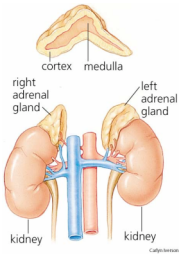
Parathyroid Abnormalities

- Hypoparathyroidism
  - Low blood calcium
  - Due to low osteoclast activity
  - May cause spontaneous depolarization of neurons and muscle fibers
    - Treat with 100,000 daily units of vitamin D and 1-2g Ca^{2+}/day
- Hyperparathyroidism
  - High blood calcium
  - Usually due to tumor
  - Women more than men
  - Decalcifies bones
  - Muscular weakness
  - Abdominal pain and constipation

Adrenal (Suprarenal) Glands

- Adrenal glands
  - Paired, pyramid-shaped organs atop the kidneys
- Structurally and functionally
  - They are two glands in one
  - Adrenal medulla
    - Nervous tissue that acts as part of the sympathetic nervous system (SNS)
  - Adrenal cortex
    - Glandular tissue derived from embryonic mesoderm



Adrenal Cortex

- Synthesizes and releases steroid hormones
  - Called corticosteroids
- Different corticosteroids are produced in each of the three layers
  - Zona glomerulosa – mineralocorticoids (chiefly aldosterone)
  - Zona fasciculata – glucocorticoids (chiefly cortisol)
  - Zona reticularis – gonadocorticoids (chiefly androgens)

Adrenal Cortex

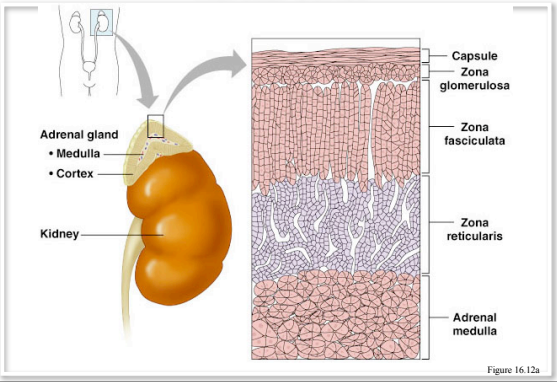
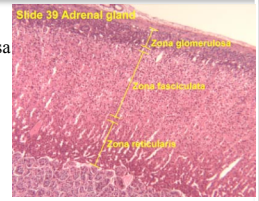


Figure 16.12a

Mineralocorticoids

- Mineralocorticoids
  - Synthesized in zona glomerulosa
    - Cells in clustered balls
  - Regulate the electrolyte concentrations of extracellular fluids
  - Aldosterone – most important mineralocorticoid
  - Maintains Na^+ balance by reducing excretion of sodium from the body
    - Effects water balance as well
  - Stimulates reabsorption of Na^+ by the kidneys



Mineralocorticoids

- Aldosterone secretion is stimulated by:
  - Rising blood levels of K^+
  - Low blood Na^+
  - Decreasing blood volume or pressure

The Four Mechanisms of Aldosterone Secretion

1. Renin-angiotensin mechanism
   - Effects blood volume and pressure
   - Kidneys release renin
     - In response to low blood pressure/volume
       - From juxtaglomerular apparatus
     - Converts angiotensinogen (plasma protein) into angiotensin II
       - Stimulates aldosterone release from zona glomerulosa
2. Plasma concentration of sodium and potassium – directly influences the zona glomerulosa cells
   - Increased K+ stimulates aldosterone secretion
3. ACTH – causes small increases of aldosterone during stress
   - Otherwise doesn't effect aldosterone release
4. Atrial natriuretic peptide (ANP) – inhibits activity of the zona glomerulosa

The Four Mechanisms of Aldosterone

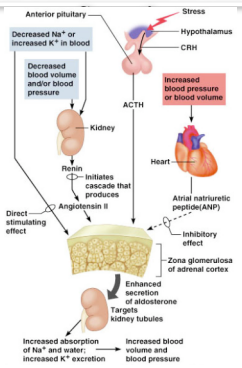


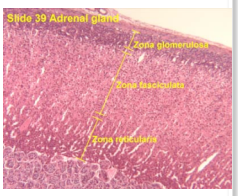
Figure 16.13

Aldosterone Related Abnormalities

- Hyperaldosteronism
  - High Na+
    - Hypertension
  - Low K+ results in hypopolarization of neuron and muscle cell membranes
    - Lowers muscle excitability
      - Leads to muscle weakness
- Hypoaldosteronism
  - Contributor to Addisons disease
  - Low Na+ and water reabsorption
    - Results in low blood volume/pressure
  - High K+
    - Heart toxicity, weakness, arrhythmia, heart failure

Glucocorticoids (Cortisol)

- Zona Fasciculata
- Cortisol, corticosterone, cortisone
  - Help the body resist stress by:
    - Keeping blood sugar levels relatively constant
    - Maintaining blood volume and preventing water shift into tissue
- Cortisol provokes:
  - Gluconeogenesis (formation of glucose from noncarbohydrates)
  - Rises in blood glucose, fatty acids, and amino acids



Excessive Levels of Glucocorticoids

- Excessive levels of glucocorticoids:
  - Depress cartilage and bone formation
    - Lowers osteoblast activity
  - Inhibit inflammation
    - By limiting histamine from mast cells
  - Depress the immune system (also used for transplants)
    - Macrophage lysosomes aren't released
      - Reduces phagocytosis, chemotaxis to injury sites, fever response
  - Promote changes in cardiovascular, neural, and gastrointestinal function
  - Chronic high levels lead to Cushing's Disease/syndrome
    - Low levels contribute to Addison's Disease

Cushing's Disease/Syndrome

- Chronic high levels of cortisol
  - If pituitary tumor causing hypersecretion of ACTH
    - Cushing's Disease
  - Clinical administration of glucocorticoid drugs
    - Cushings Syndrome

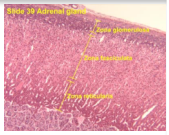
Cushing's Disease/Syndrome

- Effects of excess cortisol
  1. Protein metabolism
     - Increased catabolism, lowered anabolism
  2. Carbohydrate metabolism
     - Stimulates gluconeogenesis, results in hyperglycemia (steroid diabetes)
  3. Fat metabolism
     - Increased lipolysis causes metabolic acidosis
  4. Fat distribution
     - Central obesity
  5. Electrolytes
     - Na+ retention = hypertension, K+/H+ loss = hyperkalemia and metabolic alkalosis

Cushing's Disease/Syndrome

- Effects of excess cortisol
  6. Immune response & inflammation
     - Suppressed antibody production, lymphoid tissue atrophy, reduced histamine production and phagocytosis
  7. Gastric secretions
     - Increased HCl and Pepsinogen = ulcers
  8. Brain function
     - Over-stimulated neurons
       - Mental defects, irritability, manic-depression, impaired cognition/memory
  9. Erythropoiesis
     - Lymphoid atrophy, increased RBC production

Gonadocorticoids (Sex Hormones)



- Zona Reticularis
  - Androgens (male sex hormones)
    - Most secreted
      - Testosterone most important
      - Initially as dehydroepiandrosterone (DHEA)
        - Converted to testosterone and estrogen in body tissues
- Androgens contribute to:
  - The onset of puberty
  - The appearance of secondary sex characteristics
  - Sex drive in females
- Androgens can be converted into estrogens after menopause

Glucocorticoid Abnormalities

- Androgenital Syndrome
  - Hypersecretion of gonadocorticoids
    - Females and prepubescent boys most effected
      - Females
        - Masculinization of facial hair, clitoris grows to resemble small penis
      - Prepubescent boys
        - Early and rapid onset of puberty, enhanced sex drive
    - Not noticeable in adult males

Adrenal Medulla

- Made up of chromaffin cells that secrete epinephrine and norepinephrine
  - Surround blood sinuses
  - Stimulated by preganglionic fibers of autonomic nervous system (ANS)
    - Therefore very rapid
  - Epinephrine and norepinephrine
    - Catecholamines known as sympathomimetic amines
- Secretion of these hormones causes:
  - Blood glucose levels to rise
  - Blood vessels to constrict - especially norepinephrine
  - The heart to beat faster
  - Blood to be diverted to the brain, heart, and skeletal muscle

Adrenal Medulla

- Epinephrine
  - More potent stimulator of the heart and metabolic activities
- Norepinephrine
  - More influential on peripheral vasoconstriction and blood pressure
- Abnormalities
  - Pheochromocytoma
    - Chromaffin cell tumor
      - Hypersecretion of catecholamines
        - Out of control sympathetic response

Stress and the Adrenal Gland

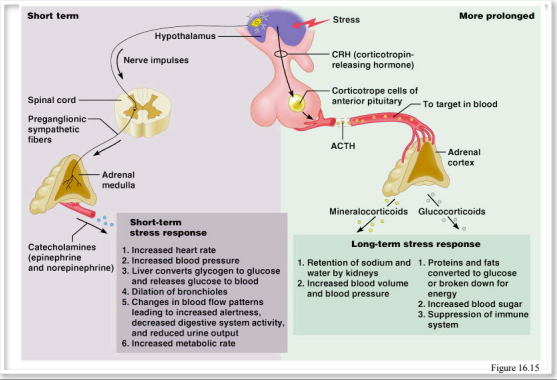
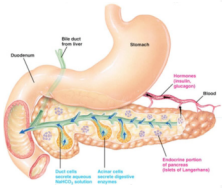


Figure 16.15

Pancreas

- Triangular, mixed gland
  - Both exocrine and endocrine functions
  - Located behind the stomach
- Acinar cells
  - Produce an enzyme-rich juice used for digestion (exocrine product)
- Pancreatic islets (islets of Langerhans)
  - Produce hormones (endocrine products)
- The islets contain two major cell types:
  - Alpha (α) cells produce glucagon
  - Beta (β) cells produce insulin
  - Delta (δ) cells produce somatostatin (GHIH)



Glucagon

- From alpha cells
- 29-amino-acid polypeptide hormone
  - Potent hyperglycemic agent
- Its major target is the liver, where it promotes:
  - Glycogenolysis – the breakdown of glycogen to glucose
  - Gluconeogenesis – synthesis of glucose from lactic acid and noncarbohydrates
    - Increased amino acid uptake
    - Lipolysis - triglyceride breakdown
  - Release of glucose to the blood from liver cells
  - Glucagonomas - glucagon secreting tumor causes hyperglycemia

Insulin

- A 51-amino-acid protein
  - Consists of two amino acid chains linked by disulfide bonds
- Synthesized as part of proinsulin
  - Then excised by enzymes, releasing functional insulin
- Insulin:
  - Lowers blood glucose levels
  - Enhances transport of glucose into body cells
    - Especially liver and muscle cells
      - Stored as glycogen
        - glycogenesis
  - Counters metabolic activity that would enhance blood glucose levels

Effects of Insulin Binding

- The insulin receptor is a tyrosine kinase enzyme
- After glucose enters a cell, insulin binding triggers enzymatic activity that:
  - Catalyzes the oxidation of glucose for ATP production
  - Polymerizes glucose to form glycogen
    - glycogenesis
  - Converts glucose to fat (particularly in adipose tissue)
    - lipogenesis

Regulation of Blood Glucose Levels

- The hyperglycemic effects of glucagon and the hypoglycemic effects of insulin

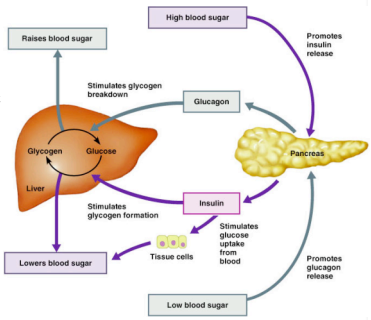


Figure 16.17

Diabetes Mellitus (DM)

- Results from hyposecretion or hypoactivity of insulin
- The three cardinal signs of DM are:
  - Polyuria – huge urine output
  - Polydipsia – excessive thirst
  - Polyphagia – excessive hunger and food consumption
- Hyperinsulinism – excessive insulin secretion, resulting in hypoglycemia

Diabetes Mellitus (DM)

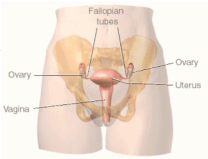
Organs/tissue involved	Organ/tissue responses to insulin deficiency	Resulting condition of: Blood	Resulting condition of: Urine	Signs and symptoms
	Decreased glucose uptake and utilization	Hyperglycemia	Glycosuria	**Polyuria** - dehydration - soft eyeballs
	Glycogenolysis		Osmotic diuresis	**Polydipsia** Fatigue Weight loss
	Protein catabolism and gluconeogenesis			**Polyphagia**
	Lipolysis and ketogenesis	Lipidemia and ketoacidosis	Ketonuria Loss of Na^+, K^+; electrolyte and acid-base imbalances	Acetone breath Hyperpnea Nausea/vomiting/ abdominal pain Cardiac irregularities Central nervous system depression; coma

= Muscle = Adipose tissue = Liver

Figure 16.18

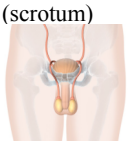
Gonads: Female

- Ovaries
  - Paired in the abdominopelvic cavity
  - Produce estrogens and progesterone
- They are responsible for:
  - Maturation of the reproductive organs
    - Production, maintenance, and maturation of oocytes
  - Appearance of secondary sexual characteristics
  - Breast development and cyclic changes in the uterine mucosa



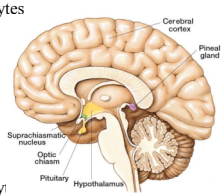
Gonads: Male

- Testes located in an extra-abdominal sac (scrotum)
  - Produce testosterone
- Testosterone:
  - Initiates maturation of male reproductive organs
  - Causes appearance of secondary sexual characteristics and sex drive
  - Is necessary for sperm production
  - Maintains sex organs in their functional state



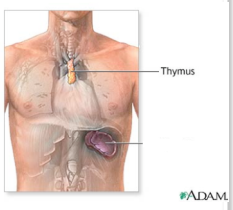
Pineal Gland

- Small gland hanging from the roof of the third ventricle of the brain
  - Composed of neuroglia and pinealocytes
  - Contains calcium salts
- Secretory product is melatonin
  - Peaks at night (10 fold)
- Melatonin is involved with:
  - Day/night cycles (circadian rhythms)
  - Physiological processes that show rhy variations (body temperature, sleep, appetite)
    - Most active in children
      - Inhibits gonadotropic hormone



Thymus

- Lobulated gland located deep to the sternum in the thorax
  - Large and active in infants and children
    - Involuted and filled with fat in adults
- Major hormonal products are thymopoietins and thymosins
  - Essential for the development of the T lymphocytes (T cells) of the immune system
    - Immunocompetency



Other Hormone-Producing Structures

- Heart
  - Produces atrial natriuretic peptide (ANP)
    - Reduces blood pressure, blood volume, and blood sodium concentration
- Gastrointestinal tract
  - Enteroendocrine cells release local-acting digestive hormones
- Placenta
  - Releases hormones that influence the course of pregnancy

Other Hormone-Producing Structures

- Kidneys
  - Secrete erythropoietin, which signals the production of red blood cells
- Skin
  - Produces cholecalciferol
    - Precursor of vitamin D
- Adipose tissue
  - Releases leptin
    - Involved in the sensation of satiety, and stimulates increased energy expenditure

Developmental Aspects

- Hormone-producing glands arise from all three germ layers
  - Endocrine glands derived from mesoderm produce steroid hormones
- Most endocrine glands show structural changes with age
  - Hormone production may or may not be affected

Developmental Aspects

- Exposure to pesticides, industrial chemicals, arsenic, dioxin, and soil and water pollutants disrupts hormone function
  - Sex hormones, thyroid hormone, and glucocorticoids are vulnerable to the effects of pollutants
- Interference with glucocorticoids may help explain high cancer rates in certain areas

Developmental Aspects

- Ovaries undergo significant changes with age and become unresponsive to gonadotropins
  - Female hormone production declines, the ability to bear children ends, and problems associated with estrogen deficiency (e.g., osteoporosis) begin to occur
- Testosterone also diminishes with age, but effect is not usually seen until very old age

Developmental Aspects

- GH levels decline with age and this accounts for muscle atrophy with age
  - Supplemental GH may spur muscle growth, reduce body fat, and help physique
- TH declines with age, causing lower basal metabolic rates
- PTH levels remain fairly constant with age, and lack of estrogen in women makes them more vulnerable to bone-demineralizing effects of PTH