Hypothalamus-pituitary complex: hypothalamus secretes specific releasing factors that regulate function of pituitary; anterior pituitary—secretes adrenocorticotropic hormone (ACTH), thyrotropin (TSH), follicle-stimulating hormone, luteinizing hormone, and prolactin; posterior pituitary—secretes oxytocin and antidiuretic hormone (ADH; vasopressin); latter plays major role in maintaining vascular tone and fluid and electrolyte balance by facilitating absorption of water in renal collecting ducts.

Diabetes insipidus (DI): deficiency of ADH results in central DI, while resistance to effects of ADH called nephrogenic DI; results in inability to absorb water in renal tubules and collecting ducts; liters of dilute urine produced each day; if water loss not supplemented, severe dehydration, hyperosmolality, hypernatremia, cardiovascular collapse, stupor, and coma may result; causes include intracranial surgery, head trauma, intracranial tumors, and infections; certain medications (eg, lithium) may cause nephrogenic DI; central DI managed with desmopressin (analogue of ADH).

Syndrome of inappropriate ADH secretion (SIADH): ubiquitous response after trauma or surgery; leads to excessive renal absorption of water, with resulting hyponatremia, decreased serum osmolality, and concentrated urine; congestive heart failure and cirrhosis can activate angiotensin-renin system and cause SIADH; strongly suggested by hyponatremia in setting of concentrated urine; management includes restriction of free water, diuretics, and control of precipitating condition; severe hyponatremia medical emergency (may require hypertonic saline under close monitoring).

Thyroid Gland

Hormones: principally T3, T4, and calcitonin; tyrosine in thyroid cells iodinated to form T3 and T4, secretion of TSH decreased by glucocorticoids, dopamine, somatostatin, and stress; physiologic effects of thyroid hormone—increases consumption of O2, as well as carbohydrate, fat, and protein metabolism; essential for normal growth; increases cardiac output by increasing heart rate and myocardial contractility; enhances effects of catecholamines.

Thyroid abnormalities: extremely low TSH with high T4 suggest hyperthyroidism; high TSH with low free T4 suggest hypothyroidism.

Hyperthyroidism: characterized by nervousness, weight loss, hyperphagia, heat intolerance, sweating, tachycardia, an increase in pulse pressure (because of vasodilation); uncontrolled symptoms should be managed medically before elective surgery; management includes decreasing hormone production (ie, administering propylthiouracil or methimazole, which compete with tyrosine for iodide) and blunting hyperadrenergic symptoms (with β-blockers); in acute situation, administer exogenous iodine to depress production of thyroid hormone; acute thyroid storm constitutes medical emergency (can develop intraoperatively)

Hypothyroidism: patients may present with vasoconstriction, poor mentation, cold intolerance, weight gain, bradycardia, and low cardiac output; treated with exogenous levothyroxine; myxedema coma—can develop in severe cases; patients exquisitely sensitive to medications and can quickly develop cardiopulmonary collapse; management requires administration of inotropic agents, T3 (has faster onset of action) or T4, fluids, hydrocortisone, and respiratory support.

Adrenal Gland

Hormones: outer cortex produces steroid hormones (ie, mineralocorticoids, glucocorticoids, and androgens); adrenal medulla produces epinephrine, and some norepinephrine and dopamine; glucocorticoids integrally involved in production and function of catecholamines; epinephrine and norepinephrine significantly increased during and after surgery; catecholamines—have short (~2-min) half-life; metabolized to vanillylmandelic acid, metanephrines, or normetanephrines, and excreted in urine.

Pheochromocytoma: primarily produces norepinephrine; patients present with hypertensive attacks and significant volume depleted due to vasoconstriction; diagnosed by measuring catecholamines and vanillylmandelic acid in 24-hr urine samples; symptoms should be managed before elective surgery; initially treated with β-blockers in conjunction with β-blockers (ie, predominant β-blockade can lead to unopposed α effects of catecholamines and worsening hypertension [HTN]).

Adrenal cortex: cholesterol precursor of all steroid hormones; production and secretion of glucocorticoids primarily controlled by ACTH; aldosterone predominantly controlled by angiotensin-2, ACTH, and levels of serum K.

Glucocorticoids: increase protein catabolism, glycogenolysis, and gluconeogenesis; have anti-inflammatory and anti-insulin effects, contribute to normal vascular reactivity, neurologic function, and water excretion; decrease eosinophils and basophils, but increase neutrophils, platelets, and red blood

Educational Objectives

The goal of this program is to improve the management of endocrine and metabolic derangements. After hearing and assimilating this program, the clinician will be better able to:

1. Identify diabetes insipidus and syndrome of inappropriate antidiuretic hormone secretion.
2. Outline the treatment of myxedema coma and thyroid storm.
3. Treat adrenal disorders and manage perioperative replacement of steroids.
4. Delineate the diagnosis and treatment of primary hyperparathyroidism.
5. Explain the metabolic effects of insulin and glucagon.

Faculty Disclosure

In adherence to ACCME Standards for Commercial Support, Audio Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, members of the faculty and planning committee reported nothing to disclose.
cells; excess leads to Cushing syndrome, which can be due to increased ACTH or increased production by adrenal gland (ACTH-independent); ACTH-dependent excess of glucocorticoids also can be caused by ACTH-secreting tumors or ectopic production by other tumors (eg, lung); causes of ACTH-independent excess include glucocorticoid-secreting tumors of adrenal gland, hyperplasia of adrenal gland, or prolonged exogenous administration of glucocorticoids; clinical effects include intolerance to glucose, with development of diabetes, muscle atrophy, retention of water, HTN, osteoporosis, truncal obesity, and psychologic complaints

Deficiency of glucocorticoids (Addison disease): causes include primary adrenal failure or lack of sufficient production of ACTH; causes of acute insufficiency include autoimmune destruction, metastatic cancer, infection, hemorrhage, and sepsis; may present with nonspecific symptoms, including chronic fatigue, muscle weakness, anorexia, weight loss, nausea and vomiting, and diarrhea; acute adrenal insufficiency frequently presents with hypotension, decreased consciousness, and shock; chronic adrenal insufficiency diagnosed by testing plasma cortisol response to ACTH-stimulation test (minimal or no response characteristic of primary adrenal insufficiency, while adequate increase suggests deficiency of ACTH); addisonian crisis requires administration of intravenous (IV) hydrocortisone and fluids

Physiologic effects of aldosterone: responsible for absorption of sodium and water to maintain intravascular volume; decreased intravascular volume leads to decreased arterial pressure in nephron, and secretion of renin by juxtaglomerular apparatus; renin converts angiotensinogen to angiotensin-1, which is then converted to angiotensin-2 by converting enzyme in lungs; angiotensin-2 potent stimulus for secretion of aldosterone; aldosterone acts on distal renal tubules and promotes absorption of Na and water; excess mineralocorticoid causes excess absorption of Na and excretion of K and H+; this causes HTN, muscle weakness, polyuria, tetany, and hypokalemic alkalosis; primary hyperaldosteronism—caused by increased production by adrenal cortex due to adrenal hyperplasia, adrenal adenoma, or carcinoma; secondary hyperaldosteronism—commonly seen in heart failure, cirrhosis, and nephropathy, which increase renin

Steroid replacement in perioperative period: exogenous administration of steroids suppresses hypothalamic-pituitary axis (HPA); suppression unlikely in patients who have received steroids for <1 wk, but presumed in patients who have received steroids for 1 to 3 wk or more, especially if receiving prednisolone >15 mg/day (or equivalent); HPA axis may require 6 to 9 mo to recover; patients who receive ≤5 mg prednisolone do not require additional supplementation if they have taken usual dose before surgery; perioperative supplementation based on expected physiologic stress (eg, for high-risk surgery, administer hydrocortisone 300 mg/24 hr in 3 divided doses; for low-risk surgery, administer hydrocortisone 25 mg at induction, followed by 100 mg in next 24 hr); preparations of glucocorticoids—dexamethasone, betamethasone, and triamcinolone have no mineralocorticoid activity and typically used for anti-inflammatory properties; fludrocortisone has 12 times more mineralocorticoid activity than anti-inflammatory activity; cortisol, hydrocortisone, and cortisone have equal mineralocorticoid and glucocorticoid activity

**Calcium Homeostasis**

Free ionized Ca: 40% to 45% of total Ca in plasma; plays critical role in regulating contraction of muscle, coagulation, release of neurotransmitters, and function of second-messenger intracellular functions; alkalosis decreases ionized Ca

**Parathyroid hormone (PTH):** increases plasma Ca; promotes excretion of phosphate, bicarbonate, and magnesium

Hyperparathyroidism: primary—caused by parathyroid adenoma, benign hyperplasia, or carcinoma; malignancies can secrete PTH-like substances; excess PTH leads to hypercalcemia with polyuria, polydipsia, generalized muscle weakness, fatigue, peptic ulceration, constipation, and psychiatric complaints; secondary—seen in conditions causing hypocalcemia or hyperphosphatemia (eg, chronic renal failure); tertiary—occurs when hyperplastic parathyroid glands lead to autonomous functioning, with resulting hypercalcemia (typically occurs after renal transplantation); treatment—treatment of hypercalcemia primary concern; administration of IV normal saline followed by loop diuretics; calcitonin, which inhibits secretion of PTH, can be used for first 24 to 48 hr

Hypoparathyroidism: causes include inadvertent removal during surgery, trauma, hemochromatosis, and infiltrative and autoimmune disorders; presents with numbness, paresthesias, muscle cramps, spasm, altered mental status, behavioral disturbances, and, rarely, seizures and laryngeal stridor; hypocalcemia with low levels of PTH confirm diagnosis; treated with Ca and vitamin D analogues; in severe cases, IV Ca administered

**Pancreas**

Cell types: cells of islets of Langerhans constitute endocrine portion of pancreas (1%-2% of pancreatic mass); β cells most abundant (~60%) and produce insulin and amylin; α cells (~25%) produce glucagon; δ cells (~10%) produce somatostatin; F cells produce pancreatic polypeptide (PP)

Insulin: anabolic hormone responsible for maintaining upper limit of blood glucose (BG) and levels of fatty acids (FAs); promotes uptake of glucose in skeletal muscle and adipose tissue while suppressing glucose output by liver; converts excess glucose into glycogen and fat; inhibits breakdown of amino acids and protein; suppresses lipolysis of adipose tissue; half-life of unbound insulin in plasma 6 min; serum glucose principal stimulus for release of insulin from β cells; entry of glucose into β cells occurs cause increase in adenine triphosphate, which inhibits influx of K into cells; in turn, this causes influx of Ca into cells, triggering insulin release; K channels mediated by sulfonylurea receptors (basis of therapeutic use of sulfonylureas in diabetes); incretin hormones (eg, glucagon-like peptide and gastric inhibitory peptide) enhance release of insulin; incretin-mimetic drugs used in management of diabetes

Glucagon: important counterregulatory hormone that increases BG by increasing output of glucose from liver; promotes production of glucose by increasing glycogenolysis and gluconeogenesis; inhibits synthesis of free FAs from glucose; stimulates ketogenesis, which provides alternative energy source for many tissues; decrease in BG major stimulus for its secretion

Other pancreatic hormones: somatostatin—inhibits all pancreatic exocrine and endocrine functions; PP—inhibits pancreatic exocrine secretion and contraction of gall bladder; may play role in feeding behavior; amylin—works with insulin to regulate BG, suppress secretion of glucagon, and slow gastric emptying; increased in obesity, HTN, and gestational diabetes; low or absent in type 1 DM

Endocrine response to surgery: plasma levels of catecholamines, vasopressin, cortisol, and glucagon increase significantly, with resulting HTN, tachycardia, fluid retention, and hyperglycemia; general anesthesia, regional anesthesia, and control of pain can blunt stress response

**Carbohydrate metabolism:** carbohydrates normally supply 40% to 50% of energy needs; while skeletal and cardiac muscle can function without glucose, nervous system and blood cells cannot; glycolysis results in breakdown of glucose to pyruvate; under aerobic conditions, pyruvate crosses into mitochondrial matrix and enters Krebs cycle; aerobic and anaerobic
metabolism — O2 required for Krebs cycle and complete oxidation of glucose; hepatic glycogen serves as glucose buffer; with prolonged fast, hepatic glycogen stores become exhausted within 24 to 48 hr; breakdown of glycogen stimulated by fall in BG, decrease in insulin, and increase in glucagon and catecholamines; muscle other major store of glycogen; if demand for O2 greater than supply (in, eg, shock, intense exercise), lactic acid accumulates and diffuses into circulation, with resulting metabolic acidosis; with shortage of nutrients, glucose synthesized from smaller molecules (eg, glycerol, lactate, amino acids) by gluconeogenesis

Fat metabolism: triacylglycerol — constitutes major energy store of body; formed from glycerol and 3 FAs; lipoprotein lipase hydrolyzes triacylglycerol to release free FAs; hydrolysis of triacylglycerol stimulated by catecholamines and inhibited by insulin; FAs used as fuel by peripheral tissues (eg, skeletal muscle, myocardium), while glycerol transported to liver and converted to glucose; FAs taken up by cells and oxidized in mitochondria, resulting in acetyl coenzyme A, which then enters Krebs cycle

Energy requirements of nervous tissue: in starvation, initial needs for energy met by gluconeogenesis, resulting in loss of lean tissue; after 10 days of simple starvation, brain adapts by obtaining one-half to two-thirds of energy from ketone bodies (synthesized in liver from free FAs)

Protein metabolism: 10% to 15% of energy needs derived from oxidation of protein; amino acid metabolism — removal of amino group produces ammonia, which undergoes rapid metabolism in liver by urea cycle; with severe sepsis or multiple injuries, protein synthesis increased and degradation increased, but relatively greater degradation results in loss of lean muscle mass; in patients with sepsis or injury, gluconeogenesis not completely suppressed; catecholamines, cortisol, glucagon, and growth hormone stimulate catabolism of protein

Acknowledgments

Dr. Akhtar’s lecture is from our newest continuing medical education program, an update of the Audio Digest Anesthesiology Board Review, a comprehensive review with approximately 40 hours of lectures presented by faculty from a variety of prominent teaching institutions across the country. This audio course offers participants a chance to benefit from firsthand expert guidance on the essential examination areas. For those not preparing for the exam, the course provides an excellent update and overview of anesthesiology. The Audio Digest Foundation thanks Dr. Akhtar for his participation in the production of this program.

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ENDOCRINE AND METABOLIC SYSTEMS

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1. Syndrome of inappropriate antidiuretic hormone secretion is associated with which of the following?
   (A) Head trauma
   (B) Lithium
   (C) Diuretics
   (D) Congestive heart failure

2. Levels of thyroid-stimulating hormone are decreased by which of the following?
   (A) Insulin
   (B) Glucagon
   (C) Dopamine
   (D) Stress

3. Management of myxedema coma includes administration of all the following, EXCEPT:
   (A) Inotropic agents
   (B) Glucocorticoids
   (C) Glucose
   (D) Fluids

4. Which of the following is the initial management of pheochromocytoma?
   (A) Fluids
   (B) α-blocker
   (C) β-blocker
   (D) Surgical excision

5. Which of the following is(are) used to manage addisonian crisis?
   1. Cortisone
   2. Intravenous fluids
   3. Inotropic agents
   4. Aldosterone
   (A) 1
   (B) 1,2
   (C) 2,3,4
   (D) 1,2,3,4

6. Recovery of the hypothalamic-pituitary axis after long-term administration of steroids takes up to:
   (A) 2 to 3 mo
   (B) 4 to 5 mo
   (C) 6 to 9 mo
   (D) 12 mo

7. Which of the following preparations has equivalent mineralocorticoid and glucocorticoid activity?
   (A) Dexamethasone
   (B) Betamethasone
   (C) Fludrocortisone
   (D) Hydrocortisone

8. The half-life of unbound insulin in plasma is:
   (A) 6 min
   (B) 15 min
   (C) 24 min
   (D) 35 min

9. For which of the following is glucose the only option for meeting energy requirements?
   (A) Heart
   (B) Skeletal muscle
   (C) Nervous system
   (D) Kidney

10. Gluconeogenesis is suppressed by which of the following?
    (A) Glucose
    (B) Catecholamines
    (C) Glucagon
    (D) Growth hormone

Answers to Audio Digest Anesthesiology Volume 57, Issue 33: 1-C, 2-D, 3-D, 4-B, 5-D, 6-A, 7-D, 8-A, 9-C, 10-C