; other issue with bubbles, the smaller the bubble, the bigger the echo signal because of size of echo wavelength; on open ventricle and aortic procedures, surgeons often ask anesthesiologist to perform more deairing maneuvers (*eg*, place head down, shift patient left or right, roll from side to side); surgeon may aspirate ventricle or aorta; inform surgeon if large bubbles noted in ventricles on echo; majority of emboli occur during aortic cannulation, cross-clamp placement or removal, side biter placement or removal, weaning from bypass, and aortic cannula removal; most of those events occur when patient still at 37°C; avoid high glucose or overly warm patient during these times; despite best efforts, 95% of patients suffer subtle neuropsychiatric changes from air emboli; can detect with neurocognitive testing

Coming off bypass: pneumonic device, wide receiver most valuable player, WRMVP; *W*— warm; is patient warm? check bladder temperature, blood temperature, ideally 37°C; do not reheat too quickly; *R*— rhythm/rate; is patient in normal sinus rhythm or do they need to be paced? is rate adequate?; if heart rate (HR) 25 bpm to 30 bpm, pace it to increase speed; if problem, likely in third-degree heart block; again, pace; *M*— monitor; all monitors/alarms turned off during bypass, need to be turned back on; *V*— ventilation; turn on ventilator (easy to forget); *P*— perfusion; assess pump flow in order to calculate systemic vascular resistance (SVR); *weaning from bypass*— requires plan; dependent on many factors (ventricular function prior to bypass, how long cross-clamp on, what heart looks like now, current SVR)

Weaning plan: communicate plan to surgeon; if planning to use drug with long side effect, *eg*, amrinone (Inocor) or milrinone (Primacor), not recommended as first choice, inform surgeon because will not clear quickly; have inotrope ready if needed; should be able to wean 80% to 90% of first-time CABG patients from bypass with no inotrope; may need some phenylephrine (*eg*, Neo-Synephrine) to vasoconstrict; calcium chloride often given, but at excessive doses (>2 g) associated with pancreatitis; standard weaning plan from bypass, calculate SVR; SVR=([MAP-CVP]/CO)x80 (MAP=mean arterial pressure, CO=cardiac output); MAP and CVP obtained from monitor; CO on bypass obtained by asking perfusionist for pump flow (*eg*, 5 L/min); SVR should be 1000 to 1200 Wood units (WU) to get off pump; usually lower in patient because CO necessary to develop reasonable blood pressure (BP) post bypass too high; to increase SVR, vasoconstrict patient to achieve better BP

Reasonable approach to coming off bypass: make educated guess about inotropic state of ventricle; if poor prior to bypass, most likely still poor, thus patient will likely need inotrope; if inotropic state of ventricle acceptable prior to bypass and cross-clamp time reasonable (≤60 mins), inotropes likely not needed; calculate SVR, correct it to 1200 WU, check requirements for coming off pump (WRMVP); be prepared to change plan

Bypass: bypass system basically large plastic pipe with holes; runs through right atrial appendage into inferior vena cava; pipe full of fluid, hooked to venous reservoir; pipe clamped

Before starting bypass: fulfill "HAD to SUE" criteria; if emergency situation and no time to check ACT, give heparin and proceed

Going on pump: perfusionist removes clamp from venous drain line, siphon effect drains blood from right atrium and inferior vena cava into venous reservoir; important to maintain siphon effect; no blood entering right ventricle, CO drops; perfusionist then turns on pump; blood heated or cooled, oxygenated, pumped back through filter into aorta; unclamping venous drain line reduces right atrial pressure and diverts blood into pump; perfusionist may then say, "Full flow," meaning achieved 4 L/min to 5 L/min of venous drainage and able to pump 4 L to 5 L into patient; at this point, turn off ventilator; PA pressure should be nonpulsatile; note that not large supply of blood in bypass machine, roughly 500 mL in reservoir; if siphon stops, must stop pump immediately

Coming off pump: exact reverse situation; fulfill all criteria for coming off pump (*ie*, WRMVP); adjust SVR; determine inotropic state; perfusionist then occludes venous drain line, which reduces amount of blood draining into venous reservoir; right atrial pressure increases as blood starts to flow into right ventricle and out PA; at this point, pump flow can be fraction of total flow (*ie*, heart doing part of job, perfusionist doing rest); surgeon may say, "Leave some in and come to 4 L/min"; PA and systemic BP become pulsatile; perfusionist gradually drops to 2 L/min, then 1 L/min, watching right and left ventricular pressures, making sure not distending, slowly loading heart; surgeon may then say, "Give 100," meaning perfusionist leaves 100 mL less blood in reservoir; perfusionist may be draining 2 L/min of blood from patient and pumping 2 L/min into patient, and will now also pump 100 mL more blood than withdrawn; inexact science; reservoir volume decreases by 100 mL; surgeon clamps venous drain line (now truly off pump); then surgeon removes venous cannula (ideally, placing it in saline), draining blood back into reservoir, keeping line full of saline; this allows perfusionist to start hemoconcentrating blood into system but keeps venous line ready in case return to bypass needed; arterial line (art-line) still in place so perfusionist can give fluid

Weaning bypass and volume orders: varies by institution and surgeon; at some institutions, anesthesiologist weans patient from bypass and gives volume orders; at others, surgeon does this job; communication key; anesthesiologist needs to tell surgeon if not ready to wean patient; if anesthesiologist feels patient needs to go back on bypass, should tell surgeon to put cannula back in; if patient doing poorly, anesthesiologist can tell surgeon not to remove arterial cannula; if patient needs more volume, anesthesiologist should communicate and/or ask

for it; anesthesiologist part of team, so critical to maintain communication during cardiac surgery

Inotropes and vasoactive compounds: if using drug that requires infusion and whose effects of incorrect or fluctuating dose would be difficult to manage (*eg*, dopamine, dobutamine, epinephrine, norepinephrine, nitroprusside [Nipride, Nitropress], nitroglycerin [*eg*, Nitro-Bid, Nitro-Dur, NitroQuick], phenylephrine, propofol [Diprivan, Propoven]), use infusion pump; fluctuations caused by relying on gravity drips unacceptable, primarily because of back pressure; all drugs must be mixed in concentrations approved by pharmacy; label all drugs and infusions

Prophylactic drugs: some surgeons believe prophylactic high-dose steroids reduce immune reaction to bypass or reduce neural injury but scientific evidence limited; downsides to steroids include infections, hyperglycemia, poor wound healing; some surgeons believe prophylactic inotropes or vasodilators work but also little evidence to suggest this; postbypass prophylactic nitroglycerin infusions suggested as preventive measure for internal mammary artery (IMA) spasm, myocardial ischemia; downsides include hypotension, supply, limit of ischemia, and more fluid requirements to keep preload adequate; magnesium thought to be antiarrhythmic and anti-ischemic; some load with magnesium prior to CABG surgery; equivocal scientific evidence for many of these theories; regardless, communicate with and ask about preference

Phosphodiesterase (PDE) inhibitors: do not start PDE inhibitor (*eg*, amrinone, milrinone) without talking to cardiac surgeon; not first-line agent; will profoundly vasodilate; will most likely require second inotrope to have vasoconstrictive properties; long-acting drug

Potassium: low potassium in cardiac surgery <4 mEq/L to 4.3 mEq/L; associated with arrhythmias; requires replacement if <4 mEq/L; high potassium depends on timing; >5 mEq/L common on bypass because of potassium in cardioplegia; ideally should be <5 mEq/L and >4 mEq/L when coming off pump; if needed once off pump, infuse slowly (10 mEq/L/hr to 20 mEq/L/hr); if potassium too high, perfusionist can ultrafiltrate patient (different from dialysis because no dialysate); ultrafiltration adds volume to reservoir, then uses dialysis cartridge to ultrafiltrate out additional fluid, which removes unwanted potassium

Hematocrit: hematocrit drops with hemodilution in bypass pump; requires correction if <20%; probably does not need correction if >26% but requires clinical judgement as well as communication with surgical team

Postbypass hemodynamics: systolic BP should be >~80 mm Hg, ideally between 100 mm Hg and 120 mm Hg; >120 mm Hg hypertension, can result in more bleeding; cardiac index >~2.0; CVP <~15 mm Hg; PA diastolic BP should be <~20 mm Hg; if CVP ≥ PA diastolic BP, likely poor calibration or right ventricular failure; in cases of hypotension, always consider surgical manipulation of heart if chest open, tamponade if closed

Protamine: "essentially salmon semen in a bottle"; allergic, anaphylactic, and histamine responses to protamine; typical dose, ~10 mg to equalize 1000 U of heparin; forming weak salt between acid and base (*ie*, heparin and protamine) and then titrating response; check response by measuring ACT; causes heparin-protamine complexes in lungs, can lead to volume-perfusion (V/Q) mismatch and postoperative shunt caused by clearance of these complexes reticuloendothelial system in lung; administer dose, then check for allergic response

Allergic response and management: manifested by hypotension, bronchospasm, rash, or pulmonary hypertension; upon seeing reaction, stop infusion; profound hypotension from protamine can occur, so be ready with phenylephrine; give 100 mg hydrocortisone and H_1 and H_2 blocker (*eg*, ranitidine [Zantac] or famotidine [Pepcid], and diphenhydramine [Banophen, Benadryl]); may also need epinephrine, vasoconstrictors, or inotropes; severe cases may need to return to bypass to allow heparin to spontaneously metabolize away

Administration: administer slowly (lecturer suggests giving over period of 20 min); once one-third administered, inform perfusionist so pump can be stopped (to prevent clotting pump); after protamine fully administered, check ACT (should be 120 secs to 130 secs); if too high, give additional protamine; can administer "pump blood" (*ie*, hemoconcentrated blood from pump) after this point; may need to give more protamine because pump blood heparinized; check ACT after giving blood products from pump or autologous blood recovery system (Cell Saver)

Postbypass bleeding: if postbypass bleeding occurs, check ACT; if elevated, correct it; if patient on aspirin in last 4 days prior to surgery, may need platelets; if bleeding medically caused, may need platelets; if bleeding from surgery, suture or cauterize

Returning to bypass: if severe hypotension, bleeding, low cardiac output, *etc*, patient may need to return to bypass; if protamine given, administer more heparin (*eg*, 400 U/kg), then check ACT; make decision before aortic cannula removed; inform surgeon if trouble maintaining BP despite inotropes, tell surgeon to delay removing aortic cannula or immediately return to bypass; unhealthy for heart to be dilated by high filling pressures and then have low coronary perfusion pressures

Balloon pumps: balloon pump not artificial heart; raises diastolic BP to improve coronary blood flow; improves coronary perfusion, can somewhat improve cardiac output; requires electrocardiogram (ECG) signal and arterial pressure signal (can have slave cable from monitor and send signal over to balloon pump, or have separate set of wires and separate arterial transducer)

Left ventricular assist device (LVAD): transportable centrifugal pumps that can be used as bridge to transplant or to allow recovery of myocardium; Impella heart pump also performs in this manner via cannulae

Closing chest cavity: closing chest raises intrathoracic pressure, may cause hypotension if volume inadequate; after chest closed, check CO; if lungs seem too large or heart lifting out of chest, patient may have bronchospasm with air trapping; may require bronchodilators or adjustments to ventilator

Transesophageal echocardiography (TEE) probe: to remove probe, unlock, then pull out; clean off biologic material

Transport: critically important to have patient monitored at all times during transport; never remove ECG or arterial pressure monitor unless another one working; place transport leads and ensure they work; ensure art-line working; if patient hemodynamically unstable, do not change art-line; fix hemodynamic problems, then transfer

it over; quickly re-zero and ensure elevation of transducer at correct level; common issue, sudden hypotension upon moving patient; phenomenon not well understood; could be from reperfusion of dependent regions (*eg*, skin); patient can have profound hypotension; many patients drop filling pressures in half; do not transfer if patient unstable or volume depleted; important preparations for transfer include volume, drug to raise BP, drug to lower BP, O_2, mask, any other drugs needed for transport

Intensive care unit (ICU): upon transfer to ICU, shift monitors in same way as from OR to transport; if using system with cartridge and transport monitor, unplug it from transport monitor and plug into ICU monitor; if not using this system, change all wires over; do not shift art-line until patient hemodynamically stable; auscult chest after hooking up ventilator; if sudden hypotension, suspect problem with ventilator (*eg*, infinite positive end-expiratory pressure [PEEP]); remove patient from ventilator, hand ventilate, use new ventilator; do not allow nurses to change inotropes or intravenous lines, or remove art-line until you (anesthesiologist) have left; patients should be monitored 100% of time

Extubation: checklist for extubation should include no evidence of myocardial ischemia, no infarction, no heart failure, hemodynamic stability, unlimited inotropic support, no balloon pump, limited bleeding without coagulopathy (*ie*, chest tube draining <50 mL/hr for 2 hrs), adequate blood gas, fraction of inspired O_2 (FiO_2) 0.4 to 0.5, tidal volume 10 mL/kg, PEEP 5 cm H_2O, patient awake and breathing; poor candidate to extubate, one in whom grafts poor, bleeding, tamponade; remain intubated until issues resolved

Minimally invasive cardiac surgery on off-pump CABG: other names include minimally invasive CABG, minimal-access CABG, etc

Heartport, Inc off-pump CABG: historically, developed to avoid opening sternum; arterial inflow cannula in femoral artery, venous outflow in femoral vein, balloon catheter advanced up aorta, balloon inflated in ascending aortic arch to administer cardioplegia; aortic atherosclerotic disease contraindication for operation; cardioplegia delivered antegrade to coronary arteries and retrograde through coronary sinus catheter; balloon advanced into internal jugular vein, PA for venting left ventricle, patient placed on essentially femorofemoral (fem-fem) bypass, and cardioplegia established; provided ability to do single-vessel CABG either through minithoracotomy or arthroscopically; risk of CABG extracorporeal circulation, not sternotomy, so this procedure worsened those risks because of extended bypass, maximizing risk of neuropsychiatric changes and strokes

Chuck Taylor Surgical (CTS) and US Surgical: next approach developed, popularized by surgeon Benetti; minithoracotomy with no bypass; single IMA to left anterior descending artery, heart stabilized by placing latex sutures under left anterior descending artery; small foot pressed on myocardium while sutures pulled heart into foot, blood flow stopped in target vessel by stabilizing sutures; technique required improved technical skill from surgeon because heart moving (both through respiratory movements and contractions); also required increased technical skill from anesthesiologist because part of myocardium ischemic and nonfunctional, prone to arrhythmias and reperfusions; advantages included lower cost, no extracorporeal circulation, reduced hospital time, possibly reduced risk of stroke; downside, operation difficult, vessels hard to approach

Octopus tissue stabilizer and Starfish heart positioner: rather than pressing on myocardium, Octopus suction stabilizes heart and reduces motion; Starfish retractor allows for lifting, moving heart to get to posterior circulation; hemodynamics much improved over CTS; ventricular fibrillation and cardiac issues persist even with better equipment, so sternotomies gaining favor again

Off-pump CABG with sternotomy: choose anesthetic that lowers HR (*eg*, opiate plus inhaled agent); median sternotomy approach; morbidity of sternotomy small compared with risk of prolonged ventricular fibrillation; have perfusion available in case on-pump transition needed; anticoagulate patient, 300 U/kg; provide prophylaxis for arrhythmias (*eg*, magnesium 2 g plus lidocaine 2 mg/min); can also start amiodarone (Nexterone, Pacerone), 150 mg over 10 mins, then 1 mg/min for 6 hrs, then 0.5 mg/min for 18 hrs)

Management: after surgeon retracts heart, places stay sutures and stabilizers, anesthesiologist loads patient with volume (*eg*, albumin), maintains BP with vasoconstrictors; try to avoid beta-adrenergic agonists (*eg*, epinephrine), because of tachycardia and proarrhythmic effects; tachycardia makes anastomosis more difficult

Hemodynamics: prepare to adjust hemodynamics frequently, knowing it will change once surgeons cease manipulating heart; prepare to perform position changes, adjustments to ventilator, reduce motion; have small tidal volumes to increase HR; plan to lower HR further (*eg*, with esmolol [Brevibloc] and adenosine); if HR regular or too low, use atrial pacing; try to avoid glycopyrrolate (Robinul) or atropine (Atropen) because pacing difficult; prepare for reperfusion arrhythmias; be prepared to inform surgeon that hemodynamics, *etc*, warrant going on pump; when heparin reversed, remember, no bypass circuit; extra care required with protamine; give slowly, possibly reduce dose; protamine reactions more of problem without bypass system; consider anticoagulation post reversal of protamine; in off-pump CABG in which coagulation system not exposed to extracorporeal circulation, coagulation system normal, so can experience pulmonary embolism, graft closure, graft clotting, myocardial infarction

Suggested Reading

Chakravarthy M: Modifying risks to improve outcome in cardiac surgery: an anesthesiologist's perspective. *Ann Card Anaesth*. 2017;20(2):226-33; **Hensley FA et al:** *The practice of cardiac anesthesia*. Boston, MA: Little, Brown; 1990; **Nowak-Machen M:** [Impact of cardiac anaesthesia on patient outcome]. *Anasthesiol Intensivmed Notfallmed Schmerzther*. 2017;52(7-8):498-511; **Renner J et al:** [Cardiac anaesthesia: anaesthesiological management]. *Anasthesiol Intensivmed Notfallmed Schmerzther*. 2018;53(5):346-62.

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Anesthesia for Vascular Surgery

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Preoperative Evaluation

Purpose: assess patient to stratify risk; optimize patient, reduce perioperative risk; "cleared for surgery" does not reduce surgical risk; perform full history and physical examination

Coronary artery disease (CAD): all patients having vascular surgery should be assumed to have CAD; important to understand severity, stability of disease, measures to improve stability (is patient medically optimized with beta-adrenergic blockers [beta blockers]?), statins, aspirin, clopidogrel (Plavix), etc; if patient medically optimized with anti-ischemic agents, not having acute medical problems (*eg*, acute new-onset angina, new-onset congestive heart failure [CHF]), can proceed

Guidelines: 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines; reading entire document recommended

Echocardiogram (echo): determine if echo needed; patients with clinically suspected moderate or greater degrees of valvular stenosis or regurgitation should undergo preoperative echocardiography if no echo in prior yr or if significant change in clinical status or physical exam since last evaluation; get echo if congestive heart failure (CHF) and no echo in last yr or 2

Monitoring: monitor if significant valvular disease; (lecturer recommends monitoring of all patients); obtain electrocardiogram (ECG) for patients with known CAD

Stress tests: useful only if results will change management (*eg*, in patient with stable anginal pattern, no CHF, no new-onset angina, no new symptoms, stress test not useful)

Procedures not recommended: coronary angiography (class III indication, do not perform); coronary artery bypass grafting (CABG) prior to noncardiac surgery; percutaneous coronary intervention (PCI) with drug-eluting stents or bare-metal stents; PCI with drug-eluting stents, should delay surgery for almost 1 yr, bare-metal stents ≥30 days; McFalls study demonstrated that these procedures did not help patients or reduce risk prior to vascular surgery

Evidence levels: class I evidence demonstrates many large studies that indicate similar results and show benefit greatly outweighs risk (*eg*, catheterization laboratory, or "cath lab"); if not performed, could be malpractice or below standard of care; class II indicates widespread agreement on use, benefit greatly outweighs risk, class II and IIb; class III shows no benefit or risk exceeds benefit, should not be performed (*eg*, coronary angiogram prior to vascular surgery)

Perioperative beta blockers: beta blockers should be continued in patients undergoing surgery who have been on beta blockers chronically (class I indication); discontinuing chronic beta blocker prior to or on day of surgery raises risk of death ~4-fold; continue beta blockers in hospital; do not withdraw beta blocker

Management of beta blockers after surgery: beta blockers reasonable after surgery, to be guided by clinical circumstances; generally recommended for patients in whom perioperative assessment for vascular surgery identifies high cardiac risk, as identified by presence of >1 clinical risk factor; risk factors include age >65 yrs, hypertension, diabetes mellitus, cigarette smoking, elevated cholesterol, male sex; useful in intermediate- and high-risk patients; probably recommended in patients with CAD; ≥3 risk factors (diabetes, CHF, renal insufficiency, CAD, cerebrovascular disease); if indicated for surgery, consider maintaining patient on beta blocker for ≥1 mo postoperatively; do not start naïve patients on higher-than-recommended dose on day of surgery

Statin therapy: should be continued in patients currently taking statins and scheduled for noncardiac surgery (class I indication); perioperative initiation of statin use reasonable in patients undergoing vascular surgery; perioperative initiation of statins may be considered in patients with clinical indications according to goal-directed therapy

Alpha-2 adrenergic agonists: *eg*, clonidine; clonidine currently not recommended for preventing cardiac events in patients undergoing vascular surgery

Angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs): continuation reasonable; if withheld before surgery, reasonable to restart as clinically feasible after surgery; discontinuing ACE inhibitors in perioperative period shown to increase perioperative mortality; potential risk for hypotension; preparation key; preoperatively insert arterial line (a-line, art-line); start phenylephrine infusion prior to induction; monitor blood pressure (BP); discontinue phenylephrine if not needed; monitor carefully

Antiplatelet agents: important in patients who have had PCI; discontinuation can lead to major cardiac events and death; 1 study demonstrated 20% mortality if antiplatelet therapy discontinued within 30 days of PCI; may need to continue therapy for ≤1 yr; if antiplatelet therapy must be discontinued, consider aspirin as

alternative perioperatively; in patients on antiplatelet drugs undergoing nonemergency or nonurgent surgery, consider delaying 1 yr

Aspirin: lasts ≥7 days in system; studies show aspirin reduces risk in patients having cardiac surgery; while likely beneficial, unlikely beneficial if initiated day of surgery

Prior to surgery: full history and physical with particular attention to cardiovascular disease; assess stability and medications; assess for myocardial ischemia; examples include restless sleep, chest pain; obtain ECG; previously, 15% of patients developed myocardial ischemia in days prior to surgery, which led to additional ischemia; now, with good medical management, occurs much less frequently, but still important to be cautious

Cardiac troponins: lecturer recommends checking preoperatively; consider how many women must take pregnancy tests prior to procedures; comparing number of actual pregnancies (very few) with number of patients with myocardial ischemia (5%-15%) warrants use; myocardial ischemia results in 4-fold increase risk of death; positive troponin level, 2 weeks after surgery, 50% mortality; obtaining troponin levels important because of potential risk of myocardial infraction (MI)

Smoking: many patients with vascular disease have history of smoking; studies have shown that if clinician tells patient to quit smoking, demonstrates slight effect, cumulative effect if multiple clinicians recommend; ~10% of people successfully quit smoking "cold turkey;" nicotine patch, ~15% quit smoking; bupropion (Wellbutrin, Zyban) buprenorphine, ~18%; varenicline (Chantix), about ~25%, barring suicidal ideation or other issues; if presenting for cardiac surgery or acute MI, physicians can get 50% of people to quit smoking; if presenting for noncardiac surgery, ~30%; important to explain to patient why smoking caused current issues and make every effort to educate and help patient quit smoking

Vascular Surgery

Anesthesia: depends on type of surgery; endovascular abdominal aortic aneurism repair (AAA), or aortofemoral bypass graft (AFBG), can use either general anesthesia (GA) or regional anesthesia; open AFBG, probably need GA; angioplasty can be performed with local anesthesia; carotid endarterectomy, regional (*eg*, superficial cervical plexus block) or GA; femoral endarterectomy, GA or regional anesthesia; femorofemoral bypass (fem-fem), femoral-distal (fem-distal), GA or regional; amputations, regional or GA; regional good for amputation because painful procedure; toe amputations, regional; discuss with surgeon

Anesthesia choice: remember, these patients have CAD, hypertension, hyperlipidemia, chronic obstructive pulmonary disease (COPD), possibly diabetes; as disease severity worsens, risk increases; severity of CAD associated with severity of peripheral vascular disease because essentially same disease process; patients who need amputation likely have vasculopathy and severe end-stage vascular disease; microvasculature often severely damaged, high risk

Procedure risk: risk of AAA less than AFBG less than fem-distal, fem-distal less than amputation; even though AAA bigger operation, these patients have less microvascular disease than those presenting for amputation; for amputations, highest risk above-knee amputation (AKA), worse than below-knee amputation, below-knee worse than transmetatarsal amputation (TMA), TMA worse than toe amputation; AKA highest-risk procedure because of severity of microvascular disease

Minimize anesthesia when possible: when choosing anesthesia, less always better; monitoring critical; regional anesthesia ideal when possible

General anesthesia: need arterial line, 2 large-bore intravenous (IV) catheters, phenylephrine infusion; larger-bore IV better (14-16 gauge); allows for rapid volume replacement or other treatments; if patient "looks like they belong in the cardiac operating room (OR), they will act like a patient in the cardiac OR when you put them to sleep," regardless of ease of procedure; must prepare appropriately regardless of type of procedure

Phenylephrine infusion: start prior to induction; allows for assessment of pump action; most patients develop hypotension upon induction, starting infusion before induction allows for management before issue occurs; dose, 25 mcg/min (if severely hypertensive, 10 mcg/min); can discontinue if not needed (5%-10% of patients)

Premedications: midazolam (Versed) can be used if needed; some concern with delirium; helps with compliance, anxiety, for placing IV catheter, etc

Catheters: place lines (*ie*, catheters, art-lines) before induction; easier, safer than waiting until after induction; use premedications if needed

Endotracheal cardiac output monitoring (ECOM) tube: measures stroke volume variation, pulse pressure variation, systemic vascular resistance (SVR) and cardiac output (CO); allows for goal-directed therapy, fluid management; if unavailable, can set monitors to see pulse pressure variation

Inotropes: ideally, avoid; inotrope use raises mortality rate ~3-fold; increases risk of arrhythmias, myocardial ischemia, and MI; can almost always adjust blood volume and SVR to optimize cardiac output without inotrope; instead, set SVR to 1200 dynes/sec/cm^{-5}, give fluids, phenylephrine; stroke volume variation <8%; cardiac index should be reasonable; fix blood volume in SVR first

Stroke volume variation and pulse pressure variation: excellent way to measure volume status; dimensionless constants measured from variation in either stroke volume or pulse pressure with ventilator; if variation ~<8%, adding fluid will not affect cardiac output; if >13%, cardiac output will increase when fluid added; if ~25%, likely experiencing atrial fibrillation, use of ventilator recommended

Anticoagulation and reversal: obtain baseline activated clotting time (ACT); should be 120 secs to 130 secs; when surgeons desire anticoagulation, ask for ACT target (usually ~250 secs); measure ACT every 30 mins to 60 mins and administer heparin to achieve target ACT; to reverse, administer protamine (*eg*, typically, ~30 mg in adult)

Protamine: dangerous medication derived from salmon semen; can cause significant histamine release, hypotension, anaphylaxis, pulmonary hypertension; if patient experiences anaphylaxis, administer 50 mg diphenhydramine (Benadryl, etc), 50 mg ranitidine, and 100 mg hydrocortisone, in order to block H_1, H_2, and mast cell degranulation; if no improvement, 0.3 mg epinephrine subcutaneously (SQ), not IV (will cause

hypertension); diabetic patients commonly experience this reaction because of neutral protamine Hagedorn (NPH) insulin ("P" stands for protamine); after reversing, check ACT, administer more protamine if needed; can give ≤3 times expected dose of protamine before risking coagulopathy

Pulmonary artery (PA) catheters: data supporting use limited; can be useful on rare occasions in critically ill patients having major surgery; if using, should also use transesophageal echocardiography (TEE) probe, because PA catheter not accurate enough on its own; TEE probe can validate conclusions made from PA catheter prior to initiating any therapy; continuous cardiac output monitoring, stroke volume variation from noninvasive monitors make PA catheter less necessary; can be useful to have venous access for vasoactive agents; may be useful in patients having suprarenal AAA procedures, procedures on celiac access, certain thoracic aortic procedures; not useful for assessing volume status

Angioplasty: new trend among vascular surgeons in which they perform angiograms in OR followed by angioplasties, with or without stents; typically simple, easy cases, can be safely done with sedation and local anesthesia for arterial access; of primary importance when choosing sedation for these procedures, ensure patient continues breathing on his or her own; any sedative acceptable; remifentanil (Ultiva) and propofol (Diprivan, etc) infusions tend to be less safe and have more effect on respiration; dexmedetomidine (Precedex) or fentanyl (Duragesic, etc) with midazolam appropriate choices; IV MAC (monitored anesthesia care) local works well for angioplasty

Regional anesthesia: spinal blocks useful for lower extremity surgery if duration of case known; may wear off before surgery finished; epidurals less commonly used because of need for anticoagulation; if epidural vein punctured and then heparin administered, can lead to epidural hematoma and permanent paralysis if laminectomy and drainage not performed immediately

Toe amputation: patients have significant CAD, whether or not documented; do not need GA; toe or ankle block optimal; may have hemodynamic collapse with GA

Arteriovenous (AV) fistulas: patients very sick; often have numerous concurrent diseases, renal failure, CAD, CHF, diabetes, hypertension, COPD, etc; ideally, use regional or local blocks; easy to oversedate such patients; if patient has pain, fix block, do not increase sedation (applies to all patients); do not inadvertently slip patient into GA without adequate monitoring to cover up poor block; do not oversedate with propofol infusions

Other procedures: aortic aneurysms, AFBGs, AAAs, femdistals; lecturer routinely uses GA; for AAA or AFBG, patients given epidural, arterial line, and 2 peripheral IV catheters; if poor IV access, insert central line; if patient is in heart failure or if suprarenal AAA procedure, use central line; large-bore IV catheters ideally (14-16 gauge); start phenylephrine infusion prior to induction; make induction "as gentle as possible"

Airway: "airway trumps all other rules;" if patient has difficult airway, secure it safely with fiberoptic intubation or video endoscopy; proceed with "gentle induction" when possible once airway secured

Sedation: no amount of sedation will control pain if poor regional block; do not inadvertently induce GA (if needed, do it intentionally); when choosing sedative, "easy is better;" midazolam-fentanyl good choice; propofol or remifentanil can lead to respiratory issues (may stop breathing) during procedure

Warmth: keep patients warm; prewarm them before surgery; can use warming-blanket system (Bair Hugger), but difficult to achieve appropriate temperature of 37°C; Kimberly-Clark adherent thermal pad, water-filled and servo-controlled, achieves appropriate warming for patients; hypothermia can interfere with coagulation; shivering after procedure can lead to myocardial ischemia; increased risk of wound infections if patient gets cold; easier to keep patient warm if prewarmed

Glucose control: many vascular patients have diabetes; withhold metformin and oral hypoglycemic agents, check glucose preoperatively; if glucose ~>200 mg/dL, start insulin infusion 1 U/hr to 2 U/hr; if >300 mg/dL, administer 3 U/hr to 4 U/hr; check glucose hourly; once glucose ~<200 mg/dL, turn rate down to 1 U/hr to 2 U/hr; ideally, keep glucose 150 mg/dL to 200 mg/dL; do not attempt tight glucose control; keep glucose ≥120 mg/dL;

Avoid hypoglycemia, which can cause permanent neurologic injury; hypoglycemia occurs easily; worse than hyperglycemia; use caution; IV infusions of insulin safer than SQ injections because IV infusions rapidly metabolized by liver (whereas SQ injections persist for 12 hrs to 24 hrs)

Case duration: vascular cases can be prolonged; numerous issues can occur; avoid hypertension (can cause leakage from grafts); hypotension worse; avoid tachycardia (significant problem); avoid myocardial ischemia; avoid medication withdrawal; check ACT and glucose regularly; pad patient; keep them warm; use caution

Hypotension: study in 50,000 patients; diastolic BP <30 mm Hg, 11% of patients; mean BP <40 mm Hg, 8% of patients; systolic pressures <60 mm Hg, 12% of patients; if these pressures persisted >15 mins, noted elevations in 2-day, 30-day, and 1-yr mortality rates; >30 mins, rates increased to 10% to 20%; thus, correct hypotension as quickly as possible

Hypertension: more common but less of problem than hypotension; same study as previously mentioned; diastolic pressure >120 mm Hg occurred in 16% of patients; mean >130 mm Hg occurred in 33%; systolic pressure >200 mm Hg occurred in 16% of patients; >30 mins at these pressures, mortality rates of 1% at 2 days, 3% at 30 days, 8% at 1 yr

Tachycardia: same study as above; heart rates >120 bpm occurred in 8% of patients; >100 bpm occurred in 29% of patients; >100 bpm, elevations in 30-day and 1-yr mortality; >120 bpm, elevations in 2-day, 30-day, and 1-year mortality; short time to achieve severe results; 5 mins of heart rate >120 bpm affects 30-day and 1-year mortality

Suggested Reading

Fleisher LA et al: 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. Developed in collaboration with the American College of Surgeons, American Society of Anesthesiologists, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Vascular Medicine Endorsed by the Society of Hospital Medicine. *J Nucl Cardiol.* 2015;22(1):162-215; **McFalls EO et al:** Coronary-artery revascularization before elective major vascular surgery. *N Engl J Med*. 2004;351(27):2795-804; **Patelis N et al:** General versus local anesthesia for carotid endarterectomy: special considerations. *Saudi J Anaesth.* 2018;12(4):612-7; **Prochaska JJ et al:** Smoking cessation and the cardiovascular patient. *Curr Opin Cardiol*. 2015;30(5):506-11.

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Anesthesia for Abdominal and General Surgery

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Introduction: most anesthesiologists provide anesthesia for abdominal procedures many times; most cases proceed without incident and do not require special monitoring or techniques; however, adverse outcomes can occur in certain situations (*eg*, regurgitation during induction in bowel obstruction, subsequent difficulties with laryngoscopy, possibly aspiration pneumonia); laparoscopic procedures have potential for catastrophic outcomes related to CO_2 embolization or disturbances in hemodynamics related to abdominal insufflation or positioning; important to be knowledgeable about strategies for prevention, diagnosis, and treatment of events that may occur during abdominal surgery

Anesthesia for Patients at Increased Risk of Aspiration

Aspiration Pneumonia: 10% of community-acquired pneumonias; risk factors related to conditions that result in altered levels of consciousness (*eg*, dementia, sedating prescription drugs, illicit drugs, alcohol, metabolic disorders, stroke, traumatic brain injury, seizures) and disorders of esophagus and stomach; aspiration with general anesthesia occurs in 1 in 2000 to 3000 elective cases; risk increases 3- to 4-fold in emergency setting; aspiration and regurgitation fifth most common adverse event during general anesthesia; mortality from pulmonary aspiration ~5%, or ~10% to 30% of all anesthesia-related deaths; risk factors related to patient, surgery, anesthesia, and airway device

Patient-related risk factors: amount of gastric material present at time of anesthesia greatest risk factor; increases in nonfasted or emergency situations; diabetes, increased intracranial pressure (ICP), hiatal hernia, gastrointestinal (GI) obstruction, gastroesophageal reflux symptoms, morbid obesity, history of upper abdominal surgery, concurrent opioid therapy, and pregnancy or labor associated with increased volume; fasting volume ~25 mL, which also increases risk; *gastric volume evaluation* — ultrasound may risk stratify patients with large residual gastric volumes; risk 2 to 3 times in children vs adults; patients aged >80 yrs have 9- to 10-fold increased risk of aspiration vs patients aged 20 to 30 yrs

Surgical risk factors: upper abdominal surgery manipulates stomach and proximal intestines, may push gastric contents toward mouth; lithotomy and Trendelenburg positions and abdominal insufflation increase aspiration risk; 19.1% risk of aspiration during tracheostomy; increased surgical duration may increase aspiration risk; insufficient anesthesia can result in gagging, regurgitation, and vomiting upon airway manipulation; positive pressure ventilation (PPV) may result in gastric inflation and increased risk of pulmonary aspiration; removal of advanced airway devices before patient regains consciousness may increase aspiration risk; *laryngeal mask airway (LMA)* — may increase risk; risk of regurgitation occurs in ≤28% of cases; incorrect airway positioning may increase risk of gastric insufflation and activation of reflexes, resulting in aspiration; second-generation LMAs may reduce risk

Gastric volume and composition: pH <2.5 and gastric volume >25 mL or 0.4 mL/kg ideal body weight associated with increased risk; bile aspiration causes greater pulmonary damage than acid alone; food particle aspiration can cause airway obstruction and severe lung damage; food particles may remain in stomach for 28 hours, so traditional nothing by mouth (NPO) guidelines may be insufficient following trauma; feculent material can result in severe damage

Pharmacologic regulation of gastric material: impacts pH and volume of gastric content; administer ≥60 minutes before induction; emergence from anesthesia often more perilous to aspiration; may still be helpful to administer agents immediately before or after induction

Antacids: gastric acid produced by stomach parietal cells; food stimulates increased acid production; parietal cells produce 0 mmol/hr to 10 mmol/hr; antacids have short half-life, administered every 1 to 2 hrs to maintain gastric pH >4; magnesium-based antacids may cause hypermagnesemia and diarrhea; aluminum-containing antacids may cause hypophosphatemia and constipation; administer nonparticulate-based antacid (*eg*, sodium citrate) prior to induction

Histamine (H_2) receptor antagonists: block H_2 receptor on parietal cells; inhibition decreases acid production and increases gastric pH; 80% to 90% of patients experience increased pH or decreased gastric volume with ranitidine; require 30 mins to 60 mins to increase gastric pH and decrease gastric volume; some patients may need continuous infusion; interstitial nephritis, thrombocytopenia, hypotension, sinus bradycardia, confusion, and CYP450 inhibition can complicate therapy

Metoclopramide: most widely utilized prokinetic drug; dopamine-receptor antagonist, increases resting gastric tone and contractile activity of GI smooth muscle; relaxes pylorus and increases lower esophageal sphincter tone, which propels gastric contents forward; decreases gastric volume in 62% to 87% of patients; antiemetic properties; common reactions include

sedation, dizziness, and faintness; risk of extrapyramidal symptoms; contraindicated in mechanical bowel obstruction

Proton pump inhibitors (PPIs): reduce gastric acid secretion by blocking effects of histamine, gastrin, acetylcholine; more potent than H_2 receptor blockers, more protection from aspiration

Rapid-sequence induction and intubation: for patients at risk for aspiration, minimize time between loss of consciousness and insertion of endotracheal tube; recommendations vary; standard regimen involves thorough preoxygenation, rapid injection of predetermined dose of induction agent, followed by succinylcholine or high-dose rocuronium, application of cricoid pressure, avoidance of PPV, and insertion of cuffed endotracheal tube; do not release cricoid pressure until endotracheal tube position confirmed

Drugs: *induction agents* — need to provide rapid intubating conditions, avoid awareness, and stable hemodynamics (*eg*, thiopental, etomidate, ketamine, midazolam, propofol); *opioids* — rapid-onset opioids (eg, fentanyl, alfentanil, remifentanil) allow administration with induction agent and do not interfere with preoxygenation; addition allows for decreased induction dose and more stable hemodynamics; *lidocaine* — blunts hemodynamic response to intubation, improves intubating conditions in setting of partial paralysis, decreases ICP within intubation, and decreases propofol injection pain; administer 1 min to 2 mins prior to induction; *succinylcholine* — when available, gold-standard muscle relaxant for rapid-sequence induction and intubation; 1 mg/kg considered ideal but may lead to O_2 saturation <80%; 60 secs after 1 mg/kg intravenous (IV) dose, ideal conditions exist in only 63% to 80% of patients; other doses also studied and advocated; *nondepolarizing muscle relaxants* — slower onset, thus possibly elevated aspiration risk; h large doses can shorten onset time but prolong block duration

Other techniques: *PPV* — avoided in rapid-sequence induction and intubation; bag-mask ventilation may result in gastric insufflation and increased risk of aspiration; according to advocates of no ventilation in rapid-sequence induction, bag-mask ventilation unnecessary with adequate preoxygenation; gentle bag-mask ventilation with inspiratory pressure <15 cm to 20 cm H_2O not shown to cause significant insufflation; *cricoid pressure* — in obese, pregnant, or critically ill, adequate preoxygenation may result in precipitous O_2 desaturation; gentle PPV until muscle relaxation onset may be indicated; application of cricoid pressure may decrease gastric insufflation if PPV required before intubation; apply 1 kg force in awake patient, increase to 3 kg after loss of consciousness

Esophageal sphincters: *lower* — region of thickened musculature at gastroesophageal junction, prevents regurgitation; relaxes on swallowing, esophageal distention, and in vomiting reflex; antiemetics, cholinergic drugs, succinylcholine, and antacids increase tone; anticholinergics, thiopental, opioids and inhaled drugs decrease tone; cricoid pressure decreases lower tone; *upper* — inhaled anesthetics relax upper esophageal sphincter; nasogastric (NG) tube increases aspiration by causing loss of sphincter integrity

Intestinal obstruction: risk factor for aspiration; small-bowel obstruction in 3% of emergency surgical admissions; admissions related to adhesions, Crohn disease, neoplasms, hernia, miscellaneous causes; can present with dehydration, acidosis, significant electrolyte abnormalities; central venous access may be needed to guide fluid administration; NG tubes may weaken lower esophageal sphincter integrity

Rapid intubation techniques: perform preoxygenation to allow for adequate nonhypoxic intubation time; suction NG tube prior to induction; second suction tube should be available; perform induction with appropriate cricoid pressure and intubate quickly; use LMA only as bridge to eventual endotracheal intubation in difficult patients

Aspiration symptoms: gastric contents visible in oropharynx, hypoxia, increased inspiratory pressures with PPV, dyspnea, apnea or hypoventilation in spontaneously ventilating patient, bronchospasm or laryngospasm; *postoperative aspiration* — no symptoms or nonproductive cough, tachypnea, bronchospasm, bloody or frothy sputum, respiratory distress 2 hrs to 5 hrs after aspiration; aspiration pneumonia presents later as tachypnea, cough, signs of pneumonia progressing to acute respiratory distress syndrome (ARDS)

Aspiration management: position patient head-down or lateral; oropharyngeal or endotracheal tube suctioning; if no endotracheal tube, secure airway via rapid-sequence intubation with cricoid pressure; initial inspiratory O_2 concentration 100%; start positive end-expiratory pressure (PEEP) 5 cm H_2O to7 cm H_2O; aspiration of particulate matter requires bronchoscopic removal to prevent obstruction and distal pulmonary atelectasis; materials may be analyzed to guide therapy; treat bronchospasm symptomatically with bronchodilators; cancel elective procedures; limit duration and extent of emergency cases; frequent blood-gas analysis for ventilator management; central venous monitoring guides fluid administration; baseline chest radiograph guides therapy; patients with difficulty maintaining O_2 saturation or with continued high inspiratory pressures should remain intubated and transported to intensive care unit (ICU); patients stable for 2 hrs following extubation and without radiographic changes may be transferred to normal hospital unit; changes in vital signs, bronchospasm, fever, or radiographic evidence of aspiration need ICU management; steroid therapy may worsen clinical outcome; chemical lung damage; 20% to 30% of aspiration events progress to aspiration pneumonia; empiric antibiotic therapy not recommended; initiate antibiotic therapy upon identification of pathogen or if secondary infection

Anesthesia for Laparoscopic Procedures

Laparoscopic procedures: generally well tolerated, but potential for serious events; *advantages* — decreased blood loss, less pain, smaller incisions, reduced postoperative ileus, preservation of respiratory function, and shorter recovery; *disadvantages* — increased expense and longer operating times; *general contraindications* — diaphragmatic hernia, acute or recent myocardial infarction, severe pulmonary disease, ventriculoperitoneal shunt, hypovolemia, congestive or valvular heart failure

Abdominal insufflation: laparoscopic surgery depends on abdominal insufflation to allow for insertion of surgical tools and anatomy visualization; *CO_2* — current

insufflation agent (does not support combustion; rapid clearance); CO_2 carried in blood secondary to bicarbonate buffering, links to hemoglobin, rapidly eliminated by lungs; easily absorbed from intraperitoneal and extraperitoneal sites; absorption into blood from pneumoperitoneum may result in hypercapnia; hypercapnia can increase minute ventilation and stimulate sympathetic nervous system

Sympathetic nervous system stimulation: increased blood pressure, heart rate, myocardial contractility, arrhythmias; creation of pneumoperitoneum can cause significant hemodynamic alterations (*eg*, hypo- or hypertension, arrhythmias, cardiac arrest); with intraabdominal pressures <10 mm Hg to 15 mm Hg, cardiac output increases secondary to increased venous return; venous return can be increased by decreased splanchnic blood volume, hypercapnia, and sympathetic nervous system-induced peripheral vasoconstriction; at greater intraabdominal pressures, inferior vena cava and collateral vessel compression decreases venous return and cardiac output, hypotension

Patient positioning: reverse Trendelenburg position decreases venous return, cardiac output, mean arterial blood pressure; increases peripheral and pulmonary vascular resistance; Trendelenburg position increases venous return and normalizes or increases mean arterial blood pressure

Arrhythmias: bradyarrhythmias occur secondary to vagal stimulation related to peritoneal stretch; light planes of anesthesia may contribute to increased incidence of vagal nerve–mediated bradycardia; other causes include instrument insertion, manipulation of intraabdominal organs, or CO_2 embolization; tachyarrhythmias caused by hypercarbia-induced sympathetic nervous system or adrenal stimulation; ICP can increase and cerebral perfusion pressure decrease secondary to hypercapnia, increased systemic vascular resistance, Trendelenburg positioning, and elevated intraabdominal pressures

ICP: patients with baseline elevations in ICP or decreases in intracranial compliance should avoid laparoscopic procedures; Trendelenburg position can increase intraocular pressure, which may cause significant blindness in patients with glaucoma or other visual deficits

Ventilation in laparoscopic procedures: with pneumoperitoneum pressures >15 mm Hg, lung volumes reduced; pulmonary compliance decrease, peak and mean airway pressures increase; reduced lung volumes and cephalad diaphragmatic excursion may cause small airway closure with atelectasis and decreased functional residual capacity; upward displacement of diaphragm may lead to endobronchial intubation, ventilation perfusion mismatch, and intrapulmonary shunting; elevated intraabdominal pressures can cause pulmonary dysfunction, pneumothorax, and pneumomediastinum

Positioning during laparoscopic procedure: Trendelenburg position can worsen respiratory function, but reverse true for head-up positioning; use abdominal deflation and slow insufflation to lower pressures and allow surgery to proceed; some patients unable to tolerate laparoscopic surgery (from pulmonary standpoint) and require conversion to open procedure

Monitoring: electrocardiogram (EKG), noninvasive arterial pressure monitors, airway pressure monitors, pulse oximetry, end-tidal $CO_{2\ mo}$nitors, peripheral nerve stimulation, temperature probes; consider arterial cannulation for patients with limited cardiac reserve requiring close blood-pressure monitoring or with significant pulmonary disease needing arterial blood-gas analysis; use mechanical ventilation to control $PaCO_2$, keep end-tidal CO_2 levels at ~35 mm Hg; limit ProSeal LMAs use to nonobese patients undergoing short laparoscopic procedures; intravascular loading with crystalloid solution may help balance decreases in venous return with abdominal insufflation

Anesthesia: maintenance with inhaled or IV agent; consider use of opioids and shorter-acting agents; avoid N_2O because of risk of nausea and diffusion into bowel lumen, causing distention and difficulties with surgical visualization; N_2O diffusion may increase risk of perioperative explosive event; naso- or orogastric tubes decompress abdominal viscera; use spinal/epidural anesthesia in patients with low insufflation pressures and low aspiration risk

Hypotension: commonly complicates laparoscopic surgery; can be resolved by decreasing insufflation pressure, and administration of IV fluids and vasoactive drugs; alpha agonists (*eg*, phenylephrine) may cause reflex bradycardia; use cautiously in patients with low heart rate secondary to vagal stimulation

CO_2 embolization: feared complication of laparoscopic procedures; incidence of venous gas embolism during laparoscopy 0.002% to 0.02%; typically presents as hypotension, cyanosis, pulmonary edema, dysrhythmia, tachycardia, right heart strain pattern on EKG, and perhaps asystole; may be sudden increase in end-tidal CO_2 following embolization, but quickly falls as cardiac output decreases; mill-wheel murmur with cardiac auscultation characteristic for gas embolization; transesophageal echocardiography sensitive for detection of gas emboli

Embolism treatment: stop abdominal insufflation and deflate abdomen; place patient into left lateral decubitus head-down position to decrease air entry into pulmonary vasculature and hyperventilate with 100% O_2; insert central venous catheter for gas aspiration; CO_2 rapidly absorbed and aggressive cardiopulmonary resuscitation may resolve embolism;

Ventilation: consider pneumothorax as cause of cardiovascular collapse during laparoscopic surgery; high ventilatory pressure or direct communication between pleura and abdomen can result in hemodynamically significant pneumothorax; initially manage hypoxia by increasing FiO_2 to 100%; hand ventilate to feel for compliance and auscultate chest for bilateral breath sounds

Bronchoscopy: to evaluate correct endotracheal tube positioning in patients with obesity or with distant breath sounds; identify large mucus plugs or other airway obstructions; airway recruitment maneuvers or addition of PEEP may be helpful if atelectasis contributing to intraoperative hypoxia

Hypoxia: arterial blood-gas analysis may help diagnose etiology or to follow treatment or progression; decreased abdominal insufflation pressure or more head-up position may improve ventilation and oxygenation; other causes include hypoxic gas-mixture administration, ventilator failure, and bronchospasm

Hypercarbia: occurs during laparoscopy secondary to CO_2 uptake from the peritoneum and decreased elimination in patients with pulmonary disease; increased metabolism in light planes of anesthesia can contribute to increased CO_2 production; impaired ventilation secondary to increased intraabdominal pressure can impair CO_2 removal; treat hypercarbia by increasing minute ventilation or decreasing intraabdominal pressure; perforation of abdominal organ or major blood vessel necessitates vigilant monitoring and appropriate venous access prior to starting surgical procedure

Patients with multiple previous abdominal procedures: secure large-bore venous access and ensure blood availability prior to procedure; significant injuries to bowel or abdominal vasculature can occur with trocar insertion; increased risk in patients with low body mass index or history of abdominal surgery

Other effects of laparoscopic surgery:

Oliguria: may complicate laparoscopic procedures; secondary to vascular and parenchymal compression and systemic hormonal effects; pneumoperitoneum release results in resumption of normal kidney function

GI system: increased intraabdominal pressure, decreased lower esophageal sphincter tone, and possibly Trendelenburg position potentially increase risk of aspiration

Thrombosis: increased intraabdominal pressure can cause lower extremity venous stasis, which increases perioperative vein thrombosis; consider perioperative subcutaneous heparin, anticoagulation, and other mechanisms to decrease incidence

Hypothermia: caused by insufflation with cool, dry gases in patients undergoing prolonged procedures

Nutrition: patients with abdominal disease may have long-term problems with obstruction or absorption, requiring nutrition via alternative routes

Enteral feedings: may occur via tubes inserted beyond level of pylorus; *benefits* — decreased complication rate, length of hospital stay, costs; improved wound healing; *contraindications* — intestinal obstruction, malabsorption, high-output fistulas, intestinal ischemia, shock or sepsis; *complications* — aspiration, tube malposition or clogging, nausea and vomiting, diarrhea, constipation, malabsorption, hyper- or hypoglycemia, electrolyte imbalances, dehydration, refeeding syndrome

Parenteral nutrition: administration of nutrition and electrolytes via central venous catheter; *benefits* — ability to deliver nutrition to person without functioning GI tract; *complications* — phlebitis, glucose intolerance, electrolyte abnormalities, hypercapnia, fatty liver, vein thrombosis, pneumothorax, infection; if infusions terminated, patients at risk for perioperative hypoglycemia

Hepatic Disease and Anesthesia

Hepatic dysfunction: patients with advanced hepatic disease at higher risk for perioperative morbidity and mortality; perioperative hepatic dysfunction acute or chronic; common causes of advanced liver disease include viral infection, alcohol abuse, autoimmune disease, drug reaction, genetic metabolic aberrations, cholestasis, and inflammatory diseases of bile tracts; advanced hepatic disease affects hepatic function (*eg*, glucose homeostasis, protein synthesis, bilirubin metabolism, drug metabolism), other organ systems; *cardiovascular* — hyperdynamic (*ie*, increased cardiac output, increased heart rate, decreased systemic vascular resistance); cardiomyopathy and dysrhythmias; *pulmonary* — pleural effusions result in significant atelectasis, intrapulmonary shunting, hepatopulmonary disease, pulmonary hypertension, impaired hypoxic pulmonary vasoconstriction; *renal* — impaired sodium and water excretion leading to hyponatremia and increased total body fluid; *other* — altered glucose homeostasis resulting in hypoglycemia may occur; coagulopathies can increase risk for perioperative bleeding; severe encephalopathies, cerebral edema, and increased ICP may accompany severe hepatic disease

Child-Pugh classification: assessment of nutrition, control of ascites, level of encephalopathy, elevation of serum bilirubin, prolonged prothrombin time, and decreased serum albumin; patients with advanced scores at increased risk for perioperative complications; *mortality* — increased with hepatic disease; 10% for class A, 30% for class B, and 82% for class C; emergency surgery associated with 50% mortality risk, increased to 100% for emergency surgery in class C; classification may not be helpful for predicting surgical outcomes

Model for end-stage liver disease (MELD) score: system for determining severity of hepatic disease; used by United Network for Organ Sharing (UNOS) to determine status for liver transplantation; relies on evaluation of serum bilirubin, creatinine, and INR to predict survival; adjustments made to MELD score in patients on dialysis and with hepatic cancer; MELD score <8 not associated with any perioperative mortality; MELD score ≥9 associated with 29% risk of mortality

Preoperative evaluation: determine acuteness of hepatic failure; in acute hepatic failure, cancel all but vitally required surgery; consider significant varices or history of variceal bleeding before gastric tube or transesophageal echocardiogram probe placement; variceal bleeding complicates visualization

Nutritional status: improvement and achievement of euvolemia can improve outcomes; laboratory analysis should focus on values that may impact clinical management and may be altered in advanced disease (*eg*, hemoglobin, white blood cell count, platelet count, electrolytes, glucose, blood urea nitrogen, creatinine, coagulation values, fibrinogen, transaminase, bilirubin, albumin); evaluate and normalize electrolyte values; correct coagulopathy by replacing deficient factors; thromboelastogram evaluation may guide factor replacement therapy; electrocardiogram (consider echocardiogram) to evaluate cardiac status in patients with severe disease or if suspicion of cardiac or valvular dysfunction

Chest x-rays: helpful to assess for pleural effusions and to prompt preoperative drainage

Acute alcohol withdrawal: cancel elective surgery; administer thiamine; replace electrolytes; prevent seizures

Anesthesia: *induction* — drug responses prolonged and unpredictable due to alteration of CYP450 and drug conjugation systems; consider agents reliant on Hofmann elimination; *rapid-sequence airway securement* — consider, since ascites fluid can raise intraabdominal pressure and increase risk of perioperative aspiration; in acute variceal bleeding, multiple suction sources and

methods for securing difficult airway should be available; consider risks of esophageal instrumentation if possible gastric tube or echocardiogram probe placement; *renal function* — maintain renal perfusion pressure and output by maintaining reasonable blood pressure; consider mannitol or furosemide; central venous monitoring to guide fluid administration; consider large-bore venous access for extensive surgery or in patients with coagulopathies

Monitoring: insert arterial line in patients with significant cardiac or pulmonary vascular abnormalities; arterial line if frequent lab draws needed; intraoperative glucose monitoring and perioperative dextrose administration to avoid unrecognized hypoglycemia; consider regional anesthesia, but be cautious of neuraxial techniques patients with preexisting coagulopathy

Postoperative hepatic dysfunction: potentially catastrophic complication of general anesthesia; hepatotoxicity caused by inhaled anesthetics immune-mediated reaction, evidenced by evaluating IgG levels

Halothane: halothane-induced hepatotoxicity characterized by fever, jaundice, nausea, anorexia; typically presents 3 to 7 days following exposure; massive hepatic necrosis from halothane occurs in 1 in 10,000; after multiple procedures, incidence rose to 1 in 3400, and after multiple halothane administrations, incidence rose to 1 in 1400; secondary exposure within 3 mos led to increased incidence of hepatotoxicity; other factors increase halothane-related hepatotoxicity (*eg*, female sex, obesity, age >30, and intraoperative hypoxia); halothane most commonly implicated agent, followed by enflurane, isoflurane, and desflurane

Sevoflurane: few cases of severe hepatic failure; undergoes limited biotransformation, results in limited alterations in hepatic blood flow; hepatic failure possible, but not immune mediated

Evaluation and management: full laboratory analysis to pinpoint dysfunction; evaluate drugs administered during anesthetic; acetaminophen overdose possible; catecholamine or vasoconstrictor administration may cause splanchnic vasoconstriction and hepatic damage; sepsis-related jaundice can be mistaken for anesthesia-related hepatic damage; evaluate transfusion record for cold hematoma or hemolysis; consider possible extrahepatic causes of hepatic failure (*eg*, congestive heart failure, pulmonary embolism); review anesthesia record for intraoperative events (*eg*, hypotension, hypoxia); consider immune-mediated hepatotoxicity

Hepatorenal syndrome: characterized by profound reductions in renal function associated with advanced portal hypertension and splanchnic vasodilation; defined as plasma creatinine >1.5 mg/dL not explained by bleeding or intrinsic disease, not improved with fluid boluses; can present rapidly or progress slowly; if rapidly progressive, may not have good outcome without transplantation; syndrome via anesthesia-associated intraoperative fluid shifts has better improvement chance

Liver transplantation: procedure occurring with increased frequency and improved perioperative outcomes; in severe hepatic disease, many organ systems may be impacted; *portal hypertension* — can cause splenomegaly, formation of esophageal varices, ascites; *cardiovascular* — systemic vascular resistance may be reduced and cardiac output may become hyperdynamic; prolonged hepatic failure may result in depressed cardiac system, pulmonary hypertension, and extensive ventilation/perfusion mismatching; anemia, thrombocytopenia, and hypocoagulability may lead to increased surgical bleeding; intraoperative course can be unstable and require extensive venous access; insert arterial catheter to monitor blood pressure; pulmonary arterial catheters or transesophageal echocardiography can measure vascular resistance, cardiac output, valvular function

Liver transplant phases: liver transplantation generally proceeds via 3 phases

Preanhepatic phase: surgical incision made, liver and porta hepatis mobilized, and hepatic artery and bile duct divided; significant blood loss may occur secondary to coagulopathy, adhesions, and varices; avoid volume overload (can result in splanchnic congestion and worsened bleeding and coagulation)

Anhepatic phases: portal and hepatic veins divided; native liver explanted; inferior vena cava prepared for implantation; new liver inserted, caval and portal anastomoses completed; no additional clotting factors produced, so significant coagulopathy can occur; hypocalcemia, acidosis, and hemorrhage additional concerns

Neohepatic phase: liver graft reperfused; hepatic artery and biliary system anastomoses completed; anesthesia concerns include hypotension and decreases in systemic vascular resistance, potassium level increase, and arrhythmia or cardiac arrest

Suggested Reading

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Anesthesa for the Obese Patient

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Overview: obesity was once thought of as a disease simply of excess adiposity; World Health Organization definition is abnormally high percentage of body fat; now know that obesity is more than a disease of excess fat mass; excess adiposity affects multiple organ systems

Body mass index (BMI): clinically is the standard scalar used to classify obesity; BMI between 20 and 25 kg/m^2 is considered normal, BMIs >25 kg/m^2 are considered overweight, and a BMI >30 kg/m^2 is considered obese; people who have BMIs >40 kg/m^2 or a BMI >35 kg/m^2 with co-existing disease, for example diabetes or hypertension, are classified as morbidly obese; BMIs >50 kg/m^2 are classified as super morbidly obese; BMIs >60 kg/m^2 are defined as super-super morbidly obese

Prevalence of obesity: has increased dramatically last 25 years; in the United States, 1/3 of population is obese and 2/3 of population is obese or overweight; fortunately this prevalence is plateauing in the US, but continuing to increase in other countries

Pathophysiology

Neurologic and psychiatric: includes high prevalence of anxiety and depression, attributed to the social stigma associated with obesity

Pulmonary pathophysiology: fat accumulation in the chest wall and abdomen reduces chest wall and lung compliance, which leads to rapid shallow breathing and increased work of breathing; reduction in chest wall compliance is exacerbated by the supine and Trendelenburg positions; total lung capacity, vital capacity, and functional residual capacity are all reduced; it is this reduction in functional residual capacity that lowers lung volumes below closing capacity during spontaneous ventilation; when this occurs, there is collapse of alveoli, otherwise known as atelectasis; this leads to ventilation/perfusion mismatching, right-to-left shunting, and ultimately hypoxia

Obstructive sleep apnea (OSA): common in obese patients; characterized by frequent episodes of apneas and hypopneas; redundant airway tissue and enlarged neck circumference may exacerbate OSA; both are positively correlated with the severity of OSA; results in CO_2 retention and hypoxemia; in severe cases polycythemia, pulmonary hypertension, and cor pulmonale may develop; important to know that patients may present with OSA, even if they do not carry a formal diagnosis; signs and symptoms of OSA must be elicited; these include snoring, daytime somnolence, and headaches; in the preoperative area, an anesthesiologist can do the STOP-BANG questionnaire, a validated predictive tool to screen for OSA with 90% sensitivity and positive predictive value (acronym STOP-BANG stands for snoring, tired, observed snoring, blood pressure or hypertension, body mass index, age, neck circumference, and gender)

Obesity hypoventilation syndrome (OHS): not as prevalent as OSA but carries severe implications; defined as severe obesity and hypercapnia ($Paco_2$ is >45 mmHg) that is unexplained by other causes of hypoventilation; although the symptoms are similar to OSA, such as daytime somnolence and fatigue, patients with OHS also suffer from daytime hypercapnia and hypoxia; pulmonary hypertension and cor pulmonale are very common; patients with OHS are very sensitive to sedative-hypnotic effects of benzodiazepines and opioids, and use of these should be limited whenever possible; patients who carry this diagnosis are reliant on hypoxic ventilatory drive and can become apneic when given 100% O_2 following general anesthesia; patients should be comprehensively evaluated and monitored during the postoperative period

Cardiovascular comorbidities: obesity is associated with increased blood volume; however, when normalized to weight, the blood volume decreases; blood volume associated with obesity is about 50 mL/kg versus 70 mL/kg in a normal adult individual; increased total blood volume associated with obesity results in increased stroke volume; together, the increased blood volume and stroke volume lead to systemic hypertension which ultimately may lead to left ventricular dilation and hypertrophy; could further lead to reductions in left ventricular compliance and ultimately diastolic dysfunction; systolic dysfunction can occur when a left ventricular dilation occurs in excess of left ventricular hypertrophy, clinical entity called obesity cardiomyopathy; anesthesiologist should become suspicious of this phenomenon if changes such as left axis deviation, low QRS voltage, and/or left atrial enlargement are observed on ECG

Myocardial ischemia: hyperlipidemia, hypercholesterolemia, and atherosclerosis may lead to coronary artery plaques; together with shift in myocardial oxygen supply and demand from left ventricular hypertrophy, secondary to hypertension, these patients are at an increased risk for myocardial ischemia; a thorough history should elicit symptoms of myocardial ischemia; patients should be asked specifically about exercise tolerance, daily activities, metabolic equivalents, and symptoms of shortness of breath or angina; signs of myocardial ischemia should be looked for on the ECG; for high risk surgery, or if there is

evidence of myocardial disease, a stress echocardiogram can be considered

Gastrointestinal (GI) system: delayed gastric emptying is common in obese patients, secondary to increased abdominal girth, causing antral distension and increased gastrin release; in addition, there is increase in parietal cell secretion, leading to decreased gastric pH; these factors place obese patients at an increased risk for gastric aspiration; obesity increases intragastric pressure and decreases lower esophageal sphincter tone; incidence of gastroesophageal reflux disease (GERD) is high and directly related to increasing weight; controversy exists about whether obese patients should have a rapid sequence induction; however, in many centers, the rapid sequence induction remains the standard of care; other common changes in the GI system include liver disease, non-alcoholic steatohepatitis (NASH), and non-alcoholic fatty liver disease (NAFLD); these may or may not be associated with significant hepatic dysfunction; liver function tests may not reflect severity of liver dysfunction

Inflammatory response: one of the hallmarks of obesity is the highly prevalent systemic inflammatory response associated with the increased adiposity; chronic lipid loading leads to adipocyte hypertrophy, which leads to release of inflammatory cytokines; chronic inflammation ultimately leads to hyperlipidemia, hyperinsulinemia, hypoadiponectinemia, and increased leptin release; this ultimately leads to insulin resistance and the metabolic syndrome; metabolic syndrome is characterized by 3 of the following criteria: increased waist circumference, hyperglycemia, hypertension, hypertriglyceridemia, and decreased HDL levels; patients with the metabolic syndrome are at a higher risk of developing coronary artery disease and diabetes

Pharmacological Management

Overview: obese patients have physiologic and anthropometric changes that affect the pharmacokinetics of anesthetic drugs; increases in total body weight, lean body weight, and fat mass affect the volume of distribution of some drugs; in addition, increases in cardiac output and total blood volume and changes in regional blood flow affect drug distribution, plasma concentrations, and drug clearance and elimination; cardiopulmonary pathophysiology associated with obesity, specifically the high prevalence of OSA, exaggerate the side effects of sedative-hypnotics and opioids, narrowing their therapeutic window; this affects the pharmacodynamics of our drugs

Dosing: there has been a great deal of confusion on how to calculate doses of drugs in obese patients; dosing recommendations are generally based on total body weight; this is valid in normal weight subjects whose total body weight, ideal body weight, and lean body weight are all similar; however, in obese patients, these are not similar; total body weight, lean body weight, and fat mass all increase with increasing obesity; fat mass increases to a greater extent than the increase in lean body weight; the ratio of lean body weight to total body weight decreases

Cardiac output: for years it was thought that the increase in fat mass vastly increases the apparent volume of distribution of our drugs, especially those drugs that are highly lipophilic; however, it has been proven that cardiac output is the major determinant of initial drug distribution and peak plasma concentration; cardiac output is highly correlated to lean body weight, the metabolically active tissue; in fact, the lean body weight receives approximately 95% of the cardiac output; the fat mass receives <5% of the cardiac output; in addition, drug clearance increases proportionately with lean body weight; these data suggest that lean body weight is the ideal weight scalar for drug administration in this patient population; drug administration based on total body weight may in fact result in overdose

IV induction agents: when specifically discussing IV induction agents, the use of lean body weight for initial induction doses of IV hypnotics, such as thiopental, propofol and etomidate, is a valid approach; induction doses of propofol have been shown to be highly correlated to both lean body weight and cardiac output; again, cardiac output, which is highly correlated to lean body weight, is responsible for these drugs' rapid distribution to the effect site and redistribution from the effect site; the higher cardiac outputs associated with obesity can result in a more rapid redistribution from the effect site and a more rapid awakening after a single bolus dose

Opioids: same pharmacokinetic principles governing IV hypnotics can be applied to opioids when determining how to properly dose obese subjects; cardiac output is the major determinant of early distribution kinetics of opioids, as with IV induction agents; when discussing opioids, we must first consider fentanyl, as it is the most commonly used opioid in the perioperative period

Fentanyl: pharmacokinetic models of fentanyl that were derived from normal weight subjects have been shown to over-predict fentanyl plasma concentrations when normalized to total body weight; in addition, clearance of fentanyl has been shown to correlate with lean body weight; these data suggest that lean body weight again be used as the optimal weight-based dosing scalar for fentanyl

Remifentanil: unique in that it undergoes ester metabolism; therefore, it has extremely short context-sensitivity; for this reason, its use has been advocated by some for administration as a continuous infusion as an adjunct to general anesthesia; a short context-sensitivity means that patients will not be exposed to the prolonged effects of the opioid once the infusion is complete; typically, doses ranging from 0.05 to 0.25 mcg/kg/min are used; an infusion based on lean body weight in obese subjects results in the same plasma concentrations as an infusion based on total body weight in normal weight subjects; in addition, infusions based on total body weight result in supra- therapeutic plasma concentrations, which may increase the risk of hypotension and bradycardia associated with remifentanil infusions

Alfentanil: the other synthetic opioid; there are no specific data analyzing the effect of obesity on alfentanil pharmacokinetics; however, theoretically, it stands to reason that lean body weight also be used as a weight-based dosing scalar for this drug; same could be said for sufentanil

Words of caution: opioids must always be used with extreme caution in obese patients, who are at increased risk for opioid-induced upper-airway obstruction and respiratory depression; use of opioids has been associated with central sleep apnea, OSA, ataxic breathing, and hypoxemia; according to the American Society of Anesthesiologists (ASA) Closed Claims

database, 48% of adverse respiratory events secondary to opioids were in obese or morbidly obese individuals, further emphasizing the increased risk opioids pose to obese patients; does this mean opioids cannot or should not be used in this patient population? the answer is no; however, knowledge of the effect of obesity on opioid pharmacology is necessary to safely administer these drugs; drugs that have a prolonged time to peak effect and/or prolonged duration of action are best avoided; to that end, it is advocated that drugs such as morphine and hydromorphone be avoided in lieu of the synthetic fentanyl congeners, which have a much shorter and more predictable time to peak effect and duration of action

Anesthesia Considerations

Perioperative: pre-procedural sedation with benzodiazepines should be avoided whenever possible, especially in patients with OSA or OHS; these medications may increase the risk of upper airway obstruction and work synergistically with opioids, further increasing this risk

Venous thromboembolism: one of the leading causes of postoperative mortality; generally, these patients are administered subcutaneous heparin for venous thromboembolism prophylaxis; this should be discussed with the surgeon prior to entry into the operating room; antibiotic prophylaxis should also be discussed with the surgeon; an antibiotic should be administered prior to, but within 1 hr of, skin incision; the doses should be weight adjusted; dosage of the commonly administered preoperative antibiotic cefazolin should be increased to 3 g every 4 hr if a patient weighs >120 kg

Positioning: placing obese patients in the supine position causes a reduction in the functional residual capacity; this causes significant ventilation-perfusion mismatching, which leads to atelectasis and hypoxia; this phenomenon is exacerbated by the Trendelenburg position; reverse Trendelenburg is preferred position, as it reduces abdominal pressure on the thorax, thereby maximizing thoracic expansion and functional residual capacity; obese patients also prone to neurologic injury, pressure sores, and rhabdomyolysis; all pressure points should be adequately padded and extremities placed in a neutral position; during induction of and emergence from anesthesia, the patient should be placed in the reverse Trendelenburg position whenever possible; this prolongs the safe apnea time, which is the time before desaturation; in the supine position, safe apnea time is only 1 to 2 min; this is doubled in the reverse Trendelenburg position

Laryngoscopy: obese patient should be placed in the head-elevated laryngoscopy position, also known as the "ramped" position; in this position, the external auditory meatus is aligned with the sternal notch; this position improves the view of the larynx and is associated with increased success in tracheal intubation

Monitoring: standard ASA monitors should be used for all patients; it must be noted that noninvasive blood pressure monitoring may be difficult or inaccurate in some obese patients, especially those at extremes of weight, due to poorly fitting blood pressure cuffs; in these situations, using the forearm or ankle may be necessary; in rare situations, invasive arterial blood pressure monitoring may be indicated; decisions to use other monitors should be based on the patient's medical comorbidities and the type and risk of surgery

Preoxygenation, induction of anesthesia, and tracheal intubation: when considering induction of anesthesia, first ensure adequate preoxygenation; as addressed before, obese patients have a reduction in functional residual capacity that makes them prone to rapid hemoglobin desaturation during periods of apnea; to maximize the safe apnea time, obese patients should be preoxygenated for at least 8 to 10 min with 100% O_2 prior to induction of anesthesia and apnea; even with adequate preoxygenation, these patients could have extremely rapid hemoglobin desaturation with pulse oximetry values decreasing to <90% within 1 to 2 min

Induction of anesthesia: the airway must be secured quickly to minimize the apneic period that follows induction of anesthesia; adequate planning is paramount to safely and quickly securing the airway in the obese patient; the anesthesiologist must perform a thorough airway examination and, when available, analyze prior anesthetic records

Tracheal intubation: signs of a potentially difficult airway include large face, presence of a beard, large neck circumference >18 cm, decreased neck extension, decreased mouth opening, small mouth size, redundant pharyngeal tissue, enlarged tongue, and Mallampati score of III or IV; Mallampati score of III or IV, coupled with an enlarged neck circumference, are the most reliable predictors of a difficult intubation; aids for a difficult intubation should be readily available and include video laryngoscopes, gum elastic bougies, laryngeal mask airways, and fiberoptic bronchoscopes; an awake fiberoptic intubation remains the gold standard for securing the airway in a known difficult airway

Mechanical ventilation: safe and effective management of the obese patient does not end in the OR; careful and attentive monitoring and consideration of specific factors in the postoperative period is necessary

Postoperative considerations: after extubation, the patient should be placed in the semirecumbent position whenever possible; this takes the abdominal pressure off the diaphragm, allowing the diaphragm to fall, thus improving functional residual capacity and oxygenation; supplemental oxygen should be administered immediately after extubation

CPAP: patients who use CPAP should be instructed to bring their equipment to the hospital for use in the post-anesthesia care unit (PACU) and while admitted; CPAP will allow alveolar recruitment during inspiration and prevent alveolar collapse during expiration

Deep venous thromboembolism: one of the biggest causes of postoperative mortality in bariatric patients; obese patients have several risk factors for venous thromboemboli: polycythemia, postoperative immobilization, increased platelet function, diabetes, and hypercholesterolemia; unless there is a contraindication, obese patients should receive anticoagulation for venous thromboembolism prophylaxis prior to surgery; sequential compression boots should also be applied; early ambulation is one of the most, if not the most, effective preventative measures and should be encouraged as soon as possible after surgery

Nausea and vomiting: in addition to administering prophylaxis for venous thromboembolism, obese patients

should also be given prophylaxis for postoperative nausea and vomiting (PONV); while obesity alone is not a risk factor for PONV, it is not uncommon for obese patients to have several risk factors for PONV; at a minimum, use at least two antiemetics intraoperatively; usually these include ondansetron and dexmedetomidine; for patients with a known history of PONV, avoidance of inhalational agents and the administration of propofol for maintenance of anesthesia should be considered

Regional Anesthesia Considerations

Overview: the changes in body habitus associated with obesity can make regional anesthesia technically difficult in these patients; difficulty with identifying and/or palpating bony landmarks and presence of adipose tissue pockets may combine to make regional blockade difficult

Block failure: BMI >25 kg/m2 is an independent risk factor for regional block failure and this rate of block failure is directly related to increasing BMI; paravertebral, epidural, supraclavicular, and superficial cervical plexus blocks are associated with the highest failure rates

Neuraxial blocks: with neuraxial blocks, such as spinal and epidural blocks, obese patients require less local anesthetic to achieve the same level of block when compared to non-obese patients; it has been shown that there is higher cephalad spread of local anesthetic in obese versus non-obese subjects: in the case of spinal blocks, this may be attributed to the smaller cerebral spinal fluid volumes associated with obesity; the reason for this higher spread in epidural blocks is unclear

Advantages: regional anesthesia offers several theoretical advantages over general anesthesia for obese patients; these include reduction in the need for airway intervention, reduced administration of opioids and other sedatives, decreased administration of drugs causing cardiopulmonary depression, and reduced incidence of PONV; can reduce PACU length of stay and overall hospital length of stay; despite these advantages, it still must be remembered that the rate of block failure is higher in obese patients; therefore, the use of regional anesthesia does not eliminate the possibility of general anesthesia

Bariatric surgery for the obese patient: these types of surgeries include gastric banding, sleeve gastrectomy, and Roux-en-Y gastric bypass; since the vast majority of these cases are now done laparoscopically, we will omit the discussion of open procedures for the sake of brevity

Pneumoperitoneum: specific to laparoscopic bariatric surgery, is the high-pressure pneumoperitoneum; normal intra-abdominal pressure is 0 to 5 mmHg; abdominal compartment syndrome occurs at pressures >20 mm Hg; in laparoscopic bariatric procedures, the high-pressure pneumoperitoneum could reach pressures of 15 to 18 mm Hg, thus approaching abdominal compartment syndrome pressures; this has a multitude of effects, especially on pulmonary function, renal function, and the cardiovascular system

Pulmonary function: mechanical pressure transmitted through the diaphragm increases intrathoracic pressure, which decreases vital capacity, functional residual capacity, and total lung compliance; in fact, pulmonary compliance can be reduced by as much as 40%; this further increases the risk of atelectasis and hypoxemia in a patient population that is already at risk; peak inspiratory pressures may also increase, potentially forcing the anesthesiologist to alter ventilatory management, eg, changing the pressure control ventilation, changing the lower tidal volumes, and allowing for permissive hypercapnia

Renal function: high-pressure pneumoperitoneum decreases renal perfusion, which has been shown to decrease by approximately 60% during insufflation and return to normal following desufflation; together with the increases in anti-diuretic hormone and aldosterone, the pneumoperitoneum causes reduced urine output perioperatively, despite adequate volume resuscitation; the anesthesiologist must be aware of this phenomenon and not blindly treat this transient oliguria with diuretics

Cardiovascular system: very stressed during the pneumoperitoneum; the increased intraabdominal pressure and increased intrathoracic pressure reduce venous return and cardiac output; usually there is a compensatory increase in heart rate, although in some patients there may be a profound, albeit transient, vagal response resulting in bradycardia; this is due to mechanical stretching of the peritoneum from the insufflation; cardiac output can be reduced by 5% to 15% during the pneumoperitoneum

Post-bariatric surgery: important consideration should be given to the patient who presents post-bariatric surgery; late complications following bariatric procedures include anastomotic strictures, gastrogastric fistulas, ventral hernias, small-bowel obstruction, protein-calorie malnutrition, and vitamin deficiencies

Vitamin deficiencies: extremely common after malabsorptive bariatric surgeries such as the Roux-en-Y gastric bypass; the most common of these deficiencies are in vitamin B12, folate, zinc, iron, calcium, and vitamin D; estimated that 50% of patients had an iron deficiency and 30% had a vitamin B12 deficiency three years following Roux-en-Y gastric bypass; anesthesiologist should look for signs and symptoms including anemia, neuropathies, and cognitive dysfunction; nutritional deficiencies may be occult, but must always be considered in a patient who presents following bariatric surgery

Conclusion: an obese patient presents many challenges to an anesthesiologist; we have seen that obesity is coupled with many pathophysiologic changes that affect multiple organ systems; the physiologic and anthropometric changes associated with obesity affect pharmacologic management; special consideration must be given to an obese patient presenting for a regional block; careful understanding of the perioperative and postoperative effects of bariatric surgery must be noted

Suggested Reading

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The Renal System and Anesthesia for Urologic Surgery

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Renal physiology: as summarized by Homer William Smith (father of renal physiology), "The composition of the blood is determined not by what the mouth ingests, but by what the kidneys keep;" highlights important central role of kidneys in homeostasis; tend to think of only serum creatinine; in addition to filtering clearance of substances and urine, kidneys function to maintain water balance, fine control over many inorganic ions in acid/base status, and hormone secretion via erythropoietin and activation of vitamin D; gluconeogenesis important component of renal function; glucose generated by kidney largely consumed by kidney as well, so tends not to contribute much to circulating glucose burden; nephron=functioning unit of kidney; each kidney has ~1 million nephrons; kidneys small, fist-sized organs, receive ~20% of cardiac output; filtration leads to modest volume of urine (how the body keeps homeostatic physiology)

Pathophysiology of Renal Disease

Chronic kidney disease (CKD): end-stage renal disease (ESRD) very common; assessed using retention of serum creatinine; serum creatinine reflects accumulation of breakdown product of muscle; when estimated creatinine clearance reaches ~15 mL/min, patients develop uremic symptoms, often requiring dialysis; greater levels of glomerular filtration associated with impaired renal function; in most classification systems, CKD officially diagnosed when glomerular filtration drops <60 mL/min; normal glomerular filtration level ~120 mL/min in young adults; after age ~30 yrs, 1% decline in glomerular filtration rate (GFR) per yr; leads to levels in average population that reflect CKD with even normal circulating levels of creatinine when patient reaches 6th or 7th decade; patient population with CKD and ESRD steadily increasing; reflected partly by expanding size of population, but also through increased incidence of patients receiving chronic dialysis; transplant surgery has allowed many patients to survive with renal transplants (which may or may not also have CKD)

Kidney disease classification: kidney diseases that progress and end up in ESRD can be grouped into 3 main types; primary kidney diseases (*eg*, IgA nephropathy); secondary kidney diseases, consequence of chronic diseases (*eg*, diabetes, hypertension, metabolic syndrome); uncommon secondary kidney diseases (*eg*, sickle cell disease, systemic lupus erythematosus, vasculitides); ~5% of adult population has CKD, vast majority attributable to diabetes and/or hypertensive disease; chronic disease more prevalent in the urban population, but acute kidney injury more common in hospital; both associated with elevated levels of serum creatinine and can exist concurrently

Acute kidney injury (AKI): defined differently from CKD; in past decades, AKI classified in various ways, making it difficult to compare studies; Society of Thoracic Surgeons (STS) definition probably first prevalently used, but others (*eg*, Risk, Injury, and Failure; and Loss; and End-stage kidney disease [RIFLE], Acute Kidney Injury Network [AKIN], and Kidney Disease Improving Global Outcomes [KDIGO] consensus definitions) have come forward; now 4 different ways of describing AKI; each requires threshold degree of elevation of serum creatinine or oliguria; oliguria hard to assess perioperatively; considerable debate about whether or not meaningful measure; many perioperative studies rely only on AKI as defined by creatinine criteria

Predicting AKI: regardless of definition, difficult to predict which surgical patients will get AKI; patient factors poor predictors of likelihood; type of surgery better predictor; cardiac surgeries, liver transplant, lung surgeries, and some major vascular surgeries (*eg*, for abdominal aortic aneurysm [AAA] and thoracic aortic aneurysm) highly associated with AKI incidence; easier to predict whether patient likely to require dialysis as consequence of AKI; higher likelihood relates to patients who present for surgery with CKD and elevated serum creatinine; difficult to predict degree of AKI that will tip patient with CKD over to need ESRD treatment

AKI risks: risks associated with onset more certain (*eg*, elevated mortality risk, extended lengths of hospital stay, increased costs for hospitalized patients with this condition); AKI has poor association with recovery (*ie*, failure to rescue) relative to other complications; in long term, AKI perioperatively associated with poorer long-term outcome and poorer 5-yr survival

Mediators of adverse consequences: many substances that accumulate mediate some adverse consequences of kidney disease; serum creatinine myocardial depressant; asymmetric dimethylarginine (ADMA) causes direct inhibition of nitric oxide (NO) synthase; limits production of NO, which causes vasoconstriction; has been attributed with some higher risks of cardiovascular (CV) disease in patients with CKD; in terms of renal protection, many therapies aimed at either prophylaxis or treatment of AKI but none has demonstrated any significant effectiveness

Treatments: those widely recognized in past include renal-dose dopamine and furosemide; no debate that both substances produce increased urine output, but no good

evidence that either one demonstrates any renoprotective effect; intravenous (IV) furosemide increases renal risk and may be renal toxin; use of mannitol as diuretic also well known, but no good evidence for renoprotective role in majority of AKI settings

Preoperative assessment: for patients at renal risk (*ie*, related to patient or procedure), some considerations in preoperative management; first surrounds exposure to intravenous pyelogram (IVP) contrast dye in early preoperative period; meta-analysis of patients who waited ≥1 day vs >3 days for surgery demonstrated that waiting >1 day not necessary (only in elective circumstances); in emergency circumstances, proceed with surgery

Preoperative management of chronic therapies: furosemide and other loop diuretics associated with increased risk of perioperative AKI; angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blocker (ARB) therapies may be associated with AKI risk; statin therapy does not appear to have effect; some procedures touted as preferable for patients at high renal risk

Perioperative cardiac surgery: minimally invasive valve surgeries performed (*eg*, minithoracotomy using heart port technology), evidence of reduced AKI risk relative to same surgery performed by median sternotomy; evidence suggesting off-pump cardiac surgery for coronary artery disease more renoprotective than on-pump more difficult to demonstrate; minimally invasive surgeries (*eg*, transcatheter aortic valve replacement [TAVR], thoracic endovascular aortic repair [TEVAR; aortic stent graft treatments], video-assisted thoracic surgery, AAA repair) associated with reduced AKI vs invasive procedures

Clinical elements in control of the anesthesiologist: use of epidural anesthesia as supplement to general anesthesia, either as intraoperative tool or in postoperative period; in both settings, associated with reduced AKI; mainly shown in patients undergoing thoracic, lung , and cardiac surgery

Cellular level contributors to AKI: 2 major pathways for cellular injury within kidney seem operative; ischemia reperfusion as consequence of hypoperfusion, involving cell necrosis; sepsis and inflammation, which can trigger cell apoptosis (programmed cell death)

Cell necrosis pathway: must address renal paradox (*ie*, situation in which kidneys responsible for ~0.5% of body weight but receive 20% of cardiac output); renal vein has elevated level of O_2; kidneys vulnerable to ischemic injury based on circulation that surrounds nephron; network of capillaries (vasa recta) follow Loop of Henle from cortex, where plasma filtered in glomerulus and plasma filtrate runs down proximal convoluted tubule into Loop of Henle; as it descends into renal medulla, complicated process occurs by which active transport produces urea gradient in presence of sluggish circulation; urea gradient underpins kidney's ability to concentrate urine; this same phenomenon (countercurrent exchange) allows sluggish blood flow to cause O_2 to escape in venous blood that departs medulla before being able to be transported into medulla for use; gradient of O_2 in renal medulla, such that even in normal patients with healthy kidneys, PO_2 values can be in the low teens, related to this countercurrent phenomenon (medullary hypoxia)

Medullary hypoxia: normal part of renal physiology; however, makes deeper part of kidney more vulnerable to ischemia; explains renal paradox; as it translates into components of patient management for anesthesiologist, first issue, management of blood pressure (BP) during surgery; decreasing BP when associated with decreasing flow associated with AKI; when decreasing BP associated with maintained flow (*eg*, during cardiopulmonary bypass), linkage with normal BP management difficult to demonstrate

Oxygen delivery management: *anemia, tolerance, and transfusion* — association (most notably in cardiac surgery) with lowest hematocrit during cardiopulmonary bypass and incidence of AKI; AKI incidence starts to rise as hematocrit descends below ~20% to 21%; seems to be common whether or not patient receives transfusion; transfusions seem to be associated with AKI; *insulin and glucose* — use of insulin and glucose in hyperglycemia associated with AKI in retrospective studies, but not demonstrated in prospective studies

Fluid management: data show role in risk of AKI; studies have suggested that avoidance of normal saline associated with benefit in terms of avoiding AKI risk, in contrast with other isotonic solutions (eg, plasma protein fraction [Plasmanate] and Ringer's lactate); other solutions associated with elevated risk of renal-related outcomes include starch solutions (associated with risk of acute renal failure requiring dialysis in patients with sepsis); strategies that manage cardiac output using goal-directed therapy appear to be associated with AKI protection; those that mediate inotrope improvements in cardiac output associated with renal protection

Treatment choices: rates of AKI related to certain procedures vary among centers; preliminary data suggest dopamine use for either inotropy or vasopressor use associated with higher risk of AKI; epinephrine vs norepinephrine associated with higher AKI rate

Dialysis: some success in terms of treating AKI or CKD; types vary and used in different settings; hemodialysis mostly used as chronic therapy for ESRD, but can be used in patients with AKI who temporarily require dialysis; continuous venovenous hemodialysis (CVVHD), continuous form of hemodialysis used most often in intensive care units (ICUs); chronic ambulatory peritoneal dialysis used for patients who prefer less invasive approach; patients instill dialysis solutions into peritoneal cavity and drain at regular intervals

Uremic toxins: goal with each approach to clear uremic toxins; uremic toxins accumulate long before dialysis threshold (ie, GFR ~15 mL/min) reached; these substances, particularly larger molecular size, cleared inefficiently as GFR declines; more amplified than for smaller molecules (*eg*, creatinine); *2 principles to guide timing of dialysis relative to surgery* — 1) try to bring patient to operating room in optimal condition; 2) avoid early adverse consequences of dialysis (*ie*, disequilibrium syndrome), often associated with considerable hypovolemia; whenever possible, dialysis should be performed on day before surgery

Selection of anesthetic agents: for patients with reduced renal function, consider factors that guide drug choice; patients have alterations in both pharmacokinetics and pharmacodynamics, relating to role of renal clearance; some agents dependent on renal clearance for loss of action; some partially dependent; some not dependent, but breakdown of components produces active or toxic

metabolites; malnutrition and/or peritoneal dialysis cause differences in binding of drugs in circulation; can lead to changes in active drug in circulation; among drugs completely dependent on renal clearance, some relatively common (*eg*, vancomycin); some muscle relaxants completely cleared by kidney, but those rarely used now; digoxin renally cleared

Dosing: medication load unaltered, but maintenance dosing lowered because of reduced substance clearance; agents partially dependent on renal clearance more common; for these drugs, load unaltered, but maintenance dosing decreased by ~30% to 50%; examples include atropine, neostigmine, vecuronium, and milrinone; common examples of medications with increased unbound fractions include barbiturate anesthetic induction agents (*eg*, thiopental, methohexital) and benzodiazepines (*eg*, diazepam); drugs with active metabolites dependent on renal clearance include morphine, midazolam, sodium nitroprusside, vecuronium, pancuronium, procainamide, and meperidine

Physiologic consequences some relevant to perioperative management: relative inability to clear certain electrolytes; hyperkalemia common; ≤40% of patients with ESRD present with elevated levels of serum potassium, which can be affected by acid/base levels; with every 0.1 unit of decline in pH (*ie*, greater acidosis), serum potassium increases 0.5 mEq/L; becomes pertinent in early postoperative period, when patient may be mildly sedated and hypercarbic, which changes pH and serum potassium; another source of potassium, exogenous boluses (most commonly from aged red blood cells (RBCs) with high potassium as part of storage lesion); can produce threatening elevations of serum creatinine; consider prewashing RBCs before transfusion, particularly in pediatric patients, in whom such potassium bolus could be very serious

Treatment: beyond avoiding original source of potassium or treatment, such as succinylcholine, other approaches to treating hyperkalemia include calcium chloride, gluconate hyperventilation, and IV sodium bicarbonate; if ineffective, try glucose and insulin to force potassium to follow inside cell; serum glucose should be monitored; extreme interventions may include emergency dialysis

Urologic Surgery

Specific urologic surgeries: specifically, lithotripsy and transurethral resection of the prostate (TURP)

Lithotripsy: shockwave lithotripsy best suited for enteronephric stones of small or moderate size; anesthetic management very similar to those for patients undergoing standard surgeries; patients with kidney stones present most commonly in 3rd to 5th decade; commonly associated with comorbidities (*eg*, obesity, hypertension, hyperparathyroidism); may have other problems relating to renal failure or CKD that produce problems associated with accumulation of renal uremic toxins (*eg*, platelet dysfunction, anemia, electrolyte abnormalities), in particular, paraplegic patients commonly have kidney problems present presenting for surgery; those with sensory deficits below T6 and who lack pain perception for cystoscopy procedure, but at risk for autonomic hyperreflexia, require anesthesia to block afferent stimulation; consider that patients with recurrent kidney stones may be receiving chronic opioid therapies

Monitoring: monitors should be as patient comorbidities dictate; significant blood loss or fluid shifts unusual; earlier shockwave lithotripsy machines conducted lithotripsy in water baths and required immersion of patient; dry-shockwave lithotripsy involves smaller water-filled coupling device that provides interface with patient and simplifies procedure; most procedures now performed in outpatient setting with topical local anesthetic and analgesic, and sedation provided; with postoperative analgesia, sufficient from nonsteroidal anti-inflammatory medications

TURP: group of procedures performed transurethrally for surveillance and resection of tissues in prostate or bladder; may be gold-standard therapy to alleviate urine obstruction symptoms related to benign prostatic hypertrophy (BPH); in therapy of BPH, TURP less common than 10 yrs to 20 yrs ago

Surgical approach: standard approach involves resectoscope (specialized endoscope with electrode for coagulating and cutting tissue); device also used for resection of tissue or tumor from bladder wall; patients presenting for TURP often elderly and have other serious comorbidities; factors worthy of consideration include cardiovascular and pulmonary status; carefully assess for ability to tolerate intravascular volume changes, sometimes associated with this procedure; *anesthesia* — assess anticoagulation status if considering spinal anesthesia; abnormal coagulation can be associated with increased risk of postoperative bleeding (important consideration for TURP surgeries); procedures performed safely with general or regional anesthesia; neuraxial block allows patient to remain awake, which may hasten diagnosis of prostatic capsule perforation and potential for transurethral resection (TUR) syndrome; may be associated with reduced blood loss compared with regional and general anesthesia

Complications: *hypothermia* — from absorption of cooled solution and/or lowering of body temperature by infusion of large volumes of cooled solution into bladder; hypothermia less common with warmed irrigation solution; average blood loss 2 mL/min to 4 mL/min; shorter procedures associated with less bleeding; ~2.5% of patients require transfusion as part of TURP surgery; *perforation of prostate capsule* — occurs in ~2% of TURP procedures, commonly resulting in extraperitoneal fluid extravasation; if patient awake, may notice abdominal discomfort or shoulder pain; *circulatory complications* — some substances released during resection (particularly if malignant) may trigger abnormal conditions in circulation (*eg*, disseminated intravascular coagulation [DIC] and/or fibrinolysis); events uncommon but may be associated with abnormal bleeding; treatment supportive with coagulation factors and platelets

TUR syndrome**:** relates to clear solutions that surgeons use to flush visual field for visualization of tissue to resect within urethra; resection can leave urinary tract injuries that may lead to absorption of irrigating solutions directly into circulation; when significant amount of fluid inadvertently enters circulation (*eg*, during TURP procedure), can cause volume overload, as well as other predictable complications, depending on quality of fluid infused; solutions have had to be electrolyte free because of disbursement of electrical

current to resect tissue; bipolar electrocautery and/or laser techniques have replaced these former techniques, allowing irrigation with isotonic crystalloid solutions; solution makeup and osmotic activity predict consequences of fluid absorption through prostate capsule, in addition to total fluid volume; each type of solution has specific side-effect considerations beyond fluid overload; anesthesiologist must know what irrigating solutions used

- Symptoms of TUR syndrome: common cluster of symptoms generally associated with hypervolemia related to water intoxication; include excessive volume expansion with respiratory distress, congestive heart failure, pulmonary edema, hypertension, bradycardia, hypotension; hyponatremia may develop with some irrigating solutions, associated with mental confusion and nausea; due to hypotonicity, water intoxication with distilled water quickly associated with severe hyponatremia with hemolysis and hemoglobinemia, and renal failure; alternate solutions (*eg*, sorbitol or other glucose solutions) associated with hyperglycemia; glycine (amino acid normally metabolized to ammonia) may cause depressed mental status and coma due to hyperammonemia that can last ≤48 hrs postoperatively; absorption of glycine solutions associated with blurred vision, minimally or nonreactive pupils, and transient blindness
- Causes of TUR syndrome: regardless of fluid type absorbed, usually occurs when large amounts of irrigant absorbed (usually >2 L); occurs in ≤1.4% of TUR procedures; rates of absorption with infusion rate into bladder of ~300 mL/min between 20 mL/min and 200 mL/min; factors that increase absorption of irrigation fluid during procedure include number and size of open venous sinuses; evidence of greater blood loss also implies greater potential for irrigation absorption; surgical disruption of prostatic capsule allows irrigant to spread into soft tissues; longer duration of resection allows for more reabsorption of fluid; higher hydrostatic pressure of irrigating fluid (*eg*, bags elevated above patient) increases pressure and, therefore, reabsorption
- Recommendations: limit resection time to <1 hr; suspend irrigation fluid bags to ≤30 cm above operating table at beginning, 15 cm in final stages of resection; avoid hypotonic IV solutions whenever possible; treat regional anesthesia-related hypotension with vasopressor agents rather than volume boluses

Dilutional hyponatremia: can cause cerebral edema with altered neurologic function; promptly intervene whenever neurologic or CV complications develop related to TUR procedures; if procedure continuing, complete as quickly as possible; reestablish normal tonicity as related to sodium level; should be performed using hypertonic saline if serum sodium concentrations <120 mEq/L; can be achieved with hypertonic NaCl 3%, infused at ≤100 mL/h in adults; monitoring should be followed, including frequent serum electrolytes, to ensure hypertonic saline discontinued when patient becomes asymptomatic, or when serum sodium concentrations >120 mEq/L; because rapid correction of low serum sodium associated with central pontine myelinolysis, once symptoms have resolved or patient has serum sodium level >120 mEq/L, hypertonic sodium therapies should cease; few reports of demyelination after correction of acute symptomatic hyponatremia; no reports in relation to TUR syndrome; treatment of volume overload should be as with any situation that includes volume excess, including use of diuretics to clear fluid

Perioperative Management of Patients with CKD and ESRD

General principles: chronic characteristics of physiology; patients with CKD common, representing ~5% of surgical population; patients with ESRD fewer in number and present for relatively small number of procedures in high frequency; majority of procedures in patients with ESRD involve vascular-access procedures; ~85% of these surgical procedures involve vascular access (*eg*, arteriovenous [AV] graft shunts in arm for hemodialysis access); patients commonly present for cardiac surgery, particularly coronary bypass graft surgery; kidney transplant common; patients at elevated risk for adverse outcomes, including 1% to 4% surgical mortality and 10% to 20% post–cardiac surgery mortality; added risks include 5-fold increased risk relative to routine patients for emergency procedures, and increased risk if patients elderly or diabetic; high postoperative morbidity rates, ranging from 14% to 64%; generally require more vasoactive drug interventions, longer ventilation dependence periods, and longer stays in ICU and hospital; greater complications such as infections, hyperkalemia, arrhythmias, hemodynamic instability, bleeding, and anemia; frequently have less-common complications, such as pericarditis, neuropathy, and clotted vascular access ports; more commonly experience stroke

Chronic anemia: characteristic of presenting ESRD patients; also common in CKD patients; deficiency of production of erythropoietin by kidneys; preoperative preparation for these patients (commonly present with hematocrit levels 25% to 28%) involves iron supplementation and exogenous erythropoietin; other causes of anemia include increased reasons for blood loss; may be dialysis related in patients with hemodialysis, but also from frequent blood sampling for blood tests, and even occult bleeding due to coagulopathy; patients have fragile RBCs that have shortened survival in circulation; exogenous recombinant human erythropoietin (EPO) therapy prior to surgery has been studied; studies have indicated reduced allogeneic blood transfusions in some patient cohorts (particularly orthopedics), but cost efficiency has yet to be proven; another management consideration, consequence of raising hematocrit too high; chronic EPO therapy for anemia associated with stroke in patients with CKD; recommended target ranges 33% to 36%, even in patients with chronic therapy

Anesthetic approaches to AV fistula creation: range from regional to general anesthesia, and in sickest patients, local anesthesia; potential considerations in avoiding general anesthesia in high-risk patients include suggestion that regional anesthesia may increase perioperative venous dilation and improve maturation of AV fistula; even with potential advantages of local anesthesia and potential for maturation of fistula, the majority of anesthetics in United States are general anesthetics

Anesthetic considerations for renal transplant: ~17,000 per yr performed in United States, with many more patients waiting for kidneys; considerable numbers of

patients with glomerular diseases (*eg*, focal segmental glomerulosclerosis [FSGS], IgA nephropathy) also present for renal transplant; some congenital defects in children

Standard preoperative assessment: approaches should include attention to state of dialysis, timing of last dialysis, type of dialysis, serum potassium values, and patient's dry weight; other associated comorbidities include CV risk, hypertension, ACE and ARB inhibitor status (if these medications have been taken), diabetes, electrolytes, and hematologic assessments; check donor kidney for human leukocyte antigen (HLA) and blood typing relative to patient; available immunosuppressant medications with standard timing throughout procedure; IV access necessary but can be challenging in patients whose vascular access has been tapped for many procedures, including for AV fistulas; in some cases, patient comorbidities and other considerations may warrant central venous pressure (CVP) monitoring and access for IV infusions; arterial lines rarely placed for renal transplant but may be considered, based on comorbidities; CVP monitoring may be used, but more commonly reason for vascular access; AV fistulas should be checked and maintained patent because they may be needed postoperatively for dialysis, even while implanted kidney recovers

Anesthesia: standard induction should include use of hypnotic and muscle relaxant (most commonly cisatracurium); maintenance often established with volatile anesthetic; IV anesthetic with propofol adequate; hemodynamic goals to keep the BP between baseline and possibly even slightly hypertensive; antibiotics used as discussed with surgeon, and opioids typically to preference of anesthesiologist (most commonly fentanyl); in terms of fluid management, colloids rarely given, crystalloid fluids usually adequate; blood transfusions rarely provided; during transplant, hemodynamic goals to keep BP elevated; once reperfusion of organ occurs, potential for use of mannitol and/or furosemide often used to induce urine production; patients generally do well with renal transplants; associated with extended graft survival and living donor survival that far extends beyond that of many other large-organ transplants

Hepatorenal syndrome: patients with hepatorenal syndrome present more commonly for liver transplants; common constellation of liver and kidney dysfunction; as related to renal dysfunction, main management components supportive, relating to correction of liver function and recovery of kidney

Summary: kidneys have profound effects on maintenance of homeostasis throughout body; dysfunction of kidneys (acute or chronic) has important implications for practice of anesthesia

Suggested Reading

Feng F et al: Anesthetic concerns for patients undergoing a transurethral resection of the prostate (TURP). *Urol Nurs*. 2016;36(2):75-81; Ismail A et al: Regional versus local anesthesia for arteriovenous fistula creation in end-stage renal disease: a systematic review and meta-analysis. *J Vasc Access*. 2017;18(3):177-84; **Hu Y et al:** The effect of the time interval between coronary angiography and on-pump cardiac surgery on risk of postoperative acute kidney injury: a meta-analysis. *J Cardiothorac Surg*. 2013;8:178; **Pauling M et al:** Severe hyperkalaemia complicating parathyroidectomy in patients with end-stage renal disease. *Anaesth Intensive Care*. 2017;45(3):365-8.

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Hematologic Diseases and Anesthesia

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Anemia: affects 2.3 billion people worldwide; most commonly affects pre-school children, followed by women of child-bearing age; high burden of disease; 4th on list of diseases with highest years lived with disability (after heart failure, cancer, and diabetes); prevalence in surgical population ranges from 20% to 70%, depending on underlying condition and surgical procedure; colon cancer patients have anemia prevalence of 70%; orthopedic patients undergoing large joint replacement have anemia prevalence of 40%; independent risk for negative outcomes associated with surgery and anesthesia; morbidity from cardiovascular and infectious complications; length of stay affected; reduced survival in surgical patients; all types of surgery pose a risk to patients with anemia, partly because of risks from transfusion; patients admitted for surgery with any level of anemia are at risk of intraoperative or postoperative transfusion; large cohorts show that, after adjustment for underlying comorbidities, those transfused have worse morbidity and survival; although these studies are retrospective or observational, they repeatedly show negative outcomes associated with transfusion; the reflex to transfuse to treat anemia can be modified to improve patient outcomes; historically, the treatment for patients with worsening anemia in the hospital has been transfusion; iron deficiency is leading cause of anemia globally and affects 30-40% of anemic surgical patients; transfusion does not address underlying disease

Iron deficiency anemia: recommendation from AABB (formerly, the American Association of Blood Banks) is not to treat iron deficiency anemia with transfusion; current recommendation is to diagnose and treat perioperatively; assess iron, B12, and folate deficiency; B12 deficiency without pernicious anemia highly prevalent among patients admitted from nursing homes for fractures or other surgical interventions

Critically ill patients: develop anemia within a few days of admission to the intensive care unit; often treated with transfusion instead of identifying underlying cause and giving appropriate treatment

Surgical patients: Canadian study suggested early transfusion before surgery to treat anemia; did not address underlying cause; transfusion as prophylactic therapy does not follow any published transfusion guidelines

Algorithms for screening, diagnosis, and treatment of anemia in surgical patient: available since 2005; guidelines rely on indices to identify patients with iron deficiency versus inflammatory anemia; iron deficiency anemia responds to iron alone; oral iron may not work for surgical patient because of short time between diagnosis and procedure; daily oral iron may actually inhibit iron absorption; master regulator of iron absorption, hepcidin (25 amino acid hormone) stimulated by oral iron ingestion; high hepcidin levels block iron absorption and very low levels enhance iron absorption; patients with iron deficiency have low hepcidin levels; patients who are septic or have high stress levels may have high hepcidin levels that block iron absorption; only situation where iron is plentiful, hepcidin low, and iron absorption continues is thalassemia

Hemoglobin: CBC is first test to screen for anemia; unfortunately, hemoglobin level has been used to define anemia; World Health Organization (WHO) definition is hemoglobin of less than 12 g/dL in females and less than 13 g/dL in males; hemoglobin is a concentration (g/dL); however, red cell mass, which cannot be measured noninvasively, is the index of interest; hemoglobin is a surrogate; range of hemoglobin from laboratory can vary by as much as 2 g/dL in either direction; a hemoglobin of 10, if plasma volume is low, can be concentrated up to 12 and a hemoglobin of 10 with increased plasma volume can dilute it down to 8, but both of these situations have same red cell mass, which is the most important marker for oxygen delivery; because hemoglobin is a concentration, it should be the same for males and females (13 g/dL); red cell mass for females is smaller than red cell mass for males, but concentration should be the same; for simplicity, we will define anemia as less than 13 g/dL; WHO is considering changing their current definition

Red cell indices: determine whether cells are macrocytic (large), normocytic (normal), or microcytic (small); multiple populations of cells (large and small) may be present, so need to look at RDW (red cell distribution width); if RDW wide, suggests multiple populations of cells, indicating a combination of 2 types of anemia; for example, nutritional (iron deficiency) and inflammatory (normocytic cells); if microcytic cells, obtain iron work-up; if reticulocyte hemoglobin content low, highly likely that patient iron deficient, and iron therapy should be started; if cells are normocytic, inflammatory condition (anemia of chronic disease) likely; if inflammatory, patient should have renal work-up prior to surgery because there is generally a reduction in endogenous erythropoietin (EPO) and patient may require exogenous erythropoietin; creatinine clearance testing and nephrology consult

advised; erythropoietin generates red cells quickly and pushes them into circulation early but does not alter iron metabolism; iron is incorporated late into red cells during production; functional iron deficiency may be created with erythropoietin therapy, but this also exists with the underlying inflammatory anemia or anemia of chronic disease, so small supplements of iron are recommended; at our institution, we do not start EPO without supplemental iron unless contraindication exists; misconception that anemia treatment takes a long time; if therapy directed towards underlying disease, rapid rise of hemoglobin within a few days

Iron: follow response to treatment; recommend IV iron for surgical patients because it works faster than oral iron; patient receiving oral iron may lose opportunity to have anemia reversed or treated; misconceptions exist about iron and its effects on hemoglobin and side effects, including anaphylactic shock; anaphylaxis rare with IV iron, but monitor patient during infusion

Surgery timing: postpone surgery while treating anemia, as would be done to modify cardiac, pulmonary, or endocrine risks; avoid transfusion because it is an important risk in itself

Transfusion indications and guidelines: first NIH Consensus Conference on transfusion guidelines in 1988; new guidelines nearly every year (most from blood establishments such as AABB, American Red Cross, American College of Pathology, and blood authorities from other countries); provide recommended thresholds ("triggers")for transfusion; 1999 TRICC trial from Canada suggested that hemoglobin of 7 safe compared to higher hemoglobin (most clinicians had been using level of 10 g/dL); remember, hemoglobin not an accurate indicator of red cell mass; need to consider clinical picture; if hypoxemia or ischemia present with anemia and volume replenishment does not address problem, consider transfusion; used to be said that if you are going to give 1 unit, you should give 2; we now understand that each transfusion unit is an independent risk; if patient requires a transfusion because low hemoglobin and clinical signs suggest ischemia, recommendation is to give 1 unit and reassess before giving more units; American Society of Anesthesiologists (ASA) suggests that patients with hemoglobin less than 6 g/dL would most likely benefit from a transfusion and those with a hemoglobin greater than 10 g/dL will not benefit but will only get the risk of transfusion; need to recognize that each patient's response or compensation to low hemoglobin or anemia varies; patients with a hemoglobin of 5 g/dL could be fine with stable vital signs and no need to transfuse because hemoglobin can be increased with an appropriate pharmacologic agent; some patients who have a hemoglobin of 9 g/dL struggle and show signs of ischemia may be helped by a single unit of blood; need to have plan B for improving hemodynamics of anemic patients; ultimately, we do not know when a patient will benefit from transfusion and when they will only experience the risks, despite many trials; acute anemia with clinical signs and symptoms that are unresponsive to other interventions to increase DO_2 (oxygen delivery) may respond to transfusion; most transfusions for medical or surgical hospitalized patients are inappropriate and provide no benefit; per the Institute of Medicine definition of overuse, transfusion for patients who do not need it and can benefit from another intervention is a risk; it is also a costly and inappropriate use of medical resources; make every effort to adhere to transfusion guidelines, considering clinical signs and symptoms

Hemoglobinopathies: 2 most concerning genetically transmitted hemoglobinopathies are sickle cell disease and thalassemia; caused by genetic mutations that result in abnormal hemoglobin molecules; cause hemolytic anemia because these are abnormal red cells; chronic complications involve lung parenchyma, vasculature, cardiac function, and gas exchange and can cause acute or chronic hypoxemia

Sickle cell disease: estimated 100,000 persons, or 1 out of 400 African American newborns in the United States has sickle cell disease; autosomal recessive, inherited condition; mutation in the sixth codon of the beta-globin gene; results in symptoms in homozygous and compound heterozygous states; resulting hemoglobin polymerizes, resulting in formation intraerythrocytic viscous gel that induces deformation of erythrocytes into sickled shapes, which then cause microvascular occlusion and hemolysis with free hemoglobin; all complications due to vasculature or hemolytic anemia are significant challenges for anesthesiologists and other clinicians caring for these patients; in addition to heart, kidney, lung parenchyma, vascular, and liver complications, disease events in sickle cell anemia patients can be associated with significant pain that can be very difficult to control; vascular events lead to acute or chronic hypoxemia, especially due to vaso-occlusive disease in the lungs, which can lead to reactive airways and bronchial constriction; resulting significant ventilation-perfusion (V/Q) mismatch may be a challenge before or during surgery; assessing pulmonary, kidney, lung, and cardiac function essential when making decisions about timing of elective surgery; no agreed-upon standards regarding timing of surgery for these patients; if there is any reserve that can be recruited, it is essential to identify the amount of reserve for any of these organs; a few publications have examined treatment and management of patients with active sickle cell disease and those with sickle cell trait who may have advanced disease; algorithms published in the literature

Thalassemia: 2 types; not as common as sickle cell disease in the United States; about 1,000 persons have beta thalassemia in US (alpha thalassemia less common); genetic disorder; patients from all corners of world; no longer thought of as Mediterranean disease; relatively common in Far East; as with sickle trait, thalassemia trait associated with less symptoms than overt disease, but anemia may be present in both sickle and thalassemia trait; patients may have microcytic anemia but do not have iron deficiency

Hemoglobinopathy treatment: patients with sickle cell disease and thalassemia live longer today because of better medical care; may present for elective surgery or for procedures involving significant blood loss; need to ensure reserve of organs with beta thalassemia (major or minor) as with sickle cell disease; need to communicate with providers who give ongoing care to patients with sickle cell or thalassemia (hematologists, internists, or pediatricians) to ensure understanding of patient reserve and biggest concerns for organ function; need to consult them about possible anemia treatment, which is not contraindicated; patients with both these anemias at risk of

transfusional iron overload; occurs in patients who receive more than 20 units of red cells over their lifetime without any bleeding episodes; most patients do not have bleeding episodes, but do have hemolysis; iron overload can cause cardiac, liver, and endocrine disfunction; anesthesia literature deplete in addressing iron overload, especially transfusional iron overload; specific therapy depends on disease penetrance and patient age; pediatric patients with homozygous sickle cell (SS) disease or severe beta thalassemia may require different interventions than those who reach adulthood with stable disease; recommendations for administering fluid to maintain urine output and maintaining normothermia to prevent cold vasoconstriction and sickling are generic; Sickle Cell Disease Society presents criteria and transfusion recommendations for patients with sickle cell disease which may also apply to thalassemia; different recommendations for infants and children than for adults; hereditary hemoglobinopathies in pregnancy challenging for anesthesiologist; consultation with high-risk obstetricians and patients' regular care providers important for treatment decisions; not every patient reacts same way to underlying condition and may require different interventions at different times

Polycythemia (erythrocythemia): condition formerly referred to all cell lines including platelets, white cells, and red cells; most cases are erythrocythemia (increase in absolute red cell mass); reflected by increased hemoglobin level or hematocrit; more common with advanced age; characterized by red cell mass greater than 36 mL/kg in males and 32 mL/kg in females; actual red cell mass may vary with altitude, geographic conditions, and ethnicity

Polycythemia vera: subtype of erythrocythemia considered potentially malignant; acquired Philadelphia-chromosome negative myeloproliferative disorder; production of all 3 cell lines (red cells, white cells, and platelets); risk for surgical patient because of increased blood viscosity; concern for progression to hematologic malignancy or leukemia; finding of high hemoglobin (red cell mass increased beyond normal range) should cause concern for elective surgery; need to determine etiology; may be first sign of underlying malignancy (renal or erythropoietin-secreting tumor); exogenous anabolic steroids are erythropoietic and anesthesiologist should consider possibility of illicit anabolic steroid use; prevalence is low (22 cases per 1,000 population); more common in patients of Eastern European and Jewish descent; much more common in males than females; etiology may be increased erythropoietin production or mutation without increase in EPO production or reduction in EPO production; careful history of cardiovascular or cerebrovascular symptoms or signs is essential; many patients have episodes of epistaxis; patients require repeated phlebotomies to reduce blood viscosity, which may cause hypovolemia; need to know when patient last phlebotomized and how much volume was removed; patients may use multiple medications including aspirin; some patients may be at risk of bleeding with subsequent anemia (very small number, not usually a problem for elective surgery); consultation with hematologist or cardiologist recommended

Thrombocytopenia: platelet count less than 150,000; many possible etiologies; can result from peripheral destruction or reduced production in bone marrow; mild thrombocytopenia is platelet count of 100,000; less than 50,000 platelets considered severe thrombocytopenia; patients with hematologic malignancies can have thrombocytopenia with less than 20,000 platelets; less than 10,000 platelets associated with increased risk of spontaneous bleeding; most common bleeding concern is into the closed space of the calvarium (central nervous system bleeding); in addition to overt bleeding, patients may present with easy bruising or skin petechiae; all infectious agents (viruses, bacteria, parasites, and rickettsial agents) can cause thrombocytopenia; bone marrow suppression due to malignancy and other diseases infiltrating the bone marrow (myelodysplastic syndrome) associated with low platelet production; pharmacologic agents may cause thrombocytopenia by reducing production or causing sequestration or destruction; sequestration of megakaryocytes and platelets can occur in autoimmune disease (eg, idiopathic thrombocytopenic purpura [ITP]); thrombocytopenia also occurs in patients who bleed and consume platelets; many medications can cause antibody-mediated thrombocytopenia by binding to platelet membranes and glycoproteins or by stimulating production of antibodies that interact with antigens on the platelet surface; heparin-induced thrombocytopenia (HIT) treated by stopping heparin and inducing anticoagulation with direct thrombin inhibitors (DTIs) in consultation hematologist; patients with chronic renal disease and uremia are thought to have platelet dysfunction and desmopressin (DDAVP) is recommended to enhance factor VIII and Von Willebrand's factor (VWF} to enhance platelet activity, but data is not robust; although risk of using DDAVP very low, need to determine if patient with petechiae or easy bruising also has uremia or chronic renal failure

Thrombocytopenia in pregnancy: two major causes: one is pregnancy-associated thrombocytopenia, in which the number of platelets is reduced but their function and activity are unchanged or increased; patients in their third trimester are hypercoagulable, so reduction in platelet count does not necessarily mean that they are at risk of bleeding, especially with regional anesthesia; no test to predict whether a patient will bleed in presence of thrombocytopenia and other coagulopathies during pregnancy; second condition is HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome; consider complete clinical condition of patient, not just risk associated with epidural or neuraxial intervention; patients with HELLP may also have blood pressure alterations and liver and kidney derangements; when considering neuraxial intervention in the parturient with thrombocytopenia, consider latest recommendations, which vary widely because of arbitrary platelet cutoff values; thought that neuraxial anesthesia can be induced safely if platelet count is 70,000 or more; safety in patients with between 50,000 and 70,000 is an individualized decision

Platelet inhibition: plays a major role in treating cardiovascular disease, with many patients taking more than just aspirin; effect of platelet inhibition may vary from patient to patient, so not all may be protected; vast majority may be at risk of bleeding with surgical intervention; understand different types of platelet inhibitors, half-life, and how long they should be discontinued prior to surgery; guidelines available regarding when to stop each platelet inhibitor prior to

surgery; patients with underlying coronary disease may take double therapy with aspirin and another agent; recommendations fairly strong that 2 drugs not needed for elective surgery; usually the more potent inhibitor should be stopped while aspirin is continued, because aspirin does not confer a significant risk of bleeding

Guidelines for platelet transfusion: very few indications for it; platelet inhibitors that patient may be taking can affect platelets that are introduced through transfusion, so they may not function well; platelet transfusion to those on potent platelet inhibitors may not remedy bleeding; best to wait for those drugs to become ineffective

Hemophilia A and B: X chromosomal recessive disorders caused by deficiency or lack of factor VIII or factor IX; absence or very low levels of these factors determine disease severity; patients receiving replenishment of these factors may develop inhibitors and not respond to therapy or may have an altered response to therapy; formerly thought to be a disease of childhood that mostly affects males; now known that there are some female patients, especially in the pediatric population; many patients reach full adulthood and present for elective surgery; availability of improved factor replenishment has been successful in reducing intra-articular bleeding; injuries from sports can bring these patients to the emergency room or operating room; chronic treatment is prophylactic or preventative against intraarticular bleeding; dose may be increased to accommodate insults of injury or surgical intervention; patients usually have extensive knowledge of their disease, manage daily activity, understand their therapy and dosing; imperative to consult preoperatively with patient's hemophilia specialist or primary physician when hemophilia patient is scheduled for elective or urgent surgery; in an emergency, increasing the factor replacement dose and adding tranexamic acid or epsilon-aminocaproic acid as an infusion is advisable; consult with treating physician as soon as possible to place patient on daily doses of replacement factors

Von Willebrand's disease (VWF): most common inherited bleeding disorder; autosomal inheritance pattern; characterized mainly by mucosal bleeding and bleeding after surgery or trauma; some patients may not be recognized early because they have had no previous insult; present operative and post-operative challenge; patients are missing Von Willebrand's factor, a carrier protein for collagen factor VIII that binds to collagen at the site of the vascular injury and mediates platelet adhesion and aggregation; VW factor has other functions and may be involved in inflammation and angiogenesis; diagnosis based on history of bleeding or laboratory evidence of abnormalities in aPTT, factor VIII, or both; affected patients have reduced VW factor; various types of disease distinguishable by characteristic phenotypes; treatment with infusion of DDAVP or exogenous Von Willebrand factor-containing concentrates; 3 major types of VW disease based on amount of factor available; patients with Type I have a partial deficiency of a functional or normal VWF; patients with Type III may have no VWF; other sub-types of VWF disease exist; anesthesiologist's major concern is bleeding during surgery; patients have variable risks that should be assessed by patient history of prior bleeding episodes and surgical history; consultation with hematologist and/or patient's primary care provider to determine therapy recommendations; therapy should commence prior to surgery; some recommend the addition of antifibrinolytic agents to support patients if they do bleed during surgery; although VW factor normally increased during the third trimester of pregnancy, patients with this disease may be at risk of significant bleeding, especially post-partum; prophylactic therapy with desmopressin and possibly factor concentrates depending on the level and the subunit of the disease is recommended

Pharmacology and anticoagulant therapy: high prevalence of vascular disease with advancing age; a major consequence of vascular disease is stroke; use of anticoagulants directed towards atrial fibrillation and its consequences of stroke or underlying cerebral vascular disease and stroke; warfarin is most commonly used anticoagulant in United States, but its use being challenged or replaced by direct oral anticoagulants (DOACs); instead of inhibiting glutamic acid residue like warfarin does for II, VII, IX, and X, newer agents target either Xa (activated form of factor X) or are direct thrombin inhibitors (DTIs) for factor II; oral anticoagulants have no specific assay, although an Xa assay is now available; no assay to determine the activity of DTIs; inability to test for those agents may represent a challenge if somebody arrives who is unconscious and bleeding and is thought to have a coagulopathy; for warfarin, an elevated INR (not predictive for DOACs) is a risk for continuous bleeding in context of trauma or surgery; currently indicated agent for reversal of warfarin is prothrombin complex concentrate (PCC) and/or plasma if PCC not available; PCC (on-label) is recommended for patients who require emergency surgery who are on warfarin and have an elevated INR or patients with active bleeding who are on warfarin and have an elevated INR; reversal of DTI uses antibody-mediated correction of DTI anticoagulation; newly FDA-approved drug (andexanet) reverses or corrects Xa; prior to availability of andexanet, reversal of DOAC and vitamin K antagonist effects was accomplished with PCC and possibly plasma; results of studies of the use of PCC to correct DOACs and bleeding associated with DOACs are inconsistent, but multiple series of patients treated with PCC to reduce bleeding have shown favorable results; direct correction agents for DTI and Xa inhibition not universally available because they are expensive; PCCs appear superior to plasma for reversal (correction) of vitamin K antagonists because they are much more concentrated and therefore require significantly less volume; PCC dose is about 1:25 the plasma dose to reverse or correct vitamin K antagonist (plasma use would be 15 to 30 mL/kg depending on the INR being targeted for correction); that is an enormous plasma volume (15 mL/kg in a 100 kg person would be 1.5 L of plasma to correct the vitamin K antagonist); factors II, VII, IX, and X have half-lives of hours (5 to 20 hours); half-life ranges have been established based upon tests on volunteers; stressed and ill persons may have shorter factor half-lives; thus, it is recommended that vitamin K infusion (1 to 10 mg IV) accompany administration of any correction agent (PCC or plasma) for correction of vitamin K antagonist; intravenous vitamin K (1 to 10 mg; some institutions prefer 5 mg) should be infused slowly over 20 to 30 minutes; all negative outcomes associated with IV vitamin K are due to rapid infusion

Suggested Reading

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ANESTHESIOLOGY
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Endocrine Diseases and Anesthesia: Part 1

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Pituitary Gland

Anterior pituitary physiology: consists of anterior pituitary, which secretes several hormones; growth hormone promotes growth in children and regulates bone, muscle mass, and fat distribution in adults (however, excess growth hormone in adults causes acromegaly); thyroid-stimulating hormone (TSH) stimulates thyroid gland to produce thyroid hormones; adrenocorticotropic hormone (ACTH) stimulates adrenal glands to produce cortisol; prolactin stimulates breast-milk production; luteinizing hormone (LH) controls ovaries and testes; follicle-stimulating hormone (FSH) regulates ovaries and testes

Posterior pituitary physiology: posterior pituitary secretes antidiuretic hormone (ADH), also known as vasopressin; ADH stimulates kidneys to increase water absorption; helps concentrate urine and regulates thirst; increased extracellular tonicity and hypovolemia stimulate ADH secretion by pituitary in feedback loop; oxytocin contracts uterus during childbirth and stimulates breast-milk production

Hypopituitarism: condition of underperformance of pituitary; etiologies include tumors, postpartum hemorrhagic shock, radiation therapy, pituitary surgery such as hypophysectomy or resection (usually for adenomas); symptoms vary and depend on affected organ; can cause hypothyroidism, adrenal insufficiency, central diabetes insipidus, impotence, amenorrhea, and anesthetic implications related to lack of hormones; treatment consists of hormone replacement therapy

Diabetes insipidus (DI): two types; *central DI* — inadequate ADH (vasopressin) production or inadequate ADH secretion from pituitary; *nephrogenic DI* — results from absence or abnormal response to ADH by kidneys; typical symptoms include excessive urination and extreme thirst; treatment usually with desmopressin (synthetic hormone; available as nasal spray, oral tablets, or by injection)

Acromegaly: results from excess growth hormone; sequelae consists of hypertrophy of tissues (skeletal, connective, and soft), hypertension, hyperglycemia, cardiomyopathy, heart failure, enlarged tongue and epiglottis, thickened vocal cords, recurrent laryngeal nerve paralysis, upper airway obstruction, and peripheral nerve entrapment (*eg*, carpal tunnel syndrome)

Anesthetic considerations: potential difficult mask ventilation and intubation; consider awake intubation with small endotracheal tube

Thyroid Gland

Physiology: has widespread effects, via thyroid hormones; regulates metabolic activity; influences cardiovascular system with effects on blood pressure (BP), contractility, cardiac output, cardiac rhythm and heart rate; also affects pulmonary system by modulating O_2 consumption, CO_2 production, respiratory rate, and tidal volume; also participates in temperature regulation and osteoclastic and osteoblastic activity of bone

Hyperthyroidism: symptoms include weight loss, heat intolerance, palpitations, tachycardia, chest pain, tremors, diarrhea, anxiety, muscle weakness, hyperactive reflexes, goiter, dermopathy or skin changes, clubbing, and ophthalmopathy

Physiologic effects: effects on cardiovascular system include hypertension, tachycardia, arrhythmias (particularly atrial fibrillation, especially in elderly patients), and increased heart rate plus increased contractility (which results in increased cardiac output); high-output cardiac failure especially common in elderly patients; effects on pulmonary system include increased O_2 consumption, CO_2 production, respiratory rate, and tidal volume

Thyroid storm: rare, life-threatening condition; etiologies include infection, stress, trauma, diabetic ketoacidosis, labor, intravenous (IV) contrast dye, and thyroid surgery; exaggeration of the usual symptoms of hyperthyroidism; altered mentation (essential part diagnosis), anxiety, coma, delirium, heart failure, tachycardia with heart rates often >140 BPM, hypotension, hepatic failure, nausea, vomiting, hyperpyrexia, and even death

Laboratory values: elevated T_3 and T_4 and low TSH; patient may also show laboratory evidence of hemoconcentration and leukocytosis, abnormal liver function tests, hyperglycemia, and hypercalcemia

Treatment: treatment for hyperthyroidism or thyroid storm consists of supportive therapy and care (particularly in intensive care unit (ICU), with cooling, IV fluids, and antipyretics to lower temperature); beta blockers can control increased adrenergic tone; propylthiouracil (PTU) or methimazole block hormone synthesis and reduce T_4 to T_3 conversion (T_3 = active form of thyroid hormone); potassium iodide, also known as supersaturated potassium iodide (SSKI) or Lugol's solution, blocks hormone release; glucocorticoids can reduce conversion of T_4 to T_3 and promote vasomotor stability; cholestyramine given orally can decrease enterohepatic recycling of thyroid hormones

Anesthetic implications**:** decrease high sympathetic tone, (can result in labile BP); important to provide sufficient anxiolysis and sufficient depth of anesthesia; for thyroid resection or thyroid surgery, neuromonitoring of

recurrent laryngeal nerve has become commonplace, so important to avoid neuromuscular blockade; typically, video laryngoscopes are used to position monitoring endotracheal tube; ~5% to 8% incidence of difficult intubations due to goiters, airway compression, or deviation; some patients have substernal goiter, which can mimic an anterior mediastinal mass; important concepts include maintaining spontaneous ventilation during intubation, considering awake fiberoptic intubation or inhalational induction, and being aware of possible hemodynamic compromise (particularly with use of muscle relaxants or supine position)

Hypothyroidism: undersecretion of thyroid hormones; be primary hypothyroidism can be caused by autoimmune disorders, radiation therapy, or can be idiopathic; secondary hypothyroidism results from pituitary and hypothalamic insufficiency

Complications: generalized reduction in metabolic activity, including lethargy, cold intolerance, weight gain, bradycardia, decreased cardiac output, decreased ventilatory response to hypoxia and hypocarbia (especially when sedated), anemia and coagulopathy, impaired free water clearance, and hyponatremia; myxedema comas can be, severe life-threatening form of hypothyroidism, with altered mental status (coma not always present), pericardial effusions, hypothermia, bradycardia, hypotension, and overt heart failure

Treatment: thyroid hormone replacement; levothyroxine can be given IV or orally, typically 200- to 300-mcg IV boluses and then 100 mcg intravenously every 24 hrs (use caution in elderly patients or those at risk for ischemic heart disease); ~5% to 10% of patients with hypothyroidism have coexisting adrenal insufficiency; consider supplemental hydrocortisone in 25- to 100-mg doses intravenously every 8 hrs (important, to avoid or minimize opioids and sedatives, if possible; patients can be particularly sensitive, with profound respiratory depression); preoperative normal thyroid state optimal, but thyroid function test, especially TSH, typically lags behind clinical state of recovery; however, only emergency surgery appropriate in patients with severe hypothyroidism or myxedema coma

Anesthetic considerations: judicious use of anesthetics and sedation because of increased sensitivity to sedatives, hypnotics, and opioids; patients also have enhanced cardiac depressant effect from many drugs, especially inhalational agents; they have depressed respiratory drive; important to maintain normothermia, normoglycemia, and intravascular volume and to avoid or treat hyponatremia

Postoperative complications: airway obstruction from hematomas, neck swelling, or recurrent laryngeal nerve injury; if recurrent laryngeal nerve injury, then unopposed action of cricothyroid muscles (tensors of vocal cords via external branch of superior laryngeal nerve); bilateral recurrent laryngeal nerve injury results in complete airway obstruction and increased risk of aspiration; more delayed postoperative complications may be associated with hypoparathyroidism if parathyroid glands inadvertently removed or injured; hypocalcemia can present 24 hrs to 96 hrs later with tetany and laryngeal stridor progressing to spasm

Parathyroid Glands

Physiology: typically 4 parathyroid glands; release parathyroid hormone (PTH), which regulates calcium; regulate serum calcium in normal range of 8.4 mg/dL to 10.2 mg/dL (however, most calcium bound to albumin); ionized calcium active form and its level is normally between 1.1 mmol/L and 1.35 mmol/L; patients with <0.5 mg/dL of ionized calcium, they at risk for tetany or arrhythmias; patients with elevated levels of ionized calcium (>1.7 mg/dL) can result in coma; PTH affects various functions and systems, including bone metabolism, nerve conduction, and cardiovascular system by regulating BP, cardiac function, and cardiac rhythm

Hyperparathyroidism: clinical manifestations summarized as "stones, bones, and groans"

Complications: hypercalcemia associated with hypertension, dysrhythmias, shortened QT interval, polyuria and polydipsia, dehydration, kidney stones, kidney injury and failure, osteoporosis, ileus, nausea and vomiting, peptic ulcer disease, pancreatitis, muscle weakness, delirium and psychosis, and coma

Treatment: surgical removal of gland or glands; temporizing measures include discontinuation of calcium supplements and thiazide diuretics; hydrating patients results in diuresis; administration of loop diuretics such as furosemide can also promote diuresis and lower calcium levels, but should only be used when patient adequately hydrated

Hypoparathyroidism: really problem of hypocalcemia, so important to monitor and replace calcium; cardiovascular effects include hypotension, heart failure, arrhythmias, and electrocardiographic changes (primarily prolonged QT); also affects musculoskeletal system, with muscle cramps and weakness; profound effects on central nervous system (CNS), resulting in irritability, laryngospasm, stridor, tetany, and seizures; altered mental status with dementia, depression, and frank psychosis can occur

Adrenal Gland

Physiology: adrenal cortex produces 3 main types of steroid hormones; *glucocorticoids* — primarily cortisol, synthesized in zona fasciculata and regulate metabolism and immune system suppression; *mineralocorticoids* — primarily aldosterone, produced in zona glomerulosa and regulate BP and electrolyte balance; *androgens* — produced in zona reticularis (innermost layer) and converted to functional sex hormones in gonads

Glucocorticoids: regulate carbohydrate metabolism by enhancing gluconeogenesis and blood glucose levels; promote hepatic glycogen synthesis; play role in protein metabolism by enhancing the degradation of muscle tissue, causing negative nitrogen balance and protein wasting; possess anti-inflammatory actions by diminishing leukocyte response to local inflammation; large doses bind to mineralocorticoid receptors with weak mineralocorticoid effects; glucocorticoids cause free water loss; direct effect on cardiovascular system by maintaining BP, vascular tone, and capillary integrity;, elevated levels of glucocorticoids suppress ACTH from pituitary in feedback loop and suppress cortisol-releasing factor from hypothalamus;

Cushing syndrome: overproduction of glucocorticoids; hyperglycemia common, but only ~20% of patients

will have overt diabetes mellitus; patients with Cushing syndrome have osteopenia and osteoporosis, impaired calcium absorption and bone formation; truncal, cervical, and facial obesity, but thin extremities and commonly, skin striae; often anxious with irritability and depression; frank psychosis can occur; typically hypertension and possibly fluid retention, heart failure, or hypokalemic alkalosis; immunosuppressed and prone to infections; caused by an anterior pituitary microadenoma (leads to adrenal hyperplasia) or by ectopic ACTH secretion (from small cell lung cancers, nonendocrine kidney tumors, or nonendocrine pancreatic tumors)

Primary disease: results from adrenal adenomas (usually unilateral; 50% of adenomas malignant) or adrenal hyperplasia (both adrenal glands enlarged); syndrome exogenous administration of glucocorticoids common cause

Diagnosis: depends on dexamethasone suppression test measuring urinary 24-hr free cortisol and ACTH levels; CT scan of abdomen can diagnose adrenal enlargement or tumors; pituitary MRI can diagnose pituitary adenomas

Anesthetic considerations: preoperative preparation by treating hypertension and hyperglycemia, normalizing fluid status, and correcting electrolytes; consider administering spironolactone (aldosterone antagonist) particularly effective in treating hypertension in patients with Cushing syndrome; during anesthesia, pay careful attention to positioning to prevent fractures, and monitor ECG; anticipate labile BP; patients will have increased sensitivity to nondepolarizing neuromuscular blockers; also, important to monitor and correct intraoperative glucose and electrolyte abnormalities

Adrenal insufficiency: multifactorial etiology; primary adrenal insufficiency (Addison disease) results from atrophy and nonproduction of adrenal glands; etiologies include autoimmune disorders, hemorrhage, infarction, and infection (*eg*, HIV, tuberculosis); secondary adrenal insufficiency results from exogenous steroids suppressing adrenals (typically, steroid doses of >7.5 mg per day for >3 weeks may suppress adrenals ≤1 yr; however, no adrenal suppression occurs if steroid doses <5 mg per day); pituitary dysfunction and hypothalamic dysfunction can also result in adrenal insufficiency

Symptoms: weakness, fatigue, anorexia, nausea and vomiting, flank pain, fever, dehydration, orthostatic hypotension, frank hypovolemic shock, altered mental status, or even coma

Diagnosis: suspected in patients with hyponatremia and hyperkalemia, especially if hypoglycemia present; diagnosis made with low plasma cortisol; does not respond to ACTH stimulation test; CT scan may show adrenal gland hemorrhage or atrophy

Treatment: supportive care with admission to ICU with advanced monitoring, volume resuscitation, electrolyte repletion, and glucose replacement; glucocorticoids mainstay; initially, hydrocortisone given in 100- to 200-mg IV boluses, and continued with 50-mg IV bolus every 6 to 8 hrs, or prednisone can be given once acute illness subsides; mineralocorticoids necessary in primary adrenal crisis, fludrocortisone 5200 mcg orally when hydrocortisone dose <100 mg per day (large doses of hydrocortisone have mineralocorticoid activity but lower doses do not)

Surgery requirements: steroid replacement necessary; for minor procedures, typical daily dose of prednisone can be administered, plus or minus 25 mg hydrocortisone or its equivalent; for major surgeries or with significant stress, ≤50 mg to 75 mg of hydrocortisone may be given IV and continued every 8 hrs for ≤3 days or until acute illness subsides; typically, hydrocortisone can be tapered rapidly to the baseline dose; in patients with sepsis with relative adrenal insufficiency, hydrocortisone doses of 200 mg to 300 mg per day in divided doses typically given until patient weaned off vasopressors; can be tapered over 3 to 5 days

Mineralocorticoids (aldosterone): not under control of pituitary or hypothalamus; regulated by renin-angiotensin system; aldosterone released in response to hypotension or dehydration; causes reabsorption of sodium and water and excretion of potassium and acid

Primary hyperaldosteronism: excessive production of aldosterone from adrenal glands resulting in low renin levels; about one-third of cases result from adrenal adenomas and two-thirds to enlargement of both adrenal glands (rarely to cancer of adrenal glands)

Symptoms: hypertension and hypokalemia most common presentation (classic but only occurs in ~25% of patients); ~10% of all patients with high BP have hyperaldosteronemia; occurs more commonly in women than in men; causes sodium retention and hypernatremic, hypokalemic metabolic alkalosis; screening typically done by measuring aldosterone-to-renin ratio in blood (aldosterone levels high, renin levels low)

Treatment: spironolactone, sodium restriction, and potassium replacement; surgery indicated if tumor >4 cm, tumors with suspicious features of cancer, or patients with refractory hypertension despite medical therapy

Adrenal medulla: located at center of adrenal gland, surrounded by adrenal cortex; connected to sympathetic division of autonomic nervous system and innervated by preganglionic nerve fibers via preganglionic fibers from T5 to T11; secretion consists of ~80% epinephrine (adrenaline), 20% norepinephrine (noradrenaline), and small amount of dopamine; secretes in response to stimulation by sympathetic preganglionic neurons

Pheochromocytomas: catecholamine-secreting tumors; typically occur in ~0.1% of all hypertensive patients; patients with pheochromocytoma may progress to heart failure and dysrhythmias; rarely present intraoperatively with hypertension and tachycardia, but may be associated with other syndromes; these syndromes include multiple endocrine neoplasia (MEN) type 2A (also known as Sipple syndrome; medullary thyroid carcinoma, pheochromocytomas, and hyperparathyroidism), or MEN type 2B (medullary thyroid carcinoma, neuromas, and pheochromocytomas); may be associated in patients with von Hippel-Lindau disease (~25% of patients will have pheochromocytoma); pheochromocytomas result in episodic hypertension but orthostatic hypotension can be present

Rule of 10: with pheochromocytomas, ~10% malignant, ~10% bilateral, ~10% familial, and ~10% extra-adrenal

Symptoms: sweating, headache, palpitations, pallor, tremor, cold extremities, diaphoresis, hypertension, labile hypertension, and tachycardia; can be precipitated by

straining, exercise, abdominal trauma, or anesthesia; rarely present unexpectedly intraoperatively

Diagnosis: high index of suspicion in susceptible populations (particularly those with associated syndromes previously mentioned) and in patients with extreme hypertension refractory to treatment and/or wide swings in BP, especially with minimal stimulus; 24-hour urinary metanephrine or normetanephrine level best diagnostic test, with and it has high specificity (99%); plasma metanephrines can be done if 24-hour urine not possible, but specificity of only ~88%; to avoid diagnosing incidental adrenal masses, CT scan for adrenal masses should be done only if biochemical tests positive; CT scan ~96% sensitive for adrenal mass but has low specificity for pheochromocytoma; metaiodobenzylguanidine (mIBG) scan best test for extra-adrenal tumors, with 80% sensitivity and 100% specificity for pheochromocytomas; other tests include plasma catecholamines, urine vanillylmandelic acid (VMA)

Anesthetic considerations: preoperative BP control key and essential; alpha blockers mainstay; phentolamine or phenoxybenzamine primarily used; beta blockers should only be used after alpha blockade to avoid unopposed vasoconstriction; adequate access and invasive hemodynamic monitoring consisting of arterial lines and central access important; adequate anxiolysis and depth of anesthesia essential; ligation of tumor's venous supply will lead to hypotension, so be prepared with fluids and phenylephrine; laparoscopic surgery with pneumoperitoneum may release catecholamines, which best treated with nitroprusside; avoid sympathomimetics (*eg*, ephedrine and ketamine) and medications that release histamine (*eg*, morphine and atracurium); important to treat acute intraoperative hypertensive crisis with sodium nitroprusside, phentolamine, and labetalol; treat cardiac dysrhythmias with beta blockers, especially esmolol, but only if previously on alpha blockers

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Endocrine Diseases and Anesthesia: Part 2

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Diabetes and Anesthesia

Overview: number of individuals diagnosed and living with diabetes has risen steadily over last 2 decades, continues to rise; perioperative hyperglycemia reported in 20% to 40% of general surgery patients and 80% of cardiac surgery patients; long-term glycemic control relates to mortality in patients with diabetes; plasma glucose levels between 60 mg/dL and 100 mg/dL (3.3 mmol/L to 5.5 mmol/L) normal in fasting state; preoperative assessment appropriate time to screen for poor glycemic control and patients with risk factors for diabetes by measuring hemoglobin $A1_c$

Type 1 diabetes: absolute insulin deficiency; autoimmune disease; antibodies directed against beta islet pancreatic cells that produce insulin; ~5% of all individuals with diabetes; these diabetic patients at greatest risk of developing diabetic ketoacidosis; typically younger, thinner patient; often present with failure to thrive; formally called insulin-dependent diabetes mellitus (IDDM)

Type 2 diabetes: relative insulin deficiency or insulin resistance; ~ 95% of all diabetics; typically, older, with central obesity, consumption of high glycemic diet; formally known as non–insulin-dependent diabetes mellitus (NIDDM)

Type 1.5 diabetes (nonofficial term): form of type 1 diabetes known as latent autoimmune diabetes in adults (LADA); typically slow onset, similar to type 2 diabetes; also autoimmune disease like type 1 diabetes; patients will almost certainly require insulin therapy at some point; ~15% to 20% of patients diagnosed with type 2 diabetes may actually have type 1.5 diabetes; medications designed to reduce insulin resistance do not work; patients with type 1.5 diabetes have little or no resistance to insulin; important to avoid use of term IDDM or NIDDM because often confusing

Insulin: pancreas produces ~50 U of insulin/day; released by beta cells; primarily triggered by blood glucose levels; insulin important anabolic hormone; moves glucose and potassium into muscle and fat cells; regulates processes that lower blood sugar, *eg*, synthesis of glycogen, fatty acid, and protein; decreases processes that raise blood sugar; inhibits glycogenolysis (breakdown of glycogen); decreases gluconeogenesis (increase in glucose), process of ketogenesis (production of ketones), lipolysis (breakdown of fat), protein catabolism

Diagnosis: variety of ways to diagnose; $A1_c$ ≥6.5% establishes diagnosis of diabetes; $A1_c$ not accurate in patients with anemia, abnormal hemoglobins, or who have recently been transfused; fasting blood sugar ≥126 mg/dL (7 mmol/L) also defines diagnose of diabetes; fasting state = no caloric intake for ≥8 hrs; oral glucose tolerance test (used frequently in past, but less currently) to establish diagnosis of diabetes, 2-hr glucose ≥ 200 mg/dL (11.1 mmol/L) after ingestion of 75 g of anhydrous glucose; classic clinical symptoms of hyperglycemia (polyuria, polydipsia, unexplained weight loss) with random glucose ≥200 mg/dL can also establish diagnosis of diabetes; hemoglobin $A1_c$ (glycosylated hemoglobin) reflects average blood sugar during previous 3 months, half of that determined by most recent month, other half from previous 2 months; better predictor of control than fasting blood sugars

Complications: patients with diabetes have 4- to 5-fold greater rate of left ventricular dysfunction than general population; higher rates of hypertension and cerebrovascular disease; worse outcomes after stroke, global brain ischemia, as with respiratory or cardiac arrest; ~75% people with diabetes die of atherosclerosis, 75% of these deaths from coronary artery disease

Autonomic neuropathy: ~20% of diabetic persons have some abnormal cardiovascular autonomic dysfunction; common findings include resting tachycardia, exercise intolerance, orthostatic hypotension, constipation, gastroparesis, erectile dysfunction, bladder dysfunction, impaired neurovascular function, brittle diabetes, abnormal vascular reflexes, loss of sweating, reduced heart rate variability, and hypoglycemic autonomic failure (loss of symptoms indicative of low blood sugar); therapies include improved metabolic control and use of prokinetics, *eg*, metoclopramide, ACE inhibitors, and beta blockers

Renal failure secondary to diabetes mellitus: leading cause of need for dialysis; 50% of all dialysis patients diabetic; patients with type 2 diabetes who have retinopathy have higher incidence of proteinuria and worse outcomes; to lower risk of acute kidney injury, important to check preoperative creatinine in diabetics planning intermediate- to high-risk procedures or those involving contrast dye; hydration and bicarbonate infusions may have benefit; patients with diabetes who have erectile dysfunction have higher prevalence of silent coronary artery disease

Hypoglycemia: results in endothelial dysfunction, production of oxygen free radicals, overproduction of free fatty acids, increase in inflammatory mediators, phagocyte dysfunction, immune dysfunction with suppression of immune processes, catecholamine elevations, platelet hyperreactivity, increased incidence

of myocardial infarction, increased infarct size, impairment in ischemic preconditioning

Diabetes and surgery: stress of surgery and anesthesia alters balance between hepatic glucose production and utilization in peripheral tissues; cortisol increases hepatic glucose production, stimulates protein catabolism, promotes gluconeogenesis resulting in elevated blood glucose levels; catecholamines increase glucagon secretion and inhibit instant release by pancreatic beta cells; stress hormones lead to lipolysis and high free fatty acids; increased free fatty acids inhibit insulin-stimulated glucose uptake; these processes lead to insulin resistance, most pronounced on postoperative day 1 but can persist for 9 to 21 days after surgery; association between perioperative hyperglycemia and adverse outcomes in surgical patients, and risk of postoperative complications and increased mortality relates to both long-term glycemic control and severity of hyperglycemia on admission and during hospital stay; diabetics with $A1_c$ levels >7% undergoing major noncardiac surgery have higher infectious complication rate, with odds ratio of 2.13; increased rates of postoperative morbidity and mortality, longer lengths of stay after surgery, higher risk of postoperative arrhythmias (especially atrial fibrillation), greater risk of hypotension on induction, throughout case, and postoperatively

Glucose management and surgery: morbidity reduced in those treated with insulin; hemoglobin $A1_c$ predicts preoperative fasting blood sugar, severity of coronary artery disease, gastric volumes, increased infection rates, perioperative adverse events, and all-cause mortality; optimal glucose management during perioperative period not well-established, but substantial evidence indicates that correction of hyperglycemia with insulin reduces hospital complications and decreases mortality in cardiac and general surgery patients; randomized controlled trials using conventional targets for glycemic control have not been associated with a significant risk of hypoglycemia (as seen with previous tight control); inpatient care targeted for moderate control of blood sugar and individualized glycemic management; control of hyperglycemia can decrease myocardial infarction size, postoperative arrhythmias (*eg*, atrial fibrillation), incidence of surgical wound infections, sternal wound infections after cardiac surgery, bloodstream infections, duration of ventilator dependency, incidence of acute renal failure, length of stay; reduces postoperative morbidity and mortality in ICU and hospital and in long term; lowers costs of care

Oral diabetes medication and surgery: on day of surgery, hold all oral agents; however, no need to hold metformin because low risk of lactic acidosis; only risk for lactic acidosis likely occurs with both hepatic and renal failure; important not to restart metformin until risk of hepatic or renal failure no longer issue

Insulin and surgery: in patients with insulin pumps, continue the lowest insulin rate (usually overnight rate); continue scheduled insulin until evening before surgery; hold all short-acting insulin on day of surgery; best to administer one-third to one-half of the AM long-acting, intermediate-acting, or combination insulin (*eg*, 70-30) on day of surgery; randomized control trial of various AM insulin regimens showed patients with type 2 diabetes treated with AM long-acting, intermediate-acting combination insulins, taking half their usual dose of insulin on day of surgery, achieved better blood-glucose control and no hypoglycemia vs no insulin on day of surgery; basal insulin must be provided to prevent ketoacidosis in patients with type 1 diabetes, given absolute insulin deficiency, even in absence of caloric intake; use of scheduled insulin improves glucose control compared with sliding-scale insulin coverage alone; no established absolute cutoff for preoperative blood glucose, but typically targeted $A1_c$ of <8.5 or <8.0 preoperatively is preferred; *recommended blood glucose levels* — American Diabetes Association (ADA) recommends glucose levels maintained between 140 mg/dL and 180 mg/dL for inter- and postoperative management; Society of Critical Care Medicine (SCCM) advises treatment for blood glucose ≥150 mg/dL with goal to maintain blood glucose below that level and absolutely below 180 mg/dL; Society for Ambulatory Anesthesia (SAMBA) recommends glucose levels <180 mg/dL; Society of Thoracic Surgeons (STS) practice guidelines recommends glucose levels <180 mg/dL for ≥24 hours after cardiac surgery; intravenous (IV) insulin infusions favored pre-, inter-, and postoperatively over subcutaneous (SC) insulin or IV bolus doses, especially postoperatively in cardiac surgery and organ transplants, for patients with type 1 diabetes while fasting, and for all critically ill patients; *management of glucose with insulin infusions* — recommended targets for certain blood glucose levels; 60 mg/dL to 120 mg/dL, no treatment necessary; 120 mg/dL to 160 mg/dL, start insulin infusion at 0.5 U/hr, 160 mg/dL to 200 mg/dL, start insulin infusion at 1.0 U/hr; 200 mg/dL to 240 mg/dL, start insulin infusion at 2.0 U/hr; during insulin infusions, check patient blood sugars every hour; if blood sugar increased, increase insulin dose; if blood sugar decreased, decrease insulin dose; however, no changes if blood sugar in target range of 80 mg/dL to 120 mg/dL; if blood sugar <60 mg/dL administer half ampule of dextrose 50% (D50) IV, followed by dextrose 10% (D10) infusion; to make D10 infusion, add half ampule of D50 to 1 L of dextrose 5% (D5); to make insulin infusion, add 50 U of regular insulin to 50 cc of either normal saline or dextrose 5% in water (D5W) for final concentration of 1 U of insulin/cc of fluid

Hypoglycemia: blood glucose level <70 mg/dL; complication of insulin therapy, more commonly occurring in type 1 diabetes; typically no symptoms present until blood glucose <50 mg/dL; common symptoms include altered mental status, dizziness, lightheadedness, diaphoresis, fatigue, delirium, seizures; often no symptoms in patients with type 1 diabetes; high-risk conditions for hypoglycemia in patients receiving scheduled insulin include sudden fasting status, reduction of oral intake, acute discontinuation of enteral feedings, discontinuation of total parenteral nutrition or intravenous dextrose, unexpected transport from nursing unit after administration of rapid-action insulin, reduction in corticosteroid doses

Treatment of hypoglycemia: immediate dextrose bolus, D50 or D50W recommended in 25- to 250-cc increments IV; 20 g to 40 g dextrose gel orally, especially in patients with no IV present; start maintenance infusion of D10W to avoid repeat hypoglycemia; frequent blood

glucose monitoring; adjunctive options include glucagon 1 mg intramuscularly (IM) or IV; hydrocortisone to empirically treat adrenal sufficiency or even octreotide (synthetic somatostatin) to suppress insulin release

Diabetic ketoacidosis (DKA): can occur with both type 1 and type 2 diabetes, though rare in type 2; precipitating factors include lack of insulin or illnesses with acute infections, trauma, myocardial infarctions, gastrointestinal bleeding, severe illnesses, or surgery; presentation includes altered mental status, lethargy, coma, abdominal pain, nausea and vomiting, polydipsia, polyuria; patients can be hypotensive, with tachycardia and tachypnea; osmotic diuresis with resulting electrolyte depletion, particularly hypokalemia; laboratory findings consists of anion gap metabolic acidosis; in anion gap metabolic acidosis, sodium minus chloride, plus bicarbonate >12 mmol/L; mixed disorders possible with associated nausea and vomiting, which cause metabolic alkalosis; lactic acidosis frequently present; patient may be uremic, particularly in chronic kidney disease; patient will typically have increased ketones, including beta-hydroxybutyrate (BHB), acetoacetic acid (AcAc), and byproduct acetone; glucose levels typically 400 mg/dL to 800 mg/dL; initially, patients have serum hyperkalemia, though frequently total body deficit of potassium

Treatment of DKA: primarily with insulin; best as IV infusion because of variable absorption of SC injections; transition to SC insulin when bicarbonate normalizes, important to continue insulin infusion for ≥2 to 3 hrs after first SC injection; initial resuscitation with isotonic 0.9% NaCl or lactated Ringer's solution; when blood glucose <200 mg/dL, start D5W and continue insulin to continue treating ketogenesis; add KCl to solution when potassium level <4 mEq/L and urine output established; check glucose hourly during initial insulin infusions, check electrolytes in arterial blood gases every 1 to 2 hrs initially

Nonketotic hyperosmolar state: usually in older patients with type 2 diabetes; insulin deficiency associated with renal dysfunction, cognitive impairment, inadequate oral intake; common precipitators include systemic illnesses, infections, myocardial infarctions, cerebrovascular accidents, bleeding, falls; laboratory findings similar to DKA, but with milder acidosis; typically non-anion gap metabolic acidosis has pH ≥7.3, no ketones present; typically severe hyperglycemia, severe hyperosmolality with osmoles >320 mmol/kg and sodium inappropriately normal despite dehydration; elevated blood urea nitrogen (BUN) and creatinine with azotemia common findings

Treatment of nonketotic hyperosmolar state: vigorous rehydration, typically with isotonic NaCl solution; need to correct electrolytes and hyperglycemia (insulin IV preferred) and to treat underlying disease or precipitating cause; monitor cardiovascular, pulmonary, renal, and central nervous system functions; monitor glucose and electrolytes frequently; endotracheal intubation may be indicated for comatose patients to protect airway

Preoperative carbohydrate loading: recommended practice, because may counteract insulin resistance due to stress and starvation; carb loading increases insulin sensitivity and decreases postoperative hyperglycemia; enhanced recovery after surgery (ERAS) programs advocate carbohydrates with drinks up to 2 hrs before surgery; in patients undergoing major abdominal surgery, carbohydrate loading associated with reduced hospital length of stay

Gestational diabetes: pregnant women; risk factors include overweight, advanced age, history of previous gestational diabetes, family history of type 2 diabetes, polycystic ovarian syndrome; affects ~3% to 9% of pregnancies; presents most commonly in third trimester; increases risk of preeclampsia, depression, intrauterine demise, intrauterine growth retardation, and need for instrumental deliveries or Cesarean section; patients with gestational diabetes have increased risk of obesity and diabetes post pregnancy; babies born to mothers with gestational diabetes at risk for macrosomia, hyperbilirubinemia, jaundice, polycythemia, hypocalcemia, hypomagnesemia; risk of hypoglycemia after birth; children are at higher risk of obesity and type 2 diabetes as they age

Treatment of gestational diabetes: diabetic diet, exercise, insulin

Anesthetic techniques for diabetics: not personalized for diabetics; anesthetic techniques like spinals, epidurals, or other regional blockade may modulate secretion of catabolic hormones and insulin secretion; perioperative increase in circulating glucose, epinephrine, and cortisol in nondiabetic patients exposed to surgical stress under general anesthesia blocked by epidural anesthetics; cataract surgery in patients with type 2 diabetes having local anesthesia compared with general anesthesia associated with less disruption of glucose metabolism, with lower blood glucose levels, lower lactate, cortisol levels, less insulin resistance; however, no evidence that regional anesthesia alone or in combination with general anesthesia for surgical patients with diabetes lowers mortality or major complications; regional anesthetics in diabetic patients somewhat controversial; diabetic neuropathic nerves (not nerves of diabetic patients *per se*) can exhibit complex functional changes, chronic hyperglycemia induces inflammation and oxidative stress, causing microvascular changes, local ischemia, and decreased axonal conduction velocity; consequently, diabetics appear more sensitive to local anesthetics, which results in longer block duration; patients with diabetes more difficult to stimulate with nerve stimulators, requiring higher thresholds, and theoretically, diabetic patients more prone to permanent injury; local anesthetics conjectured to be more toxic in diabetic neuropathy, but equivocal evidence; diabetes independent risk factor for infections when peripheral nerve catheters used postoperatively

Pancreatic transplantation: most pancreas transplants performed to treat type 1 diabetes; ~10% done in type 2 diabetes (low insulin resistance and low insulin production present); usually, pancreatic transplant performed in conjunction with kidney transplant; isolated pancreatic transplants can be done in patients with type 1 diabetes if severe frequent hypoglycemia or poor control; pancreatic transplants rarely used in treatment of pancreatic or bile duct cancers; pancreatic transplant recipients usually have severe diabetes with systemic complications associated with disease; optimization of metabolic and hemodynamic parameters can improve graft function; islet cell transplantation consists of IV injection of insulin-producing islet cells from pancreas of deceased donor (experimental procedure)

Emergency surgery in diabetic patient: all principles discussed regarding risk of diabetes and hyperglycemia apply to uncontrolled diabetic for emergency surgery; controlling metabolic derangements most important; safest to use IV insulin infusions as previously described; targeting moderate control of blood sugar with ranges of blood glucose from 140 mg/dL to 180 mg/dL optimal for patients undergoing emergency surgeries

Carcinoid Syndrome

Overview: excessive secretion of serotonin and other hormones from neuroendocrine cells; these cells can occur anywhere in body, most commonly from primitive gut (90% in distal ileum and appendix); appendiceal carcinoids most common; ileal carcinoids more commonly metastasize to liver; presentation includes flushing, diarrhea, wheezing, cardiac murmurs, hypotension, and dizziness

Diagnosis and treatment: screening tests using 5-hydroxyindoleacetic acid (5-HIAA), metabolite of serotonin; urine 5-HIAA of >25 mg/day establishes diagnosis; diagnosis confirmed with octreotide scan; treatment for carcinoid includes resection of tumor or symptomatic treatment with octreotide;

Anesthesia concerns: maintain anesthesia with appropriate depth; avoid sympathomimetics

Carcinoid heart disease: affects ~≥50% of patients; results from serotonin release from primary tumor and metastases, causing thickening and dysfunction of right-sided cardiac valves with subsequent valve regurgitation; carcinoid heart disease always involves tricuspid valve and pulmonary valve; left-sided valve disease occurs in ~10% of patients; thought to occur primarily with intracardiac shunt, allowing serotonin-rich blood to bypass filter of lungs, or from very active metastasis in high circulatory serotonin; ranges from asymptomatic disease discovered on echocardiogram to patients presenting with fatigue, dyspnea, edema, ascites, or overt heart failure; cardiac involvement reduces survival compared with no cardiac involvement

Diagnosis: elevated brain natriuretic peptide (BNP) level raises clinical suspicion of carcinoid heart disease in asymptomatic patients; use of BNP as screening test in all patients with carcinoid syndrome has been suggested; if high clinical suspicion, echocardiography test of choice to establish diagnosis; echocardiographic appearance of heart valves pathognomonic, and valvular dysfunction can be quantified; cardiac magnetic resonance imaging or computerized tomography may provide additional important information such as assessment of right heart size and function in selected patients

Treatment: somatostatin analogs (*eg*, octreotide) for symptoms; limited medical treatment options for patients with symptomatic carcinoid heart disease; diuretics may improve edema and ascites, but generally not dyspnea and fatigue; valve replacement if symptoms related to valve disease and progressive right-heart enlargement or dysfunction; elevated right atrial pressures from carcinoid heart disease increases liver surgery risks and best treated with valve replacement before liver resection or transplantation

Anesthesia: anesthetic management of patients with carcinoid syndrome same as for any critical ill patient; consider use of invasive monitoring; important to prevent mediator release; best to use anxiolytics without histamine-relating properties, especially in preoperative period or for placement of invasive monitoring (*eg*, arterial lines) if done while patient awake; important to avoid sympathomimetics; beta-adrenergic agents (*eg*, epinephrine) can stimulate release of vasoactive hormones in tumor, and exacerbate hypotension; important to maintain appropriate depth of anesthesia; primary treatment for hypotension includes IV fluids, octreotide, and phenylephrine; immediate availability of vasopressors (*eg*, phenylephrine) and vasodilators important; ondansetron has antiserotonin action, but octreotide (somatostatin) treatment of choice; relieves vasoactive symptoms and restores hemodynamic stability; octreotide administered in boluses of 250 mcg to 500 mcg; for minor procedures, single bolus may be enough; for more lengthy procedures or for major operations, bolus of 250 mcg to 500 mcg, followed by infusion of 100 mcg to 500 mcg/hr

Suggested Reading

American Diabetes Association: Glycemic targets: standards of medical care in diabetes — 2018. *Diabetes Care*. 2018;41(suppl 1):S55-64; **Castillo J et al:** Anesthetic management of patients with carcinoid syndrome and carcinoid heart disease: the Mount Sinai algorithm. *J Cardiothorac Vasc Anesth.* 2018;32(2):1023-31; **Duggan EW et al:** Perioperative hyperglycemia management: an update. *Anesthesiology*. 2017;126(3):547-60; **Fayfman M et al:** Management of hyperglycemic crises: diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Med Clin North Am*. 2017;101(3):587-606.

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Anesthesia and Adult Neuromuscular Disease

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Neuromuscular diseases in adults: include demyelinating diseases (multiple sclerosis), motor neuron diseases (amyotrophic lateral sclerosis, spinobulbar muscular atrophy, hereditary spastic paraplegia), peripheral neuropathies (Guillain-Barré, chronic inflammatory demyelinating polyneuropathy, critical illness neuropathy, and Charcot-Marie-Tooth disease), disorders of neuromuscular transmission (myasthenia gravis, Lambert-Eaton Syndrome, periodic paralysis, hyperkalemic periodic paralysis, potassium-aggravated myotonia, paramyotonia congenita, hypokalemic periodic paralysis), and postpolio syndrome

Demyelinating Disease

Multiple sclerosis (MS): autoimmune disease affecting central nervous system; occurs in genetically-susceptible persons after an environmental exposure; no clear understanding of the immunopathogenic process that determines the sites of tissue damage in the central nervous system, variation in natural history, severity of disability caused by the disease; twice as common in women as men; pathologically, MS characterized by a diverse combination of inflammation, demyelination, and axonal damage in the CNS; loss of myelin covering axons is followed by formation of well-described demyelinated plaques; peripheral nerves unaffected

Anesthesia management: consideration of the impact of surgical stress on the natural progression of disease is important; likely that symptoms will be exacerbated during postoperative period; informed consent is crucial, because patients should know that the disease may worsen after surgery; any increase in body temperature more likely than drugs to exacerbate MS during postoperative period; controlling body temperature is a major aim; possible that increased body temperature completely blocks conduction in demyelinated nerves

Regional anesthesia in MS: the changing and unpredictable neurological picture in patients with MS during the perioperative period must be appreciated when selecting regional anesthetic technique; spinal anesthesia has been implicated in exacerbation of MS more than other techniques; exacerbation after epidural anesthesia or peripheral nerve block has not been described; mechanism by which spinal anesthesia may be more likely than epidural anesthesia to exacerbate clinical manifestations unknown, but may reflect local anesthetic neurotoxicity; it is speculated that lack of a protective nerve sheath around the spinal cord and demyelination may render the spinal cord more susceptible to potential neurotoxic effects of local anesthetics; epidural anesthesia may be less risky, because the concentration of local anesthetic in the white matter of the spinal cord is 3 to 4 times lower after epidural than after spinal anesthesia; nevertheless, both epidural and spinal anesthesia have been used in parturients with MS

General anesthesia in MS: general anesthesia often chosen; no unique interactions between MS and drugs used for general anesthesia; no evidence to support recommendations for specific inhaled or injected anesthetic drugs

Muscle relaxants in MS: when selecting a muscle relaxant, consider the possibility of an exaggerated release of potassium following administration of succinylcholine; prolonged responses to the paralyzing effect of non-depolarizing muscle relaxants may reflect proliferation of extra-junctional cholinergic receptors characteristic of upper motor neuron lesions

Other considerations: corticosteroid supplementation during perioperative period may be indicated in patients being treated chronically with these drugs; efforts should be made during perioperative period to recognize and prevent even modest increases in body temperature (more than 1°C), as this change may lead to deterioration of nerve tissue at sites of demyelination; neurologic evaluation during postoperative period useful and recommended for detecting evidence of MS exacerbation

Motor Neuron Diseases

Amyotrophic lateral sclerosis (ALS): degenerative disease of the motor ganglia in anterior horn of spinal cord and spinal pyramidal tracts; cause unknown, but occasional genetic pattern present; viral etiology also a consideration; general anesthesia may be associated with exaggerated ventilatory depression; patients with lower motor neuron disease such as ALS are vulnerable to hyperkalemia following administration of succinylcholine; patients may show prolonged responses to non-depolarizing muscle relaxants; changes of ALS (as displayed on the electromyogram) resemble those of myasthenia gravis; bulbar involvement with dysfunction of the pharyngeal muscles that may predispose to pulmonary aspiration; no evidence that a specific anesthetic drug or drug combination is best for patients with this disease; regional anesthesia is likely to be avoided for fear of exacerbating the disease; epidural anesthesia has been successfully administered to patients with ALS without neurologic exacerbation or impairment of pulmonary function

Spinobulbar muscular atrophy, Duchenne muscular dystrophy, and Becker muscular dystrophy: X-linked inherited diseases; occur in 1 per 300 to 3500 male newborns; caused by recessive mutations in the dystrophy gene on the short arm of chromosome X (Xp21); Becker muscular dystrophy has partially functional dystrophin gene; Duchenne has total absence of dystrophin gene; as the sarcolemma breaks down, myofibrial atrophy, necrosis, and fibrosis occur; both diseases have progressive muscular weakness, cardiomyopathy, respiratory muscle weakness, cardiac rhythm abnormalities, autonomic dysfunction, and limited ability to [10:09]; perioperative complications include respiratory failure, aspiration, atelectasis, postoperative pneumonia, congestive heart failure (CHF}, and cardiac arrhythmias; patients commonly undergo procedures such as major spine surgery and diagnostic muscle biopsies; patients can experience life-threatening perioperative complications after exposure to agents that can induce muscular tissue breakdown (rhabdomyolysis, hyperkalemic cardiac arrest, and hypermetabolism); a review of 117 anesthetic cases for Becker and Duchenne showed that succinylcholine may trigger rhabdomyolysis, hyperkalemia, and cardiac arrest and that dystrophinopathies do not increase the susceptibility to malignant hyperthermia or hypermetabolism after exposure to volatile anesthetics; thus, the hypothesis that volatile anesthetics could destabilize the sarcolemma, making it more prone to second insults such as muscle agitation and shivering in the postoperative setting, appears not to be true; several patients experienced major thrombotic events; study published in *European Journal of Anesthesiology* in 2012 of 323 cases of Duchenne showed that patients have a reduced vital capacity and 5% had a difficult direct laryngoscopy; total intravenous anesthesia (TIVA) was used safely in these patients

American College of Chest Physicians and the American Academy of Pediatrics recommendations for TIVA in patients with Duchenne and Becker: patients should have a baseline cardiac and pulmonary function evaluation, optimize medical therapy before surgery, avoid succinylcholine, avoid exposure to inhaled anesthetics, measure expired carbon dioxide concentration, monitor body temperature, maintain oxygen delivery and ventricular preload, take antithrombotic precautions, and have postoperative cardiac monitoring

Hereditary spastic paraplegia (Strumpell disease): progressive lower limb spasticity; very rare; occurs in 2 to 10 persons per 100,000; autosomal dominant disease in 70% to 80% of cases; neuropathology shows axonal degeneration of corticospinal tract and dorsal columns; degeneration maximal at the terminal portion of the corticospinal tract and the cervical part of the dorsal column in 50% of patients; pure (uncomplicated) and complicated disease forms exist; pure form is predominantly motor impairment, late onset of symptoms, and slow progression; complicated form has additional signs and symptoms such [14:18] signs, pes cavus, wasted hands, optic atrophy, and sensory symptoms

Anesthetic considerations: very little literature; some successful anesthesia case reports; Thomas et al. reported spinal anesthesia in manual removal of a placenta using bupivacaine, fentanyl, and morphine; Deruddre et al. published a case of subarachnoid anesthesia for C-section delivery using bupivacaine plus fentanyl; McIver et al reported a case of general anesthesia for C-section using thiopental, rocuronium, sevoflurane, and nitrous oxide; Franco-Hernandez et al reported 2 successful cases of general anesthesia with TIVA for laparoscopic subtotal colectomy and inhaled anesthetic for a cholecystectomy with both patients receiving sugammadex for reversal of muscle relaxation; concern for exaggerated response to non-depolarizing neuromuscular antagonists and possible hyperkalemia; possible that long-acting neuromuscular blockers should be avoided; routine monitoring of neuromuscular relaxation throughout operation using a standard peripheral nerve stimulator recommended; before awakening, confirm an appropriate train-of-four (TOF) ratio greater than 0.9

Peripheral Neuropathies

Guillain-Barré syndrome: characterized by a sudden onset of skeletal muscle weakness or paralysis that manifests initially in the legs and spreads cephalad over the ensuing days to involve skeletal muscles of the arms, trunk, and face; impact on functioning of the autonomic nervous system and depression of lower motor neuron lesions are the 2 key considerations for anesthesia management; compensatory cardiovascular responses may be absent, resulting in profound hypotension in response to changes in posture, blood loss, or positive airway pressure; noxious stimulation (such as direct laryngoscopy) can manifest as an exaggerated increase in systemic blood pressure, which reflects labile autonomic nervous system activity; prudent to monitor systemic blood pressure, perhaps continually with an intra-arterial catheter; exaggerated response to indirect-acting vasopressors should be considered if selecting these drugs instead of intravenous infusion of fluid to treat hypotension; succinylcholine should not be administered, as there is a risk of excessive potassium release due to denervated skeletal muscles; non-depolarizing muscle relaxants that have minimal circulatory effect are a better choice; avoid pancuronium; even if spontaneous ventilation present preoperatively, very likely that anesthetic drugs will necessitate mechanical ventilation of patients after surgery; continuous ventilatory support likely to be necessary during postoperative period

Chronic inflammatory demyelinating polyneuropathy (CIDP): sensory and motor diffuse polyneuropathy with generalized areflexia that evolves proximally over more than 8 weeks; more common in elderly patients; prevalence is 1 to 5 in 100,000 patients; inflammation-mediated demyelination appears to be the most prominent pathophysiology; triggering agent usually unknown; inflammatory markers such as tumor necrosis factor (TNF) and interleukin (IL)-2 are increased; selective involvement of peripheral nervous system; involvement of proximal and distal limb structures; involvement of both motor and sensory fibers; in some cases, only motor or sensory fibers are affected; recurring, continuously worsening, or fluctuating curves may be seen; different types may occur, according to an article published in 2010 in *The Lancet*; pure motor form has symmetrical and selective involvement of motor fibers; sensory CIDP frequently presents with numbness in extremities; ataxia can be prominent; are minimal forms, in which strength is usually normal; there is a

multifocal form, distal form, as well as a chronic immune sensory polyradiculopathy

Anesthetic implications: consider concomitant pathologies and adverse effects of treatments; CIDP has been associated with hepatitis C, inflammatory bowel disease (IBD), lymphoma, monoclonal gammopathy of undetermined significance (MGUS), HIV/AIDS, organ transplantation, and connective tissue disorders; treatments for these patients is with corticosteroids, intravenous immune globulin (IVIG), plasma exchange, and immunosuppression

Critical illness polyneuropathy and myopathy: characterized by structural changes, axonal nerve degeneration, muscle myosin loss, and muscle necrosis; functional changes can cause electric inexcitability of nerves and muscles, with reversible muscle weakness; microvascular changes and syncopatic hypoxia may disrupt energy supply and use; an acquired sodium channelopathy causing reduced muscle membrane end nerve excitability is a possible mechanism underlying chronic illness polyneuropathy (CIP) or critical illness myopathy (CIM); it is the most common polyneuropathy seen in ICU; systematic review published in *The Lancet* in 2011 shows CIP and CIM in up to 50% of patients in ICU who have had lengthy mechanical ventilation, sepsis, or multiorgan failure; for diagnosis, determine if patient is critically ill, has multiorgan dysfunction and failure, limb weakness, or difficulty weaning from the ventilator; electrophysiological evidence of axonal motor and sensory polyneuropathy and absence of a decrement of response to repetitive nerve stimulation; risk factors are severity of illness, duration of multiple organ dysfunction with or without systemic inflammatory response syndrome (SIRS), duration of vasopressor and catecholamine support, duration of ICU stay, hyperglycemia, female sex, renal failure and renal replacement therapy, hyperosmolality, parenteral nutrition, low albumin, and neurologic failure; aminoglycosides, neuromuscular blocking agents, and [23:55] have been associated with some cases

Anesthetic considerations: adjust neuromuscular blocking agents according to renal and hepatic function; stabilize other factors that prolong neuromuscular blockade (such as hypermagnesemia, metabolic acidosis, and concomitant use of aminoglycosides and clindamycin); periodically monitor neuromuscular blockade in OR and avoid prolonged muscular blockade; identify patients at risk of rhabdomyolysis by estimating serum creatinine phosphokinase; cisatracurium may be an option, as it appears to improve survival and increase time without ventilation in some patients; intensive insulin therapy to maintain normal glucose concentration appears to reduce the incidence of electrophysiologically diagnosed CIP; there is a protocol where daily interruption of sedative with spontaneous awakening and interruption of mechanical ventilation with spontaneous breathing trials appears to reduce mechanical ventilation, coma, and length of ICU and hospital stay; ABCDE trial (awakening, breathing, coordination of awakening and breathing, delirium assessment, and early exercise) has been proposed, as it has appeared to reduce the problem of muscle weakness and delirium; use of nondepolarizing muscle relaxants and steroids should be limited as much as possible

Charcot-Marie-Tooth disease: most common inherited cause of chronic motor and sensory peripheral neuropathy; autosomal dominant disorder that manifests as distal skeletal muscle weakness; wasting and loss of tendon reflexes usually become evident in the mid-teenage years; anesthesia concerns include response to neuromuscular blocking drugs, potential for development of malignant hyperthermia, and possibility of postoperative respiratory failure; these patients do not seem to be susceptible to malignant hyperthermia, and response to neuromuscular blocking drugs seems predictable; avoid succinylcholine, based on the theoretical concern for exaggerated potassium release following administration of these drugs (patients with neuromuscular disease in general); succinylcholine has been used safely in these patients without producing hyperkalemia or triggering malignant hyperthermia

Disorders of Neuromuscular Transmission

Myasthenia gravis: acquired chronic autoimmune disorder caused by a decrease in functioning acetylcholine receptors at the neuromuscular junction owing to destruction or inactivation by circulating antibodies; origins of this antibody unknown, but thymus appears to have a role because of association of myasthenia gravis with thymus gland abnormalities; clinical course marked by periods of exacerbations and remissions; ptosis and diplopia resulting from extraocular muscular weakness are the most common initial complaints; weakness of pharyngeal and laryngeal muscles results in dysphagia, dysarthria, and difficulty eliminating oral secretions; skeletal muscle atrophy uncommon; patients at high risk for pulmonary aspiration of gastric contents; myocarditis may result in atrial fibrillation and heart block; patients may have cardiomyopathy

Different types of myasthenia gravis: generally, the longer the therapy and the higher the dose, the more severe is the disease process; type 1 limited to extraocular muscles; type 2a mild, and the respiratory muscles are spared; type 2b more rapidly progressing with respiratory muscle involvement; type 3 with acute onset and rapid progression with very high mortality; type 4 most severe and usually a progression from type 1 or 2

Anesthetic implications: patients may require thymectomy; preoperatively, drugs such as opioids should be used with caution or not at all; likely that patients will require ventilatory support after surgery; anesthesia induction should be done with a short-acting intravenous anesthetic; however, respiratory depression effect of this drug can be accentuated; tracheal intubation can be accomplished without muscle relaxants; in those patients, take advantage of the existence of skeletal muscle weakness to work as a relaxing effect; there is an increased relaxing effect of the volatile anesthetic on skeletal muscles; succinylcholine can be used to facilitate tracheal intubation, keeping in mind the need to decrease the initial dose of succinylcholine until response of the neuromuscular junction can be documented with a peripheral nerve stimulator; with respect to muscle relaxants, antibodies decrease the number of functional acetylcholine receptors, which results in an increased sensitivity to nondepolarizing muscle relaxants; it is very possible that the drugs used to treat myasthenia gravis influence the response to muscle relaxants independently of the disease process; short-acting intravenous

anesthetics acceptable; respiratory depression effect will be accentuated with these drugs; tracheal intubation can be accomplished with induction drugs only; volatile anesthetics will help; maintenance of the anesthesia can be done with volatile anesthetics alone or volatile plus nitrous oxide; use of volatile anesthetics may reduce the dose of muscle relaxants needed or even eliminate them altogether; if administration of nondepolarizing muscle relaxants necessary, initial dose should be decreased by 1/2 to 2/3; observe response using a nerve stimulator and assess the situation again; at conclusion of surgery, leave the tracheal tube in place until patients demonstrate ability to maintain adequate level of ventilation; skeletal muscle strength often seems adequate during the early stage after anesthesia and surgery, but it will deteriorate over a few hours

Lambert-Eaton syndrome: patients with myasthenic syndromes are sensitive to the effects of both succinylcholine and nondepolarizing muscle relaxants; antagonism of neuromuscular blockade with anticholinesterase drugs may be inadequate; potential presence of myasthenic syndrome and the need to decrease muscle relaxants should be considered in patients with known cancers; syndrome should be considered in patients undergoing diagnostic procedures such as bronchoscopy, mediastinoscopy, or exploratory thoracotomy for suspected lung cancer

Hyperkalemic periodic paralysis: characterized by episodes of flaccid skeletal muscle paralysis associated with increased serum potassium concentration; preoperatively, consider depletion of total body potassium by administration of furosemide or thiazide diuretics; potassium-containing fluids and drugs that evoke the release of potassium are avoided; intravenous glucose infusions are administered to minimize carbohydrate depletion during fasting; intravenous calcium gluconate suggested in the emergency treatment of hyperkalemia-induced skeletal muscle weakness; intraoperative maintenance of body temperature is prudent

Potassium-aggravated myotonia: autosomal dominant inherited disease; characterized by muscle stiffness without weakness and mild to severe myotonia exacerbated by increasing serum potassium levels; results from a missense mutation in the gene that codes for the skeletal muscle sodium channel called NAV 1.4; channel dysfunction induces disruption of the entry and fast inactivation and increasing persistent sodium current and/or accelerated recovery from fast inactivation; causes a hyperexcitability state

Paramyotonia congenita: myotonic syndrome characterized by cold-induced muscle stiffness and weakness; produced by a gene mutation (SCN4A, ARG1440s, or CYS mutation in the sodium channel gene, and others); exacerbated by cold, exercise, potassium-rich fruits, and anesthesia

Hypokalemic periodic paralysis: preoperative considerations include carbohydrate balance, correction of electrolyte abnormalities, and avoidance of events known to trigger hypokalemic attacks; large carbohydrate meals are known to trigger hypokalemic episodes and should be avoided during the 24 hours preceding surgery; glucose-containing intravenous solutions and drugs known to cause intracellular shift of potassium should be avoided; mannitol administered in place of potassium-losing diuretics; frequent perioperative monitoring of serum potassium every 15 to 60 minutes is useful; aggressive interventions should be considered; hypokalemia may precede the onset of skeletal muscle weakness by several hours; may be able to avoid symptoms with potassium supplementation; administration of a short-acting neuromuscular blocking agent should be recommended only when skeletal muscle relaxation is needed; succinylcholine can increase serum potassium concentration transiently and seems acceptable in these patients; use of succinylcholine and other drugs known to trigger malignant hyperthermia is influenced by report of this syndrome in patients with hypokalemia periodic paralysis; regional anesthesia has been used safely in these patients; however, hypokalemia may be a consequence of epidural and other regional anesthetic techniques

Postpolio Syndrome

Usually manifests as fatigue, skeletal muscle weakness, joint pain, cold intolerance, and swallowing difficulties; sleeping and breathing problems presumably reflect neurologic damage from the regional poliovirus infection; poliovirus may damage the reticular activating system and cause exquisite sensitivity of these patients to the sedative effects of anesthetic with delayed awakening from anesthesia; not only do patients have sensitivity to sedative drugs, but also to muscle relaxants that can be predicted; severe back pain following surgery may be due to coexisting skeletal muscle atrophy and scoliosis; postoperative shivering may be profound; these individuals are highly sensitive to cold; postoperative pain sensitivity seems to be increased and is presumed to be caused by poliovirus damage to the endogenous opioid-secreting cells in the brain and spinal cord; same-day surgery may not be appropriate for postpolio patients; patients should be admitted to a hospital to perform the surgery

Suggested Reading

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Acute and Chronic Pain and Its Management

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Pain definition: the International Association for the Study of Pain is an international body of clinicians, scientists, policymakers, legislators, and other stakeholders; they describe pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of damage; there is a sensory (physiological) and pathophysiological transduction and perception of pain, and emotional modulation processing; actual/potential tissue damage or description by patient in terms of damage

States of pain: time course — acute vs chronic pain

- Acute pain: begins suddenly; usually a sharp sensation; often a warning sign; some signal of impending/actual tissue damage or threat to the body; can range from mild to very severe; lasts for a momentary period of time, but can last longer; every chronic pain condition has a precursor acute pain; acute pain does not last longer than 3-6 months because natural healing takes place during that time period; common examples include surgical pain, labor pain, ischemic pain, and traumatic pain
- Chronic pain: unrelieved acute pain leads to chronic pain; defined as >3-6 months of persistent pain despite healing of initial injury; physical effects (eg, muscle tension, limited ambulation/mobility, changes in sleep, interest, appetite, and energy, fatigue) and emotional manifestations (eg, anxiety, depression, irritability, fear behaviors of reinjury) affect social and occupational functioning; examples are neuropathic pain, fibromyalgia, musculoskeletal pain, and arthritic pain

Types of pain by pathophysiology:

- Nociceptive pain: activation of nociceptive afferent fibers; collecting information from the periphery (afferent) and nociceptive (a pain-sensing type of fiber); respond to a variety of different stimuli — temperature (thermal), mechanical (pressure or vibration), and chemical stimulation; based on where nociceptors are in the body, divide into visceral, deep somatic, or superficial somatic pain
- Neuropathic pain: caused by damage or disease process to the somatosensory system; we use neurological principles and divide peripheral neuropathic pain from central pain; peripheral neuropathic pain is damage or dysfunction to the peripheral nervous system (eg, painful diabetic neuropathy, complex regional pain syndrome, postherpetic neuralgia, radicular pain); patients often describe as a burning sensation, pins and needles, tingling paresthesia sensation, or electrical stabbing; in central pain, the lesion or dysfunction lies in the central nervous system (ie, the CNS, the brain and spinal cord), and is associated with noxious stimuli, temperature hypersensitivity, and abnormal perceptions; includes post-stroke pain, spinal cord injury-related pain, multiple sclerosis (MS)-related pain, phantom pain (pain felt in a lost body part or part from which the brain no longer receives signals); with nerve conduction or blockade, can result in numbness, weakness, and loss of the deep tendon reflexes in affected nerve area; aberrant symptoms of spontaneous or stimulus-evoked pain occur
- Spontaneous pain: continuous pain; commonly described as a burning, shooting, shock-like sensation
- Stimulus-evoked pain: allodynia — if something normally is not painful but produces pain; hyperalgesia — if something normally is painful and there is an exaggerated or enhanced response to that pain stimulus; allodynia can be caused by light stimulation (eg, skin contact with clothing, a light breeze, or normal-temperature water); sensory abnormalities can go beyond the typical nerve distribution; sometimes inappropriately classified as a psychosomatic disorder because does not abide by normal distributions; most neuropathic pain diagnoses are made by history and physical examination; classic conditions include complex regional pain syndrome, postherpetic neuralgia, phantom limb pain, post-stroke pain, and peripheral neuropathy
- Psychogenic pain: caused by mental, emotional, or behavioral influences; somatoform pain; people are often stigmatized because healthcare practitioners feel that this pain is unreal; it is harmful to the physician-patient relationship to consider psychogenic pain to be of inferior quality or require less resources, treatment, or management than physical pain
- Mixed pain: a common type; pain is complex; includes multiple mechanisms of action and pathophysiology (eg, complex regional pain syndrome, fibromyalgia, and musculoskeletal types of pain); arthritic pain has inflammatory plus neuropathic components; therapeutic approaches depend on pain mechanisms

Pain pathways: nociceptors are peripherally located in the neurons, called A-delta and C fibers; A-delta are larger, myelinated fibers; C are smaller, unmyelinated fibers; A-delta are of medium diameter and carry well localized pain signals; A-delta fibers are not heavily myelinated, so they permit a relatively rapid transmission of impulses from the periphery through the spinal cord and are responsible for initial pain sensation; these fibers further subdivided — type I fibers are high-threshold, mechanical nociceptors and respond to mechanical and chemical stimuli; type II nociceptors have a heat threshold ~42 °C

and have thermal pain insult sensation; C fibers are small diameter, unmyelinated fibers and are responsible for the second wind of pain — poorly localized pain; have 10-fold slower transduction than A-delta fibers; physiological pain is an adaptive, protective, survival-based mechanisms

Pain perception: a cascade of events occurs with pain perception — transduction, conduction, transmission, modulation, and perception; for the first sensation of pain, A-delta fibers carry a well localized pain signal from the periphery; then C fibers are recruited, poorly localize where the pain is; signals go through the dorsal root ganglion of the spinal cord; in painful conditions, first-order neurons synapse at lamina Rexed number 1; second-order neurons cross the midline and ascend to the brainstem via spinothalamic tracts; second-order neurons synapse with a third-order neuron in the thalamus which projects to the cortex; the second- and third-order neurons are responsible for emotional experience, behavior, and arousal; relay not just to sensory cortex, but also limbic system, olfaction, emotional processing areas; afferent pain signals are modulated by the brainstem, cortex, and dorsal horn; inhibitory interneurons and descending pathways put the brakes on the system; endogenous nociceptive pain signals cause inhibition, using opiate receptors and modulators to activate the descending inhibitory system through the periaqueductal gray and other neuroanatomical regions

- Pain modulation: the Melzack and Wall gate control theory of pain was described in 1965; a sensation of a non-painful stimulus, such as touch, diminishes the ability to sense painful input; non-painful stimuli close a gate to transmission of noxious stimuli; theory later modified and refined; principle behind transcutaneous electrical nerve stimulation (TENS), in which a not-very-noxious peripheral electrical stimulation is applied in order to close the gates, thereby limiting the painful stimulation; descending pain-modulating pathways, the periaqueductal gray, the raphé nuclei, and the rostral ventral medulla are involved with endogenous opiates (eg, enkephalins, endorphins, dynorphins), which inhibit the pathway; the periaqueductal gray is the main pathway; found in midbrain; has excitatory and inhibitory neurotransmitters to facilitate its input
- Sensitization: there are two types of sensitization, peripheral and central; pathological process; despite intensive research in the field, the mechanism of acute to chronic pain transformation is poorly understood; peripheral sensitization occurs when sustained, painful stimuli result in spinal sensitization; first-order neuron in lamina Rexed 1; there is a heightened sensitivity to spinal neurons and reduced activation threshold; requires less input for the phenomenon to be transduced up the pathway; enhances responsiveness to input (ie, more likely to transmit pain to the brain); this can manifest in the expansion of affected area, increased response to painful inputs (hyperalgesia), transmission of pain following a non-painful stimulus (allodynia); central sensitization is mediated largely through the N-methyl-D-aspartate (NMDA) receptor, disinhibition, and microglial activation; NMDA receptor blockade studied experimentally, suppresses central sensitization, but the narrow therapeutic windows of NMDA antagonists have limited therapeutic use

Pain assessment: pain is a subjective experience; there might not be a direct relationship between how much physical insult or injury patients have experienced and the reported intensity of the pain; need to take a proper pain assessment — history, physical examination, standardized assessment tools, and diagnostic tests — to elucidate cause; an individual with untreated pain has many reactions based in various organ systems

- Cardiovascular system: tachycardia, hypertension, increased peripheral vascular resistance; increased myocardial oxygen consumption can cause ischemia; may be regional blood flow alterations, deep-vein thromboses (DVTs), pulmonary emboli (PEs)
- Respiratory system: decreased lung volumes, atelectasis, decreased cough reflex, and retained sputum, which predisposes to infection and hypoxemia
- GI system: decreases gastric and bowel motility
- Genitourinary system: untreated pain can cause urinary retention
- Neuroendocrine and metabolic systems: increased catabolic hormones reduce anabolic hormones, and that catabolism can lead to hypoglycemia, protein breakdown, negative nitrogen balance, poor wound healing, and muscle wasting
- Musculoskeletal system: spasms, immobility, and wasting
- CNS: development of allodynia and hyperalgesia
- Psychologically: untreated pain can cause anxiety, fear, sleep deprivation, helplessness, long-term psychological effects, making pain much more resistant to therapy; certain patients or groups may present differently in pain, eg, elderly patients or patients from different cultural backgrounds may require adjustments in our interaction (cultural competence involved)
- Pain scales: the most common standardized pain scale is the NRS (Numerical Rating Scale); we often elicit this verbally, but can be visual; it's a 0 to 10 scale; generally, it's a verbal command to define what's the most pain or least pain; it is less reliable in very young and elderly patients; we have the Visual Analog Scale (VAS), using that 10 or 100 mm line, no pain to worst pain possible; the Wong-Baker FACES® Pain Rating Scale uses a range of facial expressions — this is the preferred pain assessment method for pediatric patients aged 3-12 years; the McGill Pain Questionnaire (MPQ) has 20 items and assesses pain quality and location; it is important in studies and research, and used in trials; the Brief Pain Inventory (BPI) has 32 questions and assesses pain intensity and functional interference and is good for monitoring progressive conditions

Pain management: acute and chronic pain management are different; every chronic pain has an acute pain precursor, and may involve recurrent episodes of acute exacerbation; chronic pain is persistent, severe pain and involves functional impairment, disability, behavioral changes, and psychological comorbidity

Psychological management: patients can have inappropriate, catastrophic thoughts; once developed, there's a high correlation with the intensity of pain complaints

- Cognitive behavioral therapy (CBT): one of the best-proven modalities in addressing chronic pain conditions; as pain worsens, automatic thoughts may occur and can lead to a tremendous amount of distress (eg, "The pain has never been as bad as this," or "I'm getting

much worse"); it's also physical distress, fear avoidance behaviors ("Don't do this because it could exacerbate that"); CBT helps patients recognize that there is an automatic thought; then they need to rationally dispute those catastrophizing cognitions and replace those automatic thoughts; helps with pain management and associated anxiety and depression; CBT restructures the negative scheme into a realistic appraisal of the patient's current condition; considers the past, present, and future, the associated gains; patients learn to better deal with their pain

Biofeedback: monitoring device measures a physiological process (eg, blood pressure, heart rate, muscle tension, or galvanic skin response); through therapy, the patient becomes adept in controlling these processes that they did not previously feel they had voluntary control over; much of this has to do with self-control, arousal states, and changing parameters

Hypnosis: inducing a state of selective attention, sometimes a trancelike state, using relaxation and imagery techniques; when patient achieves a sufficient level of relaxation, he/she is in a state of mind receptive to suggestion; often mediated by a hypnotherapist; in self-hypnosis, therapist teaches patients to hypnotize themselves

Meditation: similar to self-hypnosis, but don't have that trance-like induction state; there are many techniques (eg, mindfulness, concentration, transcendental, movement); self-hypnosis and meditation techniques are done by the patient on the patient, and there's an increased sense of restoring control in their lives; chronic pain is a disease of feeling lack of control over one's life, related to sleep, eating, social and occupational responses, and physical activities

Physical modalities:

Active exercises: strengthening, endurance, stretching exercises; TENS (transcutaneous electrical nerve stimulation), acupuncture, massage, hot and cold thermal therapy with/without compression, passive motion, and bracing; TENS has evidence behind it; small, portable device with a very low-voltage electrical current, applied right over the skin; it is based on gate theory, but also activates descending inhibitory pathways that work on opiate receptors and reduce central excitability and stimulatory effects

Acupuncture: involves needle placements at predefined acupuncture points; acupressure is a related technique — pressure, rather than needles, in those particular points; auricular acupuncture is applied to the ear; electroacupuncture involves electrical current applied to the needles; evidence is mixed; negative trials in post-operative pain and for reduction of other analgesics

Pharmacological management: know the types of opiates (synthetic and semi-synthetic), their affinity for the various receptors, and what those receptors do (from euphoric states to anesthesia, or the cognitive function to addiction); evidence suggests that IV opiate administration is not superior to oral administration in various conditions, including postoperative pain; when given the option, and there is no contraindication to oral administration, oral is preferred; intramuscular analgesics for postoperative pain, particularly opiate-based analgesics, have unreliable absorption and produce inconsistent periprocedural perioperative analgesia; recommendations are against its use; patient-controlled analgesia (IV PCA) is recommended over healthcare provider-initiated intermittent bolusing; in children, PCA can safely be done by a proxy (parent or caregiver); in adults, it should be highly avoided, particularly when patients are sleeping; PCA is recommended over intermittent bolusing in adults because of excess sedation and respiratory depression risk; close monitoring (assessments of alertness, signs and symptoms of hypoventilation or hypoxia) is needed with systemic opiates; pulse oximetry is frequently used to monitor, but it is unclear whether it is superior to nurse observation of respiratory rate and mental status; pulse oximetry has a very low sensitivity for hypoventilation, particularly when supplemental oxygen is being given; limited evidence on capnography; is more sensitive than pulse oximetry in identifying respiratory depression; with individuals who are frequently or continuously being dosed with opiates or other CNS-sedating medications, capnography and frequent nurse observation are germane to safe practice; is a synergistic effect between acetaminophen and NSAIDs with opiates, because they work on different mechanisms; acetaminophen and NSAIDs reduce opiate requirements (and possibly hospital stays); highly recommended unless contraindicated; look at the NSAIDs' durations of action, COX-1 and COX-2 effects, and specific contraindications; evidence of reduced opiate requirements peri-procedurally with certain medications at certain times, eg, preoperatively, a dose of celecoxib is recommended; perioperatively, gabapentin, pregabalin, IV ketamine, or IV lidocaine infusions may be used, particularly in opiate and laparoscopic abdominal surgery if no contraindications (eg, cardiac)

Local anesthetic toxicity: practitioner should know esters and amides, maximum doses and mg/kg, and the duration of action; the absorption of local anesthetics, from most to least, is IV, intercostal, caudal epidural, lumbar epidural, brachial plexus, subcutaneous; this list parallels the vascular supply of each tissue; CNS and cardiotoxic effects occur with local anesthetics

CNS toxic effects: tinnitus, blurred vision, dizziness, paresthesias, particularly of tongue, and circumoral numbness; excitatory signs (eg, nervousness, agitation, restlessness, muscle twitching) because of blocked inhibitory pathways; muscle twitching is often a precursor to tonic-clonic seizure; early signs of advancement to CNS depression are slurred speech, drowsiness, unconsciousness, and respiratory arrest; under general anesthesia, may not have all manifestations

Cardiotoxicity: largely prolonged PR interval, QRS, and QT intervals; potentiates reentrant tachycardias; aberrant conduction may herald toxicity

Treatment: basic principles apply to any cardiopulmonary resuscitation; follow BLS (basic life support) and ACLS (advanced cardiac life support) principles; with local anesthetic toxicity, proven therapy with IV infusion of 20% lipid emulsion; it is becoming an accepted part of treatment for any systemic toxicity from local anesthetics and in cardiac arrest unresponsive to standard therapy; ASRA (American Society of Regional Anesthesia and Pain Management) guidelines recommend lipid emulsion therapy with a first sign of systemic toxicity and after airway management

Interventional pain management: common procedures for low back pain include epidural steroid injections; various types — medial branch blocks, sacroiliac joint blocks, sympathetic nerve blocks, stellate ganglion blocks; other procedures include peripheral nerve blocks, occipital blocks, trigger points, and botulinum toxin procedures

Epidural steroid injection: indications are radicular pain — pain in peripheral nerve distribution; often, etiology is disc herniation and acute disc herniation; inflammatory mediators present; the nucleus pulposus has a tear and break, and those materials are now exposed and irritating either exiting nerve root, causing pain; there are different approaches for epidural steroids; intralaminar — go right through the laminae; transforaminal approaches — select which exiting nerve root to block (may do multiple levels); cervical — in the neck region; caudal is through the caudal foramen; there are particulate (eg, Kenalog [triamcinolone]) and nonparticulate steroids (eg, dexamethasone); comes into play at the cervical site; if you inject particulate matter into a vascular structure, can cause a thromboembolic or embolic phenomenon, or thrombosis at that site, leading to cerebral ischemia; caution against the use of particulate matter, particularly in areas where vascular structures are approached; addition of a local anesthetic is common; generally, mixtures of long- and short-acting lidocaine and bupivacaine; complications can occur, particularly dural punctures leading to low CSF pressure; orthostatic postural headaches have evidence for hydration, caffeine intake, and epidural blood patches to fix; intermittent paresthesias, nicking one of these exiting nerves; extremely rare reports of paralysis; epidural hematomas or epidural abscesses cause compression phenomena; hematomas, we generally screen; look at the latest ASRA guidelines on neuraxial procedures, anticoagulants, and anti-platelet agents; abscesses can form — survey the site beforehand, making sure there are no systemic or localized skin infections or bone or soft tissue infections before procedure; for spinal stenosis, you can look at the variety of trials or look at lidocaine versus steroids; no difference in outcomes; mixed modelling on prevention of surgical corrections, disability, morbidity

Facet joint medial branch blocks: joints on both sides of the spine, from cervical to lumbar regions; often subject to arthritis, hypertrophy, or arthropathy of the facet joints; axial strain (eg, bending, twisting, lifting) can cause an axial or localized low back pain without much radiation; injections are done in medial branches that come off of the level above below, exiting spinal nerve root, and supply that particular capsule of that joint; we can block nerves or inject steroids and numbing medication into the facet joint; if effect is short-lived, move to radiofrequency lesioning or ablation (RFL or RFA)of involved nerves, which offers longer-term relief; in sacroiliac joints, a common presentation is pain caused by prolonged sitting, generally in truck drivers, long-distance commuters, or men who have wallets on one side, who complain of SI pain on ipsilateral side; provocation maneuvers (eg, the FABER or Patrick's test of flexion, abduction, external rotation) elicit pain unilaterally in the upper buttock/ lower back; other provocation maneuvers can be tested; SI joint strengthening and stretching exercise is the most proven therapy; can use steroid injections

Sympathetic nerve blocks: particularly stellate ganglion, lumbar sympathetic, celiac plexus block, hypogastric plexus blocks; part of the autonomic nervous system, sympathetic system; C unmyelinated fibers are part of the process; neuropathic pain conditions, as with complex regional pain syndrome, are mediated through these ganglia and pathways; can block these nerve confluences, for both diagnostic and therapeutic purposes as long-term blocks

Peripheral nerve blocks: common are occipital nerve blocks, greater and lesser occipital nerves, at the back of the head, near the inion, along the nuchal ridge, halfway from the mastoid to the most protuberant process; local anesthetics and steroids for occipital neuralgia; trigeminal nerve can be approached; sphenopalatine ganglion can be approached; intercostal nerves, particularly for fractures; lateral femoral cutaneous nerve, with meralgia paresthetica (lateral femoral cutaneous nerve neuralgia); along the midline thigh, pain, particularly in response to a tight belt, tight clothing, weight gain, pregnancy — can be blocked for therapeutics/diagnostics

Ilioinguinal nerve blocks: for certain types of abdominal pain, particularly abdominal wall pain; to determine if you have abdominal wall pain, use the Carnett's test; bring legs and shoulders together in a crunch-like position, tensing the abdominal muscles; if that elicits the index pain, it's positive for abdominal wall pain and may respond to abdominal wall nerve blocks; depending on its location, you have ilioinguinal nerves, transverse abdominal plane; for genital pain or scrotal pain, genital femoral nerve blocks can be performed; these blocks are ultrasound guided

Trigger points vs tender points: tender points are areas of localized tenderness — often seen in fibromyalgia, where there are diffuse tender points; localized pressure on a trigger point causes a larger distribution or referred pain; can cause a local muscle-twitch response; trigger points, very localized myofascial pain syndromes can respond to myofascial pain release or trigger point injections; trigger point injections involve taking a small needle and putting it directly into the point that causes the referred pain and muscle twitching, using the needle to break up the tender, taut band of muscle; you can add local anesthetics to ameliorate the pain associated with the needling procedure; the needling of the muscle causes a local inflammatory reaction and relaxes that myofascial taut band; trigger points are distinct from tender points; tender points do not respond to trigger point injections

Botulinum toxin: FDA approved for chronic migraine headaches; must have 15 or more headache days per month for more than 3 months, meet other criteria from International Classification of Headache Disorders; botulinum toxin also has utility for myofascial pain syndromes, dystonia, muscle spasm, and neuropathic pain; intradermal or subcutaneous injection; 3-month time course for action; requires 3-month dosing; can develop autoantibodies for it, reducing its efficacy

Surgical management of pain: spinal cord stimulation, which is a form of neuromodulation; based on the principles of the gate control theory, but many other mechanisms support its use, such as neuropeptide suppression involved in pain, like CGRP (calcitonin gene-related peptide); basic principles of spinal cord

stimulation are to take a lead, which transmits electrical activity, put it into the epidural space so it is over the spinal cord and the dura and in the epidural space, stimulating the dorsal columns; dorsal columns are responsible for vibration and thermal sensation, and some forms of touch; by stimulating that region, you can reduce noxious stimuli; classic indications are complex regional pain syndrome, failed back surgery syndrome, peripheral vascular disease, ischemic heart disease, and others; least level of efficacy is for pure axial; patient selection is important because the procedure marries the individual to a stimulating device; if pain is evolving, you could be chasing moving pain with a static device; you could alter its electrical frequency, polarity, and coverage, but if you are trying to hit a fast-moving target, it's tough with a spinal cord stimulator; with chronic pain populations, psychosocial issues must be worked out and expectations set; usually a psychological evaluation about coping skills, resiliency, and expectations related to the stimulator; stimulator hardware — the lead has electrodes that submit signals, and it is connected to a battery pack, the implantable pulse generator, which contains the battery and is usually implanted in the abdominal region or in the buttock/flank; can address neuropathic pain through various forms of programming; newer types of software and hardware don't produce a paresthesia (older stimulators produce a paresthesia over the coverage area) — called sub-perception threshold or paresthesia-free devices with high frequency systems; evidence for use in the non-neuropathic, fast-moving target syndromes; psychologic comorbidities blur lines

Intrathecal drug delivery systems: pain pumps; considered for use in the cancer pain population and non-malignant, chronic pain population; for cancer pain, patients need to be recalcitrant to oral or IV opiate medications; they may be having dose-related side effects that are limiting its potential or use; might not have sustained response to nerve blocks; they must have a life expectancy >3 months; cannot have CSF flow obstructions; contraindicated if there are metastases in the spine or brain that impact CSF flow; main contraindication is infection; for non-malignant, chronic pain population, this is a last resort; there is a screening period trial of the agent that could be done intrathecally, epidurally, or as a one-time bolus; opiate conversions are based on the route of administration — intrathecal to epidural (1:10), intrathecal to intravenous (1:100), intrathecal to oral (1:300); thus trial will be done with 1/300 of patient's usual oral dose; in conjunction with opiates, often add local anesthetics (eg, bupivacaine) or alpha-adrenergic agents (eg, clonidine for its neuropathic benefit)

Special pain populations: burn patients have baseline pain due to burn severity and incidental pain (eg, associated with dressing changes); incidental pain may require medications before each dressing change; baseline pain may respond better to continuous opiate therapy; in patients with sickle cell disease, acute crises are treated with opiates, fluids, and supportive care; prevent recurrent crises through behavioral modifications and trigger avoidance (eg, dehydration, alcohol intake, extreme temperatures, exertion); important to know that this population does not have an increased susceptibility to addiction; hydroxyurea and L-arginine supplementation have proven pain efficacy in sickle-cell disease

Appropriate prescribing of opiate-based therapy: 1) must have a strong indication for use of chronic opioid therapy; 2) should have functional goals (eg, to achieve walking distance of 2 blocks) or goals to achieve more functional, restorative outcomes (eg, sleep, physical activity, social relationships, return to school or work); 3) should have a monitoring plan in place — often includes urine toxicology testing, random pill counts, and a contract with terms for the prescriber and the recipient of the opiate-based medication, along with communication, when refills can be taken, questions asked, etc; at follow-up, conduct a reappraisal of continued use of opiates

Prescription drug monitoring programs: state-run initiatives with a database of prescribers, patients, pharmacies, doses, routes of administration; may include additional data (eg, payers, insurance vs self-payment, number of pills); can be useful for opiate risk-stratification; opiate risk-stratification tools, such as the SOAPP (Screener and Opioid Assessment for Patients with Pain) or ORT (Opiate Risk Tool), can help predict propensity for misuse, abuse, tolerance, dependence, and addiction; various guidelines by the CDC (Centers for Disease Control) and the WHO (World Health Organization); a ladder-based approach could be useful in this scenario

Suggested Reading

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Basic Considerations for Pediatric Anesthesia

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Neonatal Physiology

Respiratory physiology: lungs develop in 5 stages; first, 0-7 weeks gestation, embryonic stage, large airways develop; second, pseudoglandular period, 7-17 weeks, bronchi branch, bronchioles form, diaphragm begins development; canalicular stage, third stage, 17-27 weeks, rudimentary alveoli begin development; epithelial cells form type 1, type 2 pneumocytes; period of limited surface area in alveoli, limited surfactant — if born early (ie, 24-27 weeks gestation), likely difficulty with respiration; fourth stage, saccular period, 28-36 weeks, surface area for gas exchange increasing; fifth, alveolar phase, 36 weeks gestation to 3 years of age, surface area of alveoli and type 2 pneumocytes increases; alveolar sacs at birth, 30-40 million, 90% more by 18 months of age; after 18 months, grow in size only until 6-8 years of age

Differences between neonatal and adult airway: neonatal occiput large relative to head, head naturally in "sniffing" position, no support to occiput needed to view larynx; tongue relatively large compared to volume of oral cavity; epiglottis long, "floppy," omega-shaped, must lift it to view larynx; larynx high in neck. ie, level of C3, C4, adult larynx at C5, C6, angulated, more anterior than in adults; cricoid ring funnel-shaped, comprises narrowest part of upper airway, only solid cartilaginous structure in airway — can restrict gas flow; if narrowed, can cause respiratory distress; cricoid ring covered by pseudocolumnar epithelium, if irritated/traumatized, could swell, decrease lumen; trachea short (ie, 4-5 cm), branches sharply into right mainstem bronchus — why many foreign bodies present there, rather than over left mainstem bronchus; 65% of airway resistance in upper airway, 35% lower airway; neonate obligate nasal breather; nose comprises much of resistance; breathing turbulent in upper airway, varies with radius to fifth power; if any portion airway narrows, eg, if cricoid lumen narrows by 50%, resistance increases 32-fold; breathing challenging; considering ribcage, ribs horizontal; unlike adults' ribs, do not move in "bucket handle" manner, do not contribute substantially to breathing; much of breathing diaphragmatic; diaphragm prone to fatigue, only 10% type 1 fast-twitch fibers in premature infant; 30% Type I fast-twitch fibers in neonate; increase to 50% at 1 year of age; 60-80% ventilation by diaphragm in children up to 6 months of age, after which decreases to 50%; chest wall compliance weak, elastic recoil of lungs reduced because fewer elastic elements present; net effect, small functional residual capacity (FRC), encroachment of closing volume on FRC may result in shunting, hypoxia; greater metabolic rate in neonate than adult, alveolar ventilation to FRC ratio 5:1 (adult 1.5:1); small FRC, limited oxygen reserve, reason supplemental oxygen administration must be more aggressive in neonates; further complicated under anesthesia by reduction in lung volume associated with loss of consciousness and increasing risk of shunt; breathing control develops from before birth into first year of life; at birth, irregular respiration, worse in premature babies; may lead to apnea, central, peripherally mediated; matures after 1-2 months of age; because of immaturity, irregular respiration stemming from limited, immature arrhythmogenicity in brain stem, immature input from peripheral and central chemoreceptors; most physiologic responses to hypoxia, hypercapnia are mature in term infants, significantly attenuated in premature babies, asphyxiated newborns, eg, premature infant, PO_2 <60 mm Hg, ventilation initially increases then decreases; by 3 weeks of age, ventilatory response to hypoxia sustained, giving 100% oxygen, ventilation decreases then turns to hyperventilation, in contrast to adult, in whom ventilation decreases; in hypercapnia in premature or term neonate, ventilation increases, but impact of increasing carbon dioxide (CO_2) blunted compared to older infants

Apnea of prematurity: phenomenon afflicting primarily premature infants (ie, born <37 weeks gestation); the younger the infant, the greater the risk of apneas; often mixed origin (ie, centrally and peripherally mediated); caused by immature development of central respiratory control center in brain stem; pause in apnea of prematurity lasts roughly 20 seconds; infant typically responds with breathing efforts, crying, to aggressive stimulation, such as rubbing the back; all anesthetics can cause post-operative apnea, even in ex-premature child with no previous apnea history; exception to anesthetics that cause apnea are regional anesthetic blocks (spinals, caudals); apneas unlikely in anesthesias without supplemental sedation; develop protocols to ensure ex-premature infants <60 weeks post-conceptional age will not develop apneas; those with complex medical problems, anemia, considered at risk for apnea after general anesthetic or sedation; monitor for 12 hours or until apnea-free; therapeutic intervention associated with reduction, not elimination, of post-operative apnea is intravenous (IV) caffeine 10 mg/kg

Pulmonary toxicity: oxygen toxicity; issue in premature infants with development of retinopathy of prematurity, bronchopulmonary dysplasia (BPD); premature infants have immature anti-oxidative mechanisms for coping with free radicals, increased risk for developing organ toxicity from excess oxygen; increased oxygen concentrations associated with vasculopathy in the eye (retinopathy of

prematurity) and chronic lung disease; however, oxygen no longer considered sole factor precipitating these organ effects, may be other predisposing factors; oxygen concentration used for resuscitation in delivery room now room air unless oxygen saturation does not increase over first few minutes after birth; limit oxygen saturation in operating room to 90%-94%; studies conflict whether lower saturations associated with mortality, other serious sequelae; higher concentrations in most studies associated with toxicity

Bronchopulmonary dysplasia (BPD): "new" bronchopulmonary dysplasia, chronic lung disorder; occurs post-surfactant administration, despite gentle, low-volume ventilation, normal CO_2; more common in extremely low birth-weight infants; often leads to non-asthmatic obstructive airway disease; some studies suggest volume-limited ventilation limits oxygen toxicity, reduces BPD risk as compared to standard, pressure-controlled ventilation

Cardiac physiology: in utero, heart develops in 2 parallel circulations — pulmonary, systemic; stroke volume of right ventricle increases from ≤1 mL at 20 weeks to 7.5 mL by term, left ventricle increases from 0.5 mL at 20 weeks to roughly 6 mL at term; total cardiac output reaches 400-425 ml/kg/min with right ventricle dominance until delivery; at 38 weeks, right ventricle 60% of cardiac output; with expansion of lungs at birth, pulmonary vascular resistance decreases, blood flows from right side of heart through lungs to left side of heart and into rest of body; 3 shunts can persist early after birth; 1) patent ductus arteriosus (PDA)- 60% close by 2 days postpartum, 98%, by 4 days; oxygen, prostaglandins primary stimuli for functional closure, anatomically, does not close until 2 weeks of age; remains visible on examination as ligamentum arteriosum; 2) ductus venosus — communication between pulmonary artery and aorta — allows blood to bypass liver, proceeds directly to right atrium via inferior vena cava; closes upon umbilical vein occlusion, 1-2 weeks of age; 3) foramen ovale — "flap valve" between right, left atriums; functional closure when left atrial pressure exceeds right; however, 50% of patients <5 years of age have functional foramen ovale

Circulation: blood volume decreases with age; highest, premature infant, 100 mL/kg; full-term neonate, 90 mL/kg; infant, 80 mL/kg; school age, 75 mL/kg; in neonate, hemoglobin (Hb) high, 18-20 g/dL, 70%-90% hemoglobin F (HbF), which has strong binding capacity for oxygen because low levels of 2,3-diphosphoglycerate (2,3-DPG); p50 HbF, 20 mm Hg (p50 HbA, adult hemoglobin, 26-27 mm Hg); Hb concentration of neonate decreases early after birth as blood volume increases, erythropoiesis wanes; Hg reaches nadir at 8-12 weeks of age in term infant, minimum Hb 9-11 g/dL, 6-8 weeks of age, premature infant, 7-9 g/dL

Pediatric Anesthesia Considerations

Temperature control: challenging; neonates poikilothermic, relatively unable to maintain temperature due to large body area to weight ratio, thin layer of subcutaneous fat, limited keratin, inability to vasoconstrict; ability to generate heat depends solely on non-shivering thermogenesis, origin in brown fat, located primarily in interscapular, perirenal areas; thermogenesis mediated by norepinephrine; thermoneutral zone, minimum oxygen demand, adult, >28 °C, neonate, 32-35 °C; must be aggressive in implementing temperature control strategies even before child comes to operating room; heat loss primarily through radiation, 39%; 34% occurs through convective heat loss, 24% evaporative, 3% by conduction; forced air warmers very effective for maintaining temperature; heat room (27 °C recommended) before child enters; once child gets cold, more difficult to warm them; warm blood if needed; monitor core temperature; keep transport incubator warmed for transfer

Monitoring: cardiac monitoring focuses primarily on heart rate, blood pressure, volume status; with limited systemic vascular resistance, systolic blood pressure excellent reflection of volume status (low blood pressure=hypovolemia until proven otherwise); acute decreases in end-tidal CO_2 suggestive of decrease in cardiac output — pulmonary blood flow dependent on cardiac output; exact hypotension definition currently debated; neonate mean arterial pressure should be maintained >39 mm Hg to prevent end-organ damage; treat by replacing volume rather than vasopressors unless congenital heart defect; urine output unreliable measure of volume status, especially first 24 hours after birth — renal function immature; central venous pressure (CVP), arterial line, limited indications unless congenital heart defect or anticipate hemorrhage; bradycardia primarily due to hypoxia, monitor with pulse oximetry, right hand, pre-ductal region; end-tidal $C0_2$ accurate with circle breathing circuits, may require catheter in endotracheal tube for non-rebreathing circuits; can be inaccurate with cyanotic heart disease, right-to-left shunt; temperature measured with esophageal or nasopharyngeal probe; avoid use in axilla if using forced air warmer; neuromuscular blocking monitors difficult to utilize but useful guide for level of blockade, judging whether to reverse or antagonize; sugammadex effective in reversing steroidal non-depolarizing muscle relaxants; bispectral index generally not used <5 years of age

Metabolic considerations: primary focus is glucose homeostasis; glycogen stores accumulate primarily third trimester; premature infant likely insufficient glycogen storage, at risk for hypoglycemia — recommend D10 solution (ie, 10% dextrose solution) with or without calcium, infuse at same rate before and throughout surgery; author prefers this because slight hyperglycemia better than risking hypoglycemic event because of circulating high insulin levels from preoperative glucose infusion; preoperatively, decrease glucose concentrations, make decision about treatment at birth; blood glucose <40 mg/dL, or, in first 24 hours of life, <45 mg/dL, constitutes hypoglycemia; administer 2-4 mL/kg D10 (ie, 200-400 mg/kg) bolus glucose, then continue infusion 5-8 mg/kg/min; avoid hypertonic solutions, risk of intraventricular hemorrhage; at risk for hypoglycemia include premature infants, those stressed at birth, septic, small for gestational age, infants of diabetic mothers, those with Beckwith-Wiedemann syndrome, and others

Fluids and electrolytes: total body water highest in youngest premature baby — 90% of body weight in infants 25-32 weeks of gestational age, two-thirds extracellular, one-third intracellular; at term birth, total body water, 80 mL/kg, extracellular fluid 50% of body weight, intracellular fluid, 35%; 1 year of age, total body water 70% body weight, intracellular fluid, 40%, extracellular fluid, 30%; percentage used to determine

level of dehydration (ie, 5%, 10%, 15% loss of body weight corresponds to mild, moderate, severe fluid losses); fluid requirements developed by Segar, Holliday, 1957, "4-2-1" rule, in the past; now standard fluid for volume replacement is lactated Ringer's, not hyponatremic glucose-containing solution; primary insult in perioperative period is upregulation of anti-diuretic hormone (ADH), resulting from prolonged fasting, surgical trauma, other sources of inflammation, ventilation, opioids, pain; resulted in hyponatremia, seizures, aspiration in the past; even with balanced salt solutions today, unless ADH inhibited, issues can still occur; therefore, Segar and Holliday, revised fluid administration rules specifically for use in operating room — administering 10-20 mL/kg balanced salt solution over first 1-2 hours "turns off" ADH, prevents risk of hyponatremia; in neonates, young infants, malnourished, children with cancer, may give fluid being used in ICU or ward, or if child not on any fluids, may give balanced salt solution with 1% glucose; always important to monitor electrolytes, glucose concentrations in perioperative period

Blood components: often have low albumin concentrations, anemia, thus important to limit amount of balanced salt solution, especially if small for gestational age, low birth weight, septic; administer blood products as needed as well as vasopressors (dopamine) to support circulation; neonates do not tolerate low Hb; transfuse as needed, though trend is to limit transfusion, even in neonates; dilutional thrombocytopenia occurs more often in sick neonate than older child; consider albumin or fresh frozen plasma (FFP) if surgery needed, platelet administration if septic (eg, abdominal perforation)

Anesthesia apparatus: 3 broad categories of breathing circuits; semi-closed circuit (ie, circle circuit), most commonly used in pediatric anesthesia, provides heat, humidity, recycling or partial rebreathing of exhaled gases, removal of CO_2 from recycled gases to maintain normal capnea; semi-open circuit (ie, Mapleson A-F systems, "F" is Jackson Rees system, "D" is Bain circuit or coaxial system), portable lightweight circuits, inexpensive, require high fresh gas flow to prevent rebreathing of exhaled gases; unlike circle circuit, no valves in Mapleson system; low resistance, optimal for spontaneous ventilation; Mapleson A circuit most economical circuit for spontaneous ventilation; Mapleson D most economical for controlled ventilation; third type, closed circuit, infrequently used, circuit completely recycles all exhaled gases, limited inflow of fresh gases, limited in that changing concentrations of gases within circuit is time-consuming

Carbon dioxide absorbents: needed in circle circuits to remove CO_2, useful because maintain heat, humidity; primary constituent of CO_2 absorbents calcium hydroxide, also smaller proportions of potassium, sodium hydroxide, has accelerant to improve efficiency of CO_2 removal; modern inhalational agents (ether anesthetics) may be degraded in soda lime canisters; sevoflurane in soda lime produces Compound A — proven toxic in rats, not demonstrated toxic in humans; other ether anesthetics (eg, desflurane, isoflurane) produce carbon monoxide if passed through desiccated soda lime (eg, if anesthetic machine left running over the weekend without a reservoir bag and gas passed retrograde through soda lime canister and desiccated it, carbon monoxide could be administered if canister not changed); Compound A, carbon monoxide issues eliminated if carbon dioxide absorbent comprised of lithium hydroxide or if potassium, sodium hydroxide removed from calcium hydroxide absorbent

Humidity issues: humidity provided in semi-open circuits by inserting heater-humidifier in circuit — must be servo-controlled to limit temperature and prevent excess heat and water from entering respiratory system; with circle circuits, cannot use heater-humidifiers; heat and moisture exchangers can provide some heat, humidity in infants due to their small tidal volumes, rapid respiratory rate

Endotracheal tubes: uncuffed endotracheal tubes mainstay of pediatric anesthesia, though recently increased use of cuffed tubes; typically made of polyvinyl chloride, have Murphy eye, sized in general by age of child in years divided by 4, plus 4 or 4.5 (mm) for tube's internal diameter; correct size of tube is one that passes through subglottis without resistance, minimal audible leak at 20-30 cm H_2O; tube tip should rest midtrachea; depth of oral tube estimated at 10 cm plus age in years with marker at gingival level; with nasal tubes, mid-tracheal level determined by using depth markings on tube

Caution with preformed tubes: eg, Ring-Adair-Elwyn endotracheal tubes (RAE tube), have predetermined distances from bend to tip of tube; uncuffed tubes well designed for use in children of appropriate ages; with nasal RAE tubes, great deal of variability in distance from bend in nose to distal tip of tube; in cuffed nasal RAE tubes, some longer than child's age requires — tube could be placed endobronchially if bend placed right at nares; with cuffed nasal-tracheal tubes, critical to ensure bilateral air entry into lungs before securing

Trend to cuffed tube use: prompted by development of elliptical cuffed tubes; cuffed tubes may reduce number of reintubations due to leaks with uncuffed tube, reduce air leak, prevent operating room (OR) pollution, provide accurate end-tidal measurements; use during laparoscopic surgery provides accurate lung compliance, reduces risk of aspiration, airway fires; note that evidence lacking for some of these advantages; micro-cuffed tube ultra-thin, elliptical cuff, low sealing pressure (10 cm H_2O inflation), exerts low pressure on mucosa, elliptical shape spreads pressure distribution over larger area; negatives — cuff thin, nitrous oxide can diffuse easily; cuff pressure should be monitored throughout anesthesia if nitrous oxide used; no Murphy eye in micro-cuffed tubes, cuff positioned closer to tip of tube — important to use tube markings, not distance from gums, to position correctly

Tracheal intubation, extubation: undertaken with Miller blade at paraglossal approach or at right commissure of mouth; laryngoscope blade inserted at right commissure, stays at right commissure, with tip aimed at larynx, epiglottis lifted by blade to gain view of laryngeal inlet; Macintosh blade can also be used; shown in recent study by lecturer's group to be equally effective in lifting tongue; in preparation for laryngoscopy, head naturally in "sniffing" position (ie, no need for occiput lift), shoulders in natural position; another study shows raising shoulders only causes anesthesiologist to lower site of vision to get direct view into larynx, ie, no benefit; extubation can be performed either awake or deep; awake extubation requires adequate gag reflex; evidence of eye opening, flexion of hips also indicative of adequate motor tone to support airway; general maxim, "if you think it's time to extubate

the airway, then it's best to wait a minute because no one has ever gotten into trouble from leaving the tube in for the extra minute;" for deep extubation, crucial patient deeply anesthetized, author prefers monitored anesthesia care (MAC) depth >2 before removing while breathing spontaneously; light anesthesia not good time for removal; may cause laryngospasm

Premedication: should confer adequate anxiolysis, facilitate smooth separation from parents; a successful premedication is important for parent confidence as well; midazolam, primary premedication, given orally, 0.75 mg/kg, 18 months to 5-6 years of age, 0.3-0.4 mg/kg, >6 years of age, maximum 20 mg; usually provides adequate sedation, smooth separation within 10-12 minutes; higher dosing for younger children parallels increasing inhalational requirement with decreasing age; alternate techniques include intranasal midazolam, 0.1-0.2 mg/kg, rapid onset, a bitter aftertaste; intranasal sufentanil, 2-3 mcg/kg, can cause postoperative nausea, vomiting, occasionally decreased chest wall compliance; oral ketamine, 5-6 mg/kg; mixture of ketamine, midazolam at half doses; intranasal dexmedetomidine, 1-2 mcg/kg, requires 60 minutes for onset, may delay emergence; for difficult child (eg, muscular autistic teenager), intramuscular ketamine, 3-5 mg/kg; sometimes parent may accompany child to induction or operating room; however, randomized controlled trials demonstrate no proof that parental presence in OR better for child or parent anxiety than no parental presence or than premedication; video games or other electronics may also be effective in calming child; if parent allowed in OR, ensure measures taken to cover you, facility from issue with parent (eg, syncopal episode and subsequent injury); allow only one parent; plan for parental exit from OR; lecturer's institution brings a parent into OR in cases where child very uncooperative or in cases of lifesaving surgery, when this may be parent's last interaction with child

Local anesthesia: in United States, among topical local anesthetics, eutectic mixture of lidocaine and prilocaine (EMLA) — most common; apply 1 hour in advance of cannulating vein, cover with Tegaderm dressing to keep it in place; side effects include venous blanching, may increase level of difficulty in finding a vein; effective in numbing skin; alternately, nitrous oxide 50% mixture does not cause skin blanching, and child becomes sedated

Inhalational agents: "wash in" (ie, equilibration of inhalational anesthetics) more rapid in neonates than in older children, adults, due to a) increased alveolar ventilation to FRC ratio in neonates, b) increased cardiac output specifically to the vessel-rich group, which comprises 18% of cardiac output in neonate (6% in adults), and c) decreased blood and tissue solubilities in neonates; particularly true for more soluble anesthetics (eg, halothane), less so for sevoflurane — less soluble, more widely used agent; pharmacodynamics — mean alveolar concentration (MAC) of inhalational agents increases as age decreases, reaching a peak in infants (eg, isoflurane peaks at 1-6 months of age; desflurane, 6-12 months of age) then decreases through neonatal, premature infants; one exception is MAC of sevoflurane, which is 2.5% for 6 months to 10 years of age, 3.2%-3.3% in neonates, infants <6 months of age, likely because sevoflurane is methyl-isopropyl ether, other anesthetics are methyl-ethyl ethers

Intravenous agents: pharmacology in children differs from that in adults; greater extracellular fluid volume in neonate than adult; protein binding, receptor density decreased in neonate; increased receptor sensitivity in neonate; metabolic pathways for elimination of drugs primarily through cytochrome P450 system immature, develops slowly over 1-2 years of age; combined with immature renal function results in delayed elimination, prolonged action of drugs; as regards IV induction agents, effect of age on thiopental dose similar to MAC of halothane, isoflurane (ie, slow in neonates, increases to peak in infancy, decreases thereafter); propofol dose requirement also decreases from infancy through to adulthood, but dose in neonates not established; clearance of infused propofol markedly reduced <1 year of age, then levels off and remains constant thereafter; infusion at <1 year of age may cause delayed emergence; this is further exacerbated by prematurity; plasma propofol concentration remains high after single dose; at <10 days of age, concentration almost 100% greater than >10 days of age for premature child; less difference in first 10 days and after for full-term child; for prolonged infusions of propofol (ie, up to 3 hours), context-sensitive half-life (ie, time it takes for blood concentration to decrease by 50%) double that of premature child compared to older children after 2 hours; decrease infusion rates in timely manner to ensure emergence

Opioid pharmacology: dose of fentanyl for PDA ligation or intra-abdominal procedures is 25-50 mcg/kg but 10-15 mcg/kg if increased intra-abdominal pressure; dose disparity for 3 reasons; 1) opening of ductus venosus, reduced metabolism of fentanyl; 2) reduced blood flow overall, clearance drug; 3) impaired hepatic metabolism due to immature cytochrome p450 enzyme; morphine pharmacokinetics also altered with age; dose for perioperative pain control in infant/child 20 mcg/kg/h, in term neonate, 5-7 mcg/kg/h, in preterm 2 mcg/kg/h; result of decrease in clearance in younger child (<1 year of age); remifentanil pharmacokinetics relatively unchanged in neonates compared to older children; bradycardia, rigidity can occur with rapid bolus

Dosing of muscle relaxants in neonates: unpredictable because neuromuscular transmission matures during first 3 months of age, when shift from fetal to adult acetylcholine receptors, increased distribution and number of acetylcholine receptors take place; changes in body composition, altered elimination pathways, effects of inhalational and other agents can potentiate effects of neuromuscular blocking drugs; in general, with all nondepolarizing agents there is decreased dose requirement per kilogram to affect the same level of blockade in infants compared to children (ie, infants more sensitive); larger doses of succinylcholine required for neonate, infant, 2 mg/kg (0.5-1 mg/kg in adults)

Drug Toxicities

Succinylcholine toxicity: 3 possible manifestations; 1) hyperkalemia, may occur in patients with burns, typically >9% body surface area, myopathies (eg, Duchenne muscular dystrophy), malignant hyperthermia, upper or lower motor neuron lesions, immobilization, chronic sepsis; 2) prolonged block may be caused by pseudocholinesterase deficiency, drugs (eg, chemotherapeutic agents), diet (eg, tomatoes, potatoes

can potentiate succinylcholine), pregnancy (20% prolongation), liver disease, malignancies, malnutrition, heart disease, renal failure; 3) shorter blockade, may be result of hyperthyroidism, obesity, nephrotic syndrome; prolongation of succinylcholine can also be due to genetic factors; pseudocholinesterase deficiency first gene identified in anesthesia associated with prolonged drug effect; pseudocholinesterase usually metabolized by standard enzyme, may be abnormal in small percentage of patients, atypical pseudocholinesterase; 3 other forms of pseudocholinesterase — silent gene, fluoride-resistant gene, Cynthiana gene defect (causes rapid metabolism of pseudocholinesterase); these all map to third chromosome, differing incidences; atypical has heterozygote frequency of 1 in 30 but prolongation of succinylcholine in heterozygote form almost unmeasurable; homozygote form, roughly 1 in 3,000, lasts 20-30 minutes; for silent gene, 1 in 10,000; for fluoride gene, 1 in 150,000; silent can lead to 4-6 hours of non-activity, prolonged succinylcholine action; treatment, sedate and wait for recovery; plasma administration to provide exogenous source of pseudocholinesterase not supported clinically

Codeine toxicity: of cytochrome isozymes responsible for termination of action, degradation of anesthetic drugs, 2 provide metabolism for most drugs, cytochrome P450 3A4 (CYP3A4), responsible for metabolism of 50% of anesthetics, cytochrome P450 2D6 (CYP2D6) for 20%; CYP2D6 single nucleotide polymorphisms have consequences for drug administration — these polymorphisms have resulted in ultra-rapid metabolism of drugs or poor metabolism; with codeine, ultra-rapid metabolism has led to rapid production of morphine; a sensitive patient may develop relatively high level of morphine, possibility respiratory arrest; ultra-poor metabolizers fail to convert codeine to morphine, analgesic benefits negligible; concerning because children with obstructive sleep apnea and sensitivity to opioids (eg, chronic intermittent nocturnal hypoxia and/or obesity) were prescribed codeine, fatal outcomes postoperatively; incidence of these polymorphisms varies dramatically among populations; federal government now prohibits use of codeine for postoperative pain in children after tonsillectomy, especially with sleep apnea; one hospital in United States slightly different approach, began to gene type CYP2D6 isoforms for children given codeine for perioperative and pain management purposes — if eliminated patients who were ultra-rapid or poor metabolizers, codeine effective, no side effects; however, note that all opioids, including oxycodone, hydrocodone, tramadol, etc, metabolized by CYP2D6 enzyme and have same polymorphism issues as codeine

Propofol infusion syndrome: 25 years ago, 5 children with colds in intensive care units (ICU) in United Kingdom were sedated with propofol for several days; during course of sedation, developed acute metabolic acidosis, bradyarrhythmias, myocardial failure, ineffective resuscitation, death; administration of propofol infusions >5 mg/kg/hr for >48 hours can result in metabolic profile that includes lipemia, hyperkalemia, metabolic acidosis, rhabdomyolysis, myocardial instability leading to heart failure and death; roughly 33 children succumbed from 6 countries; syndrome carries high mortality; only effective treatment hemodialysis, hemoperfusion, and partial exchange blood transfusion; essentially, propofol poisons cytochrome enzyme system in mitochondria in the heart, leads to glycolysis, anaerobic metabolism; heart unable to function effectively; now, black box warning against use of propofol for sedation in ICU; compounding factors include presence of inflammation, multi-organ failure, calorie deprivation; when combined with prolonged propofol infusion, the long-chain triglycerides in propofol are utilized for calories, resulting in toxicity

Key Points

1. Neonatal physiology is important to understand for proper anesthetic technique.
2. Equipment and preparation for pediatric anesthesia can differ from that in adults.
3. Metabolism of anesthetic drugs differs in pediatric patients when compared with adults.
4. Propofol, succinylcholine, and opioid drugs have potential for causing toxicity in pediatric patients.

Suggested Reading

Basel A et al: Preoperative evaluation of the pediatric patient. *Anesthesiol Clin* 2018 Dec;36(4):689-700; **Brockel MA et al:** Anesthesia in the pediatric patient. *Urol Clin North Am* 2018 Nov;45(4):551-60; **Mai CL et al:** A history of pediatric anesthesia: a tale of pioneers and equipment. *Paediatr Anaesth* 2012 Jun;22(6):511-20.

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Neonatal Surgical Emergencies

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Introduction: will discuss 8 different congenital anomalies which may present in operating room (OR): congenital diaphragmatic hernia, tracheoesophageal fistula, lobar emphysema, necrotizing enterocolitis, omphalocele, gastroschisis, myelomeningocele, and pyloric stenosis

Congenital Diaphragmatic Hernia

Overview: defect in diaphragm; occurs about 7 to 10 weeks gestation while diaphragm is forming; 90% are Bochdalek hernia and most on left side; 9% of these hernias are called Morgagni hernias and occur in anterior region of diaphragm; only 1% are central defects; at this time in gestation, lungs, and possibly other organs in chest, are compressed by bowel; result is pulmonary hypoplasia and pulmonary hypertension (because blood vessels do not develop)

Associated anomalies: congenital heart defects occur in 20% to 40% of cases, chromosomal defects in about 10%, (specifically trisomy 13, 18, 12, 15 and DiGeorge syndrome), malrotation of gut in 40%, and genitourinary anomalies; one particular group of defects is known as Cantrell's Pentalogy which is congenital diaphragmatic hernia with omphalocele, sternal cleft, ectopia cordis, and intracardiac defects, such as ventricular septal defect (VSD)

In utero surgery: from antenatal diagnosis; improves the ultimate clinical outcome; includes tracheal plugging and ex utero intrapartum treatment (EXIT procedure)

Primary physiology: extremely stunted lung growth with decreased alveoli and decreased type II cells; therefore, less surfactant in affected lung; pulmonary blood flow to affected lung is diminished due to hypoplasia of pulmonary vasculature; results in persistent fetal circulation and right-to-left shunting through patent foramen ovale (PFO); patent ductus arteriosis (PDA) may occur (particularly in early newborn period); 3 possible presentations

First presentation: severe respiratory distress associated with severe hypoplasia of lung; child presents with tachypnea, tachycardia, and cyanosis at birth; abdomen is scaphoid because most abdominal contents are actually in chest, most commonly left side; may be mediastinal shift due to mass effect

Second presentation: sudden deterioration in child's status after honeymoon period and unrecognized presence of diaphragmatic hernia; key is correction of hypoxemia and pulmonary hypertension if identified and reversible

Third presentation: delayed onset with feeding difficulties, pneumonia, and bowel obstruction 24 hours later; associated with good prognosis

Survival: has increased dramatically; now about 75%; 80% if no extracorporeal membrane oxygenation (ECMO) is needed or other anomalies are present and child has normal birth weight and good Apgar scores; however, if anomalies are associated with diaphragmatic hernia, survival may only reach 20%

Lung management: use small tidal volumes, avoid overdistension of the hypoplastic lung (with worst complication being pneumothorax in good lung, which is potentially devastating), use of higher positive end-expiratory pressure (PEEP), and permissive hypercapnia; degree of pulmonary hypertension basically determines survival; if pulmonary vascular resistance normalizes within first 3 weeks or so after delivery, then child is likely to have good recovery; airway secured without mask ventilation; endotracheal tube inserted with intermittent mandatory ventilation after an IV induction with low airway pressures and PEEP

Anesthetics: muscle relaxants very effective in facilitating ventilation; primary anesthetic is opioids; high-dose opioids very effective in reducing stress response, reducing pulmonary hypertension, and preventing persistent fetal circulation during surgical stimulation; important to recognize that with return of chest contents to abdominal cavity, the abdominal cavity may be under increased pressure; pressure on the diaphragm reduces compliance of good lung; therefore, postoperative ventilation should be anticipated in these children; survival improved if infant stabilized for 24 to 72 hours before coming to OR, in contrast to previous surgical strategy where child is transferred directly from delivery room to OR

Optimization: optimize ventilation to maintain oxygenation and acceptable level of hypercapnia (whether intermittent mandatory ventilation, high-frequency oscillation, or even ECMO); optimize acid-base balance; if $PCO_2 \geq 60$ millimeters of mercury (mmHg) and preductal saturation <70%, may decide to use high-frequency oscillation; if pulmonary hypertension is identified and not responsive to any therapeutic interventions, then nitric oxide should be considered; finally, once baseline ultrasound of head is performed, ECMO may be considered to stabilize child; surgical approach may be laparoscopic, thoracoscopic, or open in either case; thoracoscopic surgery generally avoided due to hypercapnia associated with insufflating CO_2 into chest (depends on child's specific condition); fentanyl-paralysis approach is stress-free anesthetic; preferred, as inhalational agents may cause hypotension, but more importantly may

not achieve desired concentration due to persistent fetal circulation and right-to-left shunting; avoid nitrous oxide; administer oxygen-air gas mixture with optimal ventilation at low peak pressures and PEEP; thermal regulation is critical in all neonates; forced air warming device should be used; if necessary warm room accordingly

Tracheoesophageal Fistula

Overview: defect usually diagnosed by inability to pass gastric tube at birth or, in some cases, due to feeding difficulties and aspiration pneumonia; associated anomalies, particularly esophageal atresia, occur in 30% to 50% of cases; anomalies associated with tracheoesophageal (TE) fistula include prematurity in 30% to 40%, congenital heart defect in 22% such as VSD, atrial septal defect (ASD), or Tetralogy of Fallot; other gastrointestinal abnormalities in 24%, such as duodenal or ileal atresia and malrotation, and genitourinary anomalies in 24%; up to 25% of children with TE fistula have 3 or more components of VACTERL (vertebral anomalies, imperforate anus, congenital heart disease, TE fistula, renal anomalies, and limb, specifically radial anomalies); before coming to surgery, imperative to perform echocardiogram as ASD-VSD combinations, such as atrioventricular canal and hypoplastic left heart syndrome, have been reported

Survival: depends on presence of congenital heart defect and birth weight; anticipate 95% to 98% survival for infant with TE fistula born >1500 grams (g) with no congenital heart defect; 60% to 80% survival when <1500 g or with major congenital heart defect; finally, 20% to 50% survival in infants born <1500 g and with major congenital heart defect

Defects: Type C most common defect in TE fistula; defined as proximal esophageal atresia and distal TE fistula; occurs in 80% of TE fistulas; second most common defect is proximal esophageal atresia with no connection between distal esophagus and tracheobronchial tree

Anesthesia: infants with TE fistula nursed in reverse Trendelenburg or lateral decubitus position before surgery; drain upper pouch by instilling oral or nasal gastric tube; surgery may be delayed in infants for the following: small for gestational age or preterm, pneumonia, sepsis, and other anomalies that require staging; when swallowed air or air that tracks across fistula occurs, gastric decompression may be required before surgical correction; central venous pressure (CVP), although used, rarely needed in full-term infants

Repairs: primary repair usually ideal approach; staged repair may be needed if gap between proximal and distal atretic pieces of esophagus is too large to bridge; increasingly, rigid bronchoscopy is performed to identify location of fistula and to confirm only one fistula (there was a case where two fistulas were present and not recognized before one of them was ligated)

Anesthetic management: several choices in TE fistula; either awake intubation with topical local anesthetic and light sedation or IV induction with propofol with or without muscle relaxant; finally, classic inhalation induction

Classic inhalation induction: traditionally, insert tracheal tube into right mainstem bronchus and withdraw it with bevel facing left to detect left lung ventilation; tape immediately when left chest auscultation is positive; then, turn bevel anterior to prevent ventilation of fistula — verifyied fiberoptically; gentle ventilation may be assisted until chest open and stomach confirmed not to be inflating; if stomach begins to inflate, then open chest and suture immediately across fistula to prevent further occurrences; oxygen saturation indicates whether tube is endobronchial at any point; presence of end-tidal CO_2 will confirm adequacy of ventilation

Endotracheal tube: important to secure endotracheal tube so not displaced; again, if gastric inflation occurs, block fistula usually with ligature to fistula; in some cases, if inflation occurs and compromises ventilation, endotracheal tube taping can be undone and advanced into right long to stop gastric inflation until ventilation managed; if concern preoperatively that gastric inflation is likely to occur, Fogarty catheter may be inserted, followed with fiberoptic bronchoscopy into left lung, inflated to prevent stomach inflation (this depends on level of fistula between trachea and esophagus); after ligation of fistula, lung should be recruited, particularly to ensure that there is bilateral air entry and that correct tissue was ligated with ligature; surgeons often request endotracheal tube be removed at end of surgery; perioperative analgesia may be confirmed with either caudal epidural catheter or local infiltration of intercostal nerves on side of surgery

Neonatal Lobar Emphysema

Overview: rare defect usually involves upper or middle lobes of left lung; associated with congenital heart disease in about 35% of cases and appears on x-ray as hyperaerated portion of lungs; rule out other defects before confirming diagnosis; gastric tube should be inserted and child nursed upright; all of the following may occur if emphysema greatly distends lung — progressive respiratory failure, unilateral expansion of thorax, atelectasis of contralateral lung, and mediastinal shift

Management: may require bronchoscopy with oxygen, atropine and sevoflurane; after diagnosis is confirmed, secure airway for surgery either with inhalation induction or awake; *avoid* nitrous oxide in all cases; maintain spontaneous respiration to avoid overdistension of affected lung or, at least, support ventilation and tolerate permissive hypercapnia until sections of lung isolated; alternately, if lobar emphysema appears to expand and present ventilation problem, endobronchial intubation of contralateral lung or use of endobronchial blocker in left lung may isolate lung lesion until removal; when chest is open and lobe isolated, add positive pressure ventilation

Necrotizing Enterocolitis

Overview: infectious complication occuring in 90% of cases in premature newborns; occurs sporadically and incidence common in premature infants <750 g; mortality not insignificant, ranging from 20% to 50%, and if surgeons must be involved, mortality closer to 50%; occurs in post-birth asphyxia with respiratory distress syndrome and in newborns born in shock

Pathophysiology: intestinal mucosal injury usually at site of defect in ileocolic region; occurs secondary to bowel ischemia; perforation and peritonitis may ensue; child may become extremely ill, septic with fluid and electrolyte disorder, endotoxic, and with coagulopathy secondary to thrombocytopenia; mucosal injury likely result of reduced mesenteric blood flow with fetal asphyxia, PDA ligation,

heart failure, arrhythmia, cardiorespiratory distress, or hypoxemia

Three stages: stage I is apnea, bradycardia, lethargy, abdominal distention and vomiting; stage II, features of stage I plus pneumatosis intestinalis, which is seen on x-ray; stage III, features from stages I and II and repeated bradycardia, hypotension, acidosis, disseminated intravascular coagulation (DIC), and anuria

Treatment: supportive — nothing by mouth, decompress bowels, aggressively manage fluids, administer blood for anemia and coagulation problems, possibly total parenteral nutrition (TPN), and possibly antibiotics for any known or potential infections; surgery indicated for bowel perforations in stages II and III; be sure to appreciate needs of premature child — a septic and acidotic child in shock or coagulopathy — and aggressively administer inotropes and blood products

Anesthesia: appropriate treatment for premature infant with blood products including platelets; management of sepsis and hypotension with antibiotics, dopamine, and possibly epinephrine infusions

Surgery: when required, patients quite unstable (possibly already on high frequency ventilation to oxygenate and clear CO_2); therefore, surgery often occurs in Neonatal Intensive Care Unit (NICU); newborns are preterm; correctly placed tube confirmed with chest x-ray; goal is to provide adequate surgical conditions by providing dose of opioid to block stress response and paralyze infant; 10 to 15 mcg/kg intravenous (IV) fentanyl should be sufficient in child with raised intraabdominal pressure to maintain stable vital signs once child adequately resuscitated; need IV access and, if necessary, arterial blood gases to confirm adequacy of oxygenation, ventilation; before opening abdomen, warm fluids; blood, calcium (if a massive transfusion is needed), coagulation factors, and platelets should be on hand; greatest impact of surgery on child's vital signs with opening of abdomen; after that challenge has been met, then remainder of anesthetic fairly straightforward

Omphalocele and Gastroschisis

Overview: anterior abdominal wall defects; occur sporadically, not genetically or ethnically related; detected on ultrasound as early as 10 to 14 weeks gestation; abdominal contents — small and large bowel, stomach, and possibly liver (in 1/3 or more of cases) — herniate through anterior abdominal wall possibly into 4 to 12 cm sack; in omphalocele, umbilical cord continues with apex of sack

Anomalies of omphalocele: 50% to 75% have associated anomalies: 30% have chromosomal defects, 30% premature, 25% malrotation and other gastrointestinal (GI) anomalies, and 10% congenital heart disease; most common syndrome is Beckwith-Wiedemann syndrome (includes triad of omphalocele, macroglossia and hypoglycemia); other defects include prune belly syndrome and trisomy 13, 15, 18, and 21; another interesting association is Cantrell's Pentalogy (associated with sternal abnormalities, diaphragmatic hernia, ectopic and anomalous heart and gene defects on the X, 25-26 chromosome)

Gastroschisis: distinct from omphalocele — defect to right of umbilicus and much smaller, about 2 to 5 cm; herniated bowel (usually, but sometimes other abdominal contents may follow) not covered with any sack or in any fluid; results in bowel becoming twisted or dried out; may be loss of fluid, and loss of heat; may lead to more serious feeding and absorption problems than in omphalocele; suggested that gastroschisis may result from in utero exposure to acetaminophen, aspirin, and/or pseudoephedrine taken by mother

Management of omphalocele and gastroschisis: depends on size of defect; primary closure is preferable, reduces risk of infection and GI dysfunction, particularly with gastroschisis; however, returning large herniated abdominal contents to small abdomen may raise intra-abdominal pressure, such that peak inspiratory pressure is excessive; venous return, cardiac output, and renal function are compromised; therefore, transduce either intragastric pressure or central venous pressure as metric to determine whether primary repair and return of abdominal contents can be undertaken in one step; if peak pressure, measured by either contractile deceleration point (CDP) or intragastric pressure, is transduced <20 mmHg, then child likely will tolerate primary repair; if not, secondary closure may be undertaken — involves application of silo pouch, followed by staged reduction in pouch until abdominal contents accommodated without compromising perfusion and ventilation

Large defects: may be painted with sulfadiazine compound and left to epithelialize over weeks or months (possibly unable to return to abdominal cavity, particularly if child is extremely premature)

Management of child: includes adequate hydration, balanced salt solution, monitoring intragastric pressure during repair, ensuring adequate ventilation and oxygenation, glucose level, and temperature control; infants with gastroschisis almost always receive TPN in preoperative period — important to maintain glucose component of TPN during surgery to avoid accidental occurrence of hypoglycemia

Myelomeningocele

Overview: open neural tube defect containing spinal cord and other neural tissue, dura, and some paravertebral tissue; if spinal cord not included, simple meningocele; associated with folic acid deficiency; to lessen occurrence, women who anticipate becoming pregnant should begin folic acid before planned conception; aggressive use of multivitamins and folic acid during preconception period has reduced frequency of myelomeningocele in the population; defect is failure of neural tube to close and occurs about 4 weeks gestation (reason why folic acid preventative management strategy should begin before conception)

Diagnosis: antenatal diagnosis of neural tube defect confirmed with serum alpha-fetoprotein test; ultrasound confirms defect

Associations: can be with hydrocephalus, Chiari malformation, possible agenesis of corpus callosum, abnormal cerebral gyrations, and vertebral anomalies; in most cases, lesion in lumbar region, but may occur farther up in spinal column

Clinical manifestations: include paralysis of lower extremities, sensory loss, bladder and bowel dysfunction, and hydrocephalus

Surgery: before surgery, infants nursed in prone position to protect neural tissue; generally, close defects surgically

within 48 hours of birth to minimize infection risk; infants present with IV in place; airway may be secured with IV induction either in left lateral decubitus position or supine position with padding around defect and spine to protect from compression; if defect in lumbar region, regular oral endotracheal tube may be used; if defect in thoracic or occipital region, then nasotracheal tube or reinforced tube may be required due to unusual position for surgery; once airway secured, place child in prone position and support chest to ensure free abdomen and easy ventilation; if small defect, often closed directly once neural tissue freed; in contrast, large defect may require plastic surgery to perform rotational flap in skin to cover defect; in most cases, blood not required for this surgery

Anesthesia: consists of general endotracheal anesthesia, inhalational agent, and small dose of opioids (many infants do not have sensation at and below myelomeningocele)

Pyloric Stenosis

Overview: usually occurs in firstborn males (male-to-female sex ratio of 5:1), white more commonly than black infants, and may be associated with smoking by mother; infants often 2 to 7 weeks of age and may be preterm; substantial hypertrophy of muscularis pyloric layer with palpable olive-shaped mass in right-upper quadrant (also demonstrable on ultrasound); child suddenly vomits in projectile manner (note — not simply spitting up, but vomiting that travels for several inches out of child's mouth) and associated with dehydration and loss of hydrochloric acid, hydrogen ions from stomach, sodium, and chloride; results in hypochloremic metabolic alkalosis; acid-base disturbance depends on how long vomiting continued before child was brought for medical evaluation; due to persistent vomiting, kidneys produce aldosterone, retain sodium, and expel potassium and hydrogen ions in urine (may lead to paradoxical aciduria); with persistent vomiting and inadequate care, dehydration may ensue and metabolic acidosis develop

Levels of dehydration: in infancy, 3 levels (mild, moderate, or severe) of dehydration reflected by amount of body weight lost; mild state refers to 5% loss in body weight (about 50 cc/kg) with poor skin turgor and dry mouth; moderate state refers to 10% loss in body weight with poor skin turgor and dry mouth, and also includes tachycardia, sunken fontanelle, and oliguria; severe state refers to about 15% loss in body weight loss (150 cc/kg) with all listed previous signs as well as sunken eyes, hypotension, and anuria

Management: not surgical emergency, but medical emergency with resuscitation of child for dehydration and electrolyte imbalance; resuscitation takes 24 to 48 hours to achieve normal fluid and electrolyte concentrations; however, trigger point for referring to surgery by pediatricians and primary care providers has resulted in shortened interval of vomiting; many enter hospital minimally dehydrated and with normal electrolytes; for surgery — if normal fluid and electrolyte concentrations and fluid resuscitated — administer atropine, then insert orogastric tube and suction stomach in supine position, left decubitus position, and right decubitus position; note — high amount of fluid can accumulate in child who recently had or still has standard orogastric tube in place; give child 20 mL/kg boluses of balanced salt solution if any evidence of dehydration until fluid resuscitation achieved; once urine output continues, potassium may be resumed in IV; when electrolytes and glucose concentrations are normal in bloodstream, child may proceed for surgery; criteria for proceeding based on the electrolytes: chloride of >88 mEq/L, potassium >3.2 mEq/L, sodium >132 mEq/L, and bicarbonate <30 mEq/L (to ensure no metabolic alkalotic state from chronic vomiting); fluid status should reflect normal vital signs and urine output of 1-2 mL/kg/hr; reminder — reinsert or insert orogastric tube and empty stomach after IV atropine, preoxygenate child, and then perform modified rapid sequence induction with propofol and muscle relaxant

Muscle relaxant: choice depends on situation; in females, use succinylcholine due to rarity of undiagnosed myopathies and hypotonia; alternately, use rocuronium or cisatracurium, which spontaneously degrades, recognizing that sugammadex reverses muscle relaxants; many surgeons complete pyloromyotomy in about 20 minutes and very difficult to reverse large dose of rocuronium in that time period

Opioid: alternately, give very small dose of opioid and large dose of propofol to intubate without muscle relaxant; associated problems are that opioid may delay emergence, as children often have very little pain after surgery

Surgery: routinely use desflurane as maintenance inhalational agent because it has most rapid pharmacokinetics in terms of washout; avoid cricoid pressure in infants because force of only 15 Newton of force may distort cricoid ring and make intubation difficult; once tube is placed, ventilate lungs and use 60% nitrous oxide and desflurane for open pyloromyotomy; after performing pyloromyotomy, surgeons often request insufflation of air into orogastric tube to distend stomach and test for leak; managed by using 60 cc syringe or 40 cc syringe and stopcock attached to end of orogastric tube; again, very little pain after open or laparoscopically conducted surgery

Perioperative: acetaminophen usually sufficient for perioperative pain management; in completely awake infants, extubate in recovery position and continue IV balanced salt solution until infant tolerant of oral feeds and ready for release from hospital

Suggested Reading

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ANESTHESIOLOGY
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Pediatric Outpatient Anesthesia

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Overview: children excellent candidates for outpatient, ambulatory, or day surgery (terms used interchangeably); key to success lies in careful selection, screening, and preparation of prospective patients; screening must be completed prior to day of surgery to identify those not fitting selection criteria or requiring special consideration; anesthetic techniques should ensure smooth onset, prompt emergence, fast recovery, and safe discharge with good control of postoperative pain and vomiting

Patient Factors

Patient selection: primary factors include child's physical status and planned surgical procedure, balanced with capability of surgical facility, surgery center or hospital-based facility, and ability of staff to deal with complications; any systemic or chronic disease under control; understanding of underlying pathophysiology and thorough preoperative evaluation to guide appropriateness of ambulatory setting (*eg*, freestanding ambulatory surgery center [ASC] vs hospital-based outpatient facility); patient conditions include prematurity, asthma, congenital cardiac disease, obesity, respiratory tract infection, and Down syndrome

Age: minimum age for scheduling premature or young full-term infants frequently debated; at increased risk for postanesthesia apnea (can be fatal after discharge); monitor postoperatively for apnea, bradycardia, and O_2 desaturation (particularly important if extremely premature, bronchopulmonary dysplasia, anemia, or other neonatal problems); American Academy of Pediatrics (AAP) recommends ≥12 hrs monitoring after anesthesia for preterm infants aged <50 to 60 wks postconception; healthy full-term infants aged <4 wks, also 12 hrs; aged 4 wks to 6 mos, monitor for ≥2 hrs after surgery (schedule surgery early in day, if possible); avoiding opioids (longer monitoring with opioid use), and use of local anesthesia for pain management increases margin of safety; American College of Surgeons (ACS) recommends limiting ASCs to only healthy infants aged >6 mos

Asthma: most common chronic disease of childhood, affecting ≤10% in United States (US), with increasing incidence; decision to accept these patients and proceed with surgery depends on severity and frequency of symptoms and adequacy of pharmacologic control; children with mild asthma, infrequent symptoms, and do not require continuous medications, excellent candidates for ambulatory surgery, including at ASC; those with moderate asthma, requiring daily medications to control symptoms, should be instructed to continue medications until and including morning of surgery; beta agonist can be administered in holding area, via nebulizer in young children or inhaler if older; if wheezing, has coexisting upper respiratory tract infection (URI), persistent cough, or tachypnea on day of surgery, best to reschedule; anesthetic technique dictated by surgical procedure; most anesthetics available today used successfully in asthmatic patients; laryngeal mask airway (LMA) may decrease intraoperative bronchospasm; if endotracheal tube used, sufficient depth of anesthesia should be established first; intravenous (IV) lidocaine and/or beta agonist inhalant may be administered before extubation; ensure no wheezing when discharged; ensure adequate hydration

Obesity: very obese children have increased risk for perioperative complications including hypertension, dyslipidemia, insulin resistance, diabetes, fatty liver disease, and psychologic problems; may require prolonged recovery and occasional overnight observation, especially after airway surgery such as tonsillectomy and adenoidectomy surgery (T&A); obstructive sleep apnea (OSA) common; body mass index (BMI) threshold difficult to assess in children because of effects of age, sex, pubertal status, race, and ethnicity on growth; cut points for childhood overweight and obesity include BMI at 85th, 90th, 95th, or 97th percentile for age; BMI Centers for Disease Control and Prevention formula found at www.cdc.gov; BMI for age percentile does not directly measure body fat; very athletic adolescents (*eg*, who frequently present for orthopedic and joint procedures) may high BMI for age due to extra muscle mass; children in >97th or 98th percentile, indication for surgery and presence of comorbidities determine if candidate for procedure at ASC; most airway surgeries (*eg*, T&A) not acceptable for ASC; referral surgery (*eg*, plastic or orthopedic) accepted on case-by-case basis; no need for longer fasting time; increased risk of airway obstruction, intraoperative O_2 desaturation, difficult mask ventilation, and challenging IV access; obesity affects pharmacokinetics of most anesthetics; lipophilic IV drugs can be based on total body weight; ideal body weight used for hydrophilic drugs; propofol induction dose based on ideal body weight, whereas maintenance infusions based on total body weight (clearance not dependent on body fat mass); opioids based on ideal body weight and titrated to effect; sevoflurane provides hemodynamic stability and minimal airway irritation, can be used for both induction and maintenance; desflurane has lower blood lipid solubility, provides faster restoration of protective airway reflexes, and has more rapid recovery profile than sevoflurane when used for maintenance

Cardiac disease: no need to exclude well-compensated congenital heart disease; consider antibiotic prophylaxis, air-bubble precautions in IV fluids, and response to anesthetic drugs; bacterial endocarditis, infrequent but severe complication of congenital heart disease; lesions associated with jet formation and vortex shedding (*eg*, aortic stenosis) at greater risk than low pressure, high flow conditions (*eg*, isolated secundum atrial septal defects); American Heart Association (AHA) recommendations for antibiotic prophylaxis indications include unrepaired cyanotic congenital heart disease (*eg*, presenting for dental surgery) or repaired defects with prosthetic material; not indicated for noncyanotic children undergoing routine genitourinary, gastrointestinal, or routine endoscopy procedures; typically oral amoxicillin 50 mg/kg, 30 mins to 60 mins prior to surgery; in operating room (OR), IV antibiotic administration as soon as IV access established after induction; with penicillin allergy, review AHA guidelines at heart.org; anesthetic agents depend on type and duration of procedure and patient's cardiovascular status; volatile anesthetic agents widely used in ambulatory surgery; inhalational induction if right-to-left shunt often prolonged because shunted blood decreases or dilutes partial pressure of anesthetic reaching brain compared with pressure leaving lungs; high inspired concentration of soluble anesthetic agents (*eg*, sevoflurane) combined with augmented ventilation used to counteract this effect; left-to-right shunt, speed of inhalation induction unchanged, recirculation through lungs of left-to-right shunt blood reduces anesthetic uptake from alveoli and promotes rapid rise in alveolar partial pressure; augmented pulmonary blood flow, however, increases anesthetic uptake from alveoli, delaying rise in alveolar anesthetic levels (*ie*, left-to-right shunt increases pulmonary blood flow and does not substantially alter rate of anesthetic induction); pharmacokinetics of IV agents also affected by shunting; left-to-right shunting and increased pulmonary blood flow, IV bolus of drug reaches brain in same time as with no shunt, but initial peak concentration lower and effect prolonged; right-to-left shunting (systemic venous blood bypasses pulmonary circulation), bolus reaches brain sooner and anesthetic effects and cardiovascular depression appear more rapidly

Upper respiratory tract infection (URTI): URTI may warrant postponing elective surgery; nasal discharge may be infectious or benign noninfectious (*eg*, seasonal or vasomotor rhinitis, in which case surgery may be performed); 20% to 30% of children have persistent nasal discharge most of yr; evaluate on individual basis; speak to parents night before surgery; history, specifically allergic, most important for differential diagnosis; parents of ambulatory patients can be instructed to call morning of surgery if new URTI symptoms overnight; if surgery postponed for uncomplicated nasopharyngitis, reschedule in 1 to 2 wks; if flu-like syndrome (*ie*, upper and lower respiratory tract signs, muscle aches and pains) delay surgery until >1 mo after recovery

Down syndrome: trisomy 21, chromosomal anomaly; airway management can difficult because of macroglossia, narrow hypopharynx, and pharyngeal muscle hypotonia causing airway obstruction; often difficult IV access (from obesity and xeroderma); cardiac anomalies, behavior and communication issues, sleep apnea, bradyarrhythmias, gastroesophageal reflux, small airway size, hypothyroidism, hypotonia, obesity, possible atlantoaxial instability; assess for cervical spine instability; assess history of neurologic issues (*eg*, wide-based gait, incontinence); inquire if neck radiographs or computed tomography (CT) performed previously; if asymptomatic, routine imagining not generally recommended, but procedures that may require hyperextension (*eg*, T&A), may warrant x-ray; maintain neutral head and neck position during airway instrumentation or intubation to prevent spinal cord injury

Ambulatory Surgery Challenges

Ambulatory procedures: planned surgical procedures should be associated with only minimal bleeding and minor physiologic derangement; length of procedure not significant limitation; frequently performed pediatric procedures, T&A, herniotomy, myringotomy, adenoidectomy (with or without myringotomy), circumcision, and eye-muscle surgery

T&A: snoring, sleep-disordered breathing, and obstructive adenotonsillar hypertrophy primary indications for surgery; chronic or recurrent tonsillitis less frequent indication; ambulatory T&A for appropriately selected patients safe and cost effective, little benefit in keeping patients in facility once predetermined discharge criteria (*ie*, absence of bleeding, adequate hydration, absence of vomiting, adequate pain relief) achieved

Contraindications for T&A in ASC:

OSA: important to distinguish OSA from benign snoring or simple obstructive breathing; OSA greater risk for developing severe perioperative respiratory adverse events and possibly death after T&A; patient with OSA not appropriate candidate for ASC scheduling; factors against ambulatory T&A include severity of OSA, age <3 yrs, and comorbidities (*eg*, craniofacial abnormalities, severe obesity, Down syndrome, neuromuscular disease, history of prematurity, failure to thrive, chronic lung disease, right ventricular hypertrophy, sickle cell disease); polysomnography (sleep study) gold-standard diagnostic test for evaluation of sleep-disordered breathing; simultaneously records electroencephalogram, electromyelogram, electrocardiogram, pulse oximetry, nasal airflow, and thoracic and abdominal movement during sleep; apnea hypoxia index (AHI), summation of number of OSA and hypopnea events per hr; *American Academy of Sleep Medicine diagnostic criteria for OSA* — mild, 2 to 4 AHI events per hr; moderate, 5 to 9 AHI events per hr; severe, >10 AHI events per hr; <10% T&A patients evaluated with sleep study prior to surgery; *evaluation often based on clinical criteria alone*- snores loudly (*ie*, heard through closed door), gasps or pauses in respiration, daytime somnolence, night terrors, nocturnal enuresis, attention deficit disorder, or poor school performance; higher incidence of OSA with Asian and African American populations and children with obesity; URTIs frequent with OSA, increased risk of respiratory compromise and hemorrhage; asthma or active airway disease frequently present

Bleeding and coagulation issues: inquire about history of bleeding tendencies; medications that interfere with coagulation include aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), and valproic acid;

discontinuation of these medications may require preoperative neurology, cardiology, and hematology consultation; careful cardiorespiratory history and physical examination essential; chronic tonsillar hypertrophy may also have longstanding hypoxemia, hypercarbia, which can lead to cor pulmonale; no evidence that routinely performed preoperative coagulation studies beneficial unless indicated by history

Anesthesia

Anesthetic options: include inhalational or total IV anesthesia (TIVA) technique, endotracheal tube or LMA, and spontaneous or controlled ventilation; spontaneous ventilation allows titration of small opioid doses to effect while monitoring respiratory rates, and end-tidal CO_2; with severe OSA, severity of nocturnal O_2 desaturation correlates with sensitivity to exogenously administered opioids; overall, opioids no longer mainstay of perioperative analgesia (now use nonopioid regimens including dexmedetomidine, acetaminophen, NSAIDs, dexamethasone, and ketamine); infusion of dexmedetomidine 1 mcg/kg to 2 mcg/kg IV may reduce postoperative opioid requirements but duration of stay in postanesthesia care unit (PACU) prolonged, thus rarely used in ambulatory patients; patients with severe OSA continue to demonstrate obstructive apnea and desaturation during sleep on first night post T&A, thus require continuous overnight monitoring

Preoperative overview: most ASCs actively participate in preoperative screening; telephone call to parents 1 to 2 days prior to surgery or established formal screening clinic to clear all patients before surgery; on day of surgery, all patients screened again for acute illness and nil per os (NPO) status; vital signs recorded, any consultation reports evaluated, and need for special preoperative psychological or pharmacologic treatment considered, before arrival into OR area; preoperative laboratory testing based on history, illness, and proposed surgery; routine hemoglobin and urinalysis usually unnecessary; preoperative pregnancy testing in adolescent girls routinely performed by ~50% of US ambulatory centers; *preoperative fasting* — solid food (including milk, formula, and milk products) not allowed on day of surgery; breastfed infants allowed to nurse ≤4 hrs preoperatively; encourage drinking clear liquids until 2 hrs before surgery; possible benefits of shorter fasting times include minimizing thirst and discomfort while awaiting surgery, decreased hypovolemia-induced hypotension during induction, and less risk of hypoglycemia

Preanesthetic drugs: decision based on age and psychologic status; midazolam orally 0.5 mg/kg, 15 mins to 30 mins before induction to facilitate separation from parents and improve cooperation during induction; minimal effect on speed of recovery

Anesthetic techniques: should ensure smooth onset, quick emergence, prompt recovery in PACU, and rapid discharge with no or minimal pain, agitation, and/or vomiting

Inhalation induction: popular choice in pediatric anesthesia; sevoflurane most common; pleasant smell, least irritating inhalational agent; can be used for both induction and maintenance; low blood-gas coefficient, results in rapid and smooth induction, no airway irritation, even with 8% inspired concentration; emergence and recovery times faster than for halothane or isoflurane; desflurane not indicated for start of anesthesia induction, results in high incidence of airway irritation, coughing, and may induce spasm; can be introduced following other induction agents (typically sevoflurane), resulting in significantly faster emergence and recovery than halothane or sevoflurane

IV induction: method of choice in older children, especially if skin analgesic applied (*eg*, lidocaine and tetracaine [Synera], lidocaine and prilocaine [EMLA]); propofol 2.5 mg/kg to 3.5 mg/kg for induction; pain on injection minimized by using large antecubital vein; if hand veins used, 1 mg to 2 mg lidocaine per 1 mL propofol immediately prior to injection; recovery fastest if propofol induction followed by propofol infusion for maintenance; because of higher volume of distribution and increased clearance, children require higher infusion rates (200 mcg/kg/min to 400 mcg/kg/min) compared with adults; propofol associated with low incidence of postoperative vomiting

Postoperative analgesia: depends on procedure and pain threshold of patient, not on whether inpatient or outpatient; regional blocks or local infiltration used whenever possible to supplement general anesthesia and limit need for narcotics; acetaminophen most commonly used mild analgesic; initial dose often administered rectally, 40 mg/kg prior to awakening or given orally in combination with premedication drugs; supplemental doses given orally, 10 mg/kg to 15 mg/kg every 4 hrs to 6 hrs to ensure continuation of analgesia postoperatively; IV acetaminophen 15 mg/kg during surgery can be used; NSAIDs (*eg*, ketorolac) proven effective in relieving postoperative pain following minor operations; ketorolac may increase risk of surgical bleeding secondary to altered platelet function (best administered after hemostasis achieved); *opioids* — if narcotics indicated, choose short-acting drugs; IV administration allows more accurate titration and avoids use of standard dosage based on weight (can lead to relative overdose); recurrent hypoxemia, especially with OSA, associated with increased analgesic sensitivity to opioids in patients undergoing T&A surgery; codeine in children no longer indicated; dexmedetomidine associated with prolonged recovery, seldom indicated for pediatric outpatients

Regional anesthesia: can be combined with light general anesthesia to provide excellent postoperative pain relief and early ambulation, with minimal or no need for narcotics; place block prior to surgery, after induction, to reduce requirement for general anesthesia; may result in more rapid recovery, earlier discharge, more rapid return of appetite, and less postoperative vomiting; types of blocks limited only by skill and interest of anesthesiologist; should be simple to perform, have minimal or no side effects, and not interfere with motor function and early ambulation; ultrasonography-guided blocks becoming reference technique for local anesthetic injections and regional anesthesia catheter placements; most commonly used blocks include ilioinguinal and iliohypogastric nerve blocks, performed by infiltration of 0.25% bupivacaine or 0.2% ropivacaine; provides postoperative analgesia following inguinal herniotomy, hydrocelectomy, or orchidopexy; for dorsal nerve block of penis, injection of 1 mL to 4 mL 0.25% bupivacaine or 0.2% ropivacaine without epinephrine provides >6 hours analgesia following circumcision with no complications; topical application of lidocaine on incision sites at conclusion

of surgery also effective; caudal block with ropivacaine 0.2% solution in dose of 0.5 mL/kg to 1 mL/kg provides excellent postoperative analgesia following variety of surgical procedures (*eg*, circumcision, hypospadias repair, orchidopexy, herniotomy); if larger volume indicated, use of.125% solution recommended to minimize risk of toxicity and motor weakness

Antiemetics: postoperative nausea difficult to assess in children; indicated if surgery >30 minutes, aged >3 yrs, strabismus surgery, history of postoperative vomiting in child or immediate family; 5-HT_3 antagonists (*eg*, ondansetron) effective for prevention and treatment of postoperative vomiting in ambulatory patients; single IV dose of 0.1 mg/kg for children <40kg and 4 mg if >40kg; multimodal approach including dexamethasone 0.15 mg/kg and ondansetron can be combined with propofol-based anesthesia for maximal benefit in high-risk patients

Postoperative emergence delirium (ED): transient state of marked irritation and dissociation after anesthesia, does not respond to consoling measures; more likely to occur in children aged 2 to 5 yrs or undergoing relatively painful procedures under inhalational anesthesia; suspected cause, rapid emergence after short-acting volatile anesthetics and their intrinsic characteristics; preventive measures and treatments include premedication, analgesic adjuncts, single dose of propofol at conclusion of surgery, or dexmedetomidine (if inpatient)

Discharge

Procedures: ensure safe discharge; traditional PACU recovery scoring tools now include pulse oximetry; bypassing PACU and allowing children to reunite with parents immediately after surgery ("fast tracking") suggestive that discharge home faster and postoperative pain and vomiting less frequent

Discharge criteria: appropriateness and stability of vital signs, absence of respiratory distress, ability to swallow oral fluids, cough or demonstrate gag reflex, ability to ambulate consistent with developmental level, absence of excessive vomiting and dizziness, and state of consciousness appropriate to developmental level; recent studies suggest that children not be required to drink before discharge because may increase likelihood of vomiting (ensure IV hydration should); every child must have escort home; escort given written instructions concerning child's home care and telephone number to call for further advice or to report complications; staff counseling about postoperative care and/or designated handouts to address care and signs of complications for specific procedures; centers may consider routine follow-up telephone calls and written questionnaires for parents (for quality assurance)

Key Points

1. Using well-defined, evidence-based selection criteria for pediatric patients undergoing outpatient surgery can ensure safety of ambulatory surgery.
2. Preterm infants high-risk group and require prolonged monitoring, even after routine procedures.
3. Proposed requirements for full-term infants based on anecdotal reports. Children aged <3 yrs, those with severe OSA syndrome, or those with comorbidities should not be scheduled for T&A surgery at freestanding ambulatory surgery center; however, may, be appropriate for outpatient facilities attached to hospitals.
4. Obese children pose logistic and medical challenges; however, some with high BMI may have high muscle mass and should be considered on individual basis.
5. Postoperative analgesia as well as vomiting prophylaxis will enhance patient comfort.
6. Using predefined discharge criteria and follow up with parents will increase patients' safety and parents' satisfaction.

Suggested Reading

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Anesthesia Considerations in Pediatric Subspecialty Surgery

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Cleft lip and palate surgery: cleft lip incidence ~1/700 to 1/1000; no known cause; environmentally induced or genetically related; cleft lip presents as unilateral or bilateral defect, repaired at ~3-6 months post-natal age; cleft palate may or may not be associated with cleft lip; repaired at age 9-18 months; surgery should be canceled in case of upper respiratory infection; many syndromes associated with cleft lip and palate; e.g. Pierre Robin sequence, Down syndrome, fetal alcohol syndrome, and others; anesthetic issues relate primarily to airway management; difficult intubations and poor laryngeal views occur in ≤7% children, mostly attributable to operators' lack of experience; intubation more difficult with bilateral cleft lip, particularly when associated with retrognathia; incidence of difficult intubation 42% with bilateral microtia compared with 2% with unilateral cleft lip; failed intubation uncommon; these children require general tracheal anesthesia and preformed oral RAE (Ring-Adair-Elwyn) tube; often uncuffed as not much bleeding; retractor should be carefully placed in the mouth, as change in tube position or kinking the tube compresses tube and makes ventilation difficult; mainstay of anesthesia inhalational; use of opioids avoided as surgeons often infiltrate soft tissues with local anesthesia and epinephrine (the latter to decrease bleeding); maximum epinephrine dose 10 mcg/kg; prophylactic antiemetics not needed for age <2 yr

Palatoplasty: to establish velopharyngeal competence and normal speech; surgery for age <1 yr; straight line or Z-plasty of soft tissues to raise flaps and cover the defect; leaves open raw areas where incisions made, may result in postoperative serosanguinous drainage; avoid inserting tubes through nose once repair completed; airways extubated when patient completely awake to reduce laryngospasm risk, as airway loss may be difficult to resecure

Pharyngoplasty: to establish competent velopalatal defect; usually performed in age 5-15 yrs; flap raised in posterior pharynx, inserted into velum; tonsillar pillars may also be rotated in order to complete defect; increased risk of hyponasality and nasal airway obstruction, particularly associated with obstructive sleep apnea (OSA); nasal splint or nasopharyngeal airway may be inserted and sutured in place for postoperative airway management; important postoperatively not to disrupt any of the tissue lines by inserting catheters or airways of any sort; airway should be extubated when patient completely awake; patient should be admitted and monitored overnight to ensure competent airway and no excessive bleeding or apneas; in addition to nasal airway, nasal stents or a tongue-retention suture are inserted in OR; child's arms should be restrained in Poseys to prevent removal of these airway-protective devices; in case of tongue edema, airway should not be extubated until edema has been addressed and child able to protrude tongue from oropharynx; pain management addressed primarily by local anesthesia and possibly nerve block (especially infraorbital, which anesthetizes maxillary division of trigeminal nerve); acetaminophen dose 10-15 mg/kg orally q4-6 h or IV; avoid opioids where possible, but small doses of morphine IV may be used; cleft palate infants should be monitored overnight with continuous oximetry and cardiorespiratory monitor; (with cleft lip surgery, child may be going home); dexmedetomidine may be recommended to provide sedation analgesia, as it is relatively devoid of respiratory depression associated with opioids

Tonsillectomy and adenoidectomy (T&A) and OSA: dramatic increase in number of children with OSA as primary indication for T&A surgery; increased from 20% to 80% from 1990s to early 2000s; only 10% have had polysomnography (PSG), gold standard for diagnosing OSA; economic factors have resulted in increase of proportion of T&As done as outpatient surgery from 0-90%; postoperative mortality of 1/10,000, surgeons conservative about admitting children with severe OSA; OSA the most severe form of sleep disorder breathing, with intermittent complete upper airway obstruction; differs from primary snoring, which carries few of the physiologic and cardiorespiratory complications associated with OSA; in OSA there is direct opposition of tongue to posterior pharyngeal wall, displacement of the soft palate by tongue against pharynx, opposition of lateral pharyngeal walls, and intermittent circular closure of the pharynx, suggesting that the entire upper airway region in part, at different phases of respiration, may be narrowed and lead to difficulty in breathing; clinical features of OSA differ in children vs adults; peak age in children is preschool; gender ratio equal; in adults, OSA more common in males, often postmenopausal in females; causes in children relate to tonsil and adenoidal hypertrophy associated with craniofacial disorders, obesity and chromosomal abnormalities (eg, Down syndrome); primary cause in adults is obesity; body habitus in children varies from failure to thrive to obesity; excessive daytime somnolence common in adults but not in children; hyperactivity, developmental delay, cognitive impairment common in children but

not in adults; potential consequences of untreated OSA are failure to thrive, growth retardation, neurocognitive impairments, including difficulty concentrating in school, attention-deficit hyperactivity disorder(ADHD), and behavioral problems; may be significant cardiovascular complications, including cor pulmonale resulting from pulmonary hypertension from intermittent hypoxia; may be further complicated by pediatric obesity

Predictive factors for OSA in children: PSG gold standard for diagnosis; other tests inferior; history has positive predictive value of ~65%, physical examination of large tonsils even poorer; more recently, exhaled 8-isoprostane and urinary 8-isoprostane found to correlate with OSA in children; other predictors include presence of 3 of the urinary biomarkers (mucoid, uromodulin, kallikrein, urocortin) and nocturnal oximetry; OSA-5 questionnaire shows promise; includes degrees of loud snoring, breath holding, choking or gasping, mouth breathing, and nighttime breathing causing concern in parents; note that many non-ENT surgery patients may carry OSA signs without having diagnosis; important for evaluating responses to opioids and/or general anesthesia

Management of children having T&A: pre-medication with oral midazolam 0.5-0.75 mg/kg; induce anesthesia but be prepared for upper airway obstruction; jaw thrust may be necessary(apply pressure at coronoids of ascending ramus of mandible, not at angle); apply CPAP by closing adjustable pressure limiting (APL) valve to 10-20 cm H_2O and monitoring child's breathing carefully; IV access established, propofol administered, and oral intubation with RAE tube, with or without cuff, performed; maintain spontaneous respiration, particularly if history of OSA, with inhalational agent, low FiO_2 with and without nitrous oxide; according to paper in the *Journal of Applied Physiology*, children who underwent tonsillectomy and were given 0.5 mcg/kg fentanyl developed apnea in 46% of cases compared to 4% of controls; unclear why children with OSA so sensitive to such small fentanyl dose; subsequent work by the group at Montréal Children's explained that these children desaturate at night to levels <85%; opioid dose required for analgesia is ≤50% usual dose required for T&A surgery; this is due to upregulation of many genes (including c-fos and c-jun) in response to hypoxia; results in production of hypoxia-inducing factor 1 and insulin growth factor binding protein 1, which increase expression of mu and delta opioid receptors and trigger systemic inflammatory mediators, all of which render child more sensitive to opioids; if suspicion child is desaturating at night because of history of OSA symptoms, small morphine dose (10-20 mcg/kg IV), or 0.5 mcg/kg fentanyl may be given while monitoring for spontaneous breathing; if apnea develops, opioid administration stopped and child monitored carefully; staff informed of opioid sensitivity; if respiration continues unabated after opioid dose, dose doubled with subsequent administrations until full dose administered(150-200 mcg/kg morphine); alternate strategies to avoid opioid respiratory depression include nonsteroidal anti-inflammatory agents, local anesthetic, ketamine or dexmedetomidine for analgesia and smooth emergence from anesthesia; in all children with OSA, airway extubation done when awake to avoid airway obstruction; lateral decubitus (recovery) positioning to drain any residual secretions or blood out of mouth and not obstruct airway; oxygen administered, child transferred to recovery room breathing spontaneously

Developments in T&A surgery not related to OSA: issue of whether and how much dexamethasone should be administered to children undergoing tonsillectomy; dexamethasone effective as antiemetic particularly combined with ondansetron (~100mcg/kg of each); no dose-response curve with dexamethasone to determine anti-emetic dose; reports of postoperative bleeding after dexamethasone given during T&A are inconclusive, but there may be increase in postoperative surgical interventions after dexamethasone use; dexamethasone with ondansetron still in use; children who are at serious risk for respiratory complications after T&A with OSA and need monitoring are admitted (eg, age <2-3 yrs, those with severe OSA [apnea-hypopnea index >10 or complications such as pulmonary hypertension and right ventricular hypertrophy], obesity, complex diseases [eg, Down syndrome], neuromuscular and craniofacial disorders, those with limited hospital accessibility)

Postoperative pain management after hospital discharge: use of codeine prohibited in T&A surgery due to risk patient may have single nucleotide polymorphisms in cytochrome P450 2D6 isozyme; if such children given codeine and sensitive to opioids or obese, large morphine dose may accumulate, resulting in apnea at home; fatalities reported; therefore, codeine not favored as postoperative analgesic; acetaminophen alternating with ibuprofen every 4-6 h orally often prescribed; limited data on oral morphine; probably best avoided in those with sleep apnea, especially in the first 48 h post-surgery

Complications after T&A surgery: primary bleeding within the first 24 h of surgery, usually within 6 h, due to surgical error or failure to completely stop bleeding; secondary bleeding 24 h to 10 days post-surgery due to premature separation of the eschar, resulting in venous or arterial bleeding; incidence 0.1%-2.5% of all bleeding, of which ~3% require exploration; in such cases of nonabating tonsillar rebleed, IV access reestablished and patient rehydrated to correct any hypovolemia; patient's blood typed and cross-matched; though patient's stomach will be full of blood, no point in trying to remove with tube because much is clotted; induction agents (ie, ketamine, etomidate, propofol) may be used with muscle relaxant endotracheal tube; opioids are generally not required; important to be aggressive in treatment of child with significant bleeding, even if tonsillectomy was straightforward; need to intubate, as failure to establish an airway in child having tonsillar rebleed may lead to death, as reintubation may be difficult; patient must be well oxygenated, and there should be 2 Yankauer suctions available; if larynx cannot be visualized for intubation, backup plan includes Trendelenburg positioning with 2 Yankauer suctions in mouth, left lateral decubitus positioning, so that any bleeding runs out the left side of the mouth, while the laryngoscopist inserts the blade in the right side and finds the larynx for intubation

Peritonsillar abscess (quinsy tonsil): occurs in older children; abscess between the tonsillar capsule and the superior constrictor muscle; may spread upwards towards the palate, including the posterior pharyngeal wall, but this is often spared; patient presents with fever,

sore throat, and pharyngeal swelling, pain on swallowing and sometimes limited mouth opening (trismus), but the latter is often due to nerve compression or pterygoid muscle spasm, neck muscle spasm and can be overcome once anesthetized; X-ray and CT scan usually delineate the extent of airway involvement and should be carefully reviewed to avoid difficulty in securing airway once patient anesthetized; quinsy on the right side of the neck is problem for laryngoscopy; best to induce anesthesia with spontaneous respiration; avoid oral airway to avoid puncturing abscess; avoid traumatizing abscess when laryngoscope blade inserted; abscess will be incised and drained and tonsillectomy performed if needed

Neurosurgery

Hydrocephalus: accumulation of excess cerebrospinal fluid (CSF) in the head; may be due to congenital abnormality such as aqueductal stenosis; acquired problems include intracranial hemorrhage as in premature infants or trauma, infection, or tumor; most common pediatric neurosurgical condition; imbalance between the production of CSF and its absorption leads to either obstructive (non-communicating) or non-obstructive (communicating) cerebrospinal flow; treatment either way is shunt; in the infant, hydrocephalus leads to slowly increasing head circumference; serial measurements can demonstrate an increase in head circumference; head circumference is of little value in older children; other clinical findings include irritability, vomiting, headache, lethargy, neck pain, blurred or double vision, and incontinence; may progress to apnea, cerebellar herniation and death; the classic sunset eyes sign occurs in 40% of children with obstructive hydrocephalus with up-gaze paresis (Parinaud's syndrome) from periaqueductal compression; hydrocephalus is decompressed by inserting shunt allowing communication between lateral ventricles in head and peritoneal cavity; shunt tunneled under skin, over clavicle, and into abdomen; performed under general anesthesia with modest hyperventilation, small dose of inhalational agents, limited opioids, and local anesthetic as needed

Chiari malformation: 4 types; type I — caudal displacement of cerebellar tonsils below foramen magnum; type II with myelomeningocele — caudal displacement of cerebellar vermis, the fourth ventricle and the lower brainstem through foramen magnum; type III — caudal displacement of cerebellum and brainstem into high cervical meningocele; type IV — cerebellar hypoplasia; clinical manifestations vary; with type II, medullar compression, possible vocal cord paralysis, apnea, aspiration in infancy, may require tracheotomy if gag absent or aspiration occurs; avoid extreme head flexion; type I occurs often in healthy children with no myelomeningocele, have milder symptoms (headache or neck pain); treatment is suboccipital craniectomy with cervical laminectomy

Brain tumors: common in children, most common solid tumor; malignancy second in incidence only to leukemia; 85% brain tumors are infratentorial in children, occur in posterior fossa and present with obstructive hydrocephalus; positioned prone in surgery and endotracheal tube is secured to accommodate adequate ventilation despite neck hyperflexion in order to expose posterior fossa; patient intubated supine; lecturer often uses nasotracheal tube (endotracheal tube in nose, not RAE tube) because it stays in place better; tests position of tube while patient supine by hyperflexing neck to make sure tube tip does not impinge on carina; once patient prone, arrhythmias and blood pressure instability may occur during brainstem exploration; should be anticipated; venous air embolism possible particularly if head is 10-20 degrees up; 15% of tumors supratentorial (craniopharyngioma or optic glioma); endocrine, growth, and vision problems may occur; ongoing treatment for preoperative thyroid function and diabetes insipidus should continue in the perioperative period

A-V malformation: most common vascular malformation of head (vein of Galen); aneurysms also occur, but not common and often managed neurointerventionally; if surgery needed, prepare for massive blood transfusions with large bore IVs, arterial line and urinary catheters; controlled hypotension particularly for aneurysm repair; use caution in the presence of raised ICP; postoperatively, whether after surgery for brain tumor or vascular malformation, antihypertensives may be needed to control blood pressure, particularly if endotracheal tube is left in place; early extubation to examine and communicate with the patient to ensure intact neurologic system

Craniosynostosis: occurs from premature closures of ≥1 cranial sutures; frequency is ~1/2000 live births; more often in males than females; embryologically, frontal and parietal bones fuse by 8 months and anterior fontanel closes between 9 and 18 months; posterior fontanel closes by 3 to 6 months; compensatory growth parallel to affected suture results in abnormally shaped head and is an attempt to compensate and decompress any elevated intracranial pressure (ICP); craniosynostosis can affect ICP, brain growth, and vision; 80% of craniosynostoses are non-syndromic, single sutures closed prematurely as isolated finding; 20% are syndromic, usually involve ≥2 sutures, often associated with clinical findings; >150 syndromes associated with craniosynostosis, most common being Crousan, Apert syndrome, Pfeiffer and Carpenter; among single suture closures, at least 50% are sagittal, 20% coronal and 10% metopic; coronal suture closure most often associated with syndromes

Apert syndrome: often associated with coronal suture closure, incidence of ~1/100,000-1/150,000; occurs sporadically with occasional autosomal dominance; known as cloverleaf skull with hypertelorism and proptosis; midface hypoplasia with cleft palate present in 30%, choanal atresia, tracheal obstruction, and OSA in 40-50%; associated cardiac anomalies in 10%, most commonly ventricular septal defect (VSD) and pulmonary stenosis; hydronephrosis and cryptorchidism; syndactyly distinguishes Apert syndrome from Crousan; cervical fusion, central nervous system (CNS) developmental delay and raised intracranial pressure; if surgery done in first year, >50% will have IQ>70, otherwise <7%

Crousan syndrome: same as Apert except for syndactyly; 50/50 sporadic and genetic etiology; premature closing sutures are coronal, lambdoid or others; frontal bossing, tower skull, midface hypoplasia, airway obstruction, and OSA as in Apert syndrome; occasional mild developmental delay and raised intracranial pressure; optic atrophy in 20%; mask ventilation difficult in Apert and Crouzon due to midface hypoplasia and OSA; tracheal intubation facile

Pfeiffer syndrome: occurs in 1/25,000 to 1/100,000; autosomal dominant inheritance pattern; also occurs sporadically; involves coronal or occasionally sagittal sutures; distinct features from Apert include broad thumb, large first toe and polydactyly; normal intelligence to mild developmental delay; raised intracranial pressure

Carpenter syndrome: tower skull and premature closure of coronal or other sutures, hypertelorism and low-set ears; cardiac defects; may have hypogonadism; have syndactyly; cognitive impairment common

Surgery for craniosynostosis: indications include raised ICP, severe exophthalmos, OSA, clinical features of craniofacial disorders, and psychosocial issues; goal is to optimize brain growth, particularly in the first few months of life, so early surgery important; reconstructive surgery may occur slightly later, often involves both anterior and posterior parts of the skull, handled through strip craniectomy in age <6 months or endoscopic strip craniectomy or spring-assisted cranioplasty, with less blood loss and blood transfusion; anesthetic issues relate primarily to the preoperative airway assessment, eye examination, intracranial pressure; surgical approach is to have blood available, as bleeding starts from beginning with skin and scalp incisions; echocardiogram should be done to disclose any heart defect; critical to avoid any air bubbles due to risk of air embolism; cervical extension should be assessed before beginning; IV access may be difficult, particularly if child has syndactyly; children are at risk for OSA, so mask ventilation may be difficult; laryngoscopy and tracheal intubation are rarely challenging; document airway management in previous surgeries, plan for postoperative monitoring; endoscopic approach for craniosynostosis most common for sagittal synostosis; performed at 3-4 months of age; less invasive and may have less blood loss; another approach is midface advancement (LeFort) performed to correct midface hypoplasia; may also be achieved with distraction osteogenesis; open calvarial vault reconstruction performed at 6 months age; accessed by coronal scalp incision; reshaping and plating of all cranial bones; substantial blood loss

Pierre Robin sequence: incidence of 1/20,000 to 1/50,000; defined by retrognathia, glossoptosis (posteriorly displaced origin of tongue)and respiratory difficulties in the first 24 h of life; is sequence rather than syndrome; absence of respiratory distress renders the diagnosis simply mandibular hypoplasia; position of base of tongue right over larynx and impaired mandibular growth *in utero* lead to respiratory difficulty after birth; may be associated with other syndromes such as hemifacial microsomia and Stickler syndrome; tongue tends to prolapse backward leading to airway obstruction; affected children may need prone or lateral positioning at birth; some insert suture in tongue or sheet or tongue clip, or suturing of tongue to mandible or lip to ensure patent airway; in more severe cases mandibular distraction or tracheotomy may be required; if tongue is sutured and anesthesia is required, tongue must be released with ketamine sedation before laryngoscopy with an inhalation induction, awake intubation, or laryngeal mask airway (LMA); if micrognathia is present, essential that Miller blade and paraglossal approach used (put blade in right commissure and keep it there); if direct laryngoscopy fails, video laryngoscope, fiber-optic intubation, or LMA may be used

Treacher Collins: mandibulofacial dysostosis; incidence of 1/50,000; results from bilateral facial clefting with mandibular hypoplasia; 1/3 children have cleft palates and macrostomia; autosomal dominant inheritance pattern with variable penetrance; maxillary and mandibular hypoplasia and choanal atresia lead to airway obstruction; airway becomes more difficult with age, so prior history of easy intubation unreliable guide; tracheotomy may be needed; hearing loss is common; congenital heart disease is uncommon; high risk of OSA and sudden death; difficult mask ventilation; laryngoscopy becomes progressively more difficult with age; LMA may be placed while patient awake; consider fiberoptic bronchoscopy; eye protection important

Hemifacial microsomia (otomandibular dysostosis): spectrum of defects of the first and second branchial arches and first cleft; known as a typical syndrome, Goldenhar syndrome; carries increasing airway difficulty and complexity depending on whether unilateral or bilateral; temporomandibular joint and auricular involvement and facial nerve defect; in Goldenhar syndrome, vertebral anomalies present in 40% congenital heart disease in 35%; facial hypoplasia may render airway management extremely difficult; difficulty of airway management does not change as child ages; right-sided and bilateral defects are more difficult to manage than left-sided; mask induction intubation done with backup airway equipment; muscle relaxants avoided before the airway is secured

Tethered spinal cord syndrome: distal end of the spinal cord is tacked down and seen on the surface as midline skin defect, dimple, hair tuft, or fat pad; need ultrasound if considering caudal block; children may present with difficulty in toilet training or walking or with back pain if older; with history of myelomeningocele repair, follow-up MRI is diagnostic for tethered cord in some cases; neurosurgical goal is to free up the nerves to relieve bowel and bladder dysfunction and allow development of proper gait; for surgery, children are positioned prone and muscle relaxants avoided to avoid risk of damage to motor nerves; generally no blood loss; airway usually manageable unless tethered cord complicated by another syndrome

Halo-vest considerations: airway management critical; child often has unstable C-spine; airway can be lost under general anesthesia; maintain spontaneous respiration; use local anesthesia, superior laryngeal nerve block with some sedation; perform fiberoptic nasal intubation or use videolaryngoscope; secure airway; once captogram confirmatory, administer IV agents and continue general anesthesia for placement of halo and vest to stabilize C-spine

Anterior mediastinal masses: discrete space behind sternum extending from xiphoid caudally, then rostrally to angle of Louis and posteriorly to middle mediastinum (heart); small space; any expanding mass in the narrow anterior mediastinum can compress vital tissues and lead to serious cardiorespiratory compromise; smaller organs in children pose greater risk of tracheobronchial and pulmonary compression; 4 most common masses (4 Ts): terrible lymphoma, teratoma, thymoma, and thyroid tumor; incidence in childhood is 45%, 24%, 17% and 15%, respectively; most problematic tissue

is lymphoma; 68% of lymphomas are non-Hodgkin's, 3 types: undifferentiated B cell, lymphoblastic T cell, and large cell (B or T cell); lymphoblastic T cell occurs primarily in the mediastinum; younger children present with more symptoms, like superior vena cava syndrome and tracheal compression with rapid doubling time; remaining 20-40% of lymphomas are Hodgkin's; cardiopulmonary arrest may occur without warning if the tumor is rapidly doubling in size, resulting in poor prognosis; doubling time can be predicted; lymphoblastic non-Hodgkins lymphoma can double every 12 hours; Hodgkin's lymphoma and large cell non-Hodgkin's lymphoma have much slower doubling time; long-term prognosis depends on correct diagnosis and early implementation; lymphoblastic non-Hodgkins lymphoma has ≥80% 5-year survival; Hodgkins has ≥85%; large cell non-Hodgkins ~60-70%; chemotherapy is the treatment for non-Hodgkin's lymphoma, addition of radiation adds only toxicity; for Hodgkin's lymphoma, radiation or radiation plus chemotherapy in case of widespread tumor; tissue type and its location will dictate optimal treatment; 50% of the children are asymptomatic on presentation and diagnosed incidentally from chest x-ray; those with signs and symptoms are more likely to have rapidly growing tumor; signs, symptoms depend on local effects(from compression) or systemic effects if tumor is secreting; presenting features generally nonspecific — weight loss, night sweats, and fatigue, respiratory (cough, cyanosis, orthopnea, or dyspnea), or cardiovascular (eg, syncope with Valsalva [which may first occur on operating table during induction of anesthesia], headaches, dyspnea, or cough); cardiovascular signs primarily result of pulmonary artery compression; superior vena cava syndrome occurs in 50% of primary mediastinal tumors; pericardial infiltration common; preoperative echocardiogram is mandatory in all anterior mediastinal masses to ensure there is no pericardial effusion, tamponade, or constrictive pericarditis

Approach: preoperative workup difficult; patients often uncooperative, may need more than local anesthesia for diagnosis and biopsy; may need general anesthesia for radiology; preoperative investigation to determine need for general anesthetic; minor surgical procedures — eg, cervical node biopsy, Broviac, or mediastinal biopsy — may possibly be done under sedation, depending on child's age and ability to cooperate and tolerate; determining suitability for anesthesia depends on child's limitations such as ability to lie flat, respiratory and cardiovascular compromise; avoid general anesthesia with huge mass; sometimes can improve surgical situation with preoperative steroids or radiation, though these may cause tumor to involute, making it impossible to get tissue adequate for diagnosis; best case is biopsy under local anesthesia; can use sedation; may need sitting or left decubitus position; multidisciplinary meeting required with oncology, general surgery, anesthesia to determine whether surgery or radiation should be embarked upon; complications may be respiratory (tracheomalacia); radiological testing will determine tracheal compression or bronchial compression; ECMO (extracorporeal membrane oxygenation) unrealistic in most cases, especially emergencies, unless groin vessel access is obtained in advance; key issue in anterior mediastinal mass is position; gravity should be used to keep the tumor off the mediastinal organs; most common problem is pulmonary artery compression with inability to generate capnogram despite adequate ventilation; place patient in left decubitus position; if capnogram unobtainable, turn patient completely prone; in superior vena cava syndrome, keep head up, place IVs in lower extremity; anesthesia preferably induced in the left decubitus position maintaining spontaneous respiration; if cardiorespiratory problems, intubate and turn patient prone; alternately, surgeon can apply towel clips to xiphoid and sternal notch and lift child in air by sternum to lift tumor off mediastinum

Single lung ventilation (for any thoracic surgery): single lumen tube inserted into the left lung, turn head to right, rotate tube 180°; tube often goes into left bronchus; use cuffed or uncuffed tube; for right lung, do opposite without rotating tube; patency of right upper lobe bronchus important; important to have Murphy eye to cannulate the right mainstem bronchus and ensure patency of the right upper lobe bronchus; verified with fiberoptic bronchoscope; Fogarty tube used in older child up to 8 years; intubate selected bronchus, pass wire, remove endotracheal tube, pass Fogarty over wire, intubate trachea; use 5 French endobronchial blocker; Univent tubes for age >6 yrs because the outer diameter is ~7.5 mm; endotracheal tube with built-in endobronchial blocker; smaller Univents have high resistance to gas flow and aren't commonly used; double lumen tubes (size 26, or ~8 mm outer diameter) for age >8 yrs, usually left side only and verified with fiber-optic bronchoscopy

Chest wall deformities: 2 types: pectus excavatum and pectus carinatum; disorders of sternum, ribs, and cartilage; congenital and often gets worse with age; can be associated with Marfan syndrome or with cardiopulmonary issues like mitral valve prolapse, or patient can be otherwise normal; reduced vital capacity and lung capacity; possible arrhythmias and decreased stroke volume; limited exercise tolerance; preoperative chest x-ray and echocardiogram important to rule out any associated defects; surgery involves excising the sternocostal cartilage or inserting Nuss bar behind the sternum with minimally invasive thoracoscopic surgery; in some centers, thoracic epidurals placed for postoperative pain management for 2 or 3 days in addition to general anesthesia for procedure; insertion of the Nuss bar can perforate the heart, lung, or liver with potentially serious or fatal outcome

Laparoscopic surgery: very often used for pediatric surgery; cost-effective, infants resume normal feeds and discharged from the hospital earlier; inflation of gas (CO_2) into the peritoneal cavity allows surgeon to see organs in the abdomen through telescopes and cameras and perform surgery with hands remaining outside patient's body; incisions are small and the impact on organ integrity is minimal

Risk of embolism from gas: about 1/5,000 to 1/10,000; can block blood flow in organs; possibility of coronary or cerebral embolism in presence of right-to-left shunt; risk of embolism increases if intra-abdominal pressure is too high from over-inflation of abdomen, hypovolemia occurs, child starts breathing spontaneously, or layers of tissues are rendered open; laparoscopic surgery performed in children using 1-4 telescopes, sometimes single

lumen or sometimes with multiple incisions ~3mm in length; CO_2 is the most common gas injected into the peritoneal cavity 1-8 L/min; pressure developed in the abdomen is <8 mm Hg for children, and 6 mm Hg for newborns; physiologic consequences of inflating gas into the abdomen — diaphragm is splinted, tidal volume decreased, peak inspiratory pressures during ventilation are increased up to 30%; compliance decreases by 40% and the net effect is an increase in CO_2; compensatory increase in ventilation and alveolar recruitment are required; saturation may decrease but can be compensated by increasing inspired oxygen concentration (FiO2); minute ventilation must be increased as CO_2 in abdomen is absorbed into bloodstream, causing hypercapnia; since 2009, 6 cases of cardiac arrest in neonates during initiation of laparoscopic surgery, probably caused by misplacing cannula into vein in falciform ligament and injecting CO_2; CPR successful in most of these; important to be aware of the signs and symptoms of CO_2 embolism — sudden decreased CO_2 because of lack of blood flow to the lungs, decrease in blood pressure and heart rate ultimately leading to cardiac arrest

Management of gas embolism: immediately inform surgeon, stop insufflation, deflate abdomen, left decubitus positioning, hydrate head down and maintain cardiac output; CPR is sometimes beneficial in breaking up the airlock if it is in the right atrium or ventricle, but hyperventilation with 100% oxygen is preferable; if central line is present, aspiration of the line may be effective in removing CO_2 lock present in the heart; nitrous oxide is avoided at all times; in general, however, gas embolisms are rare; normal physiologic changes with laparoscopic surgery — decreasing tidal volume, increased peak inspiratory pressure, not usually problem if intra-abdominal pressure kept below 6-8 mm Hg, so if there are changes in vital signs, important to do alveolar recruitment, increase peak inspiratory pressure and tidal volume; saturation may decrease up to 5%; can increase FiO_2; end-tidal CO_2 will increase; should increase minute ventilation to compensate; note that these physiological responses can be much greater with thoracoscopic surgery; end-tidal CO_2 tends to track arterial CO_2 but may overestimate it by as much as 8-9 mm Hg; may be decreased venous return, especially if intra-abdominal pressure >15 mm Hg; substantial changes in cardiovascular signs are rare as peak abdominal pressures seldom exceed 8 mmHg; concern about patient becoming cold from CO_2 (dry gas) rarely a problem; heating the CO_2 has not been shown helpful; if brain compliance is decreased because of existing neurological lesion in patient, then consult neurosurgeon, especially if child has V-P shunt; however, modern shunts can take intra-abdominal pressures up to 80 mm Hg; If neurosurgeon concerned, however, shunt can be externalized; renal function often decreases during laparoscopic surgery because of increased intra-abdominal pressure, upregulation of ADH (antidiuretic hormone), endothelin, and nitric oxide but returns to normal right after abdomen deflation; can be complications of laparoscopic surgery in children with cyanotic heart disease, who might have right-to-left shunts; air embolism is a risk although rare and is the reason to avoid nitrous oxide; adequate preoperative hydration (10-15 mL/kg balanced salt solution) if any chance of dehydration to ensure adequate intra-arterial pressure; serious life-threatening complications are rare in pediatric laparoscopic surgery

Orchidopexy: occurs in up to 1% of 1-y.o. males; associated with myotonia congenita and sometimes inguinal hernia; due to delayed descent of the testicle into the scrotum; risk of malignancy escalates with longer duration of testicle in the abdomen; risk of postoperative nausea and vomiting, intraoperative bradycardia and laryngospasm if the anesthetic is not deep enough and airway not secure; prophylactic antiemetics are used and deep levels of anesthesia maintained if using an LMA; caudal epidural block may be used; testicular torsion, acute onset of scrotal pain without trauma, is urologic emergency; ultrasound used to establish diagnosis and assess viability of testicle; surgery performed within 6 h to save testis, <50% testicular survival rate after 6 h; anesthesia requires rapid sequence induction and endotracheal intubation because these children are assumed to have full stomachs from onset of pain

Tumors in the Abdomen

Neuroblastoma: most common extracranial solid tumor; 10% of all tumors and 15% of deaths; second most common abdominal tumor; 50% of neuroblastomas in adrenals, 30% below diaphragm, 30% in cervicothoracic region; 90% occur in the first 5 yrs of life and 50% in the first month; symptoms are the result of pressure on adjacent organs (ie, liver, kidney, spine), metastases to the lymph nodes, bone marrow, liver, or skin, or paraneoplastic neurohumoral production, eg, of catecholamines; urinary catecholamines elevated in 90%; staging — good prognostic indicators include age <18 months, extra-abdominal location, favorable histology, and no metastases; survival is 88% in age <18 months, 49% in age 18 months to 12 yrs, and 10% in age >12 yrs; treatment includes surgical excision and chemotherapy; preoperative assessment includes assessment of respiratory system and any mediastinal involvement; in case of hypertension, increased circulating catecholamines may require alpha and beta blockade; beta blockade alone may result in rebound hypertension; <3% of patients have increase in catecholamines while manipulating the tumor; risk of hypotension after tumor removal warrants use of volume and inotropes to support circulation; risk for major blood loss; IV access and cross-matched blood should be immediately available

Wilms tumor: most common intra-abdominal tumor in children; 6% of all tumors; primary finding increasing abdominal girth; 80% diagnosed in yrs 1-5 and occur bilaterally in 5% patients; arise from persistent immature parenchymal renal tissue in the periphery of the kidney, enclosed by pseudo-capsule; 12% of children have congenital anomalies (eg, aniridia, genitourinary abnormalities); associated with Beckwith–Wiedemann syndrome, horseshoe kidney, dysplastic kidneys, neurofibromatosis; other symptoms may include hypertension in 60%, hematuria 10-25%; von Willebrand's disease may be present; metastases can occur to the heart via the renal vein and also possibly to atrium, lungs, and lymph nodes; prognosis is 80% (local disease) and 50%

(metastases); oncoproteins identified as predictors of long-term survival; prognosis depends on cell type and child's age; chemotherapy, radiation and surgery may have a role depending on staging; preoperative workup includes assessment for metastases to lungs, previous administration of adriamycin (echocardiogram for assessment of cardiac contractility); children assumed to have full stomachs from the large tumor and require large IV access and arterial line; risk of massive blood loss and tumor spillage; open surgery preferred for larger tumors; no nitrous oxide; pain control and postoperative nausea, vomiting management needed

Sedation in children: history of significant risks and adverse events led to guidelines for sedation generated and adopted by the American Academy of Pediatrics and the American Society of Anesthesiology; addressed preoperative assessment of the child with mandatory consent and fasting rules for sedation; need for standardized sedation equipment and monitors, including wall oxygen and suction, pulse oximetry and capnography in addition to other standard monitors; required qualifications of individuals specifically to manage the airway should a deeper level of sedation occur than anticipated; requirement that sedationist had only the responsibility to monitor the child and not assist the proceduralist in doing the procedure; documentation of medications used, doses, child's recovery, and discharge criteria; children with comorbidities require consultation with the anesthesia department to ascertain whether level of vigilance requires more than a monitor for sedation; immediate availability of resuscitation equipment, especially in the area of the MRI scanner, where usual CPR (cardiopulmonary resuscitation) equipment cannot be brought close to the scanner; non-anesthesia providers must be approved by head of anesthesiology after assessment of their qualifications to provide sedation; areas to be evaluated include preoperative assessment, selection criteria of cases, proficiency with airway management, drug dosing and potential complications, appropriate monitoring, and ability to assess the patient's suitability for discharge; ability to pinpoint the depth of sedation in any child is very poor, as there is a great deal of interindividual variability in depth of sedation with the same drug dose; sedationist needs to be qualified to manage a level of sedation that is deeper than intended; risk of airway obstruction with over-sedation; Pediatric Sedation Consortium looked at ~50,000 sedations and found that anesthesiologist-provided sedation equally effective as that given by non-anesthesiologists given the training background and knowledge now required in order to administer propofol; sedation and quality care with few side effects can be provided in a host of different settings with properly trained sedationists

Suggested Reading

American Society of Anesthesiologists: Standards and Guidelines. https://www.asahq.org/standards-and-guidelines. Accessed November 27, 2018; **Coté CJ et al:** Adverse sedation events in pediatrics: a critical incident analysis of contributing factors. *Pediatrics* 2000 Apr;105:805-14; **Cravero JP et al:** The incidence and nature of adverse events during pediatric sedation/anesthesia with propofol for procedures outside the operating room: a report from the Pediatric Sedation Research Consortium. *Anesth Analg* 2009 Mar;108(3):795-804; **Green SM et al:** Predictors of airway and respiratory adverse events with ketamine sedation in the emergency department: an individual-patient data meta-analysis of 8,282 children. *Ann Emerg Med* 2009 Aug;54(2):158-68.

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Pediatric Anesthesia Challenges

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Pediatric airway anatomy and physiology: larger occiput in infants causes neck flexion in supine position**,** leading to airway obstruction**, especially after anesthesia induction**; large tongue-to-mouth ratio; cephalad position of larynx; omega-shaped**,** floppy epiglottis; anteriorly angled vocal cords (providing additional challenges for visualization during laryngoscopy); young children **often** have loose teeth that can be dislodged and possibly become aspirat**ed** (wiggly teeth may be electively removed **after induction of anesthesia**); careful preoperative history from parents and examination essential

Variation in pediatric airway size: children's airways have more sizes than in adults; **need** accurate measurements of oral and nasopharyngeal devices prior to insertion; posterior position of tongue in small children can worsen obstruction if oral airway too short, resulting in further backward tongue displacement; **if** oral airway too long, epiglottis may **be** push**ed** into larynx, worsening airway obstruction; aggressive mask ventilation against obstructed airway can lead to gastric insufflation, further decreasing functional residual capacity (FRC) and worsening hypoxemia (since children depend on diaphragmatic movement for air excursions during anesthesia)

Laryngoscopic blades for pediatric laryngoscopy: variety of laryngoscope blades available for pediatric laryngoscopy and intubation; **because** anterior larynx and floppy epiglottis **can** obstruct or obscure view, many anesthesiologists prefer using straight pipe blade or semicurved blade for children aged <1 yr to be able to actually lift epiglottis and expose larynx for intubation

Multiple intubation attempts: sometimes multiple (≥2) intubation attempts required; multiple intubation attempts significantly increase complication rates; alternative modes for securing airway (*eg*, laryngeal mask airway [LMA]), should be considered and made available after 2 failed attempts; better to ask for help than produce trauma and damage laryngeal structures

Laryngospasm: laryngospasm probably most feared anesthetic event in pediatric anesthesia practice (second only to cardiac arrest); problematic reflex that can occur under light general anesthesia, often encountered during induction or emergence in children; can rapidly progress to, and result in, hypoxemia, bradycardia, even cardiac arrest; may be triggered by combination of anesthetic-, patient-, or surgery-related factors

Anesthetic factors: light anesthesia at time of intense stimulus; use of potentially irritant, volatile anesthetic agents such as isoflurane or desflurane; presence of blood or secretions in airway; instrumentation of airway during light planes of anesthesia

Patient factors: young children with hypersensitive airway, such as those suffering from upper respiratory tract infection (URI) or those exposed to passive smoking have higher risk of laryngospasm

Surgery-related factors: children undergoing tonsillectomy and adenoidectomy known to have high instance of laryngospasm, probably because of manipulation around airway and possible presence of blood and secretions in pharynx during emergence

Etiology: primitive protective airway reflex that exists in awake individuals to protect against pulmonary aspiration; in conscious state, laryngeal closure reflex enables individual to regain control of airway soon after potential aspiration episode or threat gone; if laryngospasm occurs during anesthesia, patient unconscious and has no voluntary control over larynx; anesthesiologist must ensure airway patency regained

Prevention: can be prevented by attentiveness to depth of anesthesia and avoidance of known risk factors

Management: if occurs, prompt recognition and early correction of laryngospasm essential to reestablish ventilation and oxygenation; during episode of laryngospasm, glottic closure occurs either through vocal cord adduction alone or in conjunction with adduction of false vocal cords; supraglottic soft tissues may be drawn into larynx by increasingly negative translaryngeal pressure gradient that happens during obstructed inspiratory effort; this soft tissue compression of larynx can be improved by application of continuous positive airway pressure (CPAP); complete vocal cord adduction may not respond to CPAP; treatment of laryngospasm starts by opening and clearing oropharynx, applying CPAP with 100% O_2, then deepening of anesthesia, usually with intravenous (IV) propofol or, if not successful, with use of paralyzing agent (*eg*, succinylcholine) or other rapidly acting drugs; when IV access not present (*eg*, during inhalational induction), succinylcholine can be administered intramuscularly in dose of 4 mg/kg, usually in deltoid muscle for faster onset than in thigh muscle; effective communication needed with surgeon to stop any stimulation and nursing staff to provide support

Pediatric difficult airway: can often be anticipated; genetic and craniofacial syndromes affecting airway well documented and plans can be formulated prior to induction of anesthesia to ensure safe management; pediatric difficult airway practice guidelines primarily adapted from adult algorithms (*eg*, key requirement

to maintain spontaneous ventilation in children with anticipated difficult airway using medications); institutions that care for children should have variety of pediatric endotracheal tube sizes readily available; value of supraglottic airway use should be emphasized (*eg*, LMA for rescue); during emergency, cannot intubate, cannot ventilate scenario, children aged <8 yrs should undergo needle cricothyrotomy rather than emergency tracheotomy if invasive surgical airway indicated; ideally, should be performed in multidisciplinary institution with experience in managing complex pediatric airways

Examples of known difficult airways: children with Pierre Robin sequence; Treacher Collins, Goldenhar, Crouzon, and Hurler syndromes; difficulties tend to improve with age as airway enlarges; but those with Hurler syndrome tend to worsen with age as more mucopolysaccharides deposited around airway

Pierre Robin sequence example: Pierre Robin characteristics include micrognathia, glossoptosis, and airway obstruction; presentation, severity of symptoms, and functional status vary, but may exhibit evidence of respiratory distress, failure to thrive, gastroesophageal reflux, and feeding intolerance; mild airway obstruction during infancy usually managed conservatively, with lateral or prone positioning or insertion of nasopharyngeal airway; in severe cases, prolonged endotracheal intubation or surgical airway intervention, such as tongue-lip adhesion, mandibular distraction, tracheostomy, and/or gastrostomy tube placement may be required

Operative considerations for pediatric airway management: thorough preoperative assessment with emphasis on airway evaluation, signs and symptoms of airway obstruction, and review of prior anesthetic and intubation records important; operating room (OR) should be prepared with appropriate drugs and equipment including pediatric difficult airway cart; young children less likely to cooperate with awake airway instrumentation (usually reserved for neonates or mature adolescents)

Managing difficult pediatric airways: majority of difficult pediatric airways managed after induction of general anesthesia or under deep sedation; supraglottic airway device can be used electively for primary airway management; for children with anticipated difficult airways who may require early intervention, preoperative instillation of lidocaine jelly 2% preparation in pharynx and on top of tongue will allow for early insertion of oral airway or supraglottic airway device without inducing untoward airway response or laryngospasm; same technique can be used to allow for possible insertion of awake LMA, if necessary; manually pulling tongue forward may also temporarily relieve obstruction prior to securing airway; decision to use muscle relaxants or to maintain spontaneous ventilation prior to securing airway depends highly on ability to mask ventilate patient (may be successfully accomplished with insertion of supraglottic airway device); diagnostic laryngoscopy and bronchoscopy for stridor one of most common airway procedures in children; many of these procedures usually of brief duration, as anesthetic management can be challenging in small infants with already compromised airway; surgical goal usually to identify pathology and size of airway; inhalational induction with sevoflurane almost always performed; supplementation with IV agents may be necessary to maintain appropriate depth of anesthesia, prevent airway reactivity, and maintain spontaneous ventilation; total intravenous anesthesia (TIVA) technique can also be used

Pediatric bronchoscopy techniques: surgeon may attempt to examine vocal cord movements in office with fiberoptic small bronchoscope through nose; surgeons also may wish to examine laryngeal aperture and vocal cord movements, after induction, which necessitates maintaining spontaneous ventilation and keeping vocal cords moving; key to stress-free bronchoscopy in small infants, properly applied topical anesthetic in addition to light general anesthesia; topically treating vocal cords and subglottic area with local anesthetic decreases instance of coughing or barking during instrumentation, minimize chances of laryngospasm, and allow child to tolerate lighter level of anesthesia; lidocaine (usually 2% solution) most frequently used topical anesthetic; dose of lidocaine should be limited to 4 mg/kg, divided between laryngeal and tracheal surfaces, as rapid absorption via tracheal mucosa can occur; in small infant, if 2% solution would result in toxic dose, more dilute solution may be used; dexamethasone dosed between 0.3 mg/kg and 0.5 mg/kg intravenously, with maximum dose of 10 mg to 20 mg, frequently administered during procedure to decrease postoperative laryngeal swelling and possibility of croup during recovery; at conclusion of rigid bronchoscopy, uncuffed endotracheal tube often placed to allow surgeon to size larynx and control airway during recovery; sizing of larynx will occur when positive pressure of ventilation to level of 10 cm, 15 cm, 20 cm, and even 30 cm of water applied; surgeon can look for air bubbles coming around endotracheal tube with direct visualization; alternative to using endotracheal tube 100% O_2 via face mask, if ventilation adequate at end of surgery and anesthetic depth not excessive

Obstructive laryngeal papillomatosis: common airway pathology in children, generally seen in older children; obstructive or recurrent juvenile laryngeal papillomatosis presents in young child with hoarseness of voice, stridor, aphonia, history of chronic cough, and respiratory infections; current treatment mainly surgical removal of papillomatous tissue using CO_2 laser under microscopic visualization; large papillomas can be surgically debulked using ultrasonic microdebrider or cup forceps prior to laser treatment; perioperative care can be very challenging, often depending on degree of airflow obstruction and type and location of papillomas; obtain careful history, including inquiring about any changes in voice or increased difficulty breathing during daily activities (may indicate progressive airway obstruction); pedunculated papillomas can act like ball valves and can produce complete airway obstruction in certain patient positions or during anesthesia induction; surgeon must be present in OR when anesthesia induced in these children, with equipment immediately available to deal with complete airway obstruction; allow patients to maintain spontaneous ventilation until airway examined and anesthesiologist certain that assisted or controlled ventilation possible; if laser used, keep flammable objects away from path of laser beam; shield unprotected surfaces such as skin and eyes to prevent burning; apply wet towels to cover skin, face, and neck when laser being used to avoid burns from deflected beams; bowl of saline

or water also appropriate in surgical or nursing setup; anesthesia management of these children depends on approach surgeon uses to remove lesions; basic choice between intubation using laser-safe endotracheal tubes or intermittent apnea technique after airway secured using paralysis, total intravenous anesthesia techniques (TIVA), and topical lidocaine; antisialagogue (*eg*, glycopyrrolate) given at beginning, along with dexamethasone 0.5 mg/kg, with maximum dose of 20 mg, to reduce mucosal swelling resulting from repeated intubations and extubations; when surgery complete, endotracheal tube reinserted and secured until child completely awakened; postoperative measures to prevent laryngeal edema, such as racemic epinephrine inhalation and/or use of dexamethasone usually indicated in postanesthesia care unit (PACU)

Foreign body aspiration: most common in toddlers aged 1 to 3 yrs; majority of aspirated foreign bodies lodge in right mainstem bronchus; history of choking while eating or playing, resistant cough or wheezing that does not respond to medical treatment may be only presentation; most foreign bodies aspirated not radiopaque and will not show on x-ray of chest or larynx; if child cooperative and inspiratory followed by expiratory films taken and foreign body producing hyperinflation of affected side of lung, may be possible to identify which side of lung foreign body lodged in; approach to anesthetic management children will depend on level, degree, and duration of obstruction

Laryngeal foreign body: laryngeal foreign body can cause complete, sudden airway occlusion and asphyxiation if not immediately retrieved; sharp object can tear mucosa or perforate surrounding major structures; peanuts especially problematic because salty, can disintegrate and cause mucosal swelling, and may be difficult to grasp and remove; child who aspirates foreign body while eating further challenges anesthesiologist by presence of full stomach; anesthesia usually maintained with 100% O_2 and sevoflurane or propofol-based TIVA technique in these cases; combined approach of sevoflurane in O_2 inhalation as well as IV propofol or dexmedetomidine may be used; often these children have irritable airways; use of topical lidocaine 3 mg/kg to 4 mg/kg divided between larynx and tracheal mucosa may be used to suppress airway reflexes and prevent coughing and bronchospasm; use of muscle relaxants mandates positive pressure ventilation that enables lighter level of anesthesia and ensures quiet field for surgeon; when foreign body removed, forceps and bronchoscope may need to come out as unit, especially if foreign body larger than diameter of bronchoscope; airway must be adequately anesthetized so foreign body not dropped from forceps; after removal of foreign body, airway should be evaluated for any other objects and impact site assessed for trauma, bleeding, or granulations

Infectious airway obstruction in children: croup and acute epiglottitis most commonly cited causes of infectious airway obstruction in children

Croup (viral laryngotracheitis): symptom complex of inspiratory stridor, suprasternal, intercostal and subcostal retractions, barking cough, and hoarseness resulting from mucosal swelling in subglottic area of larynx; usually follows URI in young children; low-grade fever common; anteroposterior radiographs of neck confirm diagnosis, showing "church-steeple" or "pencil-tip" appearance; most cases resolve quickly with simple, conservative measures (*eg*, breathing humidified air or O_2; parents of children who have frequent episodes of croup know they can manage with cold shower or car ride in cold, humid weather; nebulized racemic or levo epinephrine administered for mild to moderate obstruction; if treatment with nebulized epinephrine unsuccessful or child becomes exhausted from increased work of breathing, relief of obstruction must be obtained through endotracheal intubation; intubation usually performed under general anesthesia, preferably in OR, sometimes in intensive care unit (ICU); uncuffed tracheal tube should be ≥1 half-size smaller than what normally would be chosen for age of child to avoid aggravating subglottic edema and causing subglottic stenosis and injury after extubation; if endotracheal tube too soft to pass easily through narrow subglottic area, dipping it in melting ice can be helpful in bypassing swollen area of larynx; since nasotracheal tubes better tolerated than orotracheal tubes and less likely to be pulled out, orotracheal tube frequently changed over to nasotracheal tube after the airway secured and depth of anesthesia confirmed; appropriate sedation in ICU minimizes chances of accidental extubation; corticosteroid therapy, such as IV dexamethasone 0.5 mg/kg up to 1 mg/kg standard of care; rapid clinical improvement in 12 to 24 hrs after steroid treatment significantly reduces need for tracheal intubation; child usually ready for extubation within 2 to 4 days; criteria to consider include abatement of fever, diminishing or change in character of tracheal secretions (becoming thin and watery), and audible air leak that develops around nasotracheal tube as edema subsides

Acute epiglottitis (supraglottitis): rarely seen in children today; can still be fatal because can produce sudden and complete unprovoked airway obstruction; all supraglottic structures become swollen and stiffened by inflammatory edema; focus of infection in supraglottic structures, but disease produces generalized toxemia; epiglottitis used to be most commonly seen children aged 3 to 5 yrs but can occur at any age; with widespread use of the *H influenzae* vaccination, incidence of epiglottitis in children has all but disappeared in medically advanced countries and has become more disease of adults; causative organisms now have expanded to include many other organisms; pediatric onset usually abrupt with high fever, severe sore throat, and difficulty swallowing; sore throat so intense that child cannot comfortably swallow, and sit up in bed drooling rather than risking painful swallowing; little or no hoarseness; child appears toxic, with flushed face, sits up leaning forward; mouth open, tongue protruding, drooling; respiratory pattern usually slow and quiet; clinical diagnosis, should not need radiologic confirmation (if done, lateral radiograph of neck show swelling of supraglottic structure and confirm diagnosis); examination of larynx and pharynx may induce complete airway obstruction and should be attempted only in area with adequate equipment and staff prepared to intervene, should upper airway obstruction develop (ideally, OR); safest, most conservative approach to managing acute epiglottitis, establish artificial airway (usually tracheal intubation) as soon as diagnosis made or strongly suspected; once airway secured, proceed

with appropriate antibiotic and supportive therapy; child should remain in sitting position at all times and never forced into supine position; unless child in morbid condition when first seen, tracheal intubation performed under general anesthesia; anesthesia induced with O_2 and sevoflurane with child still sitting up; spontaneous respiration continued as child gently allowed to recline; airway obstruction becomes more apparent but responds to gentle assistance with ventilation; since epiglottis stiff from swelling, concern about ball-valve effect completely blocking larynx with positive pressure ventilation but not seen in real life; when surgical plane of anesthesia achieved, IV access secured, and large fluid bolus infused (children often dehydrated and require deep plane of anesthesia to permit tracheal intubation while preserving spontaneous inspirations); styletted orotracheal tube inserted first and may be replaced by nasotracheal tube of appropriate size after airway established; visualization of vocal cords may be difficult because of large size of epiglottis; use of straight-blade laryngoscope, applying gentle pressure on larynx from outside, looking for air bubbles moving in and out during spontaneous ventilation, will help guide anesthesiologist to where laryngeal opening should be; once airway secured, obtain pharyngeal and blood cultures and administer cephalosporins; when child resumes swallowing and fever abates (usually in 24-48 hrs), acute supraglottic edema should be resolving and child may be prepared for tracheal extubation

Implications of providing anesthesia in non-OR locations (NORA): recent advances in diagnostic radiology and imaging studies have made them important part of preoperative workup for many surgical patients; majority of studies brief and cause no discomfort; some long and require total immobility for prolonged periods; other studies can be painful or extremely uncomfortable and require sedation or analgesia for all children; in many institutions, anesthesiologists provide essential service for children undergoing radiologic diagnostic and/or therapeutic procedures; those services include anesthesia, deep sedation, sedation analgesia, and supervising provision of other types of sedation administered by radiology staff

Magnetic resonance imaging (MRI): one of most challenging remote-location procedures requiring anesthesiologist involvement; examination painless but requires total immobility for 30 to 90 mins; cold and harsh environment, magnet produces loud noise, and child placed inside tube that can cause severe claustrophobia; general anesthesia and/or deep sedation required in most children aged <6 yrs and in some adolescents

Challenges of anesthesia in MRI environment: radiology suite often located far from the OR environment and PACU; anesthesiologist often alone; room cold, patient inaccessible, strong magnetic field disables normal anesthesia monitoring systems and radiofrequency can cause burns, *eg*, if ECG wires crossed and become overheated; many newer MRI systems have strong magnetic fields that may cause unknown long-term biologic changes; American College of Radiology designates 4 zones in MRI suites correlating with intensity of magnetic field; radiology staff and anesthesia personnel should monitor patients remotely using compatible monitoring equipment and video systems; choice of anesthesia or deep sedation techniques vary among practitioners and institutions, from general inhalation anesthesia with oral endotracheal intubation or LMA; MRI-compatible anesthesia machines that can be placed inside scanning room must be used; add-on accessories to machine also MRI compatible and nothing can be inadvertently placed on machine (*eg*, oxygen tanks, laryngoscopes); American Society of Anesthesiologists (ASA) has practice advisory for emergency situations within MRI environment; in case of cardiac or airway emergency, child should be brought out of magnet immediately to previously designated adjacent location for resuscitation equipment to be used; proper training and monitoring essential to prevent or treat oversedation and ensure child's safety

Sedation or anesthesia for pediatric MRI: propofol deep sedation or anesthesia with natural airway supplemented with nasal O_2 administration common choice; brief period of general anesthesia started in induction area outside scanning room using inhalational NO_2 and sevoflurane until IV line established; in older children, IV can be started directly with help of skin analgesia (*eg*, with lidocaine and prilocaine cream [*eg*, EMLA, Dermacin, Relador] or lidocaine and tetracaine [Rapydan, Synera] patch) followed by induction dose of propofol, usually 1 mg/kg or 2 mg/kg; lidocaine and tetracaine patch has ferromagnetic heating component and should be removed prior to patient entering magnets; when sedation maintained with propofol, most children require initial infusion rate of 150 mcg/kg/min up to 300 mcg/kg/min or 400 mcg/kg/min, for first ~10 mins; even with this dose, many children respond to mild stimulation; with escalation of propofol dosing or administration of supplementary medications such as midazolam or dexmedetomidine to limit movement, many children in state of general anesthesia and must be monitored accordingly; reports of children requiring infusion rate of 75 mcg/kg/min to 100 mcg/kg/ min of propofol not reproducible in clinical practice unless residual inhaled anesthetics still present

Ventilation needs in MRI: spontaneous ventilation with natural airway usually adequate in children with normal airway anatomy; nasal cannula to supply supplementary O_2 (1-2 L/min) and also to monitor exhaled CO_2 continuously; ECG monitor should be carefully placed using pads to minimize risk of overheating leads and wires if they cross; children with large adenotonsillar hypertrophy or with impaired muscle tone may require careful head and neck positioning and may benefit from small roll under shoulder to keep airway patent; use of oral or nasal pharyngeal airway lubricated with lidocaine jelly may improve airflow through pharynx and limit head bobbing that can interfere with imaging quality; in some difficult cases, use of LMA or tracheal intubation may be required; can be connected to MRI-compatible anesthesia machine that delivers O_2 and sevoflurane, or similar option to deliver O_2, if propofol chosen anesthetic

Alternative management options: various adjuncts have been tried to reduce dose of propofol needed to prevent

movement; use of small (0.5 mg/kg or 1 mg/kg) boluses of midazolam or ketamine at beginning of scan can be effective in reducing required dose of propofol and will not significantly delay recovery time; deep sedation with propofol can easily progress into general anesthesia; practitioner must be constantly aware of that possibility and be prepared, trained, and equipped to rescue patient from general anesthesia; ASA guidelines state propofol should be administered only by or under direct supervision of anesthesiologist; alternatives to propofol have been introduced; recent experience with IV dexmedetomidine have shown it to be effective, but maybe less predictable than propofol and may require frequent dose escalation and supplementation to prevent movement

Other areas of concern during MRI examination: protect ears from loud banging noise that can produce temporary hearing loss; risk of hypothermia in extremely cold environment or increasing cold temperature in longer scans; contrast administration during MRI, usually gadolinium, can be concern in children with impaired renal function

Computed tomography (CT) scan considerations: CT scans very fast; most healthy children can be sufficiently cooperative and easily comforted to undergo CT scans without sedation; presence of parent, warm blanket, or recent feeding can be helpful; use of minimal sedation techniques with rectal chloral hydrate or midazolam may be required; attention to airway patency and monitoring of O_2 saturation and ventilation essential; if study with IV contrast planned, use of topical anesthesia to start IV warranted; occasionally use of oral contrast required to perform abdominal CT examination, which poses challenge to management, since child given large volume of oral contrast equals child with full stomach; some anesthesiologists perform rapid-sequence intubation to secure airway, following ingestion of contrast; alternatively, patients can be anesthetized and intubated first, followed by insertion of orogastric tube, through which contrast slowly introduced into gastrointestinal (GI) system; use of IV metoclopramide may hasten movement of contrast through GI system and greatly reduce waiting time for full viewing from standard 60 to 90 mins

Suggested Reading

Coté CJ et al: Guidelines for monitoring and management of pediatric patients before, during, and after sedation for diagnostic and therapeutic procedures: update 2016. *Pediatrics*. 2016;138(1); **Deen J et al:** Challenges in the anesthetic management of ambulatory patients in the MRI suites. *Curr Opin Anaesthesiol*. 2017;30(6):670-5; **Ferrari LR:** Updates in pediatric anesthesia. *Curr Opin Anaesthesiol*. 2016;29(3):325-6; **Harless J et al:** Pediatric airway management. *Int J Crit Illn Inj Sci*. 2014;4(1):65-70; **Karsli C:** Managing the challenging pediatric airway: continuing professional development. *Can J Anaesth*. 2015;62(9):1000-16.

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Anesthesia for Pediatric Neuromuscular Diseases

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Primary Muscle Diseases

Muscular Dystrophies: 4 Types

Duchenne's muscular dystrophy (DMD): occurs with X chromosomal deletions (most common) and point mutations or small insertions; prevalence of about 1 in 3500 male births; rare in females; 90% of patients have family history of muscular dystrophy; 10% occur sporadically; presents in children age 2-6; manifests as proximal muscle girdle weakness and Gower's sign (difficulty straightening from squatting position); diagnostic test is muscle biopsy with absence of dystrophin; random CK level is often 5000-150,000; dystrophin an integral part of the cytoskeleton, reinforcing the myoskeleton and is present in skeletal muscle, heart, and brain; in children with Duchenne's muscular dystrophy, the concentration of dystrophin is <3% of normal; without dystrophin, muscle is fragile and tears easily, releasing intracellular contents that include potassium, CK, and myoglobin; there is no specific treatment for Duchenne's muscular dystrophy, except steroids (given with inflammation), gene therapy (under investigation), and cardiorespiratory support

Children <10 years: muscle is degrading, fragile, and susceptible to breakdown due to lack of dystrophin; disease is characterized by fatty infiltration of muscle leading to pseudo-hypertrophy, especially in calf muscles; children usually present with muscle degradation for muscle biopsy; as a result of instability and degradation of muscles, their response to inhalational agents, and succinylcholine, may lead to rhabdomyolysis, release of muscle intracellular components, hyperkalemia, and cardiac arrest; inhalational agents are not commonly used in this age group, and succinylcholine is generally prohibited

Children >10 years of age: diagnosis has often already been confirmed; muscle degradation has usually ceased; children most commonly present for surgery to maintain a sitting position or correct scoliosis and prevent progressive respiratory dysfunction; primary complication associated with anesthesia is cardiomyopathy, arrhythmias, or cardiac arrest; preoperative echocardiogram important before general anesthesia to assess for cardiomyopathy

Anesthesia: DMD not associated with malignant hyperthermia; clinical approach begins with age-related preoperative assessment, including organ system evaluation (DMD is multisystem disease) and any laboratory testing; avoid any drugs that may precipitate rhabdomyolysis, including succinylcholine and potent inhalational agents

Technique: subject of debate; many prefer total IV anesthesia; inhaled agents have been used in the past without difficulties, but there is risk of Halothane — triggered rhabdomyolysis; may be a less common occurrence with newer anesthetic agents such as Sevoflurane; airway support depends on the severity of lung disease, but muscle relaxants should be used judiciously because of the muscle wasting present, potential for protracted weakness, and difficulty extubating; opioids similarly may have respiratory depressant effect out of proportion to child's size — may be a manifestation of undiagnosed underlying obstructive sleep apnea (OSA); children with Duchenne's muscular dystrophy may be at risk for increased bleeding due to defective vascular endothelium; some recommend treatment with Amicar; use of antifibrinolytics should be discussed during the perioperative period

Hyperkalemia: one review of children with undiagnosed muscular dystrophy who arrested following succinylcholine administration and a hyperkalemic reaction showed 30% mortality; calcium is the definitive treatment to reverse hyperkalemic response to succinylcholine; whenever succinylcholine is administered to any patient, especially those who present with hypotonia or in an emergency situation, confirm calcium chloride or calcium gluconate is immediately available to be administered IV; a single dose of calcium may transiently return the electrocardiogram to a normal sinus rhythm, but the ongoing muscle degradation and slow release of potassium from torn muscle cells may then cause a recrudescence and prompt a need for a second dose of IV calcium; for children <10 years of age whose muscles continue to degrade, some recommend preparing the anesthesia workstation as in malignant hyperthermia and washing out inhaled agents to prevent rhabdomyolysis — not malignant hyperthermia — from occurring; malignant hyperthermia is not associated with muscular dystrophy; it is just as easy to insert a charcoal filter on inspiratory limb of the breathing circuit and proceed with anesthetic; there are no cases of rhabdomyolysis triggered after an anesthetic machine has been flushed

Becker's muscular dystrophy: milder form of Duchenne's muscular dystrophy; much less frequent occurrence in the

population — about 1 in 40,000 cases; later onset, in the second decade

Emery-Dreifuss: X-linked disorder afflicting primarily males; occurs with a later onset in the second decade; milder form of muscular dystrophy compared to Duchenne's; caused by absence of emerin and laminin instead of dystrophin; these are intracellular components of the cytoskeleton and structure of muscle cells; manifestations are primarily conduction defects, and patients may present with syncope; less likely to manifest in a cardiomyopathy

Limb-girdle dystrophy: results from a mutation in the sarcoglycan component of muscle cell; affects primarily the shoulder and hip muscles, leading to respiratory effects and possibly cardiac conduction difficulties; symptoms are muscle weakness, atrophy of the muscles, myoglobinuria, increased serum CK, and in 20% of patients, a cardiomyopathy; onset is between 10-30 years of age, with an equal prevalence in both males and females; inherited mostly as an autosomal recessive gene defect, with progression which leads to patient requiring a wheelchair by 20-30 years of age

Anesthesia in limb-girdle dystrophy: avoid succinylcholine and non-depolarizing agents because of variable response; no risk of malignant hyperthermia but a possible risk of rhabdomyolysis in response to inhaled agents; many advocate a total IV anesthetic technique and flushing the anesthetic machine to remove trace concentrations of inhaled agents, although this is not an evidence-based recommendation

Mitochondrial Myopathies

Mitochondrial disorders: represent abnormalities of the mitochondrial respiratory chain; many and varied clinical manifestations, affecting eyes, brain, heart muscles, kidney, liver, and pancreas; due to fact that 5 respiratory chain complexes of mitochondria are under bigenomic control; 85% are the result of nuclear DNA and 15% are under control of mitochondrial DNA; nuclear DNA is responsible for Mendelian inheritance and is the source of many mitochondrial myopathies affecting children; mitochondrial DNA follows a maternal inheritance pattern 90% of the time, resulting in manifestations in adulthood; histologically**,** red ragged fibers are classic finding; intracellular crystalline inclusions seen on electron microscopy; identified genetic markers are not all fully characterized; plasma CK tends to be normal, although lactic acid may be increased; defects in complexes one, four, and combinations of paired respiratory complexes in the mitochondria in children, leading to the varied manifestations

Identified syndromes: Kearns-Sayre syndrome has an onset between 5-15 years and affects primarily the eyes and cardiac conduction system; may include cardiomyopathy; MELAS syndrome (mitochondrial encephalopathy with lactic acidosis and stroke-like syndrome) occurs later in childhood with primarily neurologic findings, although cardiac conduction defects and cardiomyopathy may also be present; particular names and terms reflect organ systems generally affected; clinician faced with host of possible abnormalities; central nervous system (CNS) effects may include seizures, ataxia, stroke; myopathies may lead to hypotonia, limited exercise tolerance; respiratory complications may include aspiration, pneumonia; cardiac complications mentioned above; hepatorenal disorders; anemia, GI disorders, hearing loss; no cure and very little treatment

Anesthetic considerations: most anesthetics depress respiratory chain in mitochondria; inhaled agents suppress complexes one and two; propofol suppresses complexes two and five and carnitine palmitoyltransferase; there is little evidence children with mitochondrial myopathies are at greater risk for propofol infusion syndrome, despite what has been stated by many neurologists; effect of muscle relaxants on children with mitochondrial myopathies unpredictable; all anesthetics have been used, in most cases without reactions; some recommend using a primarily non-inhalational, non-propofol anesthetic — involving dexmedetomidine, midazolam, nitrous oxide, and remifentanil; not an evidence-based recommendation, but may represent best combination of available drugs, particularly if the neurologist has informed parents their child should not receive inhaled agents and propofol, a restriction which makes it difficult to administer an anesthetic; try to avoid stress and avoid hypoglycemia; use local anesthetic, maintain thermal homeostasis and avoid tourniquets and pressure

Other considerations: effects of muscle relaxants in children with mitochondrial myopathies are unpredictable; it is not necessary to flush the anesthetic machine in the anesthetic management of children with mitochondrial myopathies because there is no risk of malignant hyperthermia or rhabdomyolysis; do a thorough preoperative assessment to assess the level of multi-organ involvement; specifically to determine whether heart is involved; those with lactic acidosis (>90% of children with MELAS) should undergo a brief fast and have a glucose infusion provided (if not on a ketogenic diet to prevent seizures), and not receive any lactated Ringers-containing solutions

Channelopathies

Definition: a heterogeneous group of disorders that affect sodium, potassium, chloride, and calcium ion channel function in muscle cell membranes; ion fluxes across membranes change with depolarization, and lead to varying degrees of muscle contraction, sustained muscle contraction, or failure of the muscle to relax; many of the disorders involve myotonia; manifestations depend both on the genetic predisposition and environmental and drug factors; types include chloride channel myotonias (myotonia congenita), sodium channel myotonias (most common is paramyotonia congenita), dyskalemic episodic paralyses (including hyperkalemic periodic paralysis), and calcium channel release channelopathies (associated with malignant hyperthermia)

Congenital myotonia: due to a decrease in chloride conductance; two forms are autosomal dominant (begins in infancy) and autosomal recessive (begins later, by the second decade and is often the more severe form); triggers for muscle contraction include succinylcholine, possibly propofol, direct strike on the skin over the muscle, cold, and stress; there are some instances where controlling the onset of a myotonic response is not possible; mutation coding for this chloride 1 channel defect is on chromosome 7; failure to stabilize and repolarize the muscle membrane; numerous associated mutations

Becker disease: recessive form often of greater clinical significance; onset is beyond the age of four years; affects lower limbs more than upper limbs, with transient weakness at beginning of muscle contraction; severity is moderate to severe with mild to obvious muscle hypertrophy; no predilection for one gender

Anesthesia: avoid succinylcholine, reduce dose of neuromuscular blocking drugs (particularly if muscle wasting is present); and muscle function monitoring mandatory; cisatracurium, or an atracurium-like muscle relaxant that undergoes spontaneous degradation is preferable, although with sugammadex, any muscle relaxant could be used and reversed; consider sugammadex or a muscle relaxant that undergoes spontaneous degradation, because anti-cholinesterase agents themselves may predict a myotonic response; to minimize the possibility of myotonia, maintain normal temperature to avoid shivering

Myasthenic syndromes: occur infrequently in the population — between 1/200,000 and 1/1,000,000); represent autoimmune disorder with antibodies against the nicotinic acetylcholine receptors in the postsynaptic membrane in >80% of cases; remainder have antibodies that bind to specific protein kinases; effectively, there are reduced acetylcholine receptors available for activation; children present with muscle weakness and fatigue; thymus may be a source of auto-sensitization; thymectomy has been used as a treatment modality; extraocular muscles are often involved in the first year; presentation with ptosis and diplopia that may become generalized by 1-3 years; three myasthenia syndromes appear in childhood — neonatal myasthenia syndrome, congenital myasthenia, and juvenile myasthenia syndrome

- Neonatal myasthenia syndrome: transient weakness due to passage of antibodies from myasthenic mothers across the placenta; usually resolves in 1-3 weeks on treatment with pyridostigmine
- Congenital myasthenia: onset in the first two years of life; more commonly found in males than females; has an autosomal recessive inheritance pattern; non-fluctuating and compatible with long-term survival
- Juvenile myasthenia syndrome: autoimmune disorder; later onset — 2-20 years; predominance in females over males in a 4:1 ratio; thymus hyperplasia; slowly progressive disorder with tendency to relapse before going into remission
- Management: follows a three-pronged approach; enhance neuromuscular transmission through use of anticholinesterases; suppress the immune response by administering steroids and other anti-inflammatory agents; plasmapheresis to decrease number of circulating antibodies; if generalized weakness persists despite medical management, thymectomy is recommended (benefits 96% of patients)
- Anesthesia: optimize preoperatively with a plasmapheresis session close to time of surgery; stop anticholinesterases if the patient can tolerate, tapering steroids up to the time of surgery; response to muscle relaxants can be unpredictable; effect of succinylcholine on neuromuscular blockade is unpredictable; patients seem to be particularly sensitive to non-depolarizing agents; avoid these agents and use predominantly inhaled agents for relaxation for surgical incision; some prefer to titrate non-depolarizing muscle relaxants and use a balanced anesthetic technique with regional anesthesia; a rapid sequence induction with propofol and remifentanil may be performed in emergency situations; in the postoperative period, respiratory failure has been reported; it is more predictable based on bulbar involvement preoperatively, and if there is severe bulbar involvement, anticipate respiratory failure may occur; if the patient has had previous respiratory failure after anesthesia or the patient depends on steroids for muscle strength, plan to give supplemental steroids during the anesthetic

Cerebral Palsy (CP)

Description: a group of permanent disorders of movement and posture; motor disorders and disturbances of sensation, perception, cognition, communication, and behavior, as well as epilepsy and musculoskeletal anomalies, complicate the disorder; attributed to non-progressive disturbances, particularly occurring in fetal or infant brain; precise etiology has not been determined; causes have been linked to perinatal ischemic stroke in 22%, congenital malformations in 15%, white matter disorders in 12%, and intrauterine exposure to inflammation in 12% (result of an unrecognized sibling in utero that died early in the pregnancy and underwent involution, triggering an inflammatory response) of cases

Diagnosis: clinical diagnosis; no laboratory test to confirm; predicated on physical examination; usually requires a child to be >18 months; incidence is strikingly high at about 1 in 500 live births; may occur as frequently as 1 in 10 births for infants <28 weeks gestational age; occurs more frequently in the premature baby — the younger the gestational age, the more likely; occurs more frequently in multiple gestations or if parturient is febrile (7-fold increased incidence); postnatal steroids increase the risk, as well as antenatal administration of magnesium

Presentation: highly variable, with a great deal of interindividual variability in motor development — may lead to over- or under-diagnosis, especially since neurologic development is so variable in infancy; may be categorized into four different groups — spastic, dyskinetic, ataxic, and mixed

- Spastic form: lesions in cerebrum; includes quadriplegia, diplegia, and hemiplegia
- Dyskinetic form: lesions in basal ganglia; includes dystonias and athetosis
- Ataxic form: lesions in cerebellum; tremors and loss of balance and speech
- Mixed form: complicated by lesions in both cerebrum and cerebellum; spasticity and athetoid movements

Preoperative evaluation: requires enumeration of medications, which may be extensive; standard pregnancy test; in a system review, focus on the respiratory system, looking for chronic aspirations, sialuria, scoliosis, gastroesophageal reflux, and presence of a gastrostomy (G)-tube; look for presence of spasticity and epilepsy (which occurs in about 30%); keep in mind, however, that many affected children are of normal intelligence, and do not underestimate; contractures cause difficulty in positioning and protecting skin from breakdown; if ulcers are present, pad and protect to avoid infection; if child

has undergone previous surgeries, examine charts to find out how the anesthetics were conducted, and discuss with parents their level of satisfaction or concern

Anesthesia: there are predictable alterations in responses to medication in CP; the ED50 (dose that produces desired effect in 50% of patients) for propofol is reduced in these children; succinylcholine, in contrast to other muscle diseases, may be used safely; this is a nervous system disorder, not a muscle disease, and has not been associated with a hyperkalemic response; non-depolarizing agents should be titrated carefully because patients may have poorly developed muscle; inhalational agents and opioids are all safe to use; the minimum alveolar concentration (MAC) of halothane has been shown to be 25% less in children with cerebral palsy; patients are poikilothermic and very susceptible to hypothermia; have very poor shivering responses; use a bear hugger from the moment the child comes in the room and warm the room up to aggressively control their temperature; some may be chronically dehydrated — hypotension is the second most common complication; ensure an adequate fluid load is given before inducing anesthesia; aim airway management at reducing risk of endobronchial intubation, as patients may have scoliosis and be contracted; proper positioning of the tube is mandatory; it is possible patients are coagulopathic due to platelet abnormalities and/or nutritional deficiencies; children who may have to undergo major surgery may benefit from doses of DDAVP (desmopressin) and/or an antifibrinolytic

Pain management: sometimes neglected in children with physical disabilities; while they may perceive pain, some are not able to use a patient-controlled analgesic (PCA) pump; multimodal pain management is preferable, recognizing that opioid dosing is less in children with cerebral palsy than in those without; epidural analgesia works effectively to control pain; PCA pumps may be effective, although nurses or parents may be needed to administer the boluses

Malignant Hyperthermia (MH)

Epidemiology: between 1 in 15,000 and 1 in 30,000; occurs more frequently in children than adults; associated with central core disease and King-Denborough syndrome myopathies; review suggested cardiac arrest rate from malignant hyperthermic reaction was 2.7%, with death occurring in 1.5% of cases; high rates need to be addressed by identification of a reaction and appropriate intervention

Cause: disorder triggered primarily by anesthesia; associated with a high incidence of fatality; result of a pharmacogenetic dysregulation of calcium metabolism in muscle

Genetics: follows autosomal dominant inheritance pattern with variable penetrance; gene defects include at least six mutations that code for MH susceptibility; ryanodine receptor on chromosome 19 — responsible for calcium flux defect in up to 70% of patients; sodium channel on chromosome 17; calcium channel CACNA2D1 present on chromosome 7 accounts for only 1% of MH susceptibility; several other defects, which account for <10% of cases of MH; may be gene defects that have not yet been identified

Diagnosis: the caffeine halothane contracture test is gold standard for diagnosis; gene testing may follow; with no caffeine halothane contracture test performed, only 20% of patients are positive for a known gene defect; in those who test positive to the caffeine halothane contracture test, only 60% are positive for a known gene defect, pointing to probability that many gene defects not yet identified

Anesthetic agents that trigger a malignant hyperthermic reaction: two groups — depolarizing muscle relaxants (typified by succinylcholine) and inhalational agents; among the inhalational agents, halothane is most likely to trigger an MH reaction, followed by isoflurane, enflurane, and sevoflurane; sevoflurane and desflurane are weak triggers; agents that do not trigger MH reaction include nitrous oxide, opioids, benzodiazepines, alpha-2 agonists, and xenon

Who needs trigger-free anesthetic? patients with a prior MH reaction themselves, a patient in whom a blood relative had an MH reaction, patients with central core disease or King-Denborough syndrome, and person who has had heatstroke with rhabdomyolysis (some are positive for the ryanodine receptor)

Preparation for elective surgery: complete history and physical examination, including documentation of the proband from the MH reaction and conditions under which reaction occurred; often histories are vague — have to assume it is an accurate story of a malignant hyperthermic reaction; on the day of surgery, it is preferable the case is the first of the day, because concentration of inhaled agent in room is low and inhalational agents have not been used in it for preceding 8-12 hours; if anesthesia workstation is not a workstation designated for use in MH patients, either flush contaminated machine for a period of time and/or use a charcoal filter with a new absorbent and circuit; once machine is flushed, do not reduce fresh gas flow, because trace concentration of inhaled agent may increase afterward

Operative management: MH susceptible patients do not benefit from prophylactic dantrolene; premedicate the patient as appropriate, using a nitrous oxide total IV anesthetic technique with regional anesthesia if appropriate; ventilation is often controlled; use standard monitors, including a temperature monitor, to evaluate both core temperature and temperature in muscle groups such as in the axilla

Post-op: patients who have undergone a trigger-free anesthetic, and who are known to be MH susceptible, still have about a 0.5% incidence of a MH reaction; these patients should be monitored throughout the operating period and in the postoperative period for several hours; the probability of a reaction after surgery is exceedingly small; patients may be monitored for two hours afterwards, and then they should be given instructions about what to monitor and whom to contact should parents observe change in child's demeanor, fever nonresponsive to acetaminophen, or tachypnea

Signs of acute malignant hyperthermic reaction: early signs include jaw and body rigidity, tachypnea, a hot soda lime canister, and tachycardia; the increased end tidal CO2, tachypnea, and tachycardia are monitored responses that reflect acidosis in muscle; intermediate signs include a warm body, cyanosis, and an irregular pulse rate; late signs include generalized rigidity, coagulopathy, dark urine from myoglobinuria, oliguria, hemodynamic instability, ventricular tachycardia, and death

Differential diagnosis: first consideration is MH; ensure ventilation has been adequate and hypercapnia or

tachypnea are not iatrogenic, there is no external heat source heating the patient, and no sepsis is present from any pre-existing or intercurrent infection; patients with osteogenesis imperfecta develop hyperthermia under anesthesia, and this reaction may be confused with MH; thyroid storm or a pheochromocytoma may share some of the presenting signs of an MH reaction; drug overdose, ischemia, and neuroleptic malignant syndrome are included in differential but often can be eliminated

Treatment: discontinue any triggers; replace the circuit and machine as needed or put in a charcoal filter to stop exposing the patient to triggers; switch to a trigger-free anesthetic and total IV anesthetic technique; prepare IV dantrolene, which is given as a bolus of 2.5 mg/kg; repeat this dose if reaction continues and continue giving dantrolene as quickly as possible until reaction stops; there is no maximum dose of dantrolene to stop MH reaction; sample both venous and arterial blood for blood gases and a baseline CK to allow a comparison with subsequent blood testing; hyperhydrate the patient, insert a urinary catheter, and test urine for myoglobin; ice is not needed; important to note that after 6 to 7 hours, it is possible that a recrudescence of the reaction will occur, and dantrolene may need to be re-dosed

Dantrolene: standard preparation is 20 mg in a vial that takes one to two minutes to dissolve in 60 mL of sterile water; also has 3 g of mannitol and a pH of 9.5, which is why thrombophlebitis has been reported as a complication from dantrolene; pain on injection, thrombophlebitis, venous occlusion, muscle weakness are all known side effects from single loading dose of dantrolene to treat an MH reaction; chronic use of dantrolene may lead to liver dysfunction; newer formulation of dantrolene. called Ryanodex, has been approved by the FDA; Ryanodex is 20-30 times more soluble than dantrolene in water and comes in a vial containing 250 mg, for which only 5 mL of sterile water is required to dissolve; the entire vial only contains 125 mg of mannitol, a far smaller dose of mannitol than in the previous preparation

2010 Malignant Hyperthermia Association review: found almost 50% of reactions occurred in patients <19 years of age; 75% of patients were males; only 6.5% had family histories of MH; many families who have malignant hyperthermia have been identified, and therefore many reactions observed are sporadic mutations; signs of MH reactions were primarily an increased end-tidal carbon dioxide associated with tachycardia and masseter muscle rigidity; 99% of patients had a respiratory acidosis, but only 26% had a metabolic acidosis; average dose of dantrolene administered was 5.9 mg/kg, but some patients did not receive dantrolene; complication rates depended on promptness of treatment; there were almost three times the incidence of complications for every two-degree increase in temperature, and 1.6 times the complications for every 30 minutes of delay in giving dantrolene; thus, if MH is suspected, it is important to treat patients promptly to minimize risk of complications

Post-reaction: patient should be monitored in ICU, particularly if they are weak, intubated, and sedated; if they are strong, they may be extubated, and their laboratory tests and vital signs are monitored for the next 24 hours; monitor them until the venous or arterial blood gases have returned to normal and the CK level has returned to normal; usually the CK level peaks at about 12 hours after a reaction; for a true MH reaction, the peak blood level of CK should be >20,000; urine must be continually tested for presence of myoglobin, and ample hydration continued until the myoglobin disappears; dantrolene should be available to treat a recrudescence of the reaction; in one report up to 20% of 300 patients who had MH reactions developed a recrudescence; time interval from initiation of original MH reaction until recrudescence was 13 hours; multivariate analysis looking at what factors predispose to a recrudescence included muscle build, how high the temperature was, and the time interval from induction to the MH reaction

Follow-up: communication of diagnosis in letter form to the family; identify triggers; family counseling regarding blood relatives; patient with reaction should subsequently wear a medical bracelet that says “malignant hyperthermia susceptible;” screening tests for muscle biopsy should be done; referral should be made to an MH center

Suggested Reading

In J et al: Incidence of malignant hyperthermia in patients undergoing general anesthesia: Protocol for a systematic review and meta-analysis. *Medicine* 2017 Dec;96(49); **Katz JA et al:** Anesthetic consideration for neuromuscular diseases. *Curr Opin Anaesthesiol* 2017 Jun;30(3):435-40; **Shaikh SI et al:** Role of anesthesiologist in the management of a child with cerebral palsy. *Anesth Essays Res* 2017 Sep;11(3):544-9.

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Anesthesia for Orthopedic Surgery

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Concomitant diseases in adults: adults undergoing orthopedic procedures often have significant concomitant diseases; profound impact on anesthetic management, outcomes; population >65 y growing, and may well have orthopedic procedures; preoperative assessment of especially heart, lungs, kidneys, nerves, including preexisting neurological conditions, joints, endocrine system, current list of medications, especially antihypertensives, chronic opioids, thromboprophylaxis, critical for anesthetic plan; older age significant risk factor for poor outcome following orthopedic surgery; most frequent perioperative complications related to cardiovascular system, respiratory system, neurological system; postoperative complications confusion, delirium; orthopedic surgery often result of concomitant disease, especially rheumatoid or osteoarthritis

Rheumatoid arthritis: chronic inflammatory condition; 1% of adult population; inflammation of synovium; symmetric polyarthropathy; significant systemic involvement, including cervical spine, leads to decreased range of motion of neck and atlantoaxial subluxation; temporomandibular joint and cricoarytenoid joint cause decreased mouth opening, narrow glottic opening, suggested by preoperative hoarseness or stridor; may need video laryngoscope or fiber-optic scope for intubation due to decreased range of motion of neck, limited mouth opening; cardiovascular system also involved, 30% of patients have pericardial effusions, myocarditis, conduction abnormalities, aortic regurgitation, valvular fibrosis; in pulmonary system pleural effusions, pulmonary fibrosis, restrictive lung disease due to costochondral involvement, ventilation-perfusion mismatching, hypoxemia; peripheral neuropathies due to nerve compression; anemia of chronic disease; patients often on nonsteroidals (NSAIDs), including aspirin; potential for GI bleeding, impaired platelet function, diminution of renal function; may be on corticosteroids, and may require perioperative steroids; disease-modifying antirheumatic drugs (DMARDs) include methotrexate, sulfasalazine, minocycline

Osteoarthritis: most common joint disease in US; degeneration of articular cartilage, minimal inflammatory reaction or systemic involvement; medications include acetaminophen, NSAIDs, corticosteroid injections

Ankylosing spondylitis: chronic inflammatory disease, involves sacrolumbar spine with subsequent cephalad progression; temporomandibular joint (TMJ) involvement; can result in fixed immobile spine; onset early adulthood; more males than females; may require use of video laryngoscope or fiber-optic scope for intubation, intraoperative controlled ventilation; other associated conditions are cardiac conduction abnormalities, aortic insufficiency, pleural effusions, upper lobe parenchymal disease, uveitis; treatment with physical therapy, stretching, NSAIDs, immunosuppressive drugs, steroids

Concomitant diseases in children: trauma, congenital abnormalities, certain syndromes, neuromuscular disease, spinal deformities most common for orthopedic intervention; careful preoperative evaluation especially important for patients with neuromuscular disease, syndromes, or scoliosis

Cerebral palsy: non-progressive disorder of movement and posture; motor weakness, poor muscle control, increased motor tone, contractures, possibly developmental delay, seizure disorders; interventions are tendon releases, hip reconstruction, spinal fusions; anesthetic concerns are aspiration, secretions, chronic lung disease, obstructive sleep apnea (OSA); after removal of endotracheal tube, upper airway obstruction can occur; seizure management, IV access can be concerns

Arthrogryposis: non-progressive joint contractures, rigidity of all limbs; normal intelligence; patients present for tendon releases, hip reconstruction, spinal fusions; concerns include difficult intubation due to micrognathia, short rigid neck, decreased mouth opening; prone to upper airway obstruction; 10% of children have congenital heart disease; pulmonary hypertension and gastroesophageal reflux common; difficult IV access due to contractures

Craniofacial diseases: Apert syndrome, Crouzon disease; craniosynostosis and multiple facial anomalies; may have increased intracranial pressure; present often for syndactyly repair; anesthetic concerns include difficult mask ventilation due to facial anomalies; difficult intubation due to mandibular hypoplasia, decreased range of motion of neck; prone to upper airway obstruction, OSA; some have congenital heart disease

Myopathies: first, Duchenne's muscular dystrophy, hereditary progressive degeneration of skeletal and cardiac muscle; patients present for tendon release and spinal fusions; concerns are respiratory insufficiency, presence of cardiomyopathy; must use care with myocardial depressants; may have succinyl-induced hyperkalemia or rhabdomyolysis from exposure to inhalational agents; possible susceptibility to malignant hyperthermia (MH); second, myotonic dystrophy,

hereditary, degenerative disease of skeletal muscle involving myotonia (persistent muscle contraction after voluntary muscle contraction); patients present for tendon release; concerns are respiratory insufficiency, cardiomyopathy, increased sensitivity to respiratory depressants; regional anesthesia effective, beneficial; avoid succinylcholine due to potential of prolonged muscle contractions

Regional Anesthesia

In adults: often done in procedures that involve upper extremities; peripheral nerve block, nerve plexus block, neuraxial block; ultrasound guidance for nerve blocks can improve success rate, lessen complication rate; additional sedation with low dose propofol, dexmedetomidine, midazolam

In children: usually have general anesthesia, which may be combined with regional anesthesia after induction; advantages of regional anesthesia include improved surgical outcome, less cardiac and respiratory depression, decreased risk of thromboembolism, reduced blood loss, decreased postoperative nausea and vomiting, improved perfusion, postoperative analgesia, and rehabilitation, shortened hospital stay; considerations for specific block and medications are location and duration of surgery, duration of postoperative analgesia, hospitalization, pre-existing neurologic deficits, degree of sensory and motor block required to allow ambulation or rehabilitation, need for postoperative sympathectomy; contraindications are lack of interest by patient, pre-existing neurological deficits, infection at block injection site, systemic anticoagulation; if contraindication for neuraxial blockage, can consider more distal peripheral nerve block; proper positioning during surgery critical to avoid nerve injury; up to 4% of patients receiving total shoulder arthroplasty may have resultant neurological deficits, especially neuropraxia, but 90% of these complications resolve in 3-4 months; in patients with contractures, proper positioning important to avoid dislocations and fractures; orthopedic surgery, especially on lower extremities, often associated with significant blood loss; critical to obtain adequate IV access; consider arterial line or central venous catheter

Shoulder and upper arm surgery: regional anesthesia with IV sedation or combination with general anesthetic and endotracheal intubation; intrascalene block of brachial plexus; caution with pre-existing brachial plexus deficits; ipsilateral diaphragmatic paresis may cause loss of 25% of pulmonary function during block; such blocks contraindicated in patients with severe pulmonary or neuromuscular disease; due to semi-sitting position, increased risk of venous air embolism, postural hypotension; head, neck, and hips must be secured to prevent lateral movement of patient, or stretching of nerves may result in injury; protection of eyes and ears important

Elbow surgery: in adults, infraclavicular and supraclavicular blocks combined with light IV sedation preferred; not recommended for outpatients due to risk of late onset pneumothorax 6-12 hours after supraclavicular block,; in children, most often traumatic fractures; if fracture recent, assume full stomach; rapid, sequence induction with endotracheal tube, awake extubation, placement in lateral position recommended; if neurovascular compromise suspected, surgeon may not want regional anesthesia, especially infraclavicular block; with older elbow fractures, requiring resetting or pinning, management better with general anesthetic and laryngeal mask airway, unless patient has had a lot of opioid pain medication, resulting in delayed gastric emptying

Wrist and hand surgery: general anesthesia or axillary or infraclavicular block effective; for minor short procedures, local anesthetic infiltration or peripheral nerve block can be used; for longer surgeries, can use IV regional anesthesia or Bier block, using double tourniquet

Surgery of lower extremity:

Hip arthroplasty: 200,000/year in US; central neuraxial blockade, including spinal or epidural anesthesia, combined with light sedation often used; lumbar plexus techniques also common; benefits of neuraxial technique include decrease in intraoperative blood loss, postoperative deep vein thrombosis, and pulmonary thromboembolism and improved postoperative analgesia and rehabilitation; potential reduced medical costs; anesthetic considerations include patient's lateral decubitus position, potential for significant blood loss; consider controlled hypotensive techniques

Knee arthroplasty: >300,000/year in US; procedures using tourniquet; requires blockade of all 4 nerves of leg — femoral, lateral femoral cutaneous, obturator, and sciatic; central neuraxial blockade or general anesthesia work well; peripheral nerve blocks including femoral nerve block with potentially indwelling catheter or lumbar plexus block minimizes potential significant postoperative pain; postoperative analgesia essential for good physical therapy, rehabilitation

Knee arthroscopy and ACL repairs: variety of techniques include neuraxial blocks, general anesthesia, or local anesthesia with sedation; no one best option; patient's preference may decide; often are outpatient procedures; repair of ACL may be outpatient procedure, but usually requires more intra- and post-operative analgesia; lumbar plexus block or femoral nerve catheter effective; to reduce postoperative pain, intra-articular injections of local anesthetic, opioids, and ketorolac can be used

Ankle and foot surgery: depending on location, blockade of femoral nerve via saphenous nerve, sciatic nerve via posterior tibial, sural and deep and superficial peroneal nerves may have to be blocked; central neuraxial blockade and peripheral blocks effective; use of tourniquet >15-20 min requires spinal or epidural block; in children, caudal block with local anesthetic or opioid effective; often surgeon prefers no regional block for proximal tibia fractures, tibial osteotomies due to risk of compartment syndrome, nerve palsy

Postoperative pain management: focus on reducing use of opioids has increased use of intravenous lidocaine, with benefits of reduction in pain, nausea, opioid requirements, ileus duration, and length of hospital stay; studies show effectiveness of perioperative lidocaine infusions in open or laparoscopic abdominal surgery, colorectal surgery, radical prostatectomies, thoracic and major spine surgery, breast surgery, ambulatory surgery; effect of lidocaine infusion shown to exceed length of infusion by ≥ 8½ hours; no benefit in hip arthroplasty; toxicity manifest as lightheadedness, dizziness, visual disturbances, cardiac dysrhythmias; extremely rare

Other Related Anesthetic Considerations

Tourniquets: reduce blood loss, provide dry surgical field, needed for IV regional blocks like Bier block; use appropriate size cuff to avoid ischemic neuromuscular injury; upper extremity surgery, cuff pressure 50 mm Hg above patient's systolic pressure, 100 mm Hg over systolic for lower extremity surgery; safe duration 1-2 hours, followed by 5 min reperfusion period, then re-inflation of cuff, process called ischemic conditioning, allows tourniquets to be used longer; inflations >2 hours have been associated with prolonged or irreversible damage to underlying skin, muscles, nerves, blood vessels; damage related to pressure and duration; skeletal muscle more susceptible to ischemic injury than nerves; cuff inflation leads to tissue ischemia, results in tissue hypoxia, acidosis; reperfusion of extremity releases toxic metabolites; rapid deflation releases lactic acid, creatine kinase; increase of potassium serum levels 5-10% and CO2 levels 1-8 mm Hg; amount of toxic metabolites correlates with duration; metabolic changes return to baseline within 30 min and rarely cause deleterious effects in healthy patients; also, with cuff release, 5-10% increase of heart rate, reduction of blood pressure; as blood redistributed into limb, post-ischemic reactive hyperemia adds to blood pressure reduction; muscle damage may release myoglobin, lead to renal impairment; increase of core body temperature with inflation, decrease with deflation; with administration of antibiotics, delay inflation >5 min to allow drug distribution in limb; tourniquets can be used in patients with sickle cell disease; decide on case-by-case basis; maintain appropriate acid-base status, oxygenation

Complications: muscle damage, especially under cuff; nerve damage, due to direct compression of cuff, is higher in upper extremity, radial nerve; in lower extremity, sciatic nerve most vulnerable; vascular damage, especially adults with atheromatous vessels; avoid tourniquet with absent distal pulses or poor capillary return; skin damage is result of pressure necrosis and friction; use skin protection before placement; deep vein thrombosis and emboli during deflation possible but rare; tourniquet pain 30-45 min after inflation, unclear etiology; dull, aching pain; increase in heart rate, blood pressure may be only signs in presence of general anesthesia; treatment — release of tourniquet; opioids, additional hypnotics sometimes used

Fat embolus syndrome: fat emboli occur in nearly all patients with fractures, orthopedic procedures; generally asymptomatic; fat embolus syndrome most common with long bone (femur, tibia) or pelvic fractures; incidence 3-4%, mortality rate 10-20%; other predisposing risk factors are shock, hypovolemia, sepsis, disseminated intravascular coagulation (DIC), younger males, intramedullary instrumentation

Diagnosis: classic triad — pulmonary distress with hypoxemia and pulmonary edema, mental status change, petechial rash over neck, shoulders or chest; signs and symptoms develop 12-72 hours after injury; fever, tachycardia may be present; most consistent abnormal lab value is decreased PaO_2; gold standard pulmonary angiography; also echocardiography and/or technetium xenon lung scan

Pathophysiology: unclear; different theories; mechanical theory is that large fat droplets released into venous system are deposited into pulmonary capillary beds and brain, act as microemboli and start inflammatory cycle; fat can be detected in pulmonary artery samples in up to 70% of patients with long bone or pelvic fractures; biochemical theory divided into two mechanisms, toxic mechanism involves release of free fatty acids at time of injury, directly impacting pneumocytes and causing acute respiratory distress syndrome (ARDS) picture; trauma-induced release of catecholamines enhances mobilization of free fatty acids and toxic effect; obstructive mechanism suggests release of unspecified mediators that alter lipid solubility, results in coalescence of lipids, consequent microembolization

Treatment: rapid recognition of condition; elimination of precipitating factors, aggressive respiratory support, including additional oxygen administration, continuous positive airway pressure, even re-intubation, immobilization of fracture; corticosteroids controversial, consider administration in high risk patients; heparin and dextran not effective

Venous thromboembolism: major cause of death following surgery or trauma, especially lower extremity surgery involving hip fractures; deep venous thrombosis (DVT) in 40-80% of orthopedic patients not on antithrombotic prophylaxis; fatal pulmonary embolus in 0.1-8% of patients following major orthopedic surgery

Thromboprophylaxis: clinical risk factors include advanced age, prolonged immobility or bed rest, prior history of thromboembolus, cancer, pre-existing hypercoagulable state, major surgery; risks are cumulative; patient with hip or knee arthroplasty, hip fracture should receive low molecular weight heparin, fondaparinux (synthetic factor Xa inhibitor), or warfarin; alternatively, intermittent pneumatic compression if high risk for bleeding, similar recommendations for acute spinal cord injury; elective spine surgery or knee arthroscopy usually do not require pharmacological prophylaxis; epidural or spinal anesthesia (instead of general anesthesia) reduces incidence of DVTs and pulmonary embolus by 20-40% in total knee or hip replacement; benefits derived from vasodilatation, which maximizes venous blood flow, excellent postoperative analgesia, which allows early ambulation; pharmacological thromboprophylaxis still recommended; with neuraxial anesthesia in patients on anticoagulants, must balance risk of thromboembolism and hemorrhagic complication; <1 in 150,000 patients receiving surgery with epidural, <1 in 220,000 patients receiving surgery with spinal will have hemorrhagic complication like spinal hematoma, which can result in permanent neurological injury; increased risk in patients on anticoagulation

Methyl methacrylate: associated with implantation syndrome; acrylic bone cement, used during arthroplastic procedures in patients >70 years; pungent smell, mutagenic, associated with sudden onset of hypotension 30 sec to 10 min after placement; severe hypotension in 5% of patients; possible factors are direct myocardial depression, dilatation of peripheral vasculature, embolization from fat, bone marrow, or air during reaming of bone; discontinue nitrous oxide during that time, could exacerbate air embolism; emboli can cause pulmonary hypertension, lysis of blood cells and

marrow; can cause exothermic reaction, allergic reaction; hypoxemia within first minute can persist for some time

Treatment for hypotension: rapid fluid administration, maximize patient's oxygen, vasopressor, eg, ephedrine

Spinal Fusions

May be healthy patients or present with medical problems including neurological disease, respiratory compromise, cardiac dysfunction, or scoliosis, which is lateral deviation of spine

Scoliosis: 4 categories; idiopathic scoliosis consists of infantile, juvenile, adolescent; congenital scoliosis includes by definition vertebral and rib abnormalities and may be associated with neural tube defect; neuromuscular scoliosis, which may be neuropathic, eg, patients with cerebral palsy, or myopathic, eg, children with Duchenne's muscular dystrophy; syndromic scoliosis, eg, patients with neurofibromatosis, Marfan syndrome, mucopolysaccharidosis; scoliosis can also be caused by trauma; magnitude of scoliosis measured by Cobb angle, which must be known preoperatively; in addition to lateral flexion of spine, rotation of vertebral bodies distorts ribs in thoracic cage and results in restriction of lung volume, mechanical insufficiencies, and reduced lung compliance; earlier onset, worse alveolar, pulmonary artery development; contributes to significant hypoxemia, hypercapnia with pulmonary hypertension and right-sided congestive heart failure

Management options for scoliosis: bracing, for idiopathic patients with curves of 20°-45° and apex of curve below T6; serial casting or elongation-derotation-flexion casting in children with early onset idiopathic (may be curative) or congenital scoliosis (usually temporary effect); growing rods or VEPTR (vertical expandable titanium prosthetic rib) rods for congenital scoliosis — patients usually later require spinal fusion; spinal fusion for idiopathic, neuromuscular, or congenital scoliosis with curve >45°-50°

Preoperative evaluation: focus on respiratory and cardiac status, coexisting diseases; determine need for preoperative echo or pulmonary function tests (PFTs); age of onset, degree of curvature have impact on PFT and possibly echo results; laboratory work, CBC, coagulation studies, chemistry panel, urinalysis, pregnancy test if appropriate; standardized approach for tests specifies preoperative echo if curves >75%, congenital scoliosis, nonambulatory, congenital heart disease, muscular dystrophies or myopathies, presence of syndrome or exercise intolerance, chronic lung disease, OSA; with PFTs most common deficiency is restrictive lung disease; degree of curvature and length of thoracic curve increase degree of pulmonary impairment; classic findings are reduction in forced vital capacity (FVC) and forced expired volume at one sec (FEV1); FEV1 to FVC ratio is normal; patients with curves >70° have pulmonary hypertension with physical activity; with curves >100°, pulmonary hypertension at rest

Anesthetic induction: for healthy patient, preoperative midazolam given and monitors placed; induction with ketamine 1 mg/kg IV and propofol 2 mg/kg IV; in patients who do not tolerate propofol, can substitute dexmedetomidine 1 mcg/kg IV; may give cisatracurium, but in patients with muscular dystrophies or other myopathies neuromuscular blockade not recommended; low-dose sevoflurane used initially until propofol and remifentanil reach steady state; also, prior to incision, fentanyl 2-3 mcg/kg and antibiotics given; tranexamic acid given because of potential blood loss; use 50 mg/kg IV over 30 min for idiopathic sclerosis or 100 mg/kg IV over 30 min for neuromuscular scoliosis

Intraoperative monitoring: standard monitors plus arterial line for frequent sampling of blood gases (ABGs); central venous line indicated in patients with decreased cardiac function, staged procedure, difficult IV access, or prolonged intubation; bispectral index (BIS), somatosensory evoked potentials (SSEPs), motor evoked potentials (MEPs), urine output, thromboelastogram, all helpful

Positioning particularly important: ensure secure airway; position arms, shoulders properly to avoid ulnar nerve or other brachial plexus injury; position hips, lower extremities properly to avoid injury to lateral femoral cutaneous nerve; place male genitalia, breasts, nipples properly; position eyes to avoid corneal abrasions, direct pressure, optic vein engorgement, retinal ischemia; pad skin under IV tubing, cables, wires; periorbital skin prone to small abrasions; allow abdomen to hang free to avoid increased intra-abdominal pressure, decreased venous return, increased engorgement of epidural veins, increased bleeding; soft bite block used to avoid tongue injury; Jackson orthopedic table ideal; provides mirrored foam head support, adjustable arm supports, abdomen-free support

Maintenance of anesthesia: initially, propofol 200 mcg/kg/min, tapered down to 92-100 mcg/kg/min, following BIS to assure <60; remifentanil 0.2 mcg/kg/min, adjusted as needed as low as 0.06 mcg/kg/min; air and oxygen; tranexamic acid 5 mg/kg/hour in idiopathic patients, 10 mg/kg/hour in neuromuscular disease; if propofol cannot be used, can give dexmedetomidine 0.4-1.0 mcg/kg/hour if necessary; ketamine 20-50 mcg/kg/min can also be used, but wake-up time significantly prolonged; to control blood pressure, reduce blood loss, and reduce postoperative pain, surgeon gives intrathecal morphine at 4-5 mcg/kg, maximum of 200 mcg in idiopathic scoliosis or mild neuromuscular disease; not used in patients severely developmentally delayed with severe neuromuscular disease; dexamethasone 0.2 mg/kg used as anti-emetic, anti-inflammatory; ondansetron 0.1 mg/kg and acetaminophen 15 mg/kg IV at end of case found effective; to raise blood pressure, dopamine 3-10 mcg/kg/min; for short elevation of blood pressure, phenylephrine 10-20 mcg total; as children with idiopathic scoliosis may be exquisitely sensitive to phenylephrine, first give very small dose to assess response; to reduce blood pressure can use nitroglycerin 1-3 mcg/kg/min instead of sodium nitroprusside; easier to avoid large swings in pressure

Neurometric monitoring: real-time continuous assessment of spinal cord, decreases postoperative neurological deficits; consists of SSEPs and MEPs — now standard of care; SSEPs monitor only dorsal column or sensory function, include measurement of amplitude and latency of signals and comparison with baseline values; 50% decrease in amplitude or 10% decrease in latency requires intervention; MEPs monitor only motor tract function or corticospinal tract, measurement of amplitude of signals, comparison with baseline values; reduction of

80% amplitude is critical, requires intervention; MEPs are more sensitive than SSEPs; MEPs very sensitive to most anesthetic agents; inhalation agents known to decrease amplitude, increase latency of both SSEPs and MEPs; nitrous oxide decreases amplitude, may increase latency; propofol and dexmedetomidine have minimal impact on amplitude, latency; ketamine increases amplitude of SSEPs, minimal effect on amplitude of MEPs, latency; etomidate very similar; remifentanil minimal effect on amplitude, latency; midazolam mildly reduces amplitude of both somatosensory, motor evoked monitoring; other factors negatively impact evoked potential monitoring, including pre-existing neurological deficits, hypotension, hypoxia, hypothermia, hypocarbia, technical issues

Surgical procedure: 3 stages, each with specific goals; stage 1, soft tissue dissection, decortication of vertebral lamina, destruction of facet joints, removal of spinous processes; stage 2, placement of spinal implants or pedicle screws; stage 3, actual correction of spinal deformity, followed by bone grafting and closure of wound; anesthetic goals stage 1, maintain mean arterial pressure 55-60; in older patients or patients with congenital heart disease, may need to keep arterial pressure 60-70; to maintain 55-60, increase anesthetic, limit IV fluid administration, occasionally use vasodilator or beta blocker; intrathecal morphine also lowers blood pressure; important to maintain normocarbia; anesthetic goal stage 2, raise mean arterial pressure to 60-65; older patients or patients with cardiac disease to 70-75; to raise blood pressure, decrease anesthetic agents, increase crystalloid, colloid administration, occasionally use low dose dopamine or other vasopressor; important to maintain normocarbia or mild hypercarbia to assure good perfusion to spinal cord; in stage 3, goal is raise arterial pressure to 75-80 to assure maximal blood flow to spinal cord by decreasing anesthetic, optimize IV fluids, give blood if indicated, dopamine or small doses of phenylephrine; ideally mild hypercarbia; for IV administration, which may involve large volumes, essential to have adequate venous access, combination of crystalloid and colloid in ratio of 3 to 1; isotonic solutions like PlasmaLyte, lactated Ringers ideal; during stage 1, give IV fluids conservatively; stage 2 and 3, more aggressive IV fluid administration; fluids should be warm, guided by patient's vital signs, estimated blood loss, urine output, serial ABGs

Blood preservation techniques: induced hypotension (mean arterial pressure of 55-65) with nitroglycerin, sodium nitroprusside, beta blocker, clonidine, calcium channel blockers, and/or intrathecal morphine; also anti-fibrinolytic agents, including tranexamic acid, aminocaproic acid, both reduce intraoperative blood loss; proper positioning to avoid venous congestion; efficient, skilled surgeon; Cell Saver® may reduce need for transfusion; autologous blood donation helpful; erythropoietin may be used

Spinal cord injury risk: 4 mechanisms; first, direct contusion of spinal cord; second, contusion by implants like screws, hooks, other devices; third, distraction of cord by rods, halo traction; fourth, reduction of spinal cord blood flow; vulnerable areas include motor pathways supplied by anterior spinal artery and important watershed area, T4-T9, prone to ischemia

Management of decreased evoked potential signs: verify electrode placement with neurology technician; request surgeon to stop procedure; raise mean arterial pressure to 85 with small dose of phenylephrine; raise PaCO2 to >40, FiO2 to 100%; consider lidocaine 2 mg/kg to treat possible vasospasm; optimize arterial blood gas, transfuse blood if indicated; consider methylprednisolone; if no improvement in evoked potential signals, consider wake-up test; potential complications include extubation, air embolism, recall, injury from malposition

Postoperative pain management: ensure patient comfortable; allows for larger breaths, earlier ambulation following surgery; intrathecal morphine provides analgesia up to 24 hours following injection; some use epidural catheters placed intraoperatively; continuous infusion of local anesthetic with ON-Q pump; patient controlled anesthesia effective in older patients and those with mental capacity; acetaminophen, ketorolac first 2-3 days postoperatively; valium for muscle spasms; opioid side effect medication

Postoperative vision loss (POVL): one of most serious complications; incidence <0.1-0.2%; ischemic optic neuropathy most common cause; in children more due to cortical blindness; POVL more common with prone spine surgery, cardiac bypass, other head and neck surgery; more common in older patients, also reported in young patients (from 10 years old) following posterior spinal fusions; prone position increases intraocular pressure by 10-12 mm Hg; increased venous pressure in head may increase intraocular pressure, subsequent ischemia to optic nerve; emboli may cause central retinal artery occlusion; direct compression on globe may also be causative; American Society of Anesthesiology (ASA) practice advisory (2006); one, consider consenting patients for risk of POVL; two, controlled hypotension not associated with POVL; three, use of colloids, crystalloids for volume replacement; four, no apparent threshold for blood transfusion to minimize risk; five, position of head equal or above level of heart; six, consider staged spinal procedure; in addition, Postoperative Visual Loss Study Group (*Anesthesiology*, 2012) identified risk factors for ischemic optic neuropathy after spinal surgery, including male sex, obesity, use of Wilson frame, anesthetic duration >6 hours, blood loss >1000 mL, lower percentage of colloid administration; authors of article in *Anesthesiology,* September, 2016, found after spinal fusion incidence of POVL due to ischemic optic neuropathy significantly decreased 1998-2012 by about 2.7 fold; aging, male sex, transfusion, obesity significantly increase risk

Postoperative concerns: ICU or regular floor; respiratory status, extubation or postoperative intubation; depends on preoperative PFTs, FVC; patients with FVC <50% fairly high need for postoperative intubation; patients with FVC <30% need prolonged postoperative intubation; other concern, ongoing blood loss, development of coagulopathy; hypovolemia can continue into postoperative period; development of syndrome of inappropriate antidiuretic hormone (SIADH); appropriate pain control, with opioid administration in long surgery, risk of paralytic ileus; extubation or continuation of intubation, depends on postoperative PFTs; in both

idiopathic and neuromuscular patients, FEV1 and FVC decrease postoperatively, nadir at postoperative day 3, 60% of baseline value at post-operative days 7-10, return to baseline 1-2 months post-operatively; long-term pulmonary function in patients with idiopathic scoliosis will improve slightly, may take months to one year; in patients with neuromuscular scoliosis, improvement of pulmonary function variable, generally minimal, surgery just stabilizes their existing pulmonary function

Anterior spinal fusion: needed in some rare spinal deformities; surgery consists of discectomies with or without instrumentation, may be accompanied by posterior spinal fusion; patient's position likely lateral decubitus; surgery through left thoracotomy or video-assisted thoracoscopic approach if no instrumentation used; procedure facilitated by single, long ventilation; complications of this approach disruption of great vessels, hemothorax, pneumothorax (placement of chest tube routine), spinal cord injury

Conclusions: lessons from lecturer's spinal cord fusion experience — protocols and standards are good; effective communication essential; avoid wake-up tests if at all possible; do not use propofol to control high blood pressure — very long wake-up time; do not combine controlled hypotension with hypocapnia; teamwork is essential

Suggested Reading

American Society of Anesthesiologists Task Force on Perioperative Blindness: Practice advisory for perioperative visual loss associated with spine surgery: a report by the American Society of Anesthesiologists Task Force on Perioperative Blindness. *Anesthesiology* 2006 Jun;104(6):1319-28; **Narouze S et al:** Interventional spine and pain procedures in patients on antiplatelet and anticoagulant medications (Second Edition): guidelines from the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anaesthesia and Pain Therapy, the American Academy of Pain Medicine, the International Neuromodulation Society, the North American Neuromodulation Society, and the World Institute of Pain. *Reg Anesth Pain Med* 2018 Apr;43(3):225-62; **Ramchandran S et al:** The Impact of Different Intraoperative Fluid Administration Strategies on Postoperative Extubation Following Multilevel Thoracic and Lumbar Spine Surgery: A Propensity Score Matched Analysis. *Neurosurgery* 2018 May 30. [Epub ahead of print]; **Rubin DS et al:** Perioperative visual loss in spine fusion surgery: ischemic optic neuropathy in the United States from 1998 to 2012 in the Nationwide Inpatient Sample. *Anesthesiology* 2016 Sep;125(3):457-64; **Suresh S et al:** The European Society of Regional Anaesthesia and Pain Therapy/American Society of Regional Anesthesia and Pain Medicine recommendations on local anesthetics and adjuvants dosage in pediatric regional anesthesia. *Reg Anesth Pain Med* 2018 Feb;43(2):211-6.

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Anesthesia for Obstetrics: Part 1

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Cardiovascular Changes of Pregnancy

Cardiovascular system: changes can exacerbate pre-existing cardiovascular conditions; increased cardiac output, arterial compliance, extracellular fluid volume; decreased blood pressure, total peripheral resistance

Blood pressure: mean blood pressure (BP), gradual decreases during pregnancy, largest decrease 22-24 weeks gestation, then rises toward normal mid-third trimester; diastolic decreases more than systolic

Cardiac output (CO): increases by 50%; largest increase by 16 weeks, plateaus at 20 weeks, with further increases during labor and postpartum; due to 25% increase in stroke volume, 15% increase in heart rate, 20% decrease in systemic vascular resistance (due to low resistance placental circulation running in parallel with systemic circulation); blood volume increases by 45%, peaking at 34 weeks; returns to normal 6 weeks postpartum; plasma volume increases 55%, but red cell volume only increases 30%; results in physiological anemia of pregnancy; increases in mean circulatory filling pressure; blood flow increases to meet increased metabolic needs of tissues; total peripheral resistance decreases early, continuing through pregnancy, to lesser extent near term; arterial compliance greatly increased; many factors involved in these hemodynamic changes; nitric oxide production elevated, role in vasodilation; estrogen, relaxin role via nitric oxide-dependent mechanisms

Aortocaval compression: maternal hypotension, reduction in utero-placental perfusion; occurs in supine position >20 weeks' gestation; can be exaggerated after inducing neuraxial blockade (sympathectomy); create left uterine tilt 15% or full left lateral position to relieve; aorta not significantly compressed, vena cava compression more significant problem; preload impaired by reduced venous return; left uterine displacement possibly unnecessary if BP maintained via phenylephrine after neuraxial block

Respiratory Changes of Pregnancy

Respiratory alkalosis: progesterone sensitizes central respiratory centers, including ventilatory response to carbon dioxide (CO2); pH lower, 7.41-7.44 (7.4 in nonpregnant); CO2 partial pressure (PaCO2) 30-32 mm Hg (~40 in nonpregnant); bicarbonate 20-21 mmol/L (24 in nonpregnant)

Lung volumes and oxygenation: tidal ventilation increased by 45%; 20% decreased functional residual capacity, impacts general anesthesia (ie, pre-oxygenation critical); 40-60% increased oxygen consumption; oxygen desaturation occurs much more rapidly during apnea, accentuated by pulmonary volume changes

Other respiratory physiological changes: pulmonary resistance decreased to 50%; 45% increase in minute ventilation

Upper airway changes: increased mucosal friability and vascularity (worse with preeclampsia); mucosal injury during laryngoscopy more likely, increased bleeding risk; requires smaller endotracheal tube; avoid nasotracheal intubation, nasogastric tubes to avoid epistaxis; Mallampati score worsens with pregnancy, labor, severe preeclampsia

Hematological Changes of Pregnancy

Dilutional anemia: red cell mass increased; plasma volume increased to greater extent

Platelets: often small or no decrease; in gestational thrombocytopenia, platelets fall to 90,000-100,000/μL; condition resolves postpartum, not associated with abnormal platelet function or clinical bleeding

Coagulation and fibrinolytic systems: profound changes; pro-coagulant changes minimize intra-partum blood loss, but cause up to 6-fold increase risk of thromboembolism during pregnancy, postpartum period; increased clotting efficiency; impaired fibrinolysis; fibrinogen levels increase throughout pregnancy, often >400 mg/dL at term (if <200 mg/dL, likely pathologic, with increased risk of postpartum hemorrhage)

Hypercoagulable state: increased pro-coagulant activity, increases in factors V, VII, VIII, IX, X, XII, Von Willebrand factor, fibrinogen; decreased endogenous anticoagulant activity, increased heparin cofactor II, alpha-1 antitrypsin (A1AT), protein S activity, activated protein C resistance, depressed fibrinolytic activity

Blood volume: 90-95 mL/kg weight; 100 mL/kg if twins

Gastrointestinal Changes in Pregnancy

Displacement: uterine enlargement displaces abdominal organs cephalad; impacts interaction of lower esophageal sphincter and diaphragm, causes increased intragastric pressure

Reflux: progesterone relaxes smooth muscle of lower esophageal sphincter, decreases barrier pressure that normally prevents gastroesophageal reflux; elevation, rotation of stomach by uterus eliminates pinch valve where esophagus goes through diaphragm, further decreasing reflux barrier; increases risk of regurgitation, aspiration of gastric contents, severity of pulmonary injury

Gastric emptying: contrary to previous thinking**,** normal in gestation; labor pain, opioids can retard gastric emptying

significantly; gastric ultrasound to confirm gastric filling/emptying, factors in determining safety of surgery

Liver Changes in Pregnancy

Changes: often not clinical issue; reversible, due to increased estrogen, progesterone, but can be problem if patient has liver disease; spider nevi, palmar erythema usually indicate liver disease, but normal in pregnancy; telangiectasia in 60%; liver size, hepatic blood flow unchanged; CO percentage to liver decreases 35%; hepatic drug clearance reduced; increased splanchnic, portal, esophageal venous pressure; 60% develop esophageal varices, which resolve postpartum; serum albumin decreases 60% (increased plasma volume); 20% reduction total serum protein by mid-pregnancy

Renal Changes in Pregnancy

Changes: renal blood flow increased by 75%; enlarged kidneys; normalize 6 weeks postpartum; glomerular filtration rate (GFR) increased to 150 mL/min by second trimester, increased creatinine clearance, decreased blood urea nitrogen (BUN), creatinine ("normal" values indicate poor renal function); decreased tubular reabsorption, increased renal excretion of glucose in some; can contribute to gestational diabetes mellitus

Changes in thyroid, pancreatic, and pituitary function: clinically unimportant in most women, but may be significant in presence of pre-existing disease

Central Nervous System (CNS) Changes in Pregnancy

Changes: sensitivity changes; anesthetic requirements for volatile anesthetic agents (minimum alveolar concentration, MAC) decrease 30%; increased sensitivity to intravenous (IV) induction, sedative agents; neuraxial anesthetic requirements decrease 25%-40% at term; changes due partly to mechanical changes — inferior vena cava compression by uterus, distention of epidural venous plexus, decreases free volume of epidural space and cerebrospinal fluid (CSF) per spinal segment; thus given dose of epidural or intrathecal anesthetic will have greater dermatomal spread than in nonpregnant woman; anesthetic sensitivity also due to biochemical changes, progesterone, and beta-endorphins

Anesthetic Implications of Pregnancy

Ventilation: increased minute ventilation, reduced functional residual capacity (FRC); maintain PaCO2 at 30-32 mm Hg; inhaled anesthetic induction rate increased (increased rise of alveolar anesthetic concentration compared with inspired gasses); adjust concentration of volatile anesthetic to account for 15%-40% MAC reduction

Hypoxemia: occurs more rapidly with apnea, result of reduced FRC, increased oxygen consumption; avoid aortocaval compression by uterus with left uterine displacement of 15° or full left lateral position; especially important in term deliveries with neuraxial block

Intubation: despite 25% reduction in plasma cholinesterase in pregnancy, give usual dose succinylcholine for endotracheal intubation 1.5 mg/kg

Muscle relaxants, paralytics: standard or slightly reduced doses rocuronium because of increased sensitivity to aminosteroid muscle relaxants (eg, rocuronium, vecuronium); atracurium action unchanged by pregnancy; if short-acting, non-depolarizing neuromuscular blockers used to maintain paralysis during cesarean delivery, hysterectomy, use peripheral nerve stimulator to guide therapy

Transfusions: blood volume increased; dilutional anemia normal; keep in mind when calculating replacement needs; if patient hemodynamically unstable with ongoing blood loss, calculate percentage of blood loss to guide therapy (eg, 15%-20% total blood volume of 95 mL/kg, 100-105 ml/kg if twins); use lower threshold to determine when to transfuse cryoprecipitate, plasma, fibrinogen concentrate when fibrinogen levels <200 mg/dL with ongoing blood loss

Spinal anesthesia: subarachnoid dose reduced by 25%, epidural dose lowered; more rapid onset, increased duration in pregnant women

Anesthetic morbidity, mortality: most often during airway management, especially during emergence from general anesthesia and immediate post-anesthetic periods; also following induction of epidural, spinal anesthesia — respiratory compromise following rapid high sensory level or cardiovascular collapse

Uterus and Placenta

Anatomy, physiology: placental growth dependent on changes to maternal circulation, responses to metabolic demands from fetal growth; uterine artery (primary), ovarian artery (secondary) provide maternal blood to uterus and branch into spiral arteries; provide blood to intervillous space, where maternal and fetal gas, nutrient, and waste exchange occur; spiral artery remodeling early in gestation converts maternal placental circulation into low resistance, high flow circulatory system, maximally vasodilated

Uterine blood flow: few mechanisms increase; avoid interventions which decrease flow; oxygen-CO_2 exchange blood-flow dependent; best maintained by avoiding aortocaval compression and maintaining adequate mean maternal BP; fetal compensatory mechanisms allow fetus to tolerate reductions in uterine blood flow for long periods without significant long-term injury; most drugs cross placenta by diffusion down concentration gradient; increased maternal-fetal gradient, decreased maternal and increased fetal protein binding, lower molecular weight, less ionization, greater lipid solubility all promote maternal-fetal transfer; 20% maternal CO goes to term uterus; increased from 70 mL/min to 700 mL/min

Teratogenicity: anesthetic agents not teratogenic; placenta imperfect barrier, almost all substances can cross, varies with degree of permeability; mechanisms that restrict fetal exposure include enzyme activity, binding of substances within placental tissue, diffusion limited by membrane thickness

Placenta: additional functions: hormonal — placental enzymes convert steroid precursors into estrogen, progesterone; placenta synthesizes binding proteins, enzymes, polypeptide hormones (eg, chorionic gonadotrophin, placental lactogen)

Placental transport: passive transport: concentration gradient, electrochemical differences across membrane; other factors include substance molecular weight, lipid solubility, degree of ionization, membrane surface area, thickness; no energy requirements; through lipid membranes or protein channels that cross lipid bilayer; facilitated transport: carrier-mediated, transports lipid-insoluble molecules down concentration gradient;

process exhibits saturation kinetics, competitive and non-competitive inhibition, stereo-specificity, temperature influences; example is transplacental glucose transport; active transport: linked to cell metabolic activity, net transport against concentration, electrical, or pressure gradient, requires cellular energy (eg, sodium, potassium transported via sodium-potassium ATPase pump); pinocytosis: way that macromolecules (eg, IgG) cross; other placental transport factors include changes in maternal-fetal blood flow, placental binding, placental metabolism, diffusion capacity, degree of protein binding, and gestational age (placenta more permeable in early pregnancy)

Oxygen transportation: placenta "lung" for fetus, supplies 8 mL/min/kg fetal body weight of oxygen; one-fifth oxygen transfer efficiency of adult lung; driving force is difference in PaO_2 between maternal, fetal blood; difference in oxyhemoglobin dissociation curves in maternal and fetal blood influence oxygen transport to fetus; fetal curve left of maternal, lower p50, enhances oxygen uptake by fetal red blood cells, promotes transfer of oxygen across placenta; double Bohr effect augments oxygen transfer; concomitant fetal-to-maternal CO_2 transfer, fetal blood more alkalotic than maternal; causes rightward shift in maternal oxyhemoglobin dissociation curve, leftward shift fetal curve (accounts for 2%-8% transplacental oxygen transfer)

Maximum fetal arterial PaO_2: ≤50-60 mm Hg, even if maternal fraction of inspired O_2 (FiO_2) 1.0; because placenta is venous equilibrator; because of shape of maternal oxyhemoglobin dissociation curve, increase in maternal PaO_2 >100 mm Hg does not substantially increase maternal O2 content; if uterine blood flow, umbilical blood flow, and fetal oxygen consumption constant, fetal PaO2 increases little if maternal FiO_2 increased; more important at low fetal PaO_2 closer to p50 of fetal blood (ie, 21 mm Hg) because steep curve; placenta high rate of oxygen consumption, decreases oxygen transferred to umbilical circulation; fetal arterial blood a mixture of oxygenated umbilical venous blood and deoxygenated inferior vena cava blood from fetal lower extremities; CO_2 crosses as dissolved carbon dioxide, carbonic acid, bicarbonate ion, carbonate ion, carbaminohemoglobin (in red blood cells); predominant forms dissolved CO_2, bicarbonate ion; fetal-maternal $PaCO_2$ difference, 40 mm Hg fetal, 34 mm Hg maternal, favors fetal-to-maternal transfer; crosses placenta because 20 times more diffusible than oxygen; as CO_2 diffuses from fetal to maternal circulation, the Le Chatelier principle causes a shift in equilibrium of the carbonic anhydrase reaction, which produces more CO_2 for diffusion; further augmentation of carbon dioxide transfer comes from the Haldane effect in maternal blood; maternal-to-fetal transfer of oxygen produces deoxyhemoglobin in maternal blood, which has greater affinity for CO_2 than oxyhemoglobin: Haldane effect accounts for 50% of transplacental CO_2 transfer

Glucose transfer: facilitated diffusion down concentration gradient, independent of insulin, sodium gradient, or cellular energy; much maternal glucose used by placenta

Drug transfer: affected by drug's lipid solubility, degree of protein binding, tissue binding, pKa, fetal blood pH, and utero-placental blood flow; pKa determines percent drug not ionized at physiological pH; fetal acidemia enhances maternal-to-fetal transfer or ionic trapping of many basic drugs, such as local anesthetics and opioids; most anesthetic drugs passively transferred, dependent on blood flow rate; inhalational agents' lipid solubility, low molecular weights facilitate rapid transfer; prolonged induction-to-delivery time results in lower Apgar scores in neonates exposed to general anesthesia; nitrous oxide crosses rapidly — fetal-to-maternal ratio of 0.83 in 3 minutes, may cause neonatal depression, exacerbated by diffusion hypoxia; local anesthetics, induction agents, and opioids rapidly cross placenta; muscle relaxants are quaternary ammonium salts, fully ionized, do not readily cross; neostigmine crosses placenta, should be added to atropine (crosses more readily than glycopyrrolate); warfarin, not heparin, crosses, and results in increased fetal loss, congenital malformations — avoided in pregnancy

Non-obstetric Surgery During Pregnancy

Overview: 2% of parturients have surgery during pregnancy; number increasing, especially with laparoscopic procedures; maternal and fetal outcomes usually good; perioperative team includes obstetric consultation, surgeons, anesthesiologist, neonatologist, obstetric nursing; maintenance of fetal oxygenation is key; provide adequate utero-placental perfusion and maternal oxygenation; other goals include pain management, early mobilization; preterm labor potential issue; difficult to treat, usually due to underlying condition or procedure, not anesthetics

Drugs of concern: nitrous oxide — no demonstrated fetal adverse effects; benzodiazepines — oral cleft anomalies reported in 1970s, but case-control studies failed to demonstrate relationship; current concern about N-methyl-D-aspartate (NMDA) receptor blockers (eg, ketamine, nitrous oxide) and gamma-aminobutyric acid (GABA) A-receptor enhancers (eg, benzodiazepines, IV induction agents, volatile agents); in animal studies, exposure to these agents causes apoptosis, neurodegeneration, and/or hippocampal synaptic function deficits; relevance to humans unclear

Fetal monitoring: intraoperative fetal heart rate monitoring and measurement of uterine contractility difficult; most obstetricians request measurement of these 2 parameters preoperatively and in immediate postoperative period

Timing and preventive measures: magnesium reduces preterm labor risk postoperatively; most surgeries best delayed until second trimester (or term); regional anesthesia preferred to general; if general anesthesia, avoid maternal hypoxemia during induction, aortocaval compression; ensure rapid sequence induction and tracheal intubation

Pain Relief During Labor

Non-pharmacological and non-neuraxial pharmacologic methods: antenatal health education, including information on benefits and risks of different pain-control measures, support during labor (ie, birth partners and doulas), relaxation techniques (eg, music, breathing exercises), complementary therapies (eg, aromatherapy, hydrotherapy, transcutaneous electrical nerve stimulation, sterile water injection) inhalation (eg, nitrous oxide and air mixture), non-opioid analgesics, sedatives, opioid analgesics; calm, soothing environment; lumbosacral massage shown to reduce back pain; hypnobirthing popular in some centers, but evidence of effectiveness lacking; acupuncture shown

to reduce pain intensity; with inhalational analgesia, ensure consciousness, avoid regurgitation, aspiration; sedatives, anxiolytics not recommended, readily cross placenta, cause side effects for mother and neonate; systemic opioids, nurse-controlled (ie, intermittent IV or intramuscular [IM] boluses) or IV patient-controlled; remifentanil, fast onset, offset; continuous pulse oximetry, 1-on-1 nursing care essential, high potency, respiratory depression potential

Epidural analgesic techniques: epidural, combined spinal-epidural (CSE) techniques common; with CSE, spinal fluid presence ensures location of posterior epidural space, confirms correct location of epidural catheter; CSE produces more rapid onset pain relief; some studies indicate that CSE requires fewer labor "top-ups" than epidural technique; informed consent required for epidural analgesia; Society of Obstetric Anesthesia and Perinatology video on risk, benefits can be shown in antenatal classes

Procedure: epidural "timeout" with nurse to identify patient; sitting position (easier to find vertebral column midline) or left lateral position; locate intervertebral space via palpation or ultrasound; clean area with antiseptic; once dry, inject local anesthetic in skin at cannulating interface (17-gauge Tuohy needle); loss of resistance technique with saline, mixture of saline and air, or air alone (preferred because any fluid present is CSF) to find epidural space; epidural space 3-8 cm deep (average 4-5 cm); pencil-point 26 or 25 gauge spinal needle to penetrate dura; intrathecal dose of 2.5-3 mg bupivacaine ± 5 mcg fentanyl injected; initial pain relief in 5 minutes; remove spinal needle, cannulate epidural space (4-5 cm in, marking at skin between 8-11 cm); small test dose of 3 mL lidocaine and epinephrine; secure epidural catheter; attach to patient-controlled analgesia pump; continuous background infusion 6 mL/hr (with self-administration doses 5 mL/5 min, to maximum 26 mL/hr, 5 minute "lockout"); newer machines can provide mandatory intermittent bolus of local anesthetics, provide more efficient analgesia than continuous infusion, better spread in short period, decreases local anesthetic requirements, less need for rescue medication

Catheter malpositioning: always risk **of** intravascular catheterization; give test dose; aspirate to check for blood; if intravascular, pull catheter back 1 cm, repeat aspiration; if blood persists, replace epidural at another level; possible intrathecal space catheterization; check with aspiration, test dose; if intrathecal, catheter can be left in place if placement was difficult; risk for adverse events (eg, high spinal block) from high doses given by other providers, so catheter should be well-labeled; communicate with nursing staff, other physicians; other catheter malpositioning includes between 2 layers of dura (ie, pia mater, arachnoid mater); provides "strange block," inadequate analgesia with profound leg weakness, high block with no leg weakness, patchy block, unilateral block; subdural block placement difficult to ascertain without radiologic imaging with dye

Monitoring and complications: after epidural, patient left lateral position, fetal heart rate monitor applied, blood pressure measured immediately; hypotension risk (lumbar sympathectomy, reduces venous return to heart, lowers blood pressure); treatment with co-load IV lactated Ringers with vasoactive agent (eg, 10 mg ephedrine, 100 mcg phenylephrine); risk with CSE, 3%-6% patients, profound fetal bradycardia, sometimes associated with uterine hyperactivity (prolonged tetanic uterine contraction or uterine tachysystole [ie, numerous contractions, short period of time; eg, >5 in 10 minutes]); contractions decrease utero-placental blood flow, causing fetal bradycardia; treatment, oxygenate mother, nitroglycerin spray 2 puffs sublingually, expected response in 45-60 seconds; maintain utero-placental perfusion (ie, normalize maternal BP, change positioning); urgent cesarean section seldom required; fetal outcome unchanged (ie, fetal bradycardia is physiological response, not harmful); reassure mother and partner

Obstetric outcomes from epidural: neuraxial analgesia most effective form of labor analgesia; may increase risk of forceps and vacuum vaginal delivery slightly; may prolong second stage labor slightly; does not increase risk of cesarean delivery compared with systemic opioid analgesia; can be provided at any stage of labor without increasing risk of cesarean delivery or prolonging labor; some evidence neuraxial analgesia associated with maternal temperature increase, need more studies; unlikely to affect breastfeeding success; concentration of epidural local anesthetic has impact on amount of motor block; lower concentrations associated with fewer instrumental deliveries, less motor blockade, less fetal malrotation; recommend 0.0625% solution bupivacaine; ropivacaine associated with less motor block, theoretically less risk of cardiotoxicity; however, cardiotoxicity risk low at low doses used for labor; in women at increased risk of cesarean delivery (eg, multiple gestations, morbidly obese, previous cesarean section scars), place epidural catheter early in labor; statistics from lecturer's institution — in nulliparous woman with induced labor cesarean risk 35%; in nulliparous woman with spontaneous labor, subsequent cesarean delivery risk 25%; in multiparous woman (induced or spontaneous labor), rate of subsequent cesarean delivery after epidural, 5%; overall cesarean delivery rate 16% (30% if elective cesarean deliveries included)

Surgical anesthesia in parturient with a labor epidural catheter: for non-urgent cesarean cases, aspirate catheter, assure no evidence of profound motor block, (eg, in case of intrathecally-placed catheter), assess fetal well-being, blood pressure, confirm adequate analgesia; epidural catheter "topped-up" with 2% lidocaine (pH adjusted) with 1:200,000 epinephrine, 5 mL increments to 10 mL total; at this point, patient usually has bilateral T4 block and evidence of S2 block, confirmed using ice test (ie, determine dermatomal level) or touch test, and clamp test (ie, surgical clamp prior to incision at incision level and T10 level); if patient reports legs "much heavier" or cannot be moved, adequate block is confirmed; if slight BP decrease after "top-up," treat with lactated Ringers IV and vasoactive drugs (prefer phenylephrine, does not cross placenta, less association with fetal acidemia than ephedrine); for more urgent surgical cases, large bolus (5-15 mL) 3% chloroprocaine has rapid onset of anesthesia but risk of profound hypotension if not treated promptly

Labor epidural catheter and inadequate intrapartum analgesia: avoid with early replacement if catheter poorly functioning rather than giving multiple larger doses of anesthetics; repeat doses of rescue medication into epidural space increase risk for cesarean delivery; if replacement

not an option, emergent need for anesthesia/surgery, either induce spinal anesthesia or induce general endotracheal anesthesia; risk/benefit analysis involves airway assessment and evaluating comorbidities

Spinal anesthesia in presence of residual epidural block: controversial; if epidural ineffective, no evidence of segmental level, spinal anesthesia safe; however, with residual block, could induce high spinal block in patient with pre-existing epidural level (eg, if block high on one side, low on other); best to place spinal with patient in sitting position, with sitting maintained 1 minute after induction; use reduced dose (eg, 1 mL bupivacaine); may still induce high spinal block, in which case, must maintain BP, heart rate, support airway — intubation may occasionally be needed

General endotracheal anesthesia: surgical urgency preventing delay for neuraxial technique or top-up; de-nitrogenate with 100% oxygen; ensure left uterine displacement 15°; propofol induction, 1.5 mL/kg succinylcholine, apply cricoid pressure, use video laryngoscope if necessary, insert endotracheal tube (eg, 7 mm with cuff), release cricoid pressure once inflated, confirm placement (eg, with CO_2 waveform); use thromboprophylaxis (eg, sequential compression stockings); cesarean section after laboring carries increased risk of uterine atony because exogenous oxytocin exhausts oxytocin receptors

Elective cesarean sections: usually with subarachnoid block; sitting position, skin antiseptic, local anesthetic to numb interspace, pencil point spinal needle (eg, 25-27 gauge) with or without introducer (midline or paramedian), 9-10.5 mg bupivacaine, 10 mcg fentanyl, 0.1-0.15 mg spinal morphine

Hypotension after spinal anesthesia: risk; prevent with phenylephrine infusion upon spinal induction through birth or incrementally; increased heart rate guides assessment

Gastrointestinal medications: patient with history of gastroesophageal reflux disease, morbidly obese, recently ate — use IV metoclopramide, famotidine; citric acid/sodium citrate (eg, Bicitra, 30 mL) to neutralize stomach contents (ie, if pH of aspirated stomach contents >0.25 less risk of pneumonitis); routine use of Bicitra semi-controversial because unpleasant to swallow, only useful if given within 20 minutes of induction, and number of patients requiring general anesthesia after failed spinal low (ie, routine use is overtreatment); still recommended by American Society of Anesthesiologists (ASA) even for elective cesareans

Oxytocin: after umbilical cord clamped, administer oxytocin to mother to increase uterine tone, decrease risk of postpartum hemorrhage; vasodilator — worsens hypotension, especially if due to hemorrhage; large boluses associated with profound hypotension, cardiovascular collapse; avoid boluses, add 20-40 units oxytocin to 1 L lactated Ringers, infuse 125 mL/hr; 2015 Boston study of oxytocin in elective cesareans; "rule of three" algorithm — giving 3-unit oxytocin bolus in 3 mL followed by 500 mL infusion normal saline with optional repeat boluses of oxytocin at 3 and 6 minutes and further rescue medications if initial 3 doses inadequate was compared to continuous infusion of 30 units oxytocin in 500 mL; no difference in rate of flushing, nausea and vomiting, ECG changes, blood loss; pain scores similar; allows one to separate IV fluid administration from oxytocin; 3-unit bolus had same effect on uterine tone as wide-open infusion of 30 units oxytocin in 500 mL, with less total oxytocin delivery, same amount of drug side effects

Postdural puncture headache: common complication following neuraxial anesthesia; treat conservatively with adequate hydration, bed rest, caffeine supplementation, oral analgesics; definitive treatment epidural blood patch; wait 24 hours after conservative measures unless headache severe; tends to be postdural (ie, worse sitting or standing, often relieved in recumbent supine position); can be associated with nausea, dizziness, visual disturbances, photophobia; epidural blood patch performed with patient in sitting position (best) or left lateral position; may require IV opioids prior to insertion if sitting position; if outpatient, IV not always necessary; epidural space found with loss of resistance technique, aseptic technique, local anesthetic injected into interspace (at level of original puncture or one space above), 20 mL patient's blood injected into epidural space slowly (ie, over 10-20 seconds) — historically successful in 90%, 10% may require second patch (of which, 90% will benefit); other studies show only 65%-70% success; not all postpartum headaches result of postdural puncture — rule out preeclampsia headache, headache associated with intracerebral conditions (eg, subarachnoid hemorrhage, subdural hemorrhage, meningitis)

Anesthetic Considerations for Obstetric Emergencies

Emergencies: maternal reasons — obstetric (eg, hemorrhage, eclampsia, amniotic fluid embolism, anesthetic complication), non-obstetric — trauma, cardiorespiratory decompensation, anaphylaxis; fetal — profound bradycardia, sinusoidal heart rate, prolapsed cord, uterine abruption, malpresentation (eg, flipping breech in advanced labor)

Anesthetic options: general endotracheal anesthesia, spinal or subarachnoid anesthesia, or if existing epidural catheter, "top-off;" infiltration anesthesia not recommended

Safety: maternal (general vs. neuraxial) maternal anesthesia-related mortality in US, 1.7 per 1 million live births; Hawkins study 2011, 1991-1996, 17 maternal deaths per 1 million live births from general endotracheal anesthesia, 2.5 deaths per 1 million live birth from neuraxial anesthesia (ie, risk ratio 6.7); ratio decreased 1997-2002 to 1.7 (6.5 deaths/million live births with general endotracheal anesthesia vs 3.8 deaths/million with neuraxial anesthesia); United Kingdom (UK) 2014, 2 maternal deaths with each

Downsides of endotracheal anesthesia: pregnant airway difficult, high rates of complications from airway management; interferes with maternal-infant bonding; increased blood loss risk (effect of volatile anesthetic agents on uterine tone); poorer pain relief after surgery (can't give neuraxial opioids); some studies, increased risk of thrombotic complications; lower Apgar scores compared with neuraxial anesthesia; high risk of patient awareness

Complication factors: full stomach, morbid obesity, non-compliant patient, comorbidities (eg, cardiac disease, lung disease, prior back surgery), drug allergies, difficult airway, available resources; ensure easily accessible emergency equipment (eg, airway) and drugs

General endotracheal anesthesia indications: coagulopathy (eg, preeclampsia with hemolysis, elevated liver enzymes, low platelets [HELLP] syndrome;

anti-coagulant use; pre-existing coagulopathy eg, idiopathic thrombocytopenia (ITP), hemophilia, some types of von Willebrand's disease; maternal cardiac disease (eg, aortic stenosis); immediate delivery needed (eg, umbilical cord prolapse, significant placental abruption, prolonged fetal bradycardia) and epidural not in place

Emergency cesarean delivery preparation recommendations: formal team organization; allows for faster and improved response times; special hospital paging system for obstetric emergencies — all team members paged simultaneously; emergency airway cart with video laryngoscope, fiberoptic tools, surgical airway equipment; rapid infusion devices; red blood cell salvage; point-of-care testing; staff should perform practice drills with simulators, know fetal and maternal early obstetric warning signs — posted in nursing stations; always immediately debrief; lack of teamwork and suboptimal communication cited as leading cause of perinatal and maternal death; standardized procedures, checklists, cognitive aids useful (eg, Stanford Anesthesia Cognitive Aid Group Emergency Manual); maternal early obstetric warning system or modified early obstetric warning system; immediate action indicated if temperature <35° C or >38° C, systolic blood pressure <90 mm Hg or >160 mm Hg, diastolic blood pressure >100 mm Hg, heart rate <40 bpm or >120 bpm, respiratory <10/m or >30/m, oxygen saturation <95%, pain score >7 unresponsive to opioids, unresponsiveness to pain or voice; particularly helpful are rapid infusion device, blood warmer, formal obstetric hemorrhage protocol (eg, immediate and continued access to blood products)

Hemorrhage: etiology severe postpartum hemorrhage in lecturer's hospital includes uterine atony 38%, invasive placenta 18%, vaginal cervical lacerations 18%, uterine rupture 6%, amniotic fluid embolism 4%, placental abruption 4%, disseminated intravascular coagulation (DIC) 6%, also broad ligament hematoma, ruptured liver, splenic artery aneurism (each 2%); massive transfusion protocol recommendations — 4 units red blood cells, 4 units frozen plasma, 1 pack platelets; cryoprecipitate not used prior to fourth cycle; in lecturer's hospital, massive transfusion protocol associated with central line placement 20% of time, general anesthesia 45% of time, neuraxial anesthesia 43% of time, conversion from neuraxial to general anesthesia remainder; 53% of patients transferred to an ICU, 32% required interventional radiology and embolization of blood vessels; massive transfusion protocol associated with 1 death at author's center

pH and anesthesia type: 2015 study *International Journal of Obstetric Anesthesia* in 2015, analysis of retrospective database found in non-emergent cases, no difference in umbilical arterial pH, base excess between general endotracheal anesthesia and neuraxial anesthesia; in emergent cases, lower pH, base excess in general anesthetic cases versus spinal anesthesia; however, if exclude cases where general endotracheal anesthesia used because no time for neuraxial anesthesia, association between general endotracheal anesthesia and lower uterine artery pH or base excess no longer present

Key Points

1. Pregnant women differ significantly from non-pregnant women physiologically.
2. Surgery and anesthesia are impacted by pregnancy.
3. Utilizing proper technique for epidural anesthesia and analgesia are important for care and outcomes

Suggested Reading

Baysinger C et al: *A Practical Approach to Obstetric Anesthesia.* 2nd ed. Philadelphia, PA: Wolters Kluwer; 2016; **Chestnut DH et al:** *Chestnut's Obstetric Anesthesia:* Principles and Practice. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014; **Gambling DR et al:** *Obstetric Anesthesia and Uncommon Disorders.* 2nd ed. Cambridge, UK: Cambridge University Press; 2008; **Hilton G et al:** Checklists and multidisciplinary team performance during simulated obstetric hemorrhage. *Int J Obstet Anesth.* 2016 Feb;25:9-16.

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Anesthesia for Obstetrics: Part 2

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Obstetric hemorrhage: major problem, with increasing incidence in US and internationally; contributes significantly to maternal morbidity and mortality, representing 11% of maternal deaths in the US; can occur before, during, or after delivery;

Placental abruption: premature separation of a normally implanted placenta from the decidua basalis after 20 weeks gestation and prior to birth; occurs in 1% of pregnancies; in acute cases, bleeding results from exposure of the decidual vessels, since the uterus is unable to selectively constrict area of abruption; separation can be complete or partial and is associated with maternal hemorrhage; can be occult or present with vaginal bleeding; loss of placental-uterine surface area reduces gas exchange and can result in fetal bradycardia and/or fetal asphyxia; many cases occur with a preterm pregnancy, and half occur before the onset of labor; fetal mortality can be as high as 40%; can also contribute to maternal mortality; implicated in 10% of preterm births

Risk factors: advanced maternal age, multiparity, hypertension, smoking, trauma, premature rupture of membranes, cocaine abuse; uterotonic drugs do not increase the incidence of abruption

Anesthetic management: based on severity of abruption and degree of maternal and fetal compromise; vaginal delivery can occur if the fetal heart rate is reassuring and there is no evidence of maternal hypertension, coagulopathy, or ongoing blood loss; under these conditions, neuraxial anesthesia is an option; general anesthetic may be required in the presence of maternal hypertension, fetal bradycardia, ongoing hemorrhage, or coagulopathy; massive blood loss is unusual in this setting

Vasa previa: occurs when the fetal vessels cross the membranes ahead of the placenta; these fetal vessels are unprotected by the placenta or the umbilical cord, causing shearing if membranes rupture; if undiagnosed, vasa previa is associated with perinatal mortality rates of 60%; rupture of fetal blood vessels can lead to exsanguination of the fetus; a rare condition occurring in about 1 in 2500 deliveries; there is a type I vasa previa, in which a velamentous cord insertion comes between the umbilical cord and the placenta and exposed fetal vessels within the amniotic membranes overlie the cervix; type II form occurs when placenta has a succensuriate lobe or is multilobed and the fetal vessels connecting the lobes pass over or near the cervix; vasa previa does not endanger the mother's life

Management: prenatal diagnosis by ultrasound allows for delivery planning and management, resulting in 95% survival rate or better; condition is managed with bed rest and frequent monitoring of fetal status; elective Cesarean delivery is usually performed at 34 weeks' gestation; undiagnosed cases may present either intrapartum or postpartum with vaginal hemorrhage and fetal bradycardia at the time of membrane rupture; survival of the fetus in these cases is only 46%; anesthetic management depends on urgency of case and individual maternal issues

Postpartum hemorrhage: anesthesiologists most often deal with uterine hemorrhage in postpartum period; usually caused by uterine atony, invasive or low-lying placenta, or genital tract lacerations

Uterine atony: more likely with long labor with oxytocin, polyhydramnios, large for gestational age babies, multiple gestations, or chorioamnionitis; especially in multiparous women

Obstetric hemorrhage protocols: since blood volume is increased in pregnant women and most pregnant women are healthy, it often takes significant time for them to develop signs of hemodynamic decompensation after significant blood loss; difficult to determine blood loss accurately because of occult blood loss, contamination of drapes, and loss on the floor; obstetrician may be unaware of extent of bleeding if busy with other aspects of delivery; incumbent on anyone present who notices hemorrhage to speak up; most hospitals now have hemorrhage protocol, which can be called by any healthcare provider; at lecturer's hospital, blood bank immediately provides 4 units of packed red blood cells (pRBCs), 4 units of plasma, and one pooled unit of platelets; if more than 4 units are needed, cryoprecipitate is added

Immediate management: involves a step-wise protocol for uterotonic medication administration; includes infusion of oxytocin (20-40 units/L), methylergonavine maleate (Methergine) 0.2 mg intramuscularly (IM); if those ineffective, prostaglandin F2α (carboprost tromethamine, Hemabate) 0.25 milligrams IM or intramyometrially can be given; other methods include prostaglandin E1 (Cytotec) rectal suppository given at end of case, Bakri intrauterine balloon insertion, operative B-Lynch suture of the uterus, hysterectomy, and/or interventional radiological arterial embolization

Resuscitation: includes oxygen administration, leg elevation, insertion of two large-bore (≥16 gauge) venous cannulae in each antecubital fossa, increments

of ephedrine or neo-synephrine, and rapid fluid administration of normal saline or uncrossed-matched blood (until a cross-match is available)

Assessing resuscitation: achieved by following hemodynamic parameters and oxygenation status and checking hematocrit and acid-base status with an arterial blood sample; old rule of thumb was to transfuse if base deficit >-10; many centers now benefit from assessment of overall coagulation status in real time using a thromboelastograph (TEG) or a thromboelastometer (ROTEM); for example, TEG may show prolonged R- and K-times, indicating depletion of clotting factors and reduced maximum amplitude, indicating diminished clot strength

Coagulation management: timely administration of fibrinogen and early use of tranexamic acid both emphasized in modern bleeding protocols; since fibrinogen levels are higher in pregnancy, there is different threshold for treating hypofibrinogenemia in parturients; cryoprecipitate or fibrinogen concentrate are administered if fibrinogen level falls to <200 mg/dL; cryoprecipitate provides a richer source of fibrinogen than plasma; many experts now de-emphasize use of plasma in treatment of massive hemorrhage; each unit of cryoprecipitate contains 140 mg of fibrinogen, along with factor VIII, factor XIII, von Willebrand's factor, and fibronectin; a typical adult therapeutic dose of cryoprecipitate is 1 unit/5-10 kg of body weight, which increases plasma fibrinogen levels by ~100 milligrams per deciliter; tranexamic acid is indicated in ongoing obstetric hemorrhage; 1 gram administered IV over 20 minutes within the first h of hemorrhage, with dose repeated at 3 h if blood loss continues; use of tranexamic acid has increased as a result of the WOMAN trial published in the *Lancet* in 2017*;* results showed use of tranexamic acid reduced death from bleeding in women with postpartum hemorrhage with no adverse effects

Invasive placenta: present when the placenta is abnormally attached to the uterus; decidua basalis is absent; most common form (78%) is placenta accreta; next most common form is placenta increta (17%), in which the placenta has invaded the myometrium; less common is placenta percreta (5%), in which placenta has penetrated serosal layer of uterus and invaded surrounding structures, eg, bladder, ureter, and bowel; invasive placenta associated with profound hemorrhage at delivery if the diagnosis is not made prior to delivery; account for 30% of all instances of massive transfusion (>10 units pRBCs); occurs in 6/10,000 deliveries; need multidisciplinary management plan for elective cesarian delivery and hysterctomy

Risk factors: low-lying anterior placenta and prior cesarean sections; each additional cesarean section significantly increases the risk of placenta accreta (after one cesarian, risk 10%, after 2, is 40%, after three or more, risk is >60%); diagnosis is made by ultrasonography and color Doppler; MRI is more useful when the placenta is adherent posteriorly; antenatal meetings of obstetrical team to plan delivery reduce perioperative blood loss, transfusion requirements, and maternal morbidity and mortality

Anesthetic management for a cesarean hysterectomy: combination of neuraxial techniques and general endotracheal anesthesia; 2016 Canadian study showed no difference in rates of blood loss and transfusion between women with invasive placentation undergoing cesarean delivery who received general anesthesia and those receiving regional anesthesia; 72% of women in study required hysterectomy; better neonatal outcomes and fewer maternal respiratory complications with use of regional anesthesia; rate of cesarian hysterectomy increasing in US (now 7/10,000 deliveries); in lecturer's institution, spinal epidural or combined spinal/epidural anesthetic is used for cesarean delivery; after delivery, general anesthesia is often induced prior to hysterectomy; obstetrician should leave placenta in situ; avoid oxytocin after delivery; if vessels are clamped and surgeons get early control of hemorrhage, an entire cesarean hysterectomy can sometimes be performed under neuraxial block alone; general anesthesia allows extension of surgical incision, better retraction, and ability to place invasive lines without distressing patient; prior to surgery, communicate with obstetricians and gynecological oncologists to decide if invasive lines are required before delivery or after delivery; though some surgeons request it, yield from cell salvage is usually small; use of preoperatively placed internal iliac balloon catheters to reduce bleeding is controversial, since much of the blood loss is from other vessels; very important to keep patient warm and to have rapid-infusion devices on hand; in small, community hospital setting, patients with invasive placenta should be referred early to tertiary center

Hypertensive Disorders of Pregnancy

Definition: systolic blood pressure >140 mm hg diastolic blood pressure >90 mm hg; complicates 6-8% of pregnancies, significant morbidity and mortality; four types discussed, gestational hypertension, chronic hypertension, preeclampsia, and chronic hypertension with superimposed preeclampsia

Gestational hypertension: occurs after 20 weeks' gestation; unlike preeclampsia, proteinuria is absent and hypertension resolves spontaneously by 12 weeks postpartum; can progress to preeclampsia, eclampsia, HELLP syndrome (hemolysis, elevated liver function tests (LFTs), low platelets); may predict future chronic hypertension

Chronic hypertension: diagnosed prior to 20 weeks gestation and persists beyond 12 weeks postpartum; most patients have a history of essential hypertension, and may have taken antihypertensives with potential adverse effects on fetus; for example angiotensin-converting enzyme (ACE) inhibitors taken after the first trimester may cause renal failure or pulmonary hyperplasia in fetus and oligohydramnios; patients with hypertension may have left ventricular hypertrophy, retinal changes, and renal disease; risk factor for the development of preeclampsia; chronic hypertension with superimposed preeclampsia requires careful monitoring of renal function and proteinuria;

Preeclampsia: presence of hypertension after 20 weeks' gestation plus proteinuria; accounts for 25% of maternal mortality in the US, with most deaths due to pulmonary edema or intracranial hemorrhage; classified as preeclampsia or preeclampsia with severe features, the latter defined as systolic >160 and/or diastolic >110; other features of severe form include headache, visual disturbance, epigastric pain, cyanosis, seizures, pulmonary edema, thrombocytopenia, right upper

quadrant pain, impaired liver function, progressive renal insufficiency (serum creatinine >1.1 mg/dL or doubling of serum creatinine in absence of preexisting renal disease); intrauterine growth retardation (IGR) no longer included, since it can have many other causes; severe preeclampsia major contributor to neonatal morbidity and mortality due to impaired uteroplacental perfusion, placental abruption, and iatrogenic premature birth; delivery of fetus is only cure for preeclampsia and must be timed carefully; HELLP syndrome may be subtype of severe preeclampsia or unique syndrome; liver function tests (AST or ALT) are elevated, platelet count <100,000, but blood pressure normal in 15% of cases; early treatment with aspirin lowers incidence of preeclampsia in women at high risk

Risk factors: chronic hypertension, chronic renal disease, obesity, diabetes, vascular or connective tissue diseases, angiotensin gene T235, age>35, multiple gestation, in vitro fertilization, family history of preeclampsia, history of preeclampsia in another pregnancy, Hispanic ethnicity, and black race

Eclampsia: onset of tonic-clonic seizures in pregnancy not attributable to another cause; seizures occur after 20 weeks' gestation and up to two weeks postpartum

Seizure prophylaxis: intravenous magnesium sulfate; Magpie study 2002 showed that magnesium halved the risk for developing eclampsia and decreased risk of cerebral palsy in premature infants; magnesium inhibits release of acetylcholine from motor nerve terminal, decreases sensitivity of postjunctional membrane to acetylcholine, and decreases excitability of muscle fibers; given as a 4 gram intravenous loading dose over 15 minutes, followed by a 1-2 gram per hour infusion; serial magnesium levels are monitored to maintain therapeutic levels in the range of 4-8 meq/L; toxic levels can lead to areflexia, sedation, and respiratory depression; cardiac arrest is possible at high magnesium levels if ventilation is not maintained; toxicity is more likely in patients with renal dysfunction, since magnesium is cleared from the body by the kidneys; because preeclamptic women often have renal dysfunction, it is important to follow serum magnesium levels, especially when GFR <30 ml/min; treatment of magnesium toxicity is to stop the infusion, give a fluid load and a diuretic, inject 1 gram of calcium gluconate intravenously, provide support ventilation if needed, and (rarely needed) hemodialysis; magnesium crosses the placenta and neonates may also have respiratory depression and motor weakness; since preeclamptics are at risk of postpartum seizures for 2-7 days, magnesium therapy is continued for at least 72 hours; other anticonvulsants can be used to treat seizures not controlled by magnesium, including midazolam, lorazepam, phenytoin, and phenobarbital, sometimes bipropofol; patients with intractable seizures unresponsive to treatment should receive further tests to rule out other causes such as intracranial neoplasm

Anesthetic management in preeclampsia: any organ system may be affected, but anesthesiologist must pay special attention to cardiac, respiratory, and coagulation systems; airway edema can make tracheal intubation difficult; although neuraxial anesthesia is a preferred mode of labor analgesia and anesthesia for cesarean section, the choice is based on an assessment of the intravascular volume, blood pressure, and coagulation status, especially the platelet count; hypertension control and assessment for possible airway edema also important

Epidural: has advantage of lowering the blood pressure and improving uteroplacental perfusion by decreasing circulating stress-induced catecholamines; regional anesthesia considered ideal for laboring women with preeclampsia as long as there is no coagulopathy and platelet count stable; many anesthesiologists will place an epidural when the platelet count is as low as 60,000; a thorough bleeding history may be useful in assessing the risk-benefits of an epidural; if an epidural catheter is placed, it should not be removed until the platelet count is normalized, especially if there was a significant fall in the platelet count after insertion of the epidural catheter

Regional anesthesia: preferred for cesarean delivery; spinal anesthesia can be used safely in women with preeclampsia with severe features if the patient is not hypervolemic or coagulopathic; any neuraxial technique (such as epidural, combined spinal epidural, or subarachnoid block) is acceptable; spinal opioids are not contraindicated

General anesthesia: should be reserved for emergency cases, for those who refuse a neuraxial anesthetic, and for those with a significant coagulopathy and/or bleeding history; as with any cesarean delivery, patients should receive antacid prophylaxis

Induction: propofol is acceptable for cesarean delivery, and succinylcholine is used in a dose of 1.5 mg/kg to facilitate endotracheal intubation after adequate denitrogenation with 100% oxygen by mask and applied cricoid pressure; since magnesium can potentiate the effect of non-depolarizing neuromuscular blockers, these drugs should be titrated in small doses, if used at all, and their impact monitored with a nerve stimulator; the intubating dose of succinylcholine may provide adequate relaxation for an entire case, and a non-depolarizing neuromuscular blocker (such as rocuronium) is not usually required; anesthesia is maintained with 1.5-2% sevoflurane and a 50% air-oxygen mixture, or other volatile agent

Hypertension in preeclampsia and tracheal intubation: labetalol and/or hydralazine, lidocaine, and a calcium-channel blocker should be considered prior to intubation; intravenous nitroglycerine or nitroprusside (rarely used) can be reserved for acute increases in blood pressure; excessive nitroprusside therapy is associated with tachyphylaxis, methemoglobinemia, and cyanide toxicity in the neonate; in doses <2 mcg/kg/min and short infusions, the risk of cyanide toxicity in the neonate after nitroprusside is almost nonexistent; patients who receive titratable drugs should have an intra-arterial catheter to assess beat-to-beat variations in blood pressure

Intraoperative hypotension: treated by temporarily stopping magnesium infusion, judicious use of intravenous fluids, and small increments of intravenous neo-synephrine and ephedrine to keep blood pressure close to 140/90

Analgesia: lecturer gives 1-2 mg IV dose midazolam once baby born; intravenous opioids for intraoperative analgesia; if possible place transverse abdominis plane (TAP) block under ultrasound guidance at end of case; a combination of intravenous patient-controlled analgesia (PCA) and around-the-clock alternating doses of a nonsteroidal anti-inflammatory drug and acetaminophen

is usually adequate for postoperative analgesia after general anesthetic

Extubation: increased risk for airway misadventure due to airway edema and maternal sedation; extubation of the trachea can be safely achieved when there is return of the "train of four," sustained head-lift on command, and a vital capacity of more than 10 mL/kg; lecturer strongly favors extubation of awake patient to avoid regurgitation-aspiration risk; adequate postoperative monitoring of cardiorespiratory status in the PACU or ICU is essential for patients with preeclampsia; since preeclamptics at risk for seizures for 2-7 days after delivery, magnesium treatment should be continued for at least 72 hours

Amniotic fluid embolism (AFE): a rare complication of pregnancy which presents with signs and symptoms similar to other obstetric complications; differential diagnosis in cardiovascular collapse and hypoxemia includes eclampsia, uterine rupture, placental abruption, other causes of acute obstetric hemorrhage, emboli (air, fat, thrombus), cardiac problems such as cardiomyopathy, myocardial infarction (MI), preexisting cardiac disease, aortic dissection, anaphylaxis, sepsis, local anesthetic toxicity, high or total spinal anesthesia, transfusion reaction, aspiration; incidence estimated at 2-8/100,000 deliveries in developed countries; in UK, 56% of cases before or during delivery, 44% after delivery; associated with 10% of direct maternal deaths in the US; survivors often report major adverse outcomes, including neurological injury; often a diagnosis of exclusion

Risk factors: advanced maternal age, multiparity, intrauterine fetal death, polyhydramnios, uterine rupture, uterine hyperirritability, meconium-stained liquor, atrophy, chorioamnionitis, and placenta accreta

Pathogenesis: unclear, but most think AFE is an immune-mediated response resulting from entry of amniotic fluid into the maternal circulation by a break in maternal-fetal interface; amniotic fluid contains several vasoactive substances (leukotrienes, arachidonic acid, bradykinin, cytokines) that may trigger disseminated intravascular coagulation (DIC); complement likely plays a role in the development of the disorder; syndrome is not due to an embolic event or amniotic fluid so "AFE" is misnomer; better considered as anaphylactoid reaction of pregnancy

Diagnosis: based on clinical presentation; common signs and symptoms include sudden onset of dyspnea and oxygen desaturation; severe hypertension, cardiac dysrhythmias, cardiovascular collapse, and cardiac arrest commonly follow the onset of respiratory signs and symptoms; sudden cardiovascular collapse is attributed to profound vasospasm of the pulmonary vasculature, resulting in severe pulmonary hypertension and right ventricular dysfunction; if general anesthesia is administered, there will be a decrease in end tidal carbon dioxide; in up to 50% of the cases, there is a rapid onset of DIC

Treatment: if AFE occurs before delivery and cardiac arrest occurs, advanced cardiac life support and uterine displacement must be initiated immediately; fetal viability should not be confirmed; perform rapid delivery of the fetus by cesarean delivery within five minutes of arrest; best chance for survival of woman and survival with minimum neurological damage for baby; defibrillation recommendations and drug dosages same as for non-pregnant individuals; initiate massive transfusion protocol as coagulopathy and hemorrhage are common; early intubation and ventilatory support are the most effective measures to improve ventilation and oxygenation; when coagulation is accompanied by hemorrhage, treatment involves administration of packed red blood cells, frozen plasma, platelets, and cryoprecipitate

Anesthetic management: correction of hemodynamic instability, hypoxemia, and coagulopathy; effectiveness of replacement and supportive therapy should be continuously monitored by the signs and symptoms of adequate oxygen delivery and tissue perfusion; hemodynamic instability is often treated with aggressive IV fluid administration, vasopressor therapy, and inotropic support; placement of intra-arterial catheters should occur early in management to monitor beat-to-beat blood pressures and facilitate analysis of blood gases and laboratory values; a pulmonary artery catheter may also be considered; in most cases, patients require endotracheal intubation and transesophageal echocardiography; less common treatments include inhaled nitric oxide, prostacyclin administration, exchange transfusion, plasma exchange, cardiopulmonary bypass, extracorporeal membrane oxygenation, and right ventricular assist device placement; maternal mortality in AFE currently 13-35%

Morbid Obesity in Pregnancy

Criteria: obese patients have body mass index (BMI) >30; morbidly obese patients have a BMI >40; acceptable weight gain in pregnancy is 11-25 pounds when the BMI >30 and 15-25 pounds when the BMI <30; physiological respiratory changes in pregnancy are exaggerated in obesity; the functional residual capacity is further reduced as a result of chest wall adipose tissue exerting pressure on the thorax, and abdominal adipose tissue enhances the cephalad shift of the diaphragm, changes exaggerated in lithotomy and Trendelenburg positions; greater closing volume produces abnormal distribution of ventilation, resulting in ventilation/perfusion (V/Q) mismatch and impaired arterial oxygenation; in obese parturient, spinal anesthesia causes decrease in vital capacity much greater than is case for normal-weight parturient

Obstructive sleep apnea (OSA): common in obese pregnant women; involves intermittent pharyngeal obstruction resulting in episodic apnea during sleep; increases the risk for cardiomyopathy, eclampsia, pulmonary embolism, preeclampsia; fivefold increased odds of in-hospital mortality; diagnosed by history, sleep-laboratory testing, and stop-bang tool; treatment includes sleeping in a 45°-60° heads-up tilt, oxygen therapy, and nasal CPAP; patients require postpartum monitoring of cardiorespiratory function, especially if they receive opioids; CPAP therapy will help minimize airway collapse and postoperative oxygen desaturation

Obesity hypoventilation (Pickwickian syndrome): chronic hypoxemia and hypercarbia may lead to polycythemia, pulmonary hypertension, and cor pulmonale; asthma rates higher in morbidly obese, possibly because of acid reflux; obese patients do not tolerate supine position; left uterine is essential but difficult to accomplish or confirm;

cardiovascular collapse and death have both been reported in supine position

Hypertension: common in morbidly obese; correlates positively with BMI; associated with adverse maternal outcomes such as acute renal failure, pulmonary edema, preeclampsia, and in-hospital mortality; the incidence of preeclampsia in morbid obesity doubles with each 5-7 kg/m^2 increase over pre-pregnancy BMI; arterial BP monitoring may be needed, as cuff readings can be inaccurate

Metabolic syndrome: major risk factor in developing cardiovascular disease; characterized by insulin resistance, dyslipidemia, elevated C-reactive protein, thrombophilia, and activation of sympathetic nervous system; puts patients at risk of coronary artery disease; routine ECG advisable

Other conditions common in morbidly obese: diabetes mellitus, hypercoagulability with increased risk of venous thromboembolism, gastroesophageal reflux disease (GERD)

Anesthesia: 50% of maternal deaths occur in women who are either overweight or obese; special challenges in airway placement and placement of neuraxial blocks, line placement, transportation of patient and positioning on operating room table; ultrasound-guided IV placement useful; wide OR tables with higher weight limitations and side attachments are essential for the morbidly obese individual; multiple personnel are required move these patients; there is a risk of patient falling onto the floor during transfer; for laboring women, it is important to place an epidural catheter early, since morbidly obese parturients are at risk for cesarean delivery, of which 50% are emergent

Epidural and spinal: reduce oxygen consumption associated with labor pain and attenuate increases in cardiac output; to improve success of the labor epidural, insertion can be facilitated with ultrasound imaging; using a combined spinal-epidural (CSE) technique is another way of ensuring correct positioning of the epidural catheter; detection of spinal fluid after dural puncture confirms positioning of the epidural catheter in the middle of posterior space; attempt a plain epidural technique when CSF cannot be obtained after attempted dural punctures if the epidural catheter threads well; if after multiple attempts to find the epidural space, there is an inadvertent dural puncture, thread an intrathecal epidural catheter and use continuous spinal anesthetic, carefully labeling the catheter, inform the patient, nurse, and obstetrician, and hang a sign on the labor room door to indicate a spinal catheter; also inform other anesthesiologists at handover rounds; lecturer uses 1-2 ml/h of 1/8% bupivacaine with 2 mcg/ml of fentanyl as continuous infusion, and reassess motor block, blood pressure, and sensory level regularly; it is easier for an epidural catheter to become dislodged in an obese parturient; instruct the patient to sit upright and then lie down laterally before securing the catheter, leaving 5-6 cm of catheter in epidural space; standard needles usually long enough, but sometimes longer epidural and spinal needle needed; use a large-bore spinal needle (22 gauge) or introduce a 25-26 gauge pencil-point needle via a stiffer epidural needle used as a guide; epidural catheters can be used for cesarean delivery; increments of 3-5 mL of local anesthetic, (either pH-adjusted 2% lidocaine with epinephrine, or 3% chloroprocaine, and then 2 mL of epidural Fentanyl) are given to achieve a bilateral T4 sensory level at the nipple line; and a bilateral S2 block; it is rare to need more than a 10 mL solution in a patient with a previously well working epidural catheter; in the case of a failed epidural, if time allows, a spinal anesthetic can be inserted; a continuous spinal technique can be used if there is concern about effect wearing off

General anesthesia: required in emergency or if neuraxial technique fails; with proper patient positioning, endotracheal intubation is often straightforward; with difficult intubation, fiberoptic intubation is an option; since laryngoscopy can be difficult if large breasts impede traction of laryngeal handle, a short handle can be used; other tools include video laryngoscopes, tube stylets, and gum elastic bougies; supraglottic airways (eg, laryngo-mask airway (LMA)) allow ventilation and oxygenation and offer fiberoptic intubation via the LMA; if endotracheal tube cannot be placed and ventilation and oxygenation are adequate, surgery can proceed with LMA alone; maintain cricoid pressure throughout surgery and avoid Trendelenburg position and exteriorization of fundus

Induction: patients should be monitored and receive acid aspiration prophylaxis, pre-induction oxygen, left uterine displacement, and rapid sequence induction; ideal dose of induction medication not well studied in this population; there is a positive correlation between BMI and blood volume, suggesting an induction dose greater than that determined by ideal body weight; lecturer uses 20-30 ml propofol to induce sleep, followed by 140-160 mg succinylcholine to facilitate intubation in obese patients; could be longer operative times and greater blood loss, and incision-to-delivery time often longer

Miscellaneous: prior to surgery, it is important to tape or suspend the panniculus to help with surgical access and relieve aortocaval compression; may improve ventilation; there is increased risk of thromboembolic events, so compression stockings and anti-coagulants are often used; increased risk of endometritis, postoperative wound infection, and wound dehiscence, so often longer length of hospital stay; continuous postoperative cardio-respiratory function monitoring in stepdown unit or ICU very important

Fetal complications of morbid obesity: neural tube defects, other congenital anomalies, macrosomia, hypoglycemia, shoulder dystocia, other birth trauma, and neonatal asphyxia

Cardiac Disease in the Obstetric Patient

Risk factors: cardiac disease present in up to 4% of obstetric patients, with 80% of such cases of congenital origin; presence of reduced left ventricular ejection fraction, left-sided obstructive lesions, New York Heart Association (NYHA) functional class >2, or history of prior cardiac events are risk factors for cardiac events in pregnancy; patients with history of congenital heart disease who received definitive surgical repair and have good functional results after surgery can be managed like normal parturients; manage patients with partial correction, palliative procedures, uncorrected lesions, and residual cardiac defects according to current cardiovascular physiology

Management principles: take a detailed history, follow patients regularly during pregnancy, and understand physiological changes of pregnancy and how they affect heart lesions; coordinate care carefully with obstetricians, cardiologists, and cardiac surgeons; patient may require endocarditis antibiotic prophylaxis; patient may be on anticoagulants; may impact choice of anesthetic

Mitral stenosis: maintain hemodynamics close to the patient's normal state; provide adequate pain control, avoid hypoxia, hypercarbia and acidosis; preserve sinus rhythm and treat atrial fibrillation aggressively; avoid aortocaval compression; monitor and maintain adequate cardiac preload; provide supplemental oxygen and avoid reductions in systemic vascular resistance (SVR)

Aortic stenosis: maintain hemodynamics close to patient's normal state; provide pain control; avoid tachycardia; maintain sinus rhythm; avoid reductions in SVR and maintain preload; aortocaval compression is poorly tolerated; avoid myocardial depression agents during general anesthesia

Mitral regurgitation and aortic incompetence: afterload reduction beneficial; avoid increases in SVR; early and effective analgesia during labor is recommended; avoid and treat atrial fibrillation aggressively; slight tachycardia is preferred, with target heart rate 80-100; bradycardia is poorly tolerated; maintain preload and avoid aortocaval compression; avoid myocardial depression

Tetralogy of Fallot: most common cyanotic lesion; 10% of congenital heart disease; syndrome consists of ventricular septal defect, pulmonic stenosis, right ventricular outflow tract obstruction, overriding aorta, and right ventricular hypertrophy; anesthetic and hemodynamic goals include avoiding changes (especially decreases) in SVR to prevent altering existing shunt; avoid increases in pulmonary vascular resistance by preventing hypoxia, hypercarbia, and acidosis and providing supplemental oxygen; maintain normal or elevated cardiac filling pressures (especially in patients with right ventricular impairment); avoid aortocaval compression; provide continuous cardiac monitoring due to high incidence of atrial and ventricular dysrhythmias; avoid tachycardia and increases in myocardial contractility in situations in which there is residual right ventricular outflow tract obstruction as it might exacerbate obstruction and cause right-to-left shunting

Transposition of the great vessels: avoid aortocaval compression; consider arterial catheter or CVP catheter; avoid excessive fluids with evidence of heart failure; avoid negative inotropic agents; monitor for dysrhythmias

Fontan procedure for tricuspid atresia and hypoplastic left heart syndrome:; the Fontan procedure creates a bidirectional Glenn shunt, superior vena cava to pulmonary artery connection; closes the atrial septal defect(ASD), ligates proximal pulmonary artery, and creates a right atrial to pulmonary artery connection; blood flow to pulmonary arteries is passive, and elevators in pulmonary vascular resistance (PVR) reduce pulmonary flow and decrease cardiac output by reducing gradient between vena cava and pulmonary artery; hemodynamic stability is dependent on high systemic venous pressure (SVP) and right atrial preload; spontaneous respiration assists forward flow by keeping PVR low; single ventricle prone to failure leading to pulmonary edema; progressive hepatic failure common due to autohepatic circulation from increased SVP; anesthetic and hemodynamic goals for patients with Fontan circulation are to maintain preload, avoid aortocaval compression, avoid elevations in PVR by preventing acidosis, hypoxemia and hypercarbia, maintain sinus rhythm and spontaneous respiration, avoid sedative medications and myocardial depressants

Eisenmenger's syndrome: most severe form of pulmonary artery hypertension in adults with congenital heart disease; chronic high-volume systemic-to-pulmonary shunting results in right ventricular hypertrophy, elevated PVR, and significant ventricular and arterial remodeling of the right side of the heart; remodeling and the elevation of PVR leads to reversal of shunt flow and hypoxemia; childbirth carries mortality ranging from 30-50% and high incidence of fetal demise, so patients advised against pregnancy; anesthetic and hemodynamic goals are avoiding elevations in PVR, preventing hypoxemia, acidosis, hypercarbia, and pain; provide supplemental oxygen at all times; maintain SVR; avoid myocardial depressants; maintain myocardial contractility, preload, and sinus rhythm; advanced pulmonary hypertension management includes inhaled nitric oxide, prostacyclin analogues, endothelin-receptor antagonists, and phosphodiesterase inhibitors

Peripartum cardiomyopathy: rare disorder affecting 1/3000-4000 live births; up to 20% mortality; idiopathic cardiomyopathy presenting with heart failure secondary to left ventricular systolic dysfunction toward the end of pregnancy or in months following delivery; diagnosis of exclusion; left ventricle may not be dilated, but ejection fraction nearly always <45%; patients present with fatigue, shortness of breath, and peripheral edema; progressive deterioration and increased severity (along with chest pains, palpitations, and pulmonary edema) indicate developing heart failure; patients can have epidural anesthesia for labor or cesarean delivery if drug is slowly titrated to reduce SVR; with general anesthesia, avoid or titrate myocardial depressants (inhalational agents and propofol); arterial catheters should be strongly considered; placing central venous or pulmonary artery catheters is often reserved for NYHA class 3 and 4 patients; with general anesthesia, transesophageal echocardiography provides rapid real-time evaluation of cardiac function

Hypertrophic obstructive cardiomyopathy: genetic disorder causing left ventricle hypertrophy; hypertrophy causes a noncompliant or stiff ventricle with diastolic dysfunction, reduction in left ventricular (LV) volumes, and LV outflow obstruction; physiological changes of pregnancy are well tolerated because decreased SVR is offset by elevation in blood volume; tachycardia is poorly tolerated and patients often treated with beta blockade; maternal mortality is ~10/1000 live births, directly related to presence of heart failure symptoms prior to pregnancy; anesthetic goals are to avoid decreased preload, avoid decreased SVR, avoid tachycardia, and avoid positive cardiac inotropy, because it can increase dynamic obstruction

Transplanted heart: no afferent or efferent autonomic innervation; relies on intrinsic adrenergic receptors, increasing sensitivity to sympathomimetic agents; lack of vagal innervation causes high resting heart rate (~100/min); heart is unresponsive to agents such as atropine (function via vagal effects); patients tend to have accelerated coronary artery disease, varying degrees of rejection, impairing cardiac function, hypertension, and

possible side effects of immunosuppressive drugs; if cardiac function good, patients tolerate pregnancy well; pregnancy places patient at increased risk for rejection, fetal growth restriction, pre-term delivery, hypertension, preeclampsia, and dysrhythmias; immunosuppressive drug regimens may need to be altered due to increased blood volume and hormonal changes; cardiac functional studies may include echocardiography, cardiac catheterization, and myocardial biopsy; cesarian delivery performed for usual obstetric indications; have been successful deliveries with spinal, epidural, and general anesthesia; anesthetic and hemodynamic goals are to maintain normal filling pressures and avoid aortocaval compression; aseptic technique are critical as patients are at high risk of infection; if signs of coronary artery disease present, avoid tachycardia and hypertension; with sign of rejection and impaired myocardial function, avoid myocardial depressants

Cardiac arrest in pregnancy: occurs in 1/20,000-30,000 pregnancies; often occurs late in pregnancy; many causes, which may include dysrhythmias, hemorrhage, AFE, pulmonary embolism, MI, heart failure, and iatrogenic causes such as pharmaceuticals or hypoxia from failed intubation attempts; fetal viability will influence therapy; before 24 weeks gestation, therapy only directed at saving mother; after 24 weeks, fetal viability is a concern; American Heart Association states that best therapy for fetus is best therapy for mother; initiate advanced cardiac life support (ACLS) protocol with defibrillation, airway control, and chest compressions; place a wedge under the right side to prevent aortocaval compression and improve blood flow; electrical cardioversion used if indicated; medications used following ACLS protocol; try to determine reason for arrest; BEAUCHOPS stands for Bleeding, Embolism (pulmonary, coronary, AFE), Anesthetic complications, Uterine atony, Cardiac disease, Hypertension/ preeclampsia, Other, Placental abruption or Placenta previa, Sepsis; if initial attempts at resuscitation are unsuccessful, immediate delivery of the fetus within 4 minutes to save life of the fetus and help resuscitate the mother; fetal resuscitation usually needed for hypoxemia, acidosis, and/or preterm delivery; other options include open heart massage or cardiopulmonary bypass, which is usually only considered in cases of pulmonary embolism or bupivacaine toxicity, in which cardiopulmonary bypass can provide support while bupivacaine dissipates

For local anesthetic systemic toxicity: American Society of Regional Anesthesia recommends initial focus on airway management, ventilate with 100% oxygen, suppress seizures (benzodiazepines preferred); avoid propofol in presence of cardiovascular instability; alert nearest facility with cardiopulmonary bypass; manage arrhythmias, basic and advanced life support may require adjustment of medications and perhaps prolonged effort; avoid vasopressin, calcium channel blockers, beta blockers, or local anesthetics; reduce individual epinephrine doses to <1 mcg/kg; lipid emulsion 20% is essential; bolus dose is 1.5 ml/kg lean body mass, intravenously over 1 minute, followed by a continuous infusion of 0.25 mL/kg/min; repeat the bolus once or twice for persistent cardiovascular collapse and double infusion rate to 0.5 mL/kg/min if blood pressure remains low; continue infusion for at least 10 minutes after obtaining circulatory stability; the upper limit for a lipid emulsion is approximately 10 mL/kg over the first 30 minutes

Suggested Reading

Baird EJ: Identification and Management of Obstetric Hemorrhage. *Anesthesiol Clin* 2017 Mar;35(1):15-34; **Hess PE:** What's New in Obstetric Anesthesia: The 2016 Gerard W. Ostheimer Lecture. *Anesth Analg* 2017 Mar;124(3):863-71; **Shakur H et al:** Effect of early Tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. *Lancet* 2017 May;389(10084):2105-16.

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Neonatal Resuscitation and PALS

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Neonatal Resuscitation

Introduction: ≤10% of newborns may need some stimulation or assistance to begin breathing; <1% need extensive resuscitation procedures; if responsible for neonatal resuscitation, should make sure facility has all equipment and drugs you may require immediately at hand; newborn infant who does not need resuscitation can be immediately identified

Term birth: if baby born at term, has good tone, breathing or crying, can have routine care (dried, placed next to mother, covered to maintain temperature, and observed for continued breathing, color, and activity); some evidence that delayed cord clamping may have benefits in infants who do not require resuscitation

Preterm: infants who do not meet criteria of term birth and have good tone and respirations should be immediately transferred to radiant heater warmer for further assessment and treatment; should be completed in first 60 secs after birth (*ie*, "golden minute")

Assessment procedure: 2 basic assessments, quality of respirations and heart rate (HR); respirations other than normal and easy or HR <100 beats per minute (BPM) indications for further treatment

Once ventilation established spontaneously or by intermittent positive-pressure ventilation (IPPV), continuing evaluation of 3 parameters crucial: adequacy of spontaneous ventilation, HR, and O_2 saturation; increased HR prime indicator of successful response throughout; determination of HR by auscultation recommended, but electrocardiogram may improve accuracy; not difficult to attach adhesive leads; pulse oximetry may underestimate HR

Temperature: during resuscitation, all measures should be adopted to prevent heat loss and maintain body temperature; use of radiant warmer and head covering advocated; preterm infants should be wrapped in plastic film; hypothermia increases mortality and morbidity from respiratory problems, intraventricular hemorrhage, and sepsis

Airway and ventilation: suctioning of airway should be limited to infants who have obstructed airway or who require positive pressure ventilation (PPV); suction mouth first, then nares; beware of inducing bradycardia by passage of suction catheters; continue monitoring during all suctioning; if meconium-stained amniotic fluid present and baby vigorous and breathing well, no additional steps apart from gentle suctioning of mouth and nose recommended; however, if such infants born through meconium and have poor tone and not breathing well, IPPV should be instituted; endotracheal intubation should be performed only if airway not easily maintained; routine intubation not recommended, (may delay institution of PPV); when PPV required, self-inflating bag or T-piece system may be appropriate; in skilled hands, optimal airway pressures and low level of positive end-expiratory pressure (PEEP) *ie*, 5 cm H_2O, may be easier to maintain with T-piece; airway pressure should be monitored and peak inspiratory pressures limited to 20 cm H_2O, although initially slightly higher pressure may be optimal; ventilation rate should be 30/min to 40/min; endotracheal intubation should be performed if clear airway cannot be obtained; use of laryngeal mask airway (LMA) should be limited to patients in whom endotracheal intubation failed; use of LMA during chest compressions not evaluated; position of endotracheal tube should be carefully checked by auscultation of both sides of chest and end-tidal CO_2 detection; term and preterm infants may be resuscitated initially using room air, pending assessment of preductal saturation; O_2 should be added if needed to obtain satisfactory normal saturation level; normal levels in newborn ≥60% immediately, rising to >90% at 5 min after birth; O_2 blender should be available for titration of O_2

Chest compressions: should be commenced if HR remains <60 BPM; however, chest compressions should not be allowed to interfere with optimal ventilation; sequence of 3 chest compressions to each ventilation recommended with compression rate of 90/min and ventilation rate of 30/min; brief pause in chest compression should permit each ventilation; chest should be allowed to completely recoil after each compression, with thumbs remaining in place; higher rates may be used in very small infants; chest compressions using thumbs with hand encircling chest preferred; chest should be compressed over lower third of sternum to extent of one-third of anterior-posterior diameter; during cardiac compressions, use of 100% O_2 suggested, but should be reduced as soon as HR improves

Drugs: seldom indicated in neonatal resuscitation; limited to epinephrine and normal saline; if HR remains <60 BPM despite ventilation and compressions, use of epinephrine or volume expansion may be indicated; epinephrine 0.01 mg/kg to 0.03 mg/kg (*ie*, 10-30 mcg/kg) may be used intravenously (IV); intratracheal epinephrine in higher dose of 0.05 mg/kg may be used if IV route not available; however, IV route preferred as soon as possible; volume

expansion may be considered in cases of possible blood loss or if weak pulse, pale skin, or lack of response to resuscitation; 10 mL/kg isotonic saline or blood may be administered slowly, and may need to be repeated; rapid volume expansion has been linked to intraventricular hemorrhage and should be avoided

Postresuscitation care: infant should be kept warm and nursed in intensively monitored area because of continued risk of deterioration; blood glucose levels should be monitored, as hypoglycemia may occur, associated with increased risks for brain injury; some special considerations for preterm infant; in preparation for birth of preterm newborn, increase temperature in room where baby will receive initial care to approximately 23°C to 25°C (74°F to 77°F); goal to maintain infant's axillary temperature between 36.5°C and 37.5°C; additional interventions to maintain body temperature (*eg*, plastic wrap or bag and thermal mattress and hat) recommended; 3-lead electronic cardiac monitor provides rapid and reliable method of continuously displaying baby's HR; pulse oximeter may not acquire stable signal; resuscitation device such as T-piece or self-inflating bag capable of providing PEEP and continuous positive airway pressure (CPAP) preferred; if anticipated gestational age <30 weeks, consider having surfactant available; consider administering surfactant if baby requires intubation if he has respiratory distress or extremely preterm; early administration of surfactant more successful than delayed administration; infants who show signs of developing hypoxic ischemic encephalopathy may benefit from induced general or local hypothermia to head

When to discontinue resuscitative efforts: presence of Apgar score of 0 at 10 mins highly predictive of mortality and morbidity; if HR remains undetectable at 10 mins despite optimal resuscitation efforts, decision to terminate ventilation may be considered; however, must take into consideration all aspects of situation, including predelivery circumstances and wishes of parents

Cardiopulmonary Resuscitation (CPR) for Infants and Children Beyond the Neonatal Period

Introduction: outcomes of cardiac arrest generally much less favorable in pediatric patients than in adults; cardiac arrest in children more commonly occurs as result of ventilatory problems, less commonly as result of primary cardiac disease; we must assume that, by time impaired ventilation and oxygenation have caused cardiac arrest, significant neurologic damage have resulted; anesthesiologists have great responsibility to detect ventilation problems early and prevent respiratory arrest from proceeding to cardiac arrest

Causes of impaired perioperative ventilation: numerous perioperative causes; must be prepared and equipped to deal with them rapidly; airway obstruction prime cause; laryngospasm common, usually resulting blood or mucus in airway, or poorly planned and managed anesthesia; infants have relatively large tongue, which may block airway, and may be compounded by improper positioning or compression of soft structures by anesthesiologist's fingers; ventilation may be compromised if infant has dilated stomach as result of excessive airway pressures, partial obstruction, crying, and swallowing air; premature removal of artificial airway may be followed by complete obstruction; in children, hypertrophied adenoids or tonsils may seriously impair airway; ventilation may also be impaired due to central depression or residual neuromuscular block

Detection and management of ventilation problems: constant vigilance required to detect and rapidly manage airway and ventilation problems; equipment to deal with compromised airway must be immediately at hand during every anesthetic administration; if problems arise, endotracheal intubation should be performed without delay; alternatives, such as LMA, should be immediately available; another set of problems may be related to relatively small blood volume and high fluid turnover rate of small infants; hypovolemia may rapidly develop; patient's volume status must be carefully evaluated; also remember that infants and small children have brisk vagal responses; IV atropine should be immediately available to manage induced bradycardia; causes of airway obstruction impeding ventilation must be detected early in children; must try to prevent ventilatory problems from proceeding to cardiac arrest

Procedure if CPR needed: first, call for help and equipment, including defibrillator; begin with ABCs

Airway: check patency and apply jaw thrust

Breathing: 4 ventilations, preferably with bag and mask

Cardiac activity: check with stethoscope, palpate brachial artery in infant, femoral or carotid artery in child

Next steps:

Check ventilation — if ventilatory efforts present, position child in lateral semiprone position and extend head to optimize airway and protect it should regurgitation occur; if this does not clear airway, apply jaw thrusts; give O_2 to all patients in this situation; if respiratory efforts present, but evidence of airway obstruction (*ie*, absent or muffled breath sounds), intercostal retraction, flaring of lateral chest margins or cyanosis, pull tongue or mandible forward by pressing behind mandibular condyles; in other words, apply jaw thrust, and remove any foreign matter from pharynx, keeping mouth slightly open; extend neck as necessary; use caution in neck injury, but ventilation first priority; give O_2 by mask; check for improved chest movement and breath sounds; *if no respiratory effort or if ventilation appears inadequate* — begin PPV at once; ventilate directly (mouth-to-mouth if necessary) until resuscitation equipment placed in your hand; ensure adequate chest expansion with each breath; if cardiac activity undetectable by auscultation or by femoral, carotid, or brachial artery palpation, or if HR <60 BPM despite ventilation and oxygenation, and signs of poor perfusion, pallor, and cyanosis, start external cardiac compressions immediately

Compressions: push hard and push fast; applying high-quality cardiac compression considered most important factor in successful resuscitation; site of compression in infant 1 fingerbreadth below intermammary line; in child, over lower sternum, 1 fingerbreadth above xiphisternum; in infant, can use 2 fingers; in child, use heel of hand; depth of compression should be one-third to one-half of anterior-posterior diameter of chest; between compressions, release completely to allow chest wall to fully recoil; rate of compression should be 100/min for infants, children, and adolescents; depth of compression should be at least one-third of

anterior-posterior chest diameter (translates to 4 cm in infants, 5 cm in older children); in adult, depth of compression should be ≥5 cm, but not >6 cm; allow full chest recoil between compressions; interruptions to chest compressions must be minimized

Defibrillation: if required, early defibrillation recommended for children who have ventricular fibrillation or pulseless ventricular tachycardia; for infants and children weighing <20 kg, use pediatric defibrillator pads (4.5 cm diameter for infants, 8 cm for children); set machine to deliver shocks appropriate to child's size to maximize chance of success and minimize danger of electrically induced myocardial damage; initial setting should be 2 joules/kg; give 1 shock, then immediately resume CPR for 2 mins and reassess; if unsuccessful, defibrillator dose should be doubled to 4 joules/kg; many automatic external defibrillators (AEDs) have potential to detect pediatric shockable rhythms and can be adjusted to deliver appropriate energy for each shock; ensure that AEDs installed in your pediatric care environment conform to these requirements; children who have received digitalis should be treated with reduced power settings initially, and then power gradually increased; normal doses of countershock may cause irreversible cardiac arrest in presence of bound digitalis in heart muscle

Shock-resistant ventricular fibrillation or pulseless ventricular tachycardia: either lidocaine or amiodarone administration suggested; amiodarone 5 mg/kg may be administered, may be repeated twice if necessary; lidocaine 1 mg/kg may be followed by infusion of 20 mcg/kg/min to 50 mcg/kg/min; if infusion not available, 1 mg/kg may be repeated after 15 mins

Drug therapy: although subsequent drug therapy necessarily individualized, standard initial protocol advantageous

Epinephrine: must be given IV to be maximally effective, preferably into central vein, or, if IV not possible, by intraosseous route; initial and subsequent doses 10 mcg/kg (equal to 0.1 mL/kg of 1 in 10,000 solution); continue CPR after this injection for 2 mins and assess response; high-dose epinephrine (*ie*, 100 mcg/kg) no longer recommended, except possibly in treatment of beta blocker overdose

Vasopressin: has been successful in some cases of prolonged cardiac arrest, but has not resulted in increased survival to neurologically intact hospital discharge

Dopamine infusion: may be required for continued hypotension and poor tissue perfusion; 5 mcg/kg/min to 20 mcg/kg/min may be titrated to achieve desired effect

Sodium bicarbonate: no longer recommended as routine, but may be considered in prolonged cardiac arrest for documented, continued severe metabolic acidosis despite adequate ventilation, oxygenation, and chest compressions; may also be useful in treatment of hyperkalemia, hypermagnesemia, or tricyclic antidepressant overdose; administration of excessive doses of sodium bicarbonate produces hyperosmolarity, hypernatremia, hypokalemia, decreased ionized calcium, impaired cardiac action, and possibly severe alkalosis after recovery

Calcium: no longer recommended except as definitive treatment for hyperkalemic-induced arrhythmias or arrest and citrate-induced hypocalcemia

Glucose: documented hypoglycemia should be treated by glucose infusions; otherwise, avoid glucose administration because hyperglycemia (*ie*, blood glucose levels >200 mg/dL) may compromise neurologic outcome after hypoxic events

Route of administration: inject epinephrine into central line if available; otherwise, use peripheral IV or intraosseous line; tracheal route used only as last resort; intracardiac injections should not be made; damage to heart and coronary arteries and/or pneumothorax may result

Fluid replacement: also important; insert large-bore IV cannula as soon as possible, first to provide route for drug therapy, second for rapid replacement of fluid; in cardiac arrest, hypoxic capillaries leak rapidly, diminishing circulating blood volume; replace losses initially with isotonic crystalloids and later with colloids, plasma, or blood as indicated; even child previously in congestive heart failure needs infusions totaling ≥10% of estimated blood volume; with recovery, extravasated fluid returns slowly to vascular compartment, giving time for assessment of fluid volume and decision as to whether diuretic therapy necessary; throughout, avoid use of dextrose-containing solutions; these may cause hyperglycemia, which may compromise cerebral survivals; if hypoglycemia suspected, should be confirmed by blood glucose determination and treated accordingly

Special situations: cardiac arrest arising from documented or strongly suspected hyperkalemia should be managed by an infusion of calcium chloride 5 mg/kg and sodium bicarbonate to correct metabolic acidosis; cardiac arrest in prone position may be difficult; may be treated initially by chest compressions delivered on back with sternal support anteriorly; should be applied immediately before attempts to turn patient; midline incision, chest compressions can be delivered over scapulae; if turning patient possible, should be done with minimal interruption of continuing chest compressions delivered to back

Postresuscitation care: postresuscitation care critical to favorable outcome; hyperventilation may be harmful and should be avoided; maintain normocarbia; hypoxemia should be carefully avoided, but hyperoxia also detrimental; ensure normal levels of oxygenation; hemodynamic support using vasoactive drugs (*eg*, dopamine) should be used when necessary to improve circulatory status; most important to maintain cerebral perfusion pressure; restrict fluid replacement; avoid large infusions of crystalloid solution once cardiovascular stability ensured; target blood glucose levels to achieve normal levels; treat seizure activity with phenobarbital or phenytoin (however, prophylactic administration of antiseizure drugs not recommended); prevention of hyperthermia absolutely essential; maintain normal body temperature; induced hypothermia (*ie*, 32-34°C for 12-24 hrs), considered for children who remain comatose after CPR; however, recent studies indicate that induced hypothermia does not increase intact survival compared with those treated with continued normothermia; normothermia most important factor in postoperative care; early neurological consultation should be obtained

Suggested Reading

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ANESTHESIOLOGY
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Anesthesiology for Ophthalmologic Procedures

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Intraocular Pressure

Overview: intraocular pressure (IOP) generated by ocular muscle contractions, partially due to rigidity of sclera and intraocular contents and venous congestion; normal IOP ranges from 10 to 22 mm Hg with slight variations during day and with each heartbeat; when globe is open, as seen during ophthalmic surgery or as result of trauma, IOP cannot increase — eye responds by draining aqueous fluid or extruding vitreous through wound; both can permanently impair vision; elevated IOP, such as in patients with glaucoma, can have significant effect on optic nerve

Techniques to lower IOP: include hypothermia, increasing respiratory rate, decreasing arterial or venous pressure, or administration of diuretics such as mannitol; inhaled and intravenous (IV) anesthetics decrease blood pressure, relax extraocular muscles, and cause pupillary constriction, all leading to decreased IOP

Increased IOP: succinylcholine increases IOP by 5-10 mm Hg; mechanism of this rise unknown; succinylcholine used during rapid sequence induction, which may be necessary in emergent airway management situations when patient has not met NPO (nothing by mouth) guidelines; if any concern that possible increase in IOP could lead to clinically significant sequelae, this should be discussed with the surgeons; with increased availability of rocuronium and sugammadex, some anesthesiologists consider those drugs a better option than succinylcholine in short duration surgeries for rapid sequence induction and rapid reversal of neuromuscular blockade; ketamine can cause slight increase in IOP and should be avoided for induction and maintenance of anesthesia if any concern

Endotracheal tube: if general anesthesia with endotracheal tube is utilized for surgery, patients are at higher risk for increase in IOP, especially during intubation and extubation if bucking or coughing occurs

Postoperative nausea and vomiting: can cause dangerous rise in IOP; decrease risk with muscle paralysis, maintenance of deep plane of anesthesia, and administration of IV lidocaine or opioids

Hypotension: vigilance about intraoperative hypotension is important because deep plane of anesthesia for low stimulation surgery increases its likelihood; have vasopressors readily available for administration

Ophthalmic surgery: general anesthesia using laryngeal mask airway (LMA) is an acceptable option for ophthalmic surgery; decreases risk of vocal cord stimulation which can lead to bucking and coughing; however, important to keep patient in deep plane of anesthesia, especially if no neuromuscular blockade is utilized, as light anesthesia can cause laryngospasm and subsequent increase in IOP

Nitrous oxide: more than 30 times more soluble than nitrogen in blood, can cause significant increase in IOP; should be avoided if air or sulfur hexafluoride is injected into eye during retina surgery

Sedation: option for anesthesia administration for ophthalmic surgery; hypercarbia and hypoxia (both can occur from moderate to deep sedation) can increase IOP; even light sedation can lead to hypercarbia and hypoxia in high risk patients, such as those with obstructive sleep apnea (OSA), obesity, and increased sensitivity to benzodiazepines or opioids; short acting medication such as propofol or remifentanil can be used for sedation during injection of ophthalmic block

Oculocardiac Reflex

Overview: aka Aschner's phenomenon, Aschner's reflex, or Aschner-Dagnini reflex; defined clinically as decrease in heart rate as result of pressure to globe or traction of ocular muscles; reported incidence varies significantly (some studies reporting up to 90%); potentially leads to significant instability in vital signs, making vigilance very important for early recognition and appropriate treatment

Pathophysiology: oculocardiac reflex mediated by nerve connections between ophthalmic branch of trigeminal nerve, via ciliary ganglion, and vagus nerve of parasympathetic nervous system; afferent nerve fibers from trigeminal nerve synapse with visceral motor nucleus of vagus nerve, which decreases output from sinoatrial node; documentation of afferent tracks arising from maxillary and mandibular divisions of trigeminal nerve, such as seen in panfacial trauma surgery

Occurrence: oculocardiac reflex can occur with local anesthetic injection or under general anesthesia; reflex triggered by traction of extraocular muscles (especially medial rectus), direct pressure on eye, manipulation of globe, and ocular pain; other triggers include pressure associated with local infiltration of medication or analgesia, such as in retrobulbar block, ocular trauma, or manipulation of tissue in orbital apex (for example, after enucleation); interestingly, retrobulbar block may prevent arrhythmias by blocking afferent limb of trigeminal nerve, but it can elicit oculocardiac reflex due to pressure associated with local infiltration

Elimination: reflex sometimes fatigues with repeated stimuli or might require intervention for surgery to proceed

Manifestation: most often manifests as sinus bradycardia; however, any cardiac arrhythmia can occur, such as ventricular tachycardia, ectopic beats, atrioventricular blocks, or even asystole

Demographics: most commonly occurs in young, healthy patients; greatest incidence in healthy neonates undergoing strabismus surgery with manipulation of extraocular muscles; significant hemodynamic instabilities can arise in pediatric patients, who are more dependent on their elevated heart rate to maintain stable blood pressure

Severity: hypoxia, hypercarbia, acidosis, and light anesthesia can increase incidence and worsen severity of oculocardiac reflex; some clinicians treat risk of effects of oculocardiac reflex by deepening anesthetic or giving glycopyrrolate or atropine prior to surgical incision

Management: if suspect oculocardiac reflex is occurring, notify surgeon to stop orbital stimulation, optimize oxygenation and ventilation, deepen anesthetic with either inhaled or IV anesthetic or opioid administration; notify surgeon to proceed if patient's cardiovascular status has stabilized; if cardiac arrhythmias persist, consider giving anticholinergic agent, such as glycopyrrolate or atropine for treatment; in extreme cases, cardiopulmonary resuscitation (CPR) or cardioversion might be required; of note, late oculocardiac reflex can occur in recovery room (PACU or post-anesthesia care unit) if retrobulbar hemorrhage is present (due to persistent bleeding which can cause steady rise in periorbital pressure)

Strabismus Surgery

Overview: one or more extraocular muscles are strengthened, weakened or moved to different location to improve alignment; in children, early surgery may be recommended to improve chance of restoring or promoting normal binocular vision; in adults, eye alignment surgery restores normal appearance and considered reconstructive, while improving depth perception, eliminating double vision, and improving social function

Anesthesia: most strabismus surgery performed under general anesthesia; high risk of oculocardiac reflex, especially bradycardia; atropine, glycopyrrolate, as well as ephedrine should be readily available; other interventions include communicating with surgeons to pause surgery as oculocardiac reflex can fatigue with repeated stimulus, deepening plane of anesthesia, administering opioids, and other medical interventions

Eye examinations under anesthesia: may be required for noncooperative pediatric patients or adults; measurement of IOP part of comprehensive exam or used to evaluate various pathologies

Techniques: 2 common techniques for induction of anesthesia are via inhaled induction or using IM (intramuscular) or IV ketamine; inhaled induction with volatile agents can cause a clinically significant decrease in IOP within minutes of induction; important for ophthalmologist to be ready to measure IOP immediately to obtain most accurate values; IM or IV ketamine can cause transient increase in IOP; recovery from inhaled induction is often quicker than dose of ketamine required for brief examination under anesthesia

Glaucoma Procedures

IOP: most accurate measurement of IOP obtained in awake and cooperative patients; seldom possible in pediatric populations; therefore, examination under anesthesia is required; accurate IOP measurement determines appropriate treatment

Anesthesia: medications such as ketamine have little to no effect on IOP; can be given in IM dose, rendering patient relatively still, spontaneously breathing, and in amnestic state; duration of ketamine is relatively long if goal is only to obtain IOP without planning for further surgical intervention; ketamine can be combined with midazolam to ease wake-up and combined with glycopyrrolate to decrease increased oral secretions caused by ketamine; IM dose can be quite disturbing for parents to witness and for child to receive; recommend swift "sleight of hand" to administer medication with distraction; advise parents that patients can be in mildly hypnotic state during recovery at home

Tonometer: most accurate tonometers should be promptly available to measure IOP; if surgery is required, airway device can be inserted and medications given to maintain anesthesia

Inhaled agents: can cause significant decrease in IOP; sevoflurane is well tolerated for inhaled induction techniques; ophthalmologists should be immediately available to measure IOP once patient is induced; some studies show that inhaled nitrous oxide does not have significant effect on IOP and can be used in conjunction with volatile agent for induction

Anesthetic interventions: tracheal intubation or administration can increase IOP; techniques such as giving small nondepolarizer prior to succinylcholine administration or giving propofol and remifentanil prior to intubation can blunt changes in vital signs

Anesthesia for open eye injury: most common ocular trauma is superficial injury to eye resulting in open wound that requires surgical intervention; extreme trauma can require immediate evisceration or enucleation if repair is not possible; preventing increase in IOP is important to prevent intraocular contents from extruding through open wound; surgeries for superficial wounds may be accomplished with regional block and sedation, while other wounds require general anesthesia

Regional Analgesia

Overview: ophthalmic surgeries increasingly performed under regional analgesia; ranges from less invasive techniques, such as topical analgesia with lidocaine or proparacaine, to more invasive techniques, such as retrobulbar or intraconal blocks

Provider: provider performing these blocks varies significantly depending on organization of surgical site; some blocks performed by ophthalmology team and other blocks performed by anesthesiology team, including certified nurse anesthetists; common for blocks to be performed in operating room by ophthalmologist, while anesthesiologist provides sedation and monitors care

Complications: several cases of complications from ophthalmic blocks performed by anesthesiologists who did not receive formal training in administration of these blocks; with increased risk and oftentimes

no compensation for performing these blocks, anesthesiologists often default to surgeon to determine type of local anesthetic analgesic to be administered

Efficiency: with several ophthalmic surgeries now in ambulatory care centers, there is motivation to improve operating room efficiency, decrease operating room turnover times, improve ocular akinesia, and increase surgical volume; at some centers, anesthesia team performs block in preoperative area, allowing for adequate time for analgesia to produce maximal effect

Topical anesthesia: consists of viscous lidocaine applied to surface of eye

Retrobulbar block involves administration of local anesthetics into space located behind globe; aims to block ciliary nerves, ciliary ganglion, and cranial nerves II, III, and VI, causing akinesis of extraocular muscles as well as sensory analgesia and anesthesia to cornea, uvea, and conjunctiva

Complications of retrobulbar blocks: allergic reactions to local anesthetics; retrobulbar hemorrhage, which is characterized by motor block, closure of upper lid, and increase in IOP, causing proptosis; central retinal artery occlusion from retrobulbar hemorrhage or injection into subarachnoid space; subconjunctival edema; globe perforation (characterized by pain, sudden loss of vision, hypotonia, and poor red reflex); central spread of anesthetic into dural cuff or atrial spread; oculocardiac reflex; optic nerve atrophy; postoperative strabismus due to direct IM injection

Central spread of local anesthetic presents as drowsiness, vomiting, contralateral blindness, convulsions, respiratory depression, and cardiac instability leading to cardiac arrest; full resuscitation includes CPR, vasopressors, mechanical ventilation, and intralipid infusion

Peribulbar (extraconal) block: involves injections above and below orbit, which deposits local anesthetic into orbicularis oculi muscle; blocks ciliary nerves and cranial nerves III and IV; anesthetic deposited outside muscle cone and less risk of intradural injection, intraocular injection, and nerve injury

Complications: include spread of local anesthetic to contralateral eye, periorbital ecchymosis, and transient blindness

Antithrombotic therapy: considerations with concurrent antithrombotic therapy are ongoing; patients receive antithrombotic medications for various medical conditions — strokes, cardiac arrhythmias, cardiac stent placements, deep venous thrombi, pulmonary embolus, hypercoagulable states, and others; risks and benefits of continuing or withholding anticoagulation in preparation for ocular surgery must be discussed between primary care physicians and surgeons; in patients who continue antithrombotic therapy, surgeons must avoid (or might avoid) retrobulbar block due to increased risk of retrobulbar hemorrhage

Importance of Communication

Overview: monitored anesthesia care (MAC) is commonly requested for ophthalmic surgeries, such as cataract, glaucoma, and simple vitrectomies; regardless of type of anesthetic technique or level of sedation, most important consideration is communication with patient and with surgeon; expectations should be discussed prior to anesthesia administration

Communication with patient: patient expectation is important; present information in realistic and calm manner; emphasize benefits of being calm and relaxed during non-painful surgery, such as avoiding risk of general anesthesia and being able to go home shortly after completion of surgery; explain to patients that they will be relaxed, but not completely asleep, may experience touch to surface of eye that is similar to applying or removing a contact lens, may see lights, shadows, and colors, and may hear conversations; explain that these experiences are part of normal sedation experience; assure patients that they are monitored completely with backup plan for general anesthesia should there be unanticipated complexities

Communication with surgeon: ascertain surgeon's preference for level of sedation, and confirm type of regional analgesic technique; often safest for patient to receive light sedation involving short acting benzodiazepine, such as midazolam, and short acting opioids, such as fentanyl; if ophthalmic block is planned, medication such as propofol or remifentanil is appropriate to render patient deeply sedated, yet spontaneously breathing with possible brief period of apnea; supplemental oxygen should be administered to patient during sedation

Ophthalmic Emergencies

Acute angle-closure glaucoma: caused by rapid, sudden increase in IOP due to imbalance of aqueous humor production and impaired drainage; a medical and/or surgical emergency

Pathophysiology: angle of eye, located between peripheral cornea and peripheral iris, contains trabecular meshwork that acts as filtration system for aqueous fluid drainage; when angle closes suddenly, elevated IOP can cause optic nerve damage and vision loss

Signs and symptoms: may present with severe eye pain, blurred vision, headache, profuse tearing, and nausea and vomiting

Treatment: laser therapy, eye drops, oral medications, and surgical drainage are treatment options

Endophthalmitis: inflammatory condition of intraocular cavities; caused by infection or noninfectious or sterile etiology (such as retained native lens material after an operation), or toxic agents

Signs and symptoms: include blurred vision, red eye, pain, and swollen lid; can be surgical emergency to prevent further systemic infection

Treatment: includes vitrectomy, intravitreal antibiotics, systemic antibiotics, corticosteroids, and reinjection

Postoperative Vision Loss

Overview: reported after spine, cardiac, and head and neck surgeries; contributing factors and etiologies include ischemic optic neuropathy, microvascular diseases, intraoperative hemodynamic instabilities, central or branch retinal artery occlusion, cortical blindness, and external ocular injury; highest incidence (0.2%) of postoperative vision loss is following spine surgery

Extraocular injury: corneal abrasions or scleral injury can range from minor irritation to significant laceration; patients usually present with painful eye and foreign body sensation; eye may appear red and injected; treatment varies depending on severity and clinical

setting; important to evaluate patients who complain of eye pain and consult appropriate ophthalmology team member for treatment plan

Prevention: corneal injuries prevented by applying ophthalmic lubricants and properly taping patient's eyes closed after induction of anesthesia; use of clear tape aids in visualization of position of patient's eyelids under tape and ensures protection of cornea with fully closed eyelids

Cortical blindness: occurs from stroke in parietal-occipital region; results from global or focal ischemia, cardiac arrest, hypoxemia, intracranial hypertension and hemorrhage, vascular occlusion, thrombosis, vascular spasm, and emboli; patient may present with inability to interpret sensory stimuli, called agnosia; pupillary reflexes and most of visual field is restored, but impairment in spatial perception and in relationship between sizes and distances may remain

Retinal ischemia: results from central retinal artery occlusion that affects entire retina or retinal artery branch occlusion that affects part of retina; usually presents unilaterally; caused by external compression of eye, decreased blood supply to eye (such as from embolism or systemic hypotension), and impaired drainage of eye

Perioperative retinal artery occlusion: most common cause is improper patient position; results in external orbital compression, increase in IOP, and decreased blood flow to central retinal artery; at higher risk are patients undergoing spine surgery in prone position; patients present with painless vision loss and abnormal pupillary reactivity; other presentations include loss of light perception, afferent pupillary defect, periorbital edema, chemosis, ptosis, proptosis, and paresthesias

Fundoscopic examination shows opacification of ischemic retina and narrowing of retinal arterioles; classic diagnostic sign in central retinal artery occlusion is cherry red macula with white ground glass appearance of retina and attenuated arterioles

Prevention of central retinal artery occlusion: all efforts made to prevent compression of orbit; if patient is supine, receiving head and neck surgery or robotic surgery, protect patient's head and eyes using egg crate and other cushions as barrier to direct pressure; if patient is prone, position of head, neck, and eyes should be checked intermittently by palpation and/or visualization

Vision loss: if one suspects potential vision loss, urgent ophthalmic consult is needed for evaluation of etiology and treatment options; obtain hemoglobin values, stabilize hemodynamics, and improve and optimize arterial oxygenation; aggressive interventions to decrease IOP may be necessary; administration of fibrinolysis into ophthalmic artery can be considered if embolism is suspected

Postoperative Management of Pain and Nausea

Intraoperative pain: managed with topical analgesia and ophthalmic blocks, supplemented with IV medications; consider nonopioid pain medications including acetaminophen or nonsteroidal drugs; for moderate to severe pain consider IV or oral opioids

Postoperative pain: if significant postoperative pain, patients should be evaluated by surgeon if they are still in surgical facility; if patient not present in facility, recommend the emergency room to patient for immediate ophthalmic evaluation due to possibly dangerously high level of IOP

Nausea and vomiting: patients receiving ophthalmic surgery are at higher risk of postoperative nausea and vomiting; increased risk if history of prior postoperative nausea and vomiting, young age, nonsmoker, and female; several risk factors may warrant multimodal interventions including benzodiazepines, ondansetron, dexamethasone, promethazine, and propofol; avoidance of opioid administration can decrease risk of postoperative nausea and vomiting; important as vomiting can cause significant increases in IOP which can compromise recovery from recent ocular surgery

Suggested Reading

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Anesthesia for Adult ENT Procedures

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Overview

Airway assessment: in otolaryngology cases, anesthesiologist must be concerned with thorough assessment of airway; important to note that no single assessment tool can necessarily predict a difficult airway, so anesthesiologist should combine multiple tools wherever possible

Patient history: first, complete a directed patient history; a documented personal history of difficult or failed direct laryngoscopy is a strong predictor of future difficult intubation, but converse does not hold true; previous easy intubation does not necessarily indicate future success, especially if patient has experienced changes in weight, symptoms, or pathologic condition; regardless, all reasonable attempts should be made to acquire previous anesthetic records; other potential history red flags peculiar to otolaryngology may include known tumors, abnormal anatomy secondary to previous surgical intervention, history of radiation to neck, previous tracheostomy, tracheal stenosis, etc

Physical examination: performed after history; necessary components include visual inspection of face and neck for deformity or trauma, assessment of mouth opening with goal being inter-incisor distance >3 cm, evaluation of dentition, assessment of neck range of motion, tests of mandibular prognathism (ie, lower jaw bite test), and assessment of submandibular space including thyromental distance and tissue compliance

Modified Mallampati score: most common physical exam tool used to assess airway; however, score shown to have poor prognostic value when used alone; recommended to observe score as part of holistic approach, especially when dealing with complex otolaryngology cases

Prior imaging: complex patients often present with imaging for review, which adds value to airway assessment by informing anesthesiologist of airway compression or encroachment by any mass; be particularly cautious with tumors at base of tongue, which may be quite vascular and lead to bleeding in airway; flexible nasopharyngoscopy by anesthesiologist or otolaryngologist may be performed at bedside with local anesthetic and helps to solidify airway exam and plan

Communication: finally, do not underestimate value of communication with surgical colleagues who previously evaluated the patient and can provide useful information; if securing airway is likely to be difficult (often the case in otolaryngology), anesthesiologist should consider multiple plans for securing it, in accordance with the American Society of Anesthesiologists (ASA) difficult airway algorithm

Anesthetic Procedures

Airway methods: many options for airway tools in modern era, including direct and video laryngoscopy, gum-elastic bougie, flexible or rigid stylets, laryngeal mask airways (LMAs), and other supraglottic ventilation devices; safest method is awake fiberoptic intubation, which allows for patient to maintain native airway until secured by anesthesiologist; if decide to proceed with awake fiberoptic intubation, achieving topical anesthesia is paramount; many methods available, such as application of nebulized or viscous lidocaine

Superior laryngeal nerve block: particularly useful technique; superior laryngeal nerve is a branch of vagus nerve and provides sensory input for much of larynx, including glottic surface of epiglottis; identify superior cornu of either hyoid bone or thyroid cartilage, then insert 25-gauge needle and walk off cornu anteriorly into thyrohyoid ligament; change in resistance should be felt while passing through ligament at typical depth of 1 to 2 cm; after confirming negative aspiration for blood and air, inject 1.5-2 mL of 2% lidocaine; repeat block on contralateral side

Transtracheal block: achieves regional anesthesia of trachea and vocal chords; identify cricothyroid membrane, insert a 22-gauge needle directed posteriorly and caudally until air is aspirated; quickly inject 4-5 mL of 2% lidocaine; patient will cough, which helps disperse local anesthetic in a form of recurrent laryngeal nerve block

Level of sedation: some debate over level of patient alertness for awake fiberoptic intubation, awake tracheostomy, and other forms of awake airway intervention; most anesthesiologists will provide some sedation, but must weigh possible benefits of anxiolysis against potential loss of airway, which could be catastrophic; sedation should be gentle and judicious

Anesthetic drugs: popular agents include dexmedetomidine and ketamine, which do not impact respiration, although the latter may increase secretions, leading to possible complications; other agents may be titrated to effect; motivated patient may require no sedation

Tubes in Otolaryngology

Microlaryngeal tubes: unique to otolaryngology cases is array of endotracheal tubes; microlaryngeal tube, commonly abbreviated MLT (technically a Covidien trademark); popular choice among otolaryngologists; available in sizes 4 mm, 5 mm (most common), and 6 mm; surgeon prefers microlaryngeal tube because its small

diameter increases visibility of surgical instrumentation in airway; anesthesiologist likes it because its length outpaces its diameter; essentially a tube with pediatric diameter, but of adult length and adult-sized cuff; small diameter creates relatively high resistance to gas flow, resulting in high airway pressure, and often need for lower I to E ratio (inspiration to expiration ratio), perhaps as low as 1:6 to accommodate resistance; microlaryngeal tube is an improvement because able to ventilate patient in a way that is not possible through traditional 5.0 mm pediatric tubes

Reinforced tube: typical left-facing bevel and Murphy eye of standard endotracheal tube but also features a metal wire coil embedded in wall; tube useful for patients with existing stoma, especially with an uncuffed tracheostomy tube at baseline; in practice, uncuffed tracheostomy typically removed after induction and replaced with reinforced endotracheal tube; when used in this fashion, tube typically secured with suture; another notable fact is outer diameter slightly larger than traditional endotracheal tube of same inner diameter; therefore, although less likely to kink than traditional tube, if kinking does occur reinforced tube will not rebound and will remain kinked; also note, reinforced tube is not considered MRI (magnetic resonance imaging) compatible

Laser tube: traditional PVC (polyvinylchloride) endotracheal tubes can ignite from laser sources, but laser tubes are shielded in various ways; dependent upon manufacturer and type of laser; made of various materials, including stainless steel, silicone, and copper; most common laser type is CO_2 laser, which allows for precise cutting and minimizes bleeding

Laser vaporization of tissue: especially virus-laden tissue, can create harmful smoke that should be evacuated with suction; all health care providers should avoid breathing smoke

Special cases: of note, in some cases, due to location of lesion, not feasible to use laser tube or endotracheal tube; in these cases, anesthesiologist may choose jet ventilation or, more commonly, intermittent ventilation with standard endotracheal tube or supraglottic device

Laser surgery: surgeon and anesthesiologist alternate with airway, one ventilates and other operates; situation best managed with total intravenous anesthetic to maintain deep level of anesthesia; remifentanil is popular choice due to short half-life; has additional advantage of being vagomimetic, which helps limit intense sympathetic response often observed with use of suspension laryngoscope

Fire risk: lasers are high-energy sources; if not controlled, potential energy source for fire; operation in and around airway or face makes fire a particular risk in otolaryngology surgery; remember that fire occurs when an ignition source, oxygen, and fuel are all present; in otolaryngology, ignition source is most commonly either surgical laser or electrocautery unit; fuel may be the drapes, surgical sponge, or, most traumatically, endotracheal tube; in terms of oxygen — when surgical laser or electrocautery unit used within the airway, advisable to titrate FiO_2 (fraction of inspired oxygen) as low as tolerated to minimize risk of airway fire; avoid use of nitrous oxide due to its flammability

Airway fire: if occurs, immediately inform surgical team to stop energy source, whether laser or electrocautery; stop ventilator and turn off flow of oxygen; remove burning electric endotracheal tube and dump into bucket of water; call for help, and extinguish the fire; after fire extinguished, ventilate patient with 100% O_2 via face mask; consider bronchoscopy to evaluate airway damage; reintubate patient if necessary for airway injury or to complete surgical procedure

Otolaryngology Surgery

Functional endoscopic sinus surgery: commonly abbreviated as FESS; indications for procedure are varied, but most commonly performed for chronic or recurrent sinusitis

Sinus surgery: easily performed with either supraglottic airway device or endotracheal tube, with advantages and disadvantages of each; for example, endotracheal tube provides more protection against aspiration (real risk in case where blood may be unseen in esophagus), while supraglottic airway may allow for smoother emergence; ultimately, anesthesiologist decides based on individual patient

Decongestion: sinus surgery begins with decongestion of nose via phenylephrine or oxymetazoline, followed by vasoconstriction with cocaine-soaked pledgets

Cocaine: important to note that application of cocaine to nose by otolaryngologist may have similar effects as in illicit use of cocaine; results from reuptake at norepinephrine terminals and manifests as hypertension and tachycardia; effects may be profound, but usually short-lived in this setting; dose of cocaine should not exceed 1.5 mg/kg

Patient immobility: due to presence of rigid surgical instruments in proximity to vital structures of face and head, important for patient to remain still; achieved via neuromuscular blockade or depth of anesthesia; consideration must be given to length of surgical procedure, which is typically short

Facial flap surgery: length of procedure may be long; 2 general types of flaps used for facial reconstruction; first is pedicle flap where vessels left intact and flap rotated from local site, such as pectoralis or latissimus; second is microvascular free flap where vessels and tissue harvested from distant donor site, such as forearm or lower leg, and grafted to face

Anesthetic management: arterial line generally required for these cases; necessary for careful blood pressure management; historically, use of vasopressors discouraged and patients often liberally hydrated to maintain blood pressure; recent literature supports judicious use of vasopressors and modern goal-directed fluid therapy; perfusion of flap is paramount, both intraoperatively and postoperatively; communication with surgeon about goals is important

Head and neck trauma: first, assume head and neck trauma patients have brain and cervical spine injuries until proven otherwise and treat with extreme caution; cervical spine fixated in rigid collar or other means; this position combined with likelihood of blood and foreign bodies in airway often makes intubation difficult; best practices include gentle but thorough suctioning, use of video laryngoscopy, and use of fiberoptic bronchoscopy with low threshold for proceeding to placement of surgical airway

Placement caution: relatively common for actual airway to be disrupted in cases of burns, bilateral mandibular

fractures, or open laryngeal trauma; in such cases, endotracheal tube may be inadvertently placed into mediastinum; placement should be confirmed with bronchoscope or at least chest x-ray

Midface fractures: typically referred to by LeFort classification, which defines degree of separation of facial structures from skull base; in these cases, nasal intubation avoided as it not only can increase bleeding, but tube can be inadvertently placed into cranial vault

Bleeding risk of procedures: facial trauma considered moderate bleeding risk, similar to septoplasty, sinus surgery, thyroidectomy, and neck dissection; tonsillectomy and tumor resections, particularly glomus tumors, are considered high bleeding risk procedures

Anticoagulated patients: bleeding risks elevated in patients who are anticoagulated, as is the case for increasing fraction of population; if surgery is elective and patient is on anticoagulant, bleeding risk should be weighed against indication for anticoagulant (eg, mechanical heart valve vs atrial fibrillation) and discuss with patient's primary prescribing physician; optimally, plan decided ahead of surgery to minimize bleeding risk; in event of urgent or emergent surgery, anticoagulants may need reversal intraoperatively

Reversal: vitamin K antagonists, like warfarin, can be reversed with vitamin K and prothrombin complex concentrates; heparin, and to an extent, low-molecular-weight heparin, can be reversed with protamine; some novel oral anticoagulants have specific antidotes, while others are not reversible

Postoperative Risks

Postoperative bleeding: important — when surgery has ended, risk of bleeding continues; postoperative bleeding a significant risk in otolaryngology

Post-tonsillectomy bleeding: likely the most common emergency in the field, even for non-anticoagulated patients; securing airway in tonsillar bleed very challenging due to amount of blood and swelling in airway; always have suction available for induction in these cases and be prepared for difficult airway, potentially proceeding to surgical airway if necessary

Hematoma: at times, postoperative bleeding occurs in subcutaneous space, and patient develops significant expanding hematoma in neck; may compress airway and cause respiratory distress; if so, notify surgeon immediately, but if surgeon is not available, anesthesiologist may need to reopen incision in recovery room to release hematoma, which then releases pressure on airway

Postoperative pain and nausea: intraoperative administration of dexamethasone helps alleviate both issues; pain best controlled with NSAIDs (nonsteroidal anti-inflammatory drugs), acetaminophen, and judicious use of opiates, as these patients at risk for loss of airway if overly sedated; for postoperative nausea and vomiting, evaluate each patient for risk factors and administer prophylaxis when appropriate; in cases where blood may enter stomach unseen, such as sinus surgery, wise to pass orogastric tube and evacuate contents prior to emergence due to blood being very emetogenic

Conclusion: otolaryngology is a special field of surgery in which surgeons and anesthesiologists often share the airway; unique bleeding and fire risks make cases dangerous; education, practice, and cooperation with surgical colleagues by anesthesiologist provides safe and effective care for patients

Suggested Reading

Aujla K et al: A study to compare the quality of surgical field using total intravenous anesthesia (with propofol) versus inhalational anesthesia (with isoflurane) for functional endoscopic sinus surgeries. *Anesth Essays Res* 2017 Jul-Sep;11(3):606; **Codère-Maruyama T et al:** Anesthesia in the elderly patient undergoing otolaryngology head and neck surgery. *Clin Geriatr Med* 2018 May;34(2):279-88; **Gökdoğan O et al:** The rate of epistaxis incidence in new-generation anticoagulants and perioperative approach in otorhinolaryngological practices. *J Craniofac Surg*. 2017;28(2):e178-82; **Helmstaedter V et al:** High-frequency jet ventilation for endolaryngotracheal surgery — chart review and procedure analysis from the surgeon's and the anaesthesiologist's point of view. *Clin Otolaryngol*. 2015 Aug;40(4):341-8; **Karabayirli S et al:** Surgical conditions during FESS; comparison of dexmedetomidine and remifentanil. *Eur Arch Oto-Rhino-Laryngology* 2017 Jan;274(1):239-45; **Kim H-J et al:** Risk factors of emergence agitation in adults undergoing general anesthesia for nasal surgery. *Clin Exp Otorhinolaryngol* 2015 Mar;8(1):46-51.

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Anesthesia for Trauma and Burns

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Major trauma: the leading cause of death in young adults in the United States; accounts for 10% of all deaths among both men and women; most common causes of mortality from trauma are hemorrhage, multiorgan dysfunction, and cardiopulmonary arrest; majority of these deaths occur within first 4 hours of injury; 2 critical phases in prevention of unnecessary trauma-related deaths — pre-hospital and immediate hospital times; "golden hour" concept stresses need for rapid intervention during the first hour following major trauma

Initial approach: after assuring scene is safe, emergency medical services should quickly assess patient for any immediately life-threatening injuries that can be corrected quickly prior to transport; care should be taken not to delay transport, as time from injury to emergency department (ED) has serious implications on survival; air travel should be considered if injuries are severe or if travel by road will delay transport to a qualified facility

En route to hospital: emergency medical services should call hospital trauma staff and relay the following information — estimated time of arrival, patient age and gender, mechanism of injury, vital signs (including lowest blood pressure and highest pulse rate), any apparent injuries, and what treatment the patient has received; should also include the Glasgow Coma Scale (GCS) assessment and any decline in function since arrival of emergency medical services; this allows emergency room staff to prepare supplies and extra staff for any procedures, such as endotracheal intubation, and clues to whether or not to anticipate a difficult airway, blood transfusion; special conditions such as severe burns or potential need for decontamination should be reported

Arrival at ED: Advanced Trauma Life Support (ATLS) guidelines should be initiated; includes a primary survey ("the ABC [DE]s"), a secondary survey if applicable, and transfer to definitive management if necessary

A: stands for airway; assessment of airway and ventilation, looking at indications for intubation; if patient is conscious, ask patient their name; asking them to talk can provide clues about need for airway protection; if patient is not able to vocalize and protect their own airway, observe neck and chest symmetry for retractions or accessory muscle use, indicating impending respiratory failure; important to reexamine airway frequently throughout exam; initial ability to protect own airway does not mean patient will continue to be able to do so

Airway exam: examine the oropharynx for foreign bodies such as teeth or other objects that may have penetrated the face, complete a visual inspection of face, mouth, and neck for lacerations, bleeding, or vomitus; access to airway may be needed later; quick mnemonic to help with airway examination is "lemon"

L: stands for look at face and neck

E: stands for evaluate the intraoral, mandibular, and hyoid-to-thyroid notch distances; should be 3 finger breadths for intraoral and mandibular distances and 2 finger breadths hyoid-to-thyroid notch distance; possibility of doing this examination indicates absence of jaw fractures or obstructions preventing patient from opening the mouth and providing laryngeal-tracheal access; mandibular and hyoid-to-thyroid notch distances indicate a potential space for the tongue to move out of the way when intubation attempted

M: stands for Mallampati; often not possible to assess in trauma patients, but should be attempted if mouth opening permits and patient is conscious; patient should sit as close to 90 degrees as possible, open mouth under their own power, and stick their tongue out; visualize soft palate, hard palate, and glottic opening with a rating of 1 through 4-1 being you can see all the way to palatal folds, and 4 being you can only see tongue and hard palate

O: stands for obstruction; can be a foreign body such as teeth, bone (or anything from an accident), edema, hematoma, or soot from smoke inhalation; will give clues if there was an inhalation injury; if oral intubation not feasible, quickly progress to cricothyroidotomy or tracheostomy, depending on whether the situation is emergent and what supplies you have

N: stands for neck mobility; all trauma patients should be treated as having an unstable C-spine; utilize manual in-line stabilization if endotracheal intubation is needed; requires an extra person to hold head during removal of C-collar and facilitate endotracheal intubation under direct laryngoscopy without moving C-spine

B: stands for breathing; includes a visual and a physical examination of chest to help rule out potential pneumothorax, hemothorax, or flail chest; examine neck and chest for crepitus, tracheal deviation, or paradoxical chest movement; if a pneumothorax is suspected, an ultrasound of the lung or anterior thorax can be helpful; however, if equipment is not readily available, do not delay, as tension pneumothorax is a life-threatening condition and is diagnosed and treated clinically; treatment should be administered using either needle decompression in the second midclavicular intercostal space, or tube thoracostomy in the fourth or fifth midaxillary intercostal space per local protocol and abilities; a standard 1.25-inch IV catheter is not sufficient to reliably enter the pleural

space through the chest soft tissue; special needles are made for this, while some institutions use a 3- to 5-inch spinal needle; if you don't have special needle or a spinal needle long enough, perform tube thoracostomy

C: stands for circulation; initially assessed by palpation of central arteries, such as femoral or carotid; if not already established, 2 large-bore IVs should be started, preferably at least 18 gauge or larger; if IV access is difficult, do not delay — obtain intraosseous access to facilitate IV medication administration; noninvasive blood pressure monitoring is generally sufficient at this time, but if staffing and supplies permit, an invasive arterial line and central venous access is typically placed to both accurately assess blood pressure and deliver vasopressor medications, if needed; central access is not required, and if unavailable, do not delay medication administration while waiting for access

Bleeding: send laboratory specimens, type and cross-match patient for blood if timing permits; do not delay blood product administration waiting for laboratory results; with hemorrhage and hypovolemia, treat promptly with O negative "trauma blood"; hemorrhage should be treated with direct pressure and/or tourniquet, pelvic binder, or surgical intervention, depending on level of care available, to decrease hemorrhage and blood loss

Hypovolemia: a potential pitfall of volume assessment is that signs of hypovolemia and tachycardia in an otherwise normal, healthy trauma patient will not show up until roughly a liter of blood has been lost; causes problems in assessing hypovolemia, as you can be well behind by the time you see signs and symptoms; given that trauma patients with signs of shock and hemorrhage have higher mortality rates, care should be taken to accurately assess hypovolemia and correct promptly, preferably with whole blood or FFP (fresh frozen plasma) and platelets in a set ratio, depending on availability; current trauma literature suggests using a 1:1:1 red blood cell (RBC) to FFP to platelet ratio if whole blood is unavailable (usually the case, except in the military); crystalloid should be avoided in the acutely hemorrhaging patient as it dilutes remaining coagulation factors and contributes to coagulopathy of trauma; consider potential need for reversal of oral anticoagulation, as a growing number of patients are using these medications; thromboeslastometry or platelet function test, if available, should be run

D: stands for disability; includes focused neurological examination with a description of GCS (Glasgow Coma Scale), pupillary size and reactivity, gross motor function, and sensation; GCS is a generally accepted scoring system that predicts mortality and morbidity; important to document initially and subsequently to note possible decline over time; maintain full spinal precautions on all trauma patients until imaging is complete

E: stands for exposure and environmental control; every trauma patient should be undressed completely and the entire body examined for injury; to help prevent hypothermia, maintain trauma room at an elevated ambient temperature, as hypothermia will contribute to coagulopathy of trauma; now is proper time to obtain all necessary radiologic exams — chest, abdominal, pelvis, CTs, FAST (focused assessment with sonography for trauma) exam, extended FAST exam, any laboratory tests and reassessments ongoing

Secondary survey: definitive management of a hemodynamically unstable patient must not be delayed in order to perform a detailed secondary evaluation; such patients must be taken directly to the operating room, angiography suite, or transferred to a major trauma center as necessary; if patient is stable enough to undergo a secondary survey, a careful head-to-toe secondary assessment should be performed to determine injuries missed in primary survey; includes detailed history, thorough but efficient physical examination, and targeted diagnostic studies; plays crucial role in avoiding missed injuries; commonly missed injuries include blunt abdominal trauma (such as hollow viscus injury), intraabdominal injury, diaphragmatic rupture, penetrating abdominal trauma (such as rectal or urethral injuries), thoracic trauma (such as aortic injuries), pericardial tamponade, esophageal perforation, extremity trauma (especially in distal extremities), vascular disruption, and compartment syndrome

Tertiary survey: delayed re-evaluation of the trauma patient; useful for preventing missed injuries and detecting injuries that present late; most helpful if patient is reevaluated when fully alert; any member of the trauma team with advanced assessment skills can perform survey, but it is best if the same clinician performs all serial exams for a given patient in order to detect subtle changes

Management of hemorrhagic shock: massive blood transfusion is historically defined as a transfusion of >10 units over a 24-hour period; are other definitions currently in use, such as replacement of >1 blood volume in 24 hours or >50% of blood volume in four hours — adult blood volume is approximately 70 mL/kg; in children, transfusion of 40 mL/kg, as the blood volume in children over 1 month old is approximately 80 mL/kg; complications of mass transfusion include hypothermia, transfusion-related lung injury, transfusion-associated circulatory overload, electrolyte abnormalities (such as hypocalcemia, hypomagnesemia, hyperkalemia), citrate intoxication, and immunosuppression

Blood salvage techniques: include autotransfusion and Cell Saver; used to reduce and prevent exposure to allogenic transfusion risks such as infections, immunosuppression, and compatibility issues; indications should be considered when anticipated blood loss is >1 L, procedures where 20% of patients are routinely transfused, or in patient populations with rare blood types or incompatibilities; absolute contraindications to blood salvage techniques are utilizing fluids such as sterile water or hypertonic fluids — these cause hemolysis; avoid blood salvage techniques if utilizing Fibrin Blue, topical thrombin, or bone cement in procedure; relative contraindications include malignancy and bacterial infection; controversial areas include obstetrical (OB) cases (such as cesarean sections), hemoglobinopathies, and cold agglutinin diseases

Technique: surgeon generally aspirates blood from the field using a suction device; blood is pulled into a machine that separates, washes, and centrifuges the blood; blood is then mixed with an anticoagulant prior to being filtered and undergoing leukoreduction and is then transfused back into the patient; the product may also be collected and stored for up to six hours before disposal; complications with blood salvage therapy include most of the same as with allogenic transfusion,

with the presumed reduction of allergenic, infectious, and immunosuppressive effects

Anesthesia management for thoracoabdominal trauma: initial management per ATLS; with a hemodynamically unstable patient, an extended FAST protocol should be used to rule out pneumothorax, pericardial tamponade; if there is still uncertainty, and patient is hypotensive, patient may also need a transesophageal echocardiogram (TEE) or a computed tomogram (CT) to evaluate and diagnose aortic dissection versus rupture; lung isolation should be considered if patient has massive hemoptysis, tracheobronchial tree disruption, or difficulty oxygenating secondary to unilateral chest wall damage; cardiopulmonary bypass may be indicated for major vascular or myocardial injuries, as patient may be too unstable and unable to stop bleeding while under normal perfusion; intubated patients with significant chest wall injury should be observed and evaluated for tracheobronchial injury; if decreased expiratory return volume and elevated peak pressures are noted on ventilator, bronchoscopy or CT with contrast should be performed to evaluate the tracheobronchial tree; venoarterial bypass or extracorporeal membrane oxygenation (ECMO) may be needed to oxygenate the patient if a repair is needed; performing anesthesia for patients with thoracoabdominal injuries should be approached cautiously, as patients can have arrhythmias from tamponade or cardiac contusion, decreased lung capacity from pneumothorax or hemothorax, and decreased circulatory volume from ongoing blood loss and coagulopathy; induction of general anesthesia will exacerbate or uncover these conditions

Anesthesia management for multiple rib fractures: rib fractures occur commonly in thoracic trauma and contribute to significant mortality and morbidity; protocol should be developed for multimodal pain management; ≥3 ipsilateral rib fractures should prompt an evaluation for regional anesthesia such as an epidural, serratus anterior block, or paravertebral blocks; although there is disagreement on the subject, lecturer believes there is evidence that regional anesthesia does reduce mortality and morbidity for multiple rib fractures, especially in the elderly and very young, as this group of patients has a high mortality rate from secondary infections such as pneumonia

Burns

Assessment of burns: first step should be a complete and careful examination of the body to determine total body surface area and type and depth, or grade, of burn; the "rule of nines" is commonly used for this; in an adult patient, each area is assigned a value; only secondary degree or partial thickness burns, or worse, are counted; in an adult, the head and neck count for 9% — four and a half percent for anterior and posterior each; each arm counts for 9% — front and back four and a half percent each; anterior thorax, 18%; posterior thorax, 18%; each leg, 18% — 9% for anterior, and 9% for posterior; perineum counts for 1%; in pediatrics, the head is larger proportionally, while the legs are smaller; there is some reduction, but it is fairly minimal; referral to a specialty burn unit indicated for any partial thickness burn >10% total body surface area, burns that include the hands, feet, face, genitalia, perineum, or major joints, full thickness or third degree burns, any electrical burns, including lightening, chemical burns, inhalation injuries, and children under the age of 16

Management for burns: controversy exists over best resuscitation management for burn patients; current guidelines reflect old beliefs and research, but goals are the same; goal is to maintain tissue perfusion in early phase of burn shock, in which hypovolemia occurs secondary to fluid extravasation from an intravascular compartment; current thinking is that in burns <20% of total body surface area, oral resuscitation is adequate, with exception of facial, hand, and genital burns or children and elderly; >20% total body surface area requires IV resuscitation in an approved formula; most common formula is Parkland Formula; in first 24 hours, lactated Ringers is infused at 4 mL/kg per percent of total body surface area for adults and 3 mL/kg per total body surface area percent for children; maintenance is also added for children — for 0-10 kg it is an extra 4 mL/kg per hour, between 10 and 20 kg it is 40 mL per hour, plus 2 mL per hour for each kg in between; for ≥ 20 kg, it is 60 mL per hour, plus 1 mL per kg per hour on top of that; no colloids are to be given in the first 24 hours; over the next 24 hours, colloids will be given as 20%–60% of the calculated plasma volume for body weight; no crystalloids will be given; glucose will be added to increase urine output from 0.5-1 mL per hour in adults, and ≥ 1 mL per hour in children; in the modified Parkland Formula, in the initial 24 hours, lactated Ringers is infused at 4 mL/kg per percent total body surface area for adults; over the next 24 hours colloid infusion of 5% albumin at 0.3 to 1 mL per kg per total surface area percentile, divided by 16 per hour; crystalloids are the most common resuscitation fluid in burns for the initial injury, as previous studies have revealed that proteins and colloids collect in the extravascular space and increase edema in the early stages of injury and thus create ischemia and further tissue damage; it is difficult to assess proper resuscitation in burn patients; multiple studies have looked at left end diastolic volume, central venous pressure, and echocardiography; however, most clinicians to date continue to use urine output as a surrogate for adequate intravascular volume status; going forward, dynamic monitoring such as FloTrac, LiDCO or PiCCO catheters may prove useful in guiding fluid protocols

Diagnosis and management of airway burns: as many as 30% of burn patients will have an associated inhalation injury; as always, initial assessment should involve airway management; one should also examine face, neck, and chest of patient for clues to airway inhalation injuries not otherwise noticed; if patient is able to converse, listen to the voice and visually inspect mouth and posterior pharynx for soot or ash or signs of edema; listening to the voice will help detect stridor, drooling, or dysphagia; any hoarseness should alert to injury and further exam; timing of injury is important, as edema can develop in <1 hour from of injury, and necrosis within 24 hours; some injuries are insidious and swelling may develop over the next several days; caution should be exercised on these patients and intubation should not be delayed if practitioner has suspicion of continued swelling; chest x-ray, ABG ± flexible bronchoscopy should be performed; if the patient needs to be intubated, the largest ET tube should be used that will easily pass; do not use a small tube anticipating swelling, as this will make bronchoscopy and extubation more difficult at a later date; cuff pressure should be monitored and kept lower than average to prevent complications and ischemia; current studies warn

against early tracheostomy, as patients are at high risk for infection, fistula, and even tracheal rupture

Disposition of anesthesia drugs in burn patients: patients with thermal injuries are resistant to action of non-depolarizing muscle relaxants; this effect takes up to a week to manifest and may be observed for as long as 18 months after burn is healed; marked resistance to non-depolarizers occurs only when the burn is above 30%; pharmacokinetic alterations do not explain this resistance, and a pharmacodynamic explanation has been proposed; burn injury appears to cause acetylcholine receptors in the muscle to proliferate under the burn and at sites distant to the burn injury; an increase in acetylcholine receptors is usually associated with resistance to non-depolarizing muscle relaxants and increased sensitivity to depolarizing muscle relaxants; acetylcholine receptors increase with as small as a 2% total body surface area burn; local irritation and inflammation of muscle can upregulate receptors; the presence of non-depolarizing muscle relaxants can actually accentuate this upregulation; the resistance to non-depolarizing muscle relaxants implies that the burn patient will require larger than normal doses of non-depolarizing muscle relaxants in order to achieve the desired effect, and that the duration of action will be shorter than normal; by the same mechanism, avoid succinylcholine, as increased acetylcholine receptors increase the sensitivity and increase potassium release, thereby causing cell damage, hyperkalemia, and possible fatal hyperkalemic arrest; studies appear to show that volatile agent choice does not seem to influence outcomes of burn patients; therefore you can choose whichever volatile anesthetic you prefer

Pain management: high-dose opioids are needed to manage pain associated with burn procedures; morphine is currently the most widely used drug; partial agonist and antagonist combinations have been used — their efficacy is limited by ceiling effect; meperidine has also been used in burn patients, but prolonged administration is contraindicated because of the potential for accumulation of the toxic metabolite normeperidine; severe pain is common and patient responses vary, so individual titration to effect and frequent reassessments are important; most burn patients rapidly develop tolerance to opioids; there is no evidence to suggest that the incidence of opioid addiction in burn patients is more common than in other acutely ill patients; patient-controlled analgesia (PCA) appears to be the ideal method for opioid administration for both acute or procedure-related pain; its safety and efficacy in burns has been documented in both children and adults

Pharmacokinetic parameters of morphine in burn patients: has been studied and the results are inconsistent; some have reported a decrease in the volume of distribution and clearance and an increase in the terminal elimination half-life of morphine in the burn patient within 2 weeks of injuries; 2 other studies found that morphine pharmacokinetics were similar in burned and unburned patients; changes at the opioid receptors have been suggested to explain the apparent tolerance to opioids seen after thermal injury; however, Silbert and others found that opioid analgesic potency is actually increased acutely after burn injuries for opioids acting at the kappa and delta receptors; peripheral antinociceptive mechanisms are also being examined

Crisis management and team work: trauma and burn patients are complex patients that require a dedicated team; most successful organizations have a dedicated trauma surgeon, anesthesiologist, and a team of nurses that both understand the nuances of the patient population and also work daily with each other and help utilize protocols that have been developed to minimize errors

Dealing with mass casualties: a mass casualty incident is defined as an event that overwhelms the local healthcare system; it exhausts not only the local resources for that incident, but also for the day-to-day tasks for that hospital; several types of mass casualties — planned sporting event, conventional (such as a motor vehicle collision), burns, factory accidents, chemical, biological, radiologic, and catastrophic natural events such as explosion, flu epidemic, or tornado; each community should have a predesignated strategy designed to identify and declare a state of emergency to effectively manage the situation; generally, this involves a disaster preparedness office that would designate a call list of people to call in crisis, and what task they would perform when called; it is dependent on what system you work in as to how the anesthesiologist will be utilized in a time of crisis, but our training makes us very flexible in what we can provide for our patients and our community; we are uniquely qualified to help with triage, stabilization of trauma patients, ICU management, intraoperative care, and other issues depending on the scenario; take time to seek out your institution's leadership and plan to find out what specific role you will play, and perhaps become involved in the decision-making, as often hospital administration and leadership are unfamiliar with skills of anesthesiologists

Terrorism: because of the increased threat of terrorism, the risk posed by various microorganisms as biologic weapons needs to be evaluated, and the historical development and use of biologic agents need to be better understood; while it is unlikely that anesthesiologists will be at the initial site of the attack, you can potentially become involved in the care of patients that were involved in such an attack; it is important to review the decontamination and isolation techniques for a specific exposure; be careful not to unnecessarily expose yourself, as you will likely be walking into a known environment; after identification, review the treatment options for the specific biologic in question; some will have antidotes, while many others will have to be managed with general supportive care such as airway or hemodynamic support and decontamination; aim to treat life-threatening injuries as quickly as possible, and realize the usual standard of care may not be possible; understand casualties will occur and it is important to triage patients and continue to care for those who can be saved; for more information, refer to the ASA's committee on trauma and emergency preparedness consensus statement currently under development

Suggested Reading

Kovacs G et al: Airway Management in Trauma. *Emerg Med Clin North Am* 2018 Feb;36(1):61-84; **Gillenwater J et al:** Acute Fluid Management of Large Burns: Pathophysiology, Monitoring, and Resuscitation. *Clin Plast Surg* 2017 Jul;44(3):495-503; **Nielson CB et al:** Burns: Pathophysiology of Systemic Complications and Current Management. *J Burn Care Res* 2017 Jan/Feb;38(1):e469-81.

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Anesthesia for Geriatric Patients

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Importance: large and growing segment of population — estimated to reach >100 million by 2025; of these, half will have at least one surgery

Objectives: discuss the physiologic implications of aging, the implications of chronic diseases in different organ systems, the pharmacologic consequences of advanced age, anesthesia for common geriatric procedures, postoperative pain management, and postoperative delirium prevention and management

Organ system changes in geriatric patients:

Central nervous system (CNS): primary changes are both structural and functional; the volume and weight of the brain declines by approximately 5% per decade after age 40 primarily due to neuronal cell death, which leads to brain atrophy; this atrophy causes the primary changes in structure, function, and metabolism; loss of neural tissue leads to decreased levels of dopamine and serotonin and increases in monoamine oxidase, thus affecting the homeostasis of neurotransmitter levels; increase in monoamine oxidase with age liberates free radicals from reactions that exceed inherent anti-oxidant reserves

Cognitive changes: memory decline is one of the cognitive changes, with episodic memory being the most commonly changed; episodic memory is defined as form of memory in which information is stored with mental tags; this change can occur even in the absence of any known neurologic disease, dementia, or neurodegenerative disease such as Alzheimer's, primarily due to the fact that neuroreceptors and neurotransmitters (eg, dopamine, serotonin, and acetylcholine) have decreased in the cortex; another important structural change is increased permeability of the blood-brain barrier; the blood-brain barrier protects the CNS from systemic insults through selective permeability; because of the increased permeability in the elderly, there is inappropriate passage of mediators from the plasma into the CNS, which can result in increased inflammatory responses as well as further structural damage to the brain with certain stresses such as anesthesia

Autonomic dysfunction: another major structural change that results in a functional change which causes geriatric patients to be more prone to hypothermia; can lead to increased shivering as well as increased oxygen demand in the elderly, who already have decreased reserve in respiratory and cardiac capacities; clinicians must be very vigilant in regards to the great risk of hypothermia, especially due to the prolonged effect of anesthetics caused by decreased hepatic and extrahepatic degradation and elimination

Effects of structural and functional changes in CNS on clinical practice of anesthesiologists: less is more when taking care of geriatric patients in the OR (operating room); many common anesthetic medications affect the CNS, and the effects of aging can alter the effects of these medications; benzodiazepines exhibit a significantly increased duration of action in the elderly; best to avoid long-acting benzodiazepines or benzodiazepines in general, because they have been associated with post-operative cognitive dysfunction and post-operative delirium; elderly patients typically require a lower dose of opioids for a similar effect; increased incidence of respiratory depression and increased duration of systemic interactional effects with opioids in the elderly primarily due to decreased volume of distribution; common induction agents such as propofol require reduced doses; propofol's hemodynamic effects are greatly exaggerated in the elderly; common maintenance medications such as propofol and other volatile anesthetics require decreased concentrations; the minimum alveolar concentration (MAC) decreases by approximately 6-7% every decade after the age of 20; thermal regulation needs to be visually watched in the elderly population due to the autonomic dysfunction and delayed elimination of volatile and intravenous anesthetics used in maintenance

Cardiovascular physiology in the elderly: age-related cardiovascular changes are the leading factors impacting perioperative outcomes in the elderly; compared with younger patients, geriatric patients tend to have higher blood pressures, similar heart rates and ejection fractions, lower left ventricular end-diastolic volumes, lower stroke volumes, and lower cardiac outputs; physiologic changes in the cardiovascular system are directly related to stiffening and decreased distensibility of the systemic arteries and cardiac wall which leads to decreased cardiac outputs and stroke volume, reduced arterial elasticity, peripheral sclerosis, sclerosis of the coronary arteries, increased sympathetic nervous system activity, and decreased size of the sinoatrial (SA) and atrioventricular (AV) nodes; important to distinguish between normal physiologic changes associated with aging and the pathophysiology of common geriatric diseases; age-related cardiovascular changes are primarily due to decreased elastin production; connective tissue stiffens within the arteries, veins, and myocardium causing them to become less compliant; when elastin is damaged, the media becomes more fibrotic because it is

replaced with fibrous tissue; arterial stiffening leads to systolic hypertension and a normal to decreased diastolic blood pressure; stiffening within the aorta causes an increase in the systolic blood pressure and a decrease in the diastolic pressure; diminished diastolic pressure leads to a decrease in coronary blood flow; fibrosis of the media within the arteries is accompanied by some degree of myocardial fibrosis as well as calcification of the valves, which is common; atherosclerosis is another normal change of the vascular system that leads to hardening of the arteries, reduced vascular compliance, and a widened pulse pressure; increased arterial wall thickness and decreased beta-mediated vasodilation is also common; aging produces a state of beta adrenergic insensitivity, and elderly patients are markedly less responsive than the younger population to beta agonists; alpha sensitivity remains intact; adrenal tissue atrophies with age; circulating norepinephrine levels increase in order to compensate for beta insensitivity; overall this leads to some degree of autonomic dysfunction or impaired autonomic responses; diminished cardiac reserve in the elderly may be manifested by exaggerated drops in blood pressure, especially upon induction or with maintenance of vasodilatory volatile anesthetics; elderly patients (similar to infants) have less ability to respond to hypovolemia, hypotension, or hypoxemia with an increased heart rate; anesthetic implications of these physiologic changes include that if hypertension occurs during induction, it is best to use an alpha agonist due to the decreased beta response; maintenance of preload is important because many elderly patients become dependent on the preload; best to avoid arrhythmias as elderly patients are prone to having arrhythmias due to fibrosis of the myocardium; elderly patients become more dependent on the atrial kick at the end of diastole which can be compromised in the presence of an arrhythmia; cardiac complications are among the most serious perioperative complications; strongest predictors of adverse outcomes are: recent myocardial infarction, uncompensated congestive heart failure, unstable ischemic heart disease, and certain cardiac arrhythmias, especially atrial fibrillation; best to follow task force guidelines on perioperative cardiac evaluation from the American College of Cardiology and the American Heart Association, these guidelines can be found on both of their websites and the American Board of Anesthesiologists website

Geriatric cardiovascular pathophysiology:

Mitral stenosis: typically associated with rheumatic processes but can also be prevalent in dialysis-dependent patients; look for mitral stenosis when interviewing patients; mitral stenosis is associated with a significant reduction in the blood flow through the mitral valve which causes a transvalvular pressure gradient that depends on cardiac output, heart rate (specifically the diastolic time), and cardiac rhythm; principal management goals in mitral stenosis patients are to maintain sinus rhythm, avoid tachycardia, avoid large increases in cardiac output, and avoid hypovolemia and fluid overload by judicious fluid administration; no ideal general anesthetic for mitral stenosis patients; all tactics should be employed to achieve desired effect of permitting sufficient diastolic time; avoid intraoperative tachycardia, which can be controlled by deepening anesthesia or with a beta blocker, if necessary; for regional anesthesia, an epidural is typically better tolerated, as a spinal can cause a sudden sympathetic blockade and lead to significant hypotension; epidural anesthetic can be managed more easily and titrated to a better effect with a more gradual onset of sympathetic blockade

Mitral regurgitation: can be associated with multiple disorders including, but not limited to: rheumatic fever, rheumatoid arthritis, and lupus; mitral regurgitation can also be congenital; the derangement is due to backward blood flow into the left atrium during systole, which over time can lead to left ventricle volume overload; primary goal in mitral regurgitation patients is afterload reduction, which has been shown to be extremely beneficial in the majority of patients; anesthetic management should be tailored to the severity of the mitral regurgitation, which should be checked with a perioperative TEE (transesophageal echocardiogram) or TTE (transthoracic echocardiogram); avoid factors that can exacerbate regurgitant flow, including slowed heart rate or acute increases in afterload; bradycardia can increase regurgitant volume by increasing left ventricular end diastolic volume and dilating the mitral annulus; heart rate should ideally be kept above 80 bpm and less than 100 bpm; avoiding light anesthetic is ideal, however care should be taken to avoid deep anesthetic with myocardial depressing agents, such as ketamine; general anesthesia is typically well tolerated in these patients, but remain cognizant of the fact that patients with severe ventricular impairment can be very sensitive to high concentrations of volatile anesthetic agents; opioid-based anesthetic is suggested for these patients as well as avoiding bradycardia; with regard to regional anesthetics, spinal and epidural are both well tolerated as long as bradycardia is avoided

Mitral valve prolapse: management of patients is based on clinical course; patients are usually asymptomatic and typically do not require special care; mitral valve prolapse patients are prone to arrhythmias, specifically ventricular arrhythmias, which can be treated with lidocaine or any beta adrenergic blocking agents; some patients develop mitral regurgitation, so it is important to look for it in the perioperative setting

Aortic stenosis: commonly encountered in the OR setting; critical aortic stenosis is when the aortic valve orifice is reduced to 0.5 to 0.7 cm^2; leads to left ventricular outflow obstruction, which typically starts off as gradual, but if in critical state can lead to sudden changes in coronary blood flow; clinically these patients have dyspnea on exertion, angina, and exertional syncope; patients also exhibit significantly decreased compliance of the left ventricle due to hypertrophy from the outflow tract obstruction; goal of care in patients with aortic stenosis is to maintain sinus rhythm and a heart rate between 60 and 90 bpm; avoid bradycardia and hypotension as they can lead to decreased coronary blood flow and myocardial ischemia; ensure that vascular resistance is maintained; intravascular volume monitoring is critical; aortic stenosis patients typically function as if they have a fixed stroke volume, so it is important to have adequate preload; if hypotension is encountered, phenylephrine is agent of choice; avoid significant

tachycardia, bradycardia, severe hypertension, and severe hypotension

Aortic regurgitation: produces left ventricular volume overload; effect of stroke volume is reduced because of backward or regurgitant flow into the left ventricle during diastole; when managing these patients, avoid bradycardia and increases in systemic vascular resistance; hypertension will lead to increased regurgitant volume; avoid excessive tachycardia (>100 bpm), which can contribute to myocardial ischemia; heart rate should be maintained between 80 and 100 bpm; be sure to maintain preload but avoid overzealous fluid replacement, which could cause pulmonary edema; regional and general anesthetics are typically tolerated; patients do well with maintenance with volatile anesthetics due to the vasodilation, which decreases the systemic vascular resistance and can decrease the regurgitant flow; if hypotension is encountered, phenylephrine tends to work well; for regional anesthetics, ensure that patients are properly hydrated and have adequate preload prior to any spinal or epidural anesthesia

Congestive heart failure (CHF): common cardiac disease state encountered in the perioperative setting; associated with increased risk of surgical mortality; important to have a proper and adequate clinical assessment, including a recent ejection fraction, analysis of the trend of brain natriuretic peptide levels, and a TEE assessment; any patient with decompensated heart failure or inadequately treated heart failure should have any elective procedure postponed; cause of decompensation should be identified and treated; be aware of the medications these patients are taking; often patients are on a beta blocker and an ACE (angiotensin converting enzyme) inhibitor at time of surgery, and a large body of data supports the continuation of these medications; however, it is not adequate to place patients with decompensated heart failure on these medications and presume that the patient is able to undergo an anesthetic; in maintenance of anesthesia, avoid anything that is a cardiac depressant; volatile aesthetics are known as cardiac depressants and have been shown to be problematic; studies show that opioid-based anesthetics result in better outcomes; positive pressure ventilation can help reduce pulmonary edema, prevent excessive diastolic filling, and help reduce CHF exacerbation post-operatively

Respiratory system changes in geriatric patients: lungs continue to develop throughout life and they achieve their maximal functional status at approximately the third decade of life, after which there are multiple changes with age in the mechanical properties of the respiratory system; patients will develop impaired response to hypoxia and arterial oxyhemoglobin saturation; total lung capacity is unchanged in the elderly population; closing capacity and residual volume increase; vital capacity decreases; this leads to an unchanged total lung capacity; functional changes are due to structural changes in elasticity; patients have decreased elastic recoil and a decrease in compliance with aging, primarily due to changes in compliance of the chest wall; changes are primarily due to structural changes in the intercostal muscles, the joints, and the articulations of the ribs and vertebrae; along with decreased chest wall compliance these structural changes lead to less chest wall muscular function, meaning decreased outward force requirements; due to change in chest wall compliance and decreased elastic recoil, there are significant changes in the mechanics of the lung; important to remember total lung capacity remains unchanged; closing capacity increases; residual volume increases; there is increased ventilation-perfusion mismatch, and this is a very important reason for increased A-a gradient with aging; these mechanical changes lead to decreased ventilatory responses to hypoxia, hypercapnia, as well as stress, such as anesthesia; also an overall increased response to the respiratory changes associated with opioids, benzodiazepines, and volatile anesthetics; ciliary function of the T cells is impaired, which leads to decreased bronchociliary clearing, resulting in impaired protective mechanisms in elderly patients; overall these physiologic and mechanical changes combined with the loss of protective mechanisms place elderly patients at a greater risk of developing respiratory failure and causes higher incidences of mechanical ventilation, mechanical ventilation dependence, and ventilator-associated pneumonia; these post-operative complications are most common in geriatric patients; site of surgery is the most significant clinical predictor of these adverse pulmonary outcomes, with thoracic and upper abdominal surgery having the highest pulmonary complication rates; measures to take in the perioperative period to reduce potential postoperative pulmonary complications in the elderly include: longer time for preoxygenation, increased inspired oxygen concentration used during the anesthetic case itself, and use of positive end-expiratory pressure; be cognizant of the fact that there is a decrease in laryngeal reflexes, so be careful in order to avoid aspiration pneumonia, which could be life threatening in geriatric patients; get a very thorough history and physical examination in the preoperative setting or the optimization clinic, primarily looking for any preexisting pulmonary disease, such as chronic obstructive pulmonary disease, sleep apnea (very common in the elderly), or malnutrition; be ready for patients with thoracic or upper abdominal surgeries as they are at increased risk for postoperative complications

Hepatic system: even in the absence of any preexisting disease or pathology, elderly individuals have gross reductions in their hepatic as well as splanchnic blood flow; actual mass of liver decreases with age (by 40% at 80 years old); the effects of many medications, including opioids, vecuronium, and other hepatically cleared drugs, can be prolonged in the elderly; decreased blood flow also contributes to the impaired ability to metabolize drugs as it results in lower levels of microsomal enzymes and their decreased function; phase two metabolism, which includes acetylation, sulfation, and glucuronidation are essentially unchanged with age; along with decreased blood flow and decreased liver size, there is a decline in plasma proteins produced by the liver, especially albumin, which causes a decrease in protein drug binding; there is also decreased production of plasma cholinesterase, the enzyme which metabolizes the depolarizing agent succinylcholine, which can result in prolonged action of this medication

Renal system: also suffers a loss in actual mass in the elderly population; the decreases in cardiac output cause a decrease in renal blood flow and a decline in glomerular filtration rate; approximately 50% to 60% of all functioning glomeruli are lost by the age of 80, the remaining tend to be less sensitive to hormones including aldosterone, vasopressin, and atrial natriuretic peptide; ability to concentrate or dilute urine is thereby effectively decreased and sometimes even lost, making it essential to appropriately manage intravascular volume in the elderly population; avoid overadministration and underadministration of fluids; elderly patients are prone to dehydration because of illness, the common use of diuretics, preoperative fasting, and the lack of a thirst response; beneficial to encourage oral intake of fluids up to two to three hours preoperatively; have adequate maintenance fluid therapy; hold diuretic in the preoperative setting; this can reduce hypotensive events after the induction of anesthesia and during the maintenance of anesthesia

Endocrine system: primary concern is diabetes, which is important because hyperglycemia (with or without diabetes) increases morbidity and mortality in patients as shown by the American Diabetic Association; geriatric patients produce less thyroid stimulating hormone, free T3, growth hormone, aldosterone, and androgens, which leads to changes in body composition, mainly decreased muscle mass and greater fat composition, which leads to accompanying responses to thyroxine, renin, and aldosterone; this change in muscle-to-fat ratio is the reason why there are changes in the volume of distribution of many medications; important to be vigilant in the management of diabetes in geriatric patients; stress of surgery will increase hyperglycemia and it is important to start insulin regimens intraoperatively or postoperatively in patients with type two diabetes after discontinuing their oral hypoglycemic agents; important to be aware of the medications that they are taking, specifically sulfonylureas and metformin, which should always be discontinued the day before surgery as sulfonylureas have been shown to increase myocardial ischemia in a hypovolemic state and metformin has been shown to predispose patients to lactic acidosis; management of blood glucose levels in these patients should aim to keep levels between 80 and 120 preprandially (as mentioned by the ADA); avoidance of hypoglycemia as well as hyperglycemia intraoperatively will minimize mortality and improve perioperative outcomes

Pharmacologic, pharmacokinetic, and pharmacotherapy changes in the elderly: decreased muscle mass in comparison to greater fat composition leads to overall decrease in total body water; all previously discussed organ systems play a major role in the changes in pharmacotherapy; GFR and hepatic function decline result in increased duration of action of several common anesthetics; because of the decrease in hepatic function, there is decreased protein binding by albumin, resulting in increased action of some drugs, specifically drugs such as barbiturates, benzodiazepines, and opioids; actions of local anesthetics are decreased; fat soluble drugs have a higher plasma concentration and water soluble drugs have a lower concentration due to the change of the body composition that occurs in elderly patients; clearance for many medications as well as the dose requirements are reduced by as much as 50% (especially true for opioids); lots of controversy regarding use of benzodiazepines, specifically midazolam, in the perioperative setting for the geriatric population, primarily because many studies show increases in the incidence of postoperative delirium as well as postoperative cognitive dysfunction; dosing requirements for midazolam are significantly reduced and it also has a very prolonged half-life, up to four to five hours; responses to neuromuscular blocking drugs are not significantly changed in the geriatric population; there is some change in response to succinylcholine, especially in elderly males, primarily due to changes in plasma cholinesterase activity; drugs that depend on renal clearance, such as pancuronium, can result in prolonged blockade

Postoperative delirium and postoperative cognitive dysfunction: important to know the difference between the two, they are not the same; postoperative delirium is a transient phenomenon in which patients experience fluctuating disturbances in consciousness; postoperative delirium is usually seen in the first three days after an anesthetic; postoperative cognitive dysfunction can be defined as a decline in higher level cognitive functions of the brain, encompassing language, imagination, perception, and planning; postoperative dysfunction can be diagnosed anywhere from days to weeks following surgery; another major difference between postoperative delirium and postoperative cognitive dysfunction is preventative measures; postoperative delirium can be prevented with good sleep hygiene leading up to the surgical day, early ambulation following surgery, and cognitive stimulation; conversely, postoperative cognitive dysfunction has some associated risk factors, such as increasing age and decreased levels of education; the underlying etiology of postoperative cognitive dysfunction is unknown, and there are no known preventative measures; many studies show that certain types of anesthetics can prevent or decrease the incidence of postoperative cognitive dysfunction, specifically the avoidance of benzodiazepines or high dose opioids as well as decreasing amounts of volatile anesthetics; there is incidence of postoperative cognitive dysfunction regardless of the anesthetic type (regional or general); it is important to use the smallest possible amount of volatile or intravenous anesthetic

Postoperative pain control: pain and pain medication can contribute to postoperative delirium and postoperative cognitive dysfunction; however pain still needs to be addressed; best method is to use a multimodal approach including the use of low doses of multiple medications aimed at different receptors; a balanced, multimodal approach includes the use of opioids in low doses, preferably patient-controlled analgesic immediately postoperatively with a weak opioid, use of non-opioid drugs such as acetaminophen, non-steroidal anti-inflammatory drugs, membrane stabilizing medications, early use of regional anesthesia when appropriate, and neuraxial anesthesia; a key point regarding neuraxial anesthesia in the geriatric population is that due to coexisting diseases, such as spinal stenosis, there is a higher incidence of longer acting spinals, and epidurals can spread to levels farther from the site of the catheter than would be expected in the younger population; typically more difficult to perform neuraxial anesthesia in geriatric patients; if available, review preoperative imaging

whenever possible; avoid scheduled pain medications whenever possible in geriatric patients; either patient controlled analgesia or PRN use of oral medications is recommended when appropriate, both of which help decrease postoperative delirium incidence

Conclusion: the overall takeaway point in dealing with geriatric patients is to be vigilant and thoughtful in the preoperative assessment of organ function and reserve; be meticulous intraoperatively in managing patients' posing disorders; be cognizant and properly address postoperative pain as well as respiratory status; this is a unique patient population, as they are vulnerable and particularly sensitive to the perioperative period

Suggested Reading

Fleisher LA et al: ?2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary. *Journal of the American College of Cardiology* 2014 Dec;64(22):2373-405; **Lin HS et al:** Frailty and anesthesia — risks during and post-surgery. *Local Reg Anesth* 2018 Oct;11:61-73; **Murthy S et al:** Controversies in anesthesia for noncardiac surgery in older adults. *Br J Anaesth* 2015 Dec;115(Suppl 2):ii15-25; **Ornek D et al:** The influence of various anesthesia techniques on postoperative recovery and discharge criteria among geriatric patients. *Clinics (Sao Paulo)* 2010;65(10):941-6.

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How to Pass the Oral and Applied Examinations

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Introduction: this session is provided to pass on some simple hints on both the written multiple choice tests and the oral or OSCE (oral structured clinical examination) sessions for the initial board examination; the information is designed for those who are candidates for the initial board certification examination; candidates for the MOCA (Maintenance of Certification in Anesthesiology) examinations may find some of the suggestions for multiple choice questions useful; the aim is to review your general knowledge concerning many of the important topics that might form the basis for questions on the examinations

Background: there is no substitute for a broad knowledge of your subject; no amount of examination technique can compensate for inadequate study; there are ways to ensure that you use the knowledge you have at the time of examination; this presentation will help you make the best use of your knowledge at examination time; everyone is a little bit anxious going into an examination; this can be quite unrelated to a lack of knowledge of the subject matter of the exam; there are some websites and other services which offer help for the acutely anxious candidate

Examination process: the first essential for all candidates is to have a clear understanding of the examination process for which you are preparing; the American Board of Anesthesiology (ABA) website, www.theaba.org has a very complete detail of all the examination processes and should be studied very carefully; at this website you will find an outline of the examination content and a tutorial which will guide you through the actual examination process and how you will record your answers; make sure that you study this so that you will know exactly what to expect; a useful feature at this website is also the opportunity to practice with many different multiple choice questions that have been previously posed; if you click on the in-training examination heading, you will be able to go through several years of previous multiple choice test papers, complete with the answers; this is an invaluable experience for all candidates and should be a part of everybody's preparation; practice reading questions carefully, word by word, together with the list of possible responses; select your chosen response and check this with the answer sheets provided; take particular note if you slip up with correctly interpreting any of the questions or the responses; analyze any of your misreadings of questions so as to avoid this slip in the future

Review: we must consider your overall review activities for the examinations; there are some methods that will make the best use of the time that you have; first of all, start early; a course of revision should start early with enough time allocated to cover the essential material in a carefully planned schedule leading up to the examination; many students and residents begin planning for the review process as they progress through their years of training; summarizing notes on important topics on compact cards consolidates your knowledge, while also providing material for future rapid review; the use of different colors or underlining in the script on these cards will make important headings stand out and assist you in organizing your overall knowledge of the subject; you must organize your final plans for review and do this well before the exam time; set up a timetable which will enable you to get through the topics you need to review well in advance of the examination; set aside a fixed time and a quiet place on a daily basis; be prepared with study materials for times when you will be on call but not actually working; well organized summaries of important topics in your card index are invaluable at this time as the examination date approaches

Study tools: design and sketch out or print out your own charts, diagrams, and algorithms as a means to plot management decisions; you will then provide a visual picture that you may more readily recall when you are in the examination room; drawing and labeling diagrams and anatomical charts adds to your understanding and will augment your memory; a simple mnemonic or linked phrase can act as an aide-mémoire for individual facts; you can invent your own memory aids for any important facts which you find particularly difficult to remember

Active review: during the pre-examination review, review actively, not passively; passive re-reading of books and review articles is less likely to lead to retention of important facts than active re-summarizing of important material; underline or highlight important headings; the review of the outlines you have previously made on file cards and flash cards is proven to be a valuable review technique; as you are reviewing topics, look out for any items that you think would make possible examination questions; phrase such questions to yourself and answer them

What do you do when the exam gets very near? last minute cramming is universally condemned; it is generally accepted that active revision should be scaled back as the date for the examination gets very close; last minute intensive reading will probably not lead to more facts being retained and may be a source of confusion on examination day; relax and take some physical exercise;

accept the fact that having gone through a course of training and perhaps been in practice for a while, you're going to understand the questions and are probably going to do all right; plenty of sleep, moderation in caffeine and alcohol, and some last-minute relaxation is probably the best course for the evening immediately before the examination; tests are designed to make you think; ensure that your brain is well rested and in optimal condition for efficient thinking; about the actual written multiple choice examination — this is where you will appreciate the value of your studies and the practice questions that you have worked on; multiple choice answers require detailed knowledge and accurate answers

Test day preparation: on the day of the examination, make sure that you arrive at the test site not too early, but early enough to have some time to relax before the exam starts; do not spend time talking about the examination with other candidates; this may increase your anxiety and confuse some of your thoughts; keep away from other candidates who are obviously anxious

Exam Overview: the basic board written examination consists of one session of 4 hours, during which you will have to answer 200 questions; this gives you just over one minute for each question; some questions will take much less time, some may need more; the advanced examination also consists of one 4-hour session with 200 questions; some questions on this exam may reference static images or video clips which will be provided; plan your time and pace yourself; your remaining time for the session will be displayed on your screen; in addition, a means to navigate back to flagged or unanswered questions is provided; read each question word by word very carefully and understand the wording of the question fully; are there any negatives or double negatives to be considered? a most common mistake is misreading the question; then, if you think you know it, decide on your answer before you look at the possible responses; only then, look at all the listed responses before selecting the one which comes closest to your answer

Multiple choice questions: the questions in the multiple choice exams will be of the A type only; you can examine samples of such questions at the ABA website under the heading "sample basic" or "advanced examination questions;" do not get upset if you come to a question you cannot answer; flag this for review and move rapidly on to one that you can answer; do not get discouraged; you do not have to answer every question correctly in order to pass; some of the questions in the examination are not going to be counted in your final tally; they are just there as experimental questions; however, you must remember to come back again to all your flagged unanswered questions later; insert an answer for every question; sometimes, you will remember the answer to one of your flagged questions as you progress through the test; a later question may even jog your memory and indicate the right response for the original question; each question must be completed even if you're not certain of the answer; flag those that you might like to come back to and reconsider; do not race through the exam, pace yourself; many candidates find it helpful to take a very short break every now and then; close your eyes and take a deep breath then get right back into it; such very short breaks serve to clear your mind for the next set of questions; do not waste time fretting with questions you cannot answer; move rapidly on to those you can answer with confidence; remember, you only have just over a minute for each question; if you take more than this, you may not have enough time for later questions that you could have easily answered

Question strategies: when you get to the end, return to all uncompleted answers; answer every question with a response even if you're not quite sure; for each uncompleted question that you're unsure of, examine all the possible responses; if there are any with absolute qualifiers; for example, "always," "never," "none," or "every," these are probably wrong and can be eliminated; if you really cannot identify the most correct answer, look for the answer that looks the least wrong; if all else fails, aim for what is the most likely looking response, having excluded any or all that are obviously wrong; do not be afraid to change an answer if you think you now have a better choice; studies have shown that such later changes more often lead to a correct response than an incorrect one; if you finish early, use the rest of your time to review any answers which are still slightly doubtful in your mind

The standardized oral examination: preparing for this is also vital; take any opportunity for practice oral sessions; for the resident approaching the initial board examination, practice oral sessions are absolutely essential; get as much experience with this as you can; it helps if these can be conducted by faculty members who are familiar with the structure of the board examination; additional practice with one of your fellow residents is also very worthwhile; practice orals are a particular help when it comes to getting experience in structuring answers with ease and clarity; develop your ability to discuss cases typical of those that pose challenges to you in your everyday clinical work; these are the types of cases that you will have to discuss in the oral examination

Oral examination review: now to the examination; all candidates should view the videos which are posted on the ABA website and depict successful candidate behaviors versus improper candidate behavior; these can be found under the headings "exams," "applied part staged exams," and "Part 2 examination videos;" the oral examination and the objective structured clinical examination are held in concurrent sessions; either one of them may be delivered first

Oral examination structure: the standardized oral examination will consist of two 35-minute sessions with an intervening break of 10 minutes; at each session, two examiners will be present; after registering for the examination, there will be a briefing session, and then you will be handed a case summary with clinical data for the first case to be discussed, and you will be allowed 10 minutes to review this; read this very carefully word by word; you will then discuss your intra-operative care with the first examiner, and your post-operative care with the second examiner; you will then have some unrelated questions posed; the second 35-minute session will be similar in content, but you will be questioned about pre-operative and intra-operative care plus some unrelated topics; the clinical scenarios that will be presented have been submitted by practicing anesthesiologists and are typical of the situations that you will likely meet in your practice

Oral examination preparation: for the oral examination, dress smartly and arrive early and well rested; look professional and act in a professional manner; the oral

examination is not just a test of knowledge; it is also an opportunity for the examiners to judge your abilities to communicate, your judgment and decision making, and your ability to adapt to a changing situation; it might be useful to remember the ABA's definition of a board-certified anesthesiologist as one who, (A) possesses knowledge, judgment, adaptability, clinical skills, technical facility, and personal characteristics to carry out the entire scope of anesthesiology practice; (B) he or she is able to communicate effectively with peers, patients, their families, and others in the medical community; (C) he or she can serve as an expert in matters relating to anesthesiology, deliberate with others, provide advice, and defend opinions in all aspects of the specialty of anesthesiology; (D) he or she is able to function as the leader of the anesthesiology care team; it is your objective to persuade the examiners that you are such a person; review the written brief on the clinical cases thoroughly and listen very carefully to any questions; request clarification of any point which you do not fully understand; make sure that you completely understand any problem being presented before framing your answer; do not interrupt before a question has been fully posed; answer promptly, but with consideration; do not rush into answers without thinking them through; answer directly to the examiners; maintain eye contact; concentrate, do not become distracted, do not ramble off the subject; examiners will not mislead you, but make sure that you do not lead them away from the topic under consideration; this is where the marks are — under the topic under consideration; speak clearly and loud enough to be easily heard; be confident; be well organized and be prepared with templates on which to design your answers; for example, a general question on anesthesia management always need consideration of a pre-operative phase, an intra-operative phase, and a postoperative phase, and each phase has to be broken down into subheadings; the pre-operative phase always includes assessment, history and physical, labs, special tests; the history is broken down always into present, past history, family history; have these templates for answers clearly prepared in your mind, so that you do not omit important points; if you cannot answer a question, admit to it, but perhaps indicate where you could rapidly find the answer; in this way, you can get quickly on to the next question, which hopefully is one that you can answer; the examiners may progress to the limits of your knowledge on a subject; it is all right to have a limit as long as you know what you could be reasonably expected to know; do not be discouraged if you have to admit that you cannot progress further with a particular question; do not be afraid to state that you need to request a consultation or second opinion on a matter which is progressing beyond your reasonably expected potential to manage; the ability to consult wisely with colleagues is an important attribute for any physician; short questions often only need short answers; be decisive and appear as someone worthy of being called a consultant in anesthesiology

Objective structured clinical examinations: OSCEs; these were introduced in 2017 as a method to assess each candidate's professionalism, answers, communication, and clinical skills; every candidate should visit the ABA website, www.theaba.org, and review the information which is provided there about the OSCEs, which includes an overview video clip; this is most useful and shows you exactly what to expect at the examination; candidates should also review the list of potential scenarios for the OSCEs which is provided on the ABA website; make sure that you are familiar with each of the clinical skills that may be evaluated and consider each of the patient interaction scenarios so that you can have a pre-planned game plan; candidates will rotate through seven different scenarios during the examination, and each will last about 8 minutes; there will be a 4-minute period after each to provide time to prepare for the next scenario; the examiner may not be present in the room, but your performance will be recorded for assessment; the total OSCE examination will last about 84 minutes

OSCE stations: the first essential with an OSCE is to make sure you understand completely what is expected of you at each examination station; read the task statement on the briefing extremely carefully; a common mistake with OSCE examinations is to misinterpret what is expected of you, often by leaping to conclusions; do not second guess what the scenario is about; standardized patients may be provided to assess your skill at history taking or other patient interactions such as obtaining informed consent or discussing possible post-anesthesia complications; whenever a patient is involved, make sure that you act in a very professional manner; knock before you enter the room, greet the patient by name, tell them who you are and the exact purpose of your visit; be warm and friendly; if asked to take a history, do so in a logical order according to your standard, pre-planned routine, which you should have clearly in your head; do not miss any steps; listen to the patient very carefully and do not interrupt; do not ask too many questions; rapid, quick-fire questions, hoping to ask the right one, will just confuse matters; start out with well chosen, open questions and progress as needed to focused questions as your evaluation continues; do not talk too much; give the patient ample time to respond; do not assume anything; assess problems logically in order to arrive at the correct conclusion

OSCE evaluation: marks are assigned for each step in a logical, progressive assessment of the particular situation; do not assume you can collect all the marks by jumping immediately to the right answer; if asked to examine a patient, make sure that you wash your hands or use antiseptic hand lotion before touching the patient; always ask the patient's permission before an examination and explain exactly what you're going to do; conduct yourself in a faultless, professional manner; if you are asked to advise a patient or to obtain informed consent, make sure you do so in an in-depth manner; avoid generalizations; you are expected to be able to advise patients on their specific circumstances, so they can make decisions on a well-informed basis; if you review the content outline for the OSCEs on the ABA website, this will tell you how to collect good marks during your informed consent visit with the patient; marks are given for each of the steps along the way; in obtaining informed consent, this will consist of first, explaining why the procedure is needed, then, explaining the procedure in terms easily understandable to the patient, then, explaining all the risks and benefits of the procedure, giving alternatives if and when these are appropriate, and explaining who will do the procedure; you then invite questions and answer these in layman's terms; you should always gain consent without any attempt

at coercion, and you should demonstrate sympathy and empathy for the patient; if you follow through with the consent process like this, you will almost certainly get good marks for this portion of the examination; have a plan like this committed to memory before you attend the examination

OSCE clinical scenario: if you are asked to review a clinical scenario and present an anesthesia plan, discuss this with the patient together with treatment options; make sure you discuss all suitable management options; you present the patient with the risks and benefits of each option; you listen carefully and answer any questions the patient may have; do not interrupt or cut the patient off before they complete their answers; present all of this to them in easily understood layman's terms; confirm with the patient your agreed treatment choice and show that you have understanding and sympathy for the patient's concerns

OSCE post-procedure complication: if you are asked to interview a patient concerning a possible post-procedure complication, do so in a logical manner; this will collect you all the marks along the way; obtain a history of the symptoms and current status; perform an appropriate physical examination, ask the patient's permission first; discuss possible causes for the symptoms; explain potential outcomes in simple language; present a plan for further investigation and treatment; invite questions and answer these in simple layman's terms; express sympathy, understanding, and concern; always, after any interview, thank the patient before you leave the room

OSCE physician consultation: your task may also be to discuss the management of a prescribed case with another physician or with a surgeon; it is most important that you demonstrate your ability to communicate in a clear, concise, and efficient manner; recognize all the priorities in the care of the described patient by listening carefully to the concerns, opinions, and objectives of the other health professional; you must reach a mutually satisfactory conclusion based on the sound practice of anesthesiology but avoiding unnecessary professional conflicts; if the OSCE represents an urgent problem or the need for an urgent intervention, make sure that you communicate your own sense of urgency of the situation; proceed to do the most important things first and set the further clinical priorities; do not get sidetracked into ordering excessive unnecessary investigations

Medical ethics: you may be set a task which involves matters of medical ethics; make sure you have read the ASA guidelines on ethical practice of anesthesiology; you can review this document at the ASA website, www.asahq.org; search under the tab "resources" and then "practice guidance resources;" particularly useful here are the guidelines for dealing with "do not resuscitate" orders and guidelines for quality incentive programs

Technical skills: OSCEs may also involve an assessment of your technical skills; make sure that you look at the range of those that may be presented as listed in the OSCE content outline on the ABA website; these are all skills that you should have learned during your residency training; for the purposes of the examination, it is also most important that you have a clear plan of how you will demonstrate your skills and present your knowledge and interpretations; when asked to interpret the results of any investigation or study, make sure that you have a template in your mind so that you present these results in a complete and logical fashion; for example, if shown physiological recordings and asked to analyze these, do so in a planned, organized fashion; you will be asked to provide a diagnosis but also to list the changes in the recordings that lead you to this diagnosis; demonstrate that you have a logical approach to arriving at your diagnosis; if the task involves the examination of an echocardiogram, you will be expected to first name the view which has been presented for analysis; you must make sure you are familiar with all the standard views and can name these immediately; the list of views you are expected to recognize can be found on the ABA website; this is a pure learning exercise which must be completed before presenting yourself at the examination

Pathology: the pathology which is presented will be a lesion that you should have seen during your training and will not be anything very obscure; you will be expected to identify anatomical structures, make a diagnosis, and suggest treatment options; if you have difficulty gaining experience with examining TEE (transesophageal echocardiogram) images in your program, or if you want to review your knowledge, there are some very good instructional programs online; some of these are free to use and quite comprehensive; a typical one has been posted by the department of anesthesia at the University of Toronto and may be found if you Google "TEE interpretation U Toronto;" you should make sure that you are familiar with the following TEE appearances — alterations in ventricular function or wall motion, presence of an ASD or an intact atrial septum, changes in volume status, pulmonary or air emboli, common valve lesions, pericardial effusion, or aortic dissection; using ultrasound is another skill that may be assessed at the OSCE; make sure you are familiar with the use of ultrasound for commonly applied vascular cannulations and for common nerve blocks; if asked to place a probe on a patient, make sure you tell the patient who you are and exactly what you're going to do

Conclusion: these are the measures you should take to demonstrate to your examiners what a wonderful attending anesthesiologist you are going to become

Suggested Reading

ABA APPLIED (Staged Exams). www.theaba.org/Exams/APPLIED-(Staged-Exam)/About-APPLIED-(Staged-Exam). Accessed November 2, 2018; ABA Written Examination. www.theaba.org/Exams/Traditional-Part-1/About-Traditional-Part-1. Accessed November 2, 2018; **Manuel SP, Grewal GK, Lee JS.** Millennial resident study habits and factors that influence American Board of Anesthesiology In-Training Examination Performance: A multi-institutional study. *J Educ Perioper Med*. 2018;20(2):E623.