ANESTHESIOLOGY

ANESTHESIA OUTSIDE THE OPERATING ROOM/
ANESTHESIA AND THE DEVELOPING BRAIN

Highlights from Survey of Current Issues in Surgical Anesthesia,
presented by the Cleveland Clinic Anesthesiology Institute

Anesthesia in the Gastrointestinal Endoscopy Suite

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Background: increasing number of requests for anesthesia being made for gastrointestinal (GI) procedures; most patients undergoing endoscopy require some level of sedation (usually administered by gastroenterologist); practice style and reimbursement undergone changes

American Society of Anesthesiologists (ASA) definitions of sedation: minimal — patient comfortable; cardiovascular (CV) and pulmonary condition undisturbed; moderate — drug-induced depression of consciousness; patients respond to verbal or light tactile stimulation; no intervention needed to maintain airway; no CV changes expected; deep — drug-induced depression of consciousness; patients not easily arousable but purposefully respond to repeated or painful stimulation; patient usually able to maintain ventilatory and CV function

Role of anesthesia team in endoscopy: sedation represents continuum between awake and under general anesthesia; practitioners require skills to rescue patient from deep sedation when moderate sedation administered, and from general anesthesia when deep sedation administered; rescue — airway management; patient must be returned to previous level of sedation (procedure halted until patient returns to that state); changing role — levels of comorbidity increasing (patients classified as ASA 4 now seen in endoscopy suite); units mostly outpatient (ie, require efficiency); endoscopist must be free to perform complex procedure

Insurance coverage: propofol has been used for routine colonoscopies and endoscopies in healthy patients without support of anesthesiologist; carriers may refuse to pay for anesthesiologist-provided sedation in routine cases; may cover if medical necessity (ie, documented significant medical comorbidity) established; provides coverage for anesthesiology support in patients with difficult airway management or those for whom earlier procedure aborted without completion; payment varies if anesthesiologist requested by patient who had difficult, but completed, prior procedure

Indications for anesthesiologist (deep sedation): required for complex, difficult, or prolonged procedures; endoscopic retrograde cholangiopancreatography — endoscopy plus fluoroscopy to visualize biliary tree; diagnostic indications include removal of gallstones, leaks in bile system, and fine needle aspiration (FNA) biopsy; therapeutic indications include removal of stones and stent insertion; complications include bleeding, perforation of viscus, acute pancreatitis (option to admit patients important), and infection; overall mortality 0.3%; endoscopic ultrasonography — uses ultrasound probe on tip of endoscope for diagnostic Imaging and therapeutic procedures; often used with FNA to obtain definitive tissue diagnosis, and to locate and drain pancreatic pseudocysts; double-balloon endoscopy — used to locate and treat lesions throughout GI tract; uses endoscope with camera, balloon, and overtube; allows telescoping of intestine; reaches large bowel from mouth, or performed from above and below; can obtain biopsy, resect polyps, place stents, and dilate strictures; other procedures — placement of feeding tube; dilation and stenting of esophageal strictures; intestinal stenting; treatment of bleeding lesions; abscess drainage

Providing sedation: quick onset of deep sedation with rapid recovery desirable; avoid postoperative nausea and vomiting; begin with midazolam, ketorolac, and glycopyrrolate (dries secretions if given 3–5 min before topical anesthesia); sedation techniques require ASA monitoring (however, addition of, eg, nasal cannula may not be possible if patient not in supine position); options include bolus and continuous infusion; start with midazolam and fentanyl with ketorolac for premedication; pure propofol — reduces risk for induced apnea (in, eg, patient in lateral or prone position with unsecured airway); has excellent rapid recovery profile; easy to titrate; mildly antiemetic; propofol plus alfentanil — second most commonly added opiate (after fentanyl); onset of sedation rapid; provides analgesia; allows rapid clearance; slightly increases postoperative nausea; ketamine — sympathomimetic; excellent analgesic; does not cause respiratory depression; increases oral secretions; causes minimal dysphoria at very low doses (especially with propofol and/or midazolam); causes confusion for 10 to 20 min after procedure in 1% to 3% of patients; may benefit patients with chronic pain due to GI pathology managed with multiple medications; dexmedetomidine — used in patients with severe cardiac comorbidity; causes some hemodynamic instability; does not depress respiration; has slow onset

Educational Objectives

The goal of this program is to improve the practice of anesthesiology for outpatient gastrointestinal (GI) procedures and for pediatric patients. After hearing and assimilating this program, the clinician will be better able to:

1. Recognize the increasing role of anesthesiology providers in providing sedation or anesthesia during GI endoscopy procedures.
2. Select appropriate anesthetic techniques for GI procedures.
3. Compare and contrast the pediatric nervous system to that in adults.
4. Anticipate the effects of anesthetics based on pediatric physiology.
5. Determine which pediatric patients are at highest risk for adverse effects due to anesthesia.

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Indications for intubation: history of difficult airway; morbid obesity; sleep apnea (possibly); significant CV comorbidity (especially if patient unable to lie flat); aspiration of large GI cysts; aggressive intubation needed for removal of stones; high esophageal stenting (consider); active GI bleeding; high index of suspicion for need of intubation

Natural orifice transendoscopic surgery: incision-free laparoscopic surgery; peritoneal cavity entered via mouth, vagina, or anus; appendectomy and cholecystectomy currently possible; used for hernia repair and removal of ovaries; surgery on heart and lungs may become possible in future

Computer-assisted personalized sedation (CAPS; SEDA-SYS): Centers for Medicare and Medicaid Services (CMS) requires anesthesiology to supervise all sedation in facilities; deep sedation must be administered by anesthesiology practitioner or airway-trained physician not involved in endoscopic procedure (propofol defined by CMS as deep sedation); CAPS computer — designed to provide propofol sedation with electronic feedback for safety; ASA gave unfavorable review because of concerns about high dose of propofol (200 μg/kg/min), clinical bolus during yellow alerts, delay in detection of hyperventilation because of high-flow oxygen, lack of capnography (initial version), and complex setup (approval by Food and Drug Administration [FDA] denied); after revision of system, 2011 study showed no serious adverse events in 1000 patients; premarket approval granted by FDA (2013), with restrictions pending further study

Restrictions and use: minimal or moderate sedation only; 1% propofol; ASA 1 and 2; GI endoscopy only; anesthesia provider must be immediately available; collaboration between anesthesiology, nursing, and gastroenterology required; considerations — standard of care must be maintained; safety requires communication; nonoperating room areas have additional considerations — anesthesia, nursing, and gastroenterology required; con considerations — standard of care must be maintained; collaboration between anesthesiology, nursing, and gastroenterology is required; use — activated in preoperative area; initial dose 75 μg/kg/min unless programmed lower; has 3-min lockout until next incremental change; dose may be increased based on automated patient module response; if no response for >30 sec, infusion reduced by one-half and oxygen increased (bolus dose allowed); incremental increases up to 200 μg/kg/min possible (using automated patient response), and respirations, capnography, and oxygen saturation normal; not recommended for high-risk patients, deep sedation, or general anesthesia

Anesthesia and the Developing Brain

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Development in utero: abnormalities can arise during first trimester or organogenesis; critical points start at 24 wk of gestation (fetus starting to become viable) to 32 wk; subplate, oligodendrocytes, and microglia increasing activity in terms of differentiation, connectivity, and apoptosis; brain size increases 50% after 30 wk gestation (premature or very-low-birth-weight infants lose time required for development); brain mass triples in first 2 yr

Brain growth: weight of brain in full-term infant ≈350 g, and increases to 1 kg at 1 yr of age; sutures close at ≈3 yr of age, but development of pathways and connectivity remains highly active

Fetal circulation: shunts (ductus venosus, foramen ovale, and ductus arteriosus) allow adaptation to cyanotic uterine environment; parallel pulmonary and systemic circulation allows differences in flow velocity; oxygenated blood from placenta largely targeted toward brain and heart; shunts optimize flow, thus allowing normal growth; brain comprises ≈20% of body surface area but receives 25% of cardiac output; oxygen saturation of 60% to 70% considered high in utero

Cranial vault: all neurons present at birth; highest rate of growth occurs between 30 wk of age and teenage years; increasing size of neurons increases brain weight; increase in support cells and myelination continues until 13 to 14 yr of age; Monro-Kellie hypothesis — sum of all volumes constant; brain and interstitial fluid makes up 80% of cranial vault contents (remainder cerebrospinal fluid [CSF] and blood); children >3 yr of age (fontanelles now closed) at increased risk for herniation after head injury due to smaller cranial volume relative to adults; hypothesis — high synaptogenesis, and thus potentially increased sensitivity to neurodegenerative agents or trauma, occurs between 30 wk gestation and 3 yr of age; intraventricular hemorrhage (IVH) — incidence decreased if clamping of umbilical cord delayed; most term infants weigh >3 kg, with ≈100 mL/kg of blood; blood volume can increase 20 mL/kg if clamping delayed 1 to 3 min; elevated intravascular volume increases blood flow (passive to brain [autoregulation minimal in neonates]), and risk for IVH (typically, venous) decreases in caudate nucleus; large bleeds can compromise movement of CSF and increase intracranial pressure (may require placement of shunt); incidence of IVH 7% to 23% in premature infants, and increases in those <1 kg; usually occurs before fourth day of life

Developmental disturbances: intrinsic — ability to influence minimal; inborn errors of metabolism; inheritance patterns; mitochondrial cytopathy (includes neurometabolic syndromes and neurotoxicity); cerebral palsy (usually results from anoxic event in utero rather than injury during birth); affected by anesthesia — prematurity; low birth weight; infections during first month of life; upper respiratory infections; maternal fever in third trimester contributes to elevated risk for increased sensitivity to anesthetics; congenital heart disease (especially cyanotic) can affect ejection fraction or partial pressure of oxygen

Physiology of young infants: most medications tested on adults or animals; organs systems immature; extracellular volume of water greater than intracellular; metabolism and consumption of oxygen high; however, multiple doses of medications or infusions can accumulate; ability to clear medications depressed; tight junctions of blood-brain barrier not fully developed until >10 yr of age; bradycardia occurs during stress and hypoxia; pretreatment with glycopyrrolate or atropine maintains parasympathetic nervous system, however, sympathetic nervous system lags

Oxygenation: oxygen tension — saturation of hemoglobin (Hb) affected by presence of fetal Hb, which binds tightly to oxygen (has consequences in face of stress and/or medications); saturation reaches adult level by 12 mo of age; high cardiac index to vessel-rich groups due to high ratio of surface area to weight; oxygen consumption in infants doubled relative to adults (increased >3-fold [ie, 9 mL/kg/min] in premature neonates); hypercapnia — infants more reactive to carbon dioxide (CO 2); amount of CO 2 that causes inspiration lags behind adults; these issues affect risk for development of seizures, herniation, flow of blood into and out of brain, and CSF; CSF production — same in children as in adults (500 mL per day); however, turnover rate higher due to smaller head size; more glucose and oxygen needed for brain growth; risk to tissues with high oxygen requirement increased by lack of autoregulation

Apnea: may be induced by surgery (for, eg, pyloric stenosis); determinant cause (central vs obstructive); consider alternatives to anesthesia for patients at risk for apnea depending on site, location, and speed of surgery; consider anemia, low birth weight, and acid-base disturbances, which affect sensitivity to respiratory-depressant medications (eg, opioids, volatile anesthetics)

Apoptosis: process of scheduled or programmed cell death, triggered by extrinsic and/or intrinsic cellular events; not always adverse; children believed most sensitive during period of rapid synaptogenesis between third trimester and 3 yr of age;
apoptosis influenced by elevation of caspases (part of signal transduction pathway), mitochondria, and other mediators (eg, inflammatory, medications); low levels of apoptosis associated with neoplasms and overgrowth; high apoptosis causes atrophy

**Causes of neurotoxicity:** difficult to determine exact causes of toxicities; receptor sites likely involved in neurogenesis interact with N-methyl-D-aspartate receptors (ketamine, nitrous oxide, methadone, chloral hydrate, trichloroethanol, and alcohol) and γ-aminobutyric acid receptors (eg, all volatile anesthetics, benzodiazepines, barbiturates, propofol, nitrous oxide, chloral hydrate); agents with negligible influence include opioids; nondepolarizing muscle relaxants; dexmedetomidine and xenon; neurotoxicity multifactorial; inflammatory factors, dose and duration of anesthesia, and complexity and time of surgery likely affect toxicity as well as anesthetics; reversibility of toxicity seen in humans not seen in animal models; consensus statement on use of anesthetics and sedatives in children (smarttots.org) — evidence shows some anesthetic medications have potential to cause harmful effects; large-scale prospective studies needed, but optimal treatment still necessary; factors that increase risk — primarily, CV or respiratory events, medication error, and equipment; 1 in 10,000 anesthetics causes serious, long-term, permanent outcome; these typically occur in patients with elevated ASA score who present for emergency surgery, and small young patients, especially those with history of congenital heart disease or if undergoing cardiac procedure; long-term outcomes — primary focus of studies; include effects on behavior, cognitive ability, and learning disabilities; short-term concerns — include emergence delirium (typically seen in young children after short procedures), anxiety, behavioral changes, nightmares, and intraoperative awareness (more common in children than in adults); conclusion — neurodegenerative effects may be caused by toxicity, or may be related to insufficient anesthesia

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**Acknowledgements**

Dr. Tetzlaff and Dr. Rodriguez were recorded at *Survey of Current Issues in Surgical Anesthesia*, held December 2-6, 2013, in Naples, FL, and sponsored by the Cleveland Clinic Anesthesiology Institute. For information on upcoming CME meetings sponsored by the Cleveland Clinic, please visit ccfecme.org. The Audio Digest Foundation thanks the speakers and the Cleveland Clinic Anesthesiology Institute for their cooperation in the production of this program.

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**Suggested Reading**


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1. Which of the following is not an appropriate role for an anesthesiologist during gastrointestinal endoscopy procedures?
   (A) “Rescuing” a patient by reducing the level of sedation when it exceeds the intended level
   (B) Providing airway management
   (C) Allowing the procedure to continue while restoring the patient to the intended level of sedation
   (D) Freeing the endoscopist to focus on performing the procedure

2. In which of the following situations is moderate sedation, delivered by an anesthesia provider, appropriate?
   1. Intestinal stenting procedures
   2. Patients with morbid obesity
   3. Drainage of abscesses
   4. Patients with difficult sedation in the past
   5. Patients with chronic pain
   (A) 1,2 (B) 3,4 (C) 1,3,5 (D) 2,4,5

3. Advantages of sedation using propofol plus alfentanil include all the following, except:
   (A) Rapid onset
   (B) Decreased postoperative nausea
   (C) Provision of analgesia
   (D) Rapid clearance

4. Which of the following is a feature of ketamine?
   (A) Has vasodilatory effects
   (B) Does not produce respiratory depression
   (C) Contraindicated in patients taking multiple medications for chronic pain
   (D) Does not have analgesic effects

5. According to guidelines from the Food and Drug Administration, use of the computer-assisted personalized sedation (SEDASYS) computer is appropriate:
   (A) Only when an anesthesiologist can be immediately available
   (B) For healthy and high-risk patients
   (C) For all types of endoscopy
   (D) For mild, moderate, and deep sedation

6. Which of the following statements about brain development in children is not true?
   (A) A critical point for developing abnormalities is at ≈24 wk of gestation (threshold of viability)
   (B) Brain mass triples during the first 2 yr of life
   (C) Development of pathways and connectivity slows after sutures close at ≈3 yr of age
   (D) In full-term infants, brain weight reaches 1 kg by ≈1 yr of age

7. Which of the following statements about intraventricular hemorrhage in neonates is true?
   (A) Incidence decreases if clamping of the cord is delayed by 1 to 3 min
   (B) Occurs in 2% to 7% of premature infants
   (C) Usually occurs in the second or third week of life
   (D) Typically has arterial origin

8. Which of the following is a characteristic of neonatal physiology?
   1. Tachycardia during stress or hypoxia
   2. Underdevelopment of junctions of the blood-brain
   3. Lower oxygen consumption, compared with adults
   4. Oxygen saturation reaches adult level by 12 mo of age
   5. Greater volume of intracellular vs extracellular water
   (A) 1,2,5 (B) 3,4,5 (C) 1,3 (D) 2,4

9. Children are believed to be most sensitive to adverse effects of anesthesia between:
   (A) Conception and the end of the first trimester
   (B) The first and second trimesters
   (C) The second and third trimesters
   (D) The third trimester and 3 yr of age

10. Which of the following anesthetic agents is most likely to have a negligible influence on neurodegeneration in children?
    (A) Dexmedetomidine
    (B) Nitrous oxide
    (C) Ketamine
    (D) Trichloroethanol

Answers to Audio Digest Anesthesiology Volume 56, Issue 41: 1-A, 2-B, 3-C, 4-C, 5-D, 6-A, 7-D, 8-B, 9-A, 10-C