See separate PowerPoint slides for all figures and tables pre-inserted into PowerPoint without notes.
Introduction

• In humans, the endocrine and nervous systems specialize in communication and coordination
• The endocrine system uses hormones; the nervous system uses neurotransmitters
• This chapter will cover the endocrine system, including:
  – The basics regarding glands, hormones, and their effects
  – The details regarding hormone chemistry, production, transportation, and mechanism of action
  – The endocrine system and stress
  – Paracrine secretions
  – Endocrine dysfunctions
Overview of the Endocrine System

• Expected Learning Outcomes
  – Define *hormone* and *endocrine system*.
  – Name several organs of the endocrine system.
  – Contrast endocrine with exocrine glands.
  – Recognize the standard abbreviations for many hormones.
  – Compare and contrast the nervous and endocrine systems.
Overview of the Endocrine System

• The body has four principal mechanisms of communication between cells
  – **Gap junctions**
    • Pores in cell membrane allow signaling molecules, nutrients, and electrolytes to move from cell to cell
  – **Neurotransmitters**
    • Released from neurons to travel across synaptic cleft to second cell
  – **Paracrines**
    • Secreted into tissue fluids to affect nearby cells
  – **Hormones**
    • Chemical messengers that travel in the bloodstream to other tissues and organs
Overview of the Endocrine System

- **Endocrine system**—glands, tissues, and cells that secrete hormones

- **Endocrinology**—the study of this system and the diagnosis and treatment of its disorders

- **Endocrine glands**—organs that are traditional sources of hormones

- **Hormones**—chemical messengers that are transported by the bloodstream and stimulate physiological responses in cells of another tissue or organ, often a considerable distance away

Figure 17.2b
Overview of the Endocrine System

Figure 17.1
Comparison of Endocrine and Exocrine Glands

- **Exocrine glands**
  - Have ducts; carry secretion to an epithelial surface or the mucosa of the digestive tract: “external secretions”
  - Extracellular effects (food digestion)

- **Endocrine glands**
  - No ducts
  - Contain dense, fenestrated capillary networks which allow easy uptake of hormones into bloodstream
  - “Internal secretions”
  - Intracellular effects such as altering target cell metabolism

- **Liver cells defy rigid classification**—releases hormones, releases bile into ducts, releases albumin and blood-clotting factors into blood (not hormones)
Comparison of the Nervous and Endocrine Systems

• Both systems serve for internal communication

• Speed and persistence of response
  – Nervous: reacts quickly (ms timescale), stops quickly
  – Endocrine: reacts slowly (seconds or days), effect may continue for days or longer

• Adaptation to long-term stimuli
  – Nervous: response declines (adapts quickly)
  – Endocrine: response persists (adapts slowly)

• Area of effect
  – Nervous: targeted and specific (one organ)
  – Endocrine: general, widespread effects (many organs)
Comparison of the Nervous and Endocrine Systems

- Several chemicals function as both hormones and neurotransmitters
  - Norepinephrine, dopamine, and antidiuretic hormone

- Both systems can have similar effects on target cells
  - Norepinephrine and glucagon both cause glycogen hydrolysis in liver

- The two systems can regulate each other
  - Neurotransmitters can affect glands, and hormones can affect neurons

- Neuroendocrine cells share characteristics with both systems
  - Neuron-like cells that secrete oxytocin into blood
Comparison of the Nervous and Endocrine Systems

- **Target organs or cells**—those organs or cells that have receptors for a hormone and can respond to it
  - Some target cells possess enzymes that convert a circulating hormone to its more active form
Comparison of the Nervous and Endocrine Systems

<table>
<thead>
<tr>
<th>Nervous System</th>
<th>Endocrine System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Communicates by means of electrical impulses and neurotransmitters</td>
<td>Communicates by means of hormones</td>
</tr>
<tr>
<td>Releases neurotransmitters at synapses at specific target cells</td>
<td>Releases hormones into bloodstream for general distribution throughout body</td>
</tr>
<tr>
<td>Usually has relatively local, specific effects</td>
<td>Sometimes has very general, widespread effects</td>
</tr>
<tr>
<td>Reacts quickly to stimuli, usually within 1–10 ms</td>
<td>Reacts more slowly to stimuli, often taking seconds to days</td>
</tr>
<tr>
<td>Stops quickly when stimulus stops</td>
<td>May continue responding long after stimulus stops</td>
</tr>
<tr>
<td>Adapts relatively quickly to continual stimulation</td>
<td>Adapts relatively slowly; may respond for days to weeks</td>
</tr>
</tbody>
</table>
Communication by the Nervous and Endocrine Systems

(a) Nervous system

(b) Endocrine system

Figure 17.2a,b
The Hypothalamus and Pituitary Gland

• Expected Learning Outcomes
  – Describe the anatomical relationships between the hypothalamus and pituitary gland.
  – Distinguish between the anterior and posterior lobes of the pituitary.
  – List the hormones produced by the hypothalamus and each lobe of the pituitary, and identify the functions of each hormone.
  – Explain how the pituitary is controlled by the hypothalamus and its target organs.
  – Describe the effects of growth hormone.
Anatomy

• The hypothalamus is shaped like a flattened funnel

• Forms floor and walls of third ventricle of brain

• Regulates primitive functions from water balance and thermoregulation to sex drive and childbirth

• Many of its functions carried out by pituitary gland
Anatomy

• The pituitary gland is suspended from hypothalamus by a stalk—infundibulum

• Location and size
  – Housed in sella turcica of sphenoid bone
  – Size and shape of kidney bean

• Composed of two structures with independent origins and separate functions
  – Adenohypophysis (anterior pituitary)
  – Neurohypophysis (posterior pituitary)
Anatomy

- **Adenohypophysis (anterior lobe)** constitutes anterior three-quarters of pituitary
  - Linked to hypothalamus by **hypophyseal portal system**
    - Primary capillaries in hypothalamus connected to secondary capillaries in adenohypophysis by portal venules
    - Hypothalamic hormones regulate adenohypophysis cells
Hypothalamic-releasing and -inhibiting hormones travel in hypophyseal portal system from hypothalamus to anterior pituitary

Different hormones are secreted by anterior pituitary
Anatomy

• **Neurohypophysis (posterior lobe)** constitutes the posterior one-quarter of the pituitary
  – Nerve tissue, not a true gland
    • Nerve cell bodies in hypothalamus pass down the stalk as **hypothalamo–hypophyseal tract** and end in posterior lobe
    • Hypothalamic neurons secrete hormones that are stored in neurohypophysis until released into blood
Hypothalamic Hormones

• Eight hormones produced in hypothalamus
  – Six regulate the anterior pituitary
  – Two are released into capillaries in the posterior pituitary

• Six releasing and inhibiting hormones stimulate or inhibit the anterior pituitary
  – TRH, CRH, GnRH, and GHRH are releasing hormones that promote anterior pituitary secretion of TSH, PRL, ACTH, FSH, LH, and GH
  – PIH inhibits secretion of prolactin, and somatostatin inhibits secretion growth hormone and thyroid-stimulating hormone by the anterior pituitary
Hypothalamic Hormones

- **Two** other hypothalamic hormones are **oxytocin (OT)** and **antidiuretic hormone (ADH)**
  - Both stored and released by posterior pituitary
  - **Paraventricular nuclei** of hypothalamus produce OT
  - **Supraoptic nuclei** produce ADH
  - Posterior pituitary does not synthesize them
## Hypothalamic Hormones

### TABLE 17.3

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Principal Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyrotropin-releasing hormone (TRH)</td>
<td>Promotes secretion of thyroid-stimulating hormone (TSH) and prolactin (PRL)</td>
</tr>
<tr>
<td>Corticotropin-releasing hormone (CRH)</td>
<td>Promotes secretion of adrenocorticotropic hormone (ACTH)</td>
</tr>
<tr>
<td>Gonadotropin-releasing hormone (GnRH)</td>
<td>Promotes secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH)</td>
</tr>
<tr>
<td>Growth hormone–releasing hormone (GHRH)</td>
<td>Promotes secretion of growth hormone (GH)</td>
</tr>
<tr>
<td>Prolactin-inhibiting hormone (PIH)</td>
<td>Inhibits secretion of prolactin (PRL)</td>
</tr>
<tr>
<td>Somatostatin</td>
<td>Inhibits secretion of growth hormone (GH) and thyroid-stimulating hormone (TSH)</td>
</tr>
</tbody>
</table>
Histology of Pituitary Gland

Figure 17.5a,b

(a) Anterior pituitary

Chromophobe
Basophil
Acidophil

(b) Posterior pituitary

Unmyelinated nerve fibers
Glial cells (pituicytes)

a: ©Dr. John D. Cunningham/Visuals Unlimited; b: ©Science VU/Visuals Unlimited
Anterior Pituitary Hormones

• Anterior lobe of the pituitary synthesizes and secretes six principal hormones

• Two gonadotropin hormones that target gonads
  – Follicle-stimulating hormone (FSH)
    • Stimulates secretion of ovarian sex hormones, development of ovarian follicles, and sperm production
  – Luteinizing hormone (LH)
    • Stimulates ovulation, stimulates corpus luteum to secrete progesterone, stimulates testes to secrete testosterone

• Thyroid-stimulating hormone (TSH)
  – Stimulates secretion of thyroid hormone
Anterior Pituitary Hormones

(Continued)

• Adrenocorticotropic hormone (ACTH)
  – Stimulates adrenal cortex to secrete glucocorticoids

• Prolactin (PRL)
  – After birth, stimulates mammary glands to synthesize milk

• Growth hormone (GH)
  – Stimulates mitosis and cellular differentiation
Hypothalamo–Pituitary–Target Organ Relationships

Figure 17.6

- Principle hormones and target organs
Figure 17.4a

Posterior Pituitary Hormones

Nuclei of hypothalamus:
Paraventricular nucleus
Supraoptic nucleus

Optic chiasm

Anterior pituitary

Posterior pituitary

Oxytocin

Antidiuretic hormone

Third ventricle of brain
Floor of hypothalamus
Posterior Pituitary Hormones

- Two hormones are produced in hypothalamus and transported to the posterior lobe of pituitary
  - Hormone released when hypothalamic neurons are stimulated

- ADH (antidiuretic hormone)
  - Increases water retention, thus reducing urine volume, and preventing dehydration
  - Also called vasopressin because it can cause vasoconstriction
Posterior Pituitary Hormones

• Oxytocin (OT)
  – Surge of hormone released during sexual arousal and orgasm
  – Promotes feelings of sexual satisfaction and emotional bonding between partners
  – Stimulates labor contractions during childbirth
  – Stimulates flow of milk during lactation
  – May promote emotional bonding between lactating mother and infant
Control of Pituitary Secretion

• Rates of secretion are not constant
  – Regulated by hypothalamus, other brain areas, and feedback from target organs

• Hypothalamic and cerebral control:
  – Brain monitors conditions and influences anterior pituitary accordingly
    • In times of stress, hypothalamus triggers release of ACTH
    • During pregnancy, hypothalamus triggers prolactin secretion
  – Posterior pituitary is controlled by neuroendocrine reflexes
    • Hypothalamic osmoreceptors trigger release of ADH when they detect a rise in blood osmolarity
    • Infant suckling triggers hypothalamic response to release oxytocin
Control of Pituitary Secretion

- **Negative feedback**—increased target organ hormone levels inhibit release of hypothalamic and/or pituitary hormones
  - Example: thyroid hormone+ inhibits release of TRH by hypothalamus and of TSH by anterior pituitary

Figure 17.7
Control of Pituitary Secretion

• **Positive feedback** can also occur
  – Stretching of uterus increases OT release, causes contractions, causing more stretching of uterus, etc. until delivery
A Further Look at Growth Hormone

- GH has widespread effects on the body tissues
  - Especially cartilage, bone, muscle, and fat

- Induces liver to produce growth stimulants
  - Insulin-like growth factors (IGF-I) or somatomedins (IGF-II)
    - Stimulate target cells in diverse tissues
    - IGF-I prolongs the action of GH
    - **Hormone half-life**—the time required for 50% of the hormone to be cleared from the blood
      - **GH half-life**: 6 to 20 minutes
      - **IGF-I half-life**: about 20 hours
A Further Look at Growth Hormone

• Induces liver to produce growth stimulants (continued)

  – **Protein synthesis increases**: boosts transcription and translation; increases amino acid uptake into cells; suppresses protein catabolism
  
  – **Lipid metabolism increases**: stimulates adipocytes to catabolize fats (protein-sparing effect)
  
  – **Carbohydrate metabolism**: glucose-sparing effect, mobilizing fatty acids reduces dependence of most cells on glucose, freeing more for the brain; stimulates glucose secretion by liver
  
  – **Electrolyte balance**: promotes Na\(^+\), K\(^+\), and Cl\(^-\) retention by kidneys, enhances Ca\(^{2+}\) absorption in intestine; makes electrolytes available to growing tissues
A Further Look at Growth Hormone

- Bone growth, thickening, and remodeling influenced, especially during childhood and adolescence
- Secretion high during first 2 hours of sleep
- Can peak in response to vigorous exercise
- GH levels decline gradually with age
- Average 6 ng/mL during adolescence, 1.5 ng/mg in old age
  - Lack of protein synthesis contributes to aging of tissues and wrinkling of the skin
  - Age 30, average adult body is 10% bone, 30% muscle, 20% fat
  - Age 75, average adult body is 8% bone, 15% muscle, 40% fat
Other Endocrine Glands

• Expected Learning Outcomes
  – Describe the structure and location of the remaining endocrine glands.
  – Name the hormones these endocrine glands produce and state their functions.
  – Discuss the hormones produced by organs and tissues other than the classical endocrine glands.
The Pineal Gland

- **Pineal gland**—attached to roof of third ventricle beneath the posterior end of corpus callosum

- After age 7, it undergoes **involution (shrinkage)**
  - Down 75% by end of puberty
  - Tiny mass of shrunken tissue in adults

- May synchronize physiological function with 24-hour **circadian rhythms** of daylight and darkness
  - **Synthesizes melatonin** from serotonin during the night
    - Fluctuates seasonally with changes in day length
The Pineal Gland

• Pineal gland may influence timing of puberty in humans

• May play a role in circadian rhythms
  – It synthesizes melatonin at night
  – **Seasonal affective disorder (SAD)** occurs in winter or northern climates
  – Symptoms: depression, sleepiness, irritability, and carbohydrate craving
  – Two to 3 hours of exposure to bright light each day reduces the melatonin levels and the symptoms (phototherapy)
The Thymus

- Thymus plays a role in three systems: endocrine, lymphatic, immune
- Bilobed gland in the mediastinum superior to the heart
  - Goes through involution after puberty
- Site of **maturation of T cells** important in immune defense
- Secretes hormones (**thymopoietin**, **thymosin**, and **thymulin**) that stimulate development of other lymphatic organs and activity of T lymphocytes

![Figure 17.8a,b](image-url)
The Thyroid Gland

- **Largest gland that is purely endocrine**
  - Composed of two lobes and an isthmus below the larynx
  - Dark reddish brown color due to rich blood supply

- **Thyroid follicles**—sacs that make up most of thyroid
  - Contain protein-rich **colloid**
  - **Follicular cells**: simple cuboidal epithelium that lines follicles

Figure 17.9a
The Thyroid Gland

- Secretes **thyroxine** ($\text{T}_4$ because of four iodine atoms) and **triiodothyronine** ($\text{T}_3$) in response to TSH
  - Increases metabolic rate, $\text{O}_2$ consumption, heat production (calorigenic effect), appetite, growth hormone secretion, alertness, reflex speed

- **Parafollicular (C or clear) cells** secrete **calcitonin** with rising blood calcium
  - Stimulates osteoblast activity and bone formation in children
The Thyroid Gland

Thyroid follicles are filled with colloid and lined with simple cuboidal epithelial cells (follicular cells).
The Parathyroid Glands

• Usually four glands partially embedded in posterior surface of thyroid gland
  – Can be found from as high as hyoid bone to as low as aortic arch

• Secrete parathyroid hormone (PTH)
  – Increases blood Ca\(^{2+}\) levels
    • Promotes synthesis of calcitriol
    • Increases absorption of Ca\(^{2+}\)
    • Decreases urinary excretion
    • Increases bone resorption

Figure 17.10a,b
• Small glands that sit on top of each kidney
• Retroperitoneal location
• Adrenal cortex and medulla formed by merger of two fetal glands with different origins and functions
The Adrenal Medulla

- **Adrenal medulla**—inner core, 10% to 20% of gland

- Has **dual nature** acting as an **endocrine gland** and a **ganglion** of the sympathetic nervous system
  - Innervated by **sympathetic preganglionic fibers**
  - Consists of modified sympathetic postganglionic neurons called **chromaffin cells**
  - When stimulated, release **catecholamines** (epinephrine and norepinephrine) and a trace of **dopamine** directly into the bloodstream
The Adrenal Medulla

• As hormones, catecholamines have multiple effects
  – Increase alertness and prepare body for physical activity
    • Mobilize high-energy fuels, lactate, fatty acids, and glucose
    • Glycogenolysis and gluconeogenesis by liver boost glucose levels
    • Epinephrine inhibits insulin secretion and so has a glucose-sparing effect
      – Muscles use fatty acids, saving glucose for brain
  – Increase blood pressure, heart rate, blood flow to muscles, pulmonary airflow, and metabolic rate
  – Decrease digestion and urine production
The Adrenal Cortex

• Cortex surrounds medulla and secretes several corticosteroids (hormones) from three layers of glandular tissue

  – Zona glomerulosa (thin, outer layer)
    • Cells are arranged in rounded clusters
    • Secretes **mineralocorticoids**—regulate the body’s electrolyte balance

  – Zona fasciculata (thick, middle layer)
    • Cells arranged in fascicles separated by capillaries
    • Secretes **glucocorticoids** and **androgens**

  – Zona reticularis (narrow, inner layer)
    • Cells in branching network
    • Secretes **glucocorticoids** and **sex steroids**
The Adrenal Cortex

- **Mineralocorticoids**—from zona glomerulosa
  - Steroid hormones that regulate electrolyte balance
  - **Aldosterone** stimulates $\text{Na}^+$ retention and $\text{K}^+$ excretion
    - Water is retained with sodium by osmosis, so blood volume and blood pressure are maintained
    - Part of the renin-angiotensin-aldosterone (RAA) system
The Adrenal Cortex

- **Glucocorticoids**
  - Secreted by zona fasciculata and zona reticulata in response to ACTH
  - Regulate metabolism of glucose and other fuels
  - **Cortisol** and **corticosterone** stimulate fat and protein catabolism, **gluconeogenesis (glucose from amino acids and fatty acids)** and release of fatty acids and glucose into blood
  - Help body adapt to stress and repair tissues
  - Anti-inflammatory effect becomes immune suppression with long-term use
The Adrenal Cortex

• **Sex steroids**
  – Secreted by zona fasciculata and zona reticularis
  – **Androgens:** set libido throughout life; large role in prenatal male development (include DHEA which other tissues convert to testosterone)
  – **Estradiol:** small quantity from adrenals, but this becomes important after menopause for sustaining adult bone mass
The Adrenal Glands

• Medulla and cortex of adrenal gland are not functionally independent

• Medulla atrophies without the stimulation of cortisol

• Some chromaffin cells of medullary origin extend into the cortex
  – They stimulate the cortex to secrete corticosteroids when stress activates the sympathetic nervous system
The Pancreatic Islets

- Pancreas is elongated gland below and behind stomach
- It contains 1 to 2 million islets—clusters of endocrine cells that secrete hormones that regulate glycemia (blood sugar)
The Pancreatic Islets

- **Glucagon**—secreted by A or alpha (α) cells
  - Released between meals when blood glucose concentration is falling
  - In liver, stimulates gluconeogenesis, glycogenolysis, and the release of glucose into the circulation raising blood glucose level
  - In adipose tissue, stimulates fat catabolism and release of free fatty acids
  - Glucagon also released to rising amino acid levels in blood, promotes amino acid absorption, and provides cells with raw material for gluconeogenesis
The Pancreatic Islets

- **Insulin** secreted by B or beta (β) cells
  - Secreted during and after meal when glucose and amino acid blood levels are rising
  - Stimulates cells to absorb these nutrients and store or metabolize them, lowering blood glucose levels
    - Promotes synthesis glycogen, fat, and protein
    - Suppresses use of already-stored fuels
    - Brain, liver, kidneys, and RBCs absorb glucose without insulin, but other tissues require insulin
  - Insufficiency or inaction is cause of diabetes mellitus
The Pancreatic Islets

• **Somatostatin** secreted by D or delta (δ) cells
  – Partially suppresses secretion of glucagon and insulin
  – Inhibits nutrient digestion and absorption which prolongs absorption of nutrients

• **Pancreas also has PP and G cells of uncertain function**

• **Hyperglycemic hormones** raise blood glucose concentration (includes hormones from other glands)
  – Glucagon, growth hormone, epinephrine, norepinephrine, cortisol, and corticosterone

• **Hypoglycemic hormones** lower blood glucose
  – Insulin
The Gonads

• **Ovaries** and **testes** are both endocrine and exocrine
  – **Exocrine** product: whole cells—eggs and sperm (cytogenic glands)
  – **Endocrine** product: gonadal hormones—mostly steroids

• **Ovarian** hormones
  – Estradiol, progesterone, and inhibin

• **Testicular** hormones
  – Testosterone, weaker androgens, estrogen, and inhibin
The Gonads

- Follicle—egg surrounded by granulosa cells and a capsule (theca)

Figure 17.13a
The Gonads

• Ovary
  – Theca cells synthesize androstenedione
  – Converted to mainly estradiol by granulosa cells

• After ovulation, the remains of the follicle becomes the corpus luteum
  – Secretes progesterone for 12 days following ovulation
  – Follicle and corpus luteum secrete inhibin

• Functions of estradiol and progesterone
  – Development of female reproductive system and physique including adolescent bone growth
  – Regulate menstrual cycle, sustain pregnancy
  – Prepare mammary glands for lactation

• Inhibin suppresses FSH secretion from anterior pituitary
The Gonads

• **Testes**
  – Microscopic **seminiferous tubules** produce sperm
  – Tubule walls contain sustentacular (Sertoli) cells
  – Leydig cells (interstitial cells) lie in clusters between tubules

• **Testicular hormones**
  – **Testosterone** and other steroids from interstitial cells (cells of Leydig) nestled between the tubules
    • Stimulates development of male reproductive system in fetus and adolescent, and sex drive
    • Sustains sperm production
  – **Inhibin** from sustentacular (Sertoli) cells
    • Limits FSH secretion in order to regulate sperm production
The Gonads

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Blood vessels
Seminiferous tubule
Germ cells
Connective tissue wall of tubule
Sustentacular cells
Interstitial cells (source of testosterone)

Testis

Figure 17.13b
Endocrine Functions of Other Tissues and Organs

• **Skin**
  – Keratinocytes convert a cholesterol-like steroid into cholecalciferol using UV from sun

• **Liver**—involved in the production of at least five hormones
  – Converts cholecalciferol into **calcidiol**
  – Secretes **angiotensinogen** (a prohormone)
    • Precursor of angiotensin II (a regulator of blood pressure)
  – Secretes 15% of **erythropoietin** (stimulates bone marrow)
  – **Hepcidin**: promotes intestinal absorption of iron
  – Source of **IGF-I** that controls action of growth hormone
Endocrine Functions of Other Tissues and Organs

• **Kidneys**—play role in production of three hormones
  – Convert calcidiol to **calcitriol**, the active form of vitamin D
    • Increases Ca^{2+} absorption by intestine and inhibits loss in the urine
  – Secrete **renin** that converts angiotensinogen to angiotensin I
    • Angiotensin II created by converting enzyme in lungs
      – Constricts blood vessels and raises blood pressure
  – Produces 85% of **erythropoietin**
    • Stimulates bone marrow to produce RBCs
Endocrine Functions of Other Tissues and Organs

• Heart
  – Atrial muscle secretes two natriuretic peptides in response to an increase in blood pressure
  – These decrease blood volume and blood pressure by increasing Na\(^+\) and H\(_2\)O output by kidneys and oppose action of angiotensin II
  – Lowers blood pressure

• Stomach and small intestine secrete at least 10 enteric hormones secreted by enteroendocrine cells
  – Coordinate digestive motility and glandular secretion
  – Cholecystokinin, gastrin, ghrelin, and peptide YY (PYY)
Endocrine Functions of Other Tissues and Organs

- **Adipose tissue** secretes leptin
  - Slows appetite

- **Osseous tissue**—osteocalcin secreted by osteoblasts
  - Increases number of pancreatic beta cells, pancreatic output of insulin, and insulin sensitivity of body tissues
  - Inhibits weight gain and onset of type 2 diabetes mellitus

- **Placenta**
  - Secretes estrogen, progesterone, and others
    - Regulate pregnancy, stimulate development of fetus and mammary glands
Hormones and Their Actions

• Expected Learning Outcomes
  – Identify the chemical classes to which various hormones belong.
  – Describe how hormones are synthesized and transported to their target organs.
  – Describe how hormones stimulate their target cells.
  – Explain how target cells regulate their sensitivity to circulating hormones.
  – Describe how hormones affect each other when two or more of them stimulate the same target cells.
  – Discuss how hormones are removed from circulation after they have performed their roles.
Hormone Chemistry

- Three chemical classes: steroids, monoamines, and peptides
  - **Steroids**
    - Derived from cholesterol
    - Sex steroids (such as estrogen) from gonads and corticosteroids (such as cortisol) from adrenals
  - **Monoamines (biogenic amines)**
    - Made from amino acids
    - Catecholamines (dopamine, epinephrine, norepinephrine), melatonin, thyroid hormone

Figure 17.14a,b
Hormone Chemistry

- **Peptides and glycoproteins**
  - Created from chains of amino acids
  - Examples include hormones from both lobes of the pituitary, and releasing and inhibiting hormones from hypothalamus
  - Insulin is a large peptide hormone

Figure 17.14c
Hormone Synthesis - Steroids

- Steroids are synthesized from cholesterol and differ in functional groups attached to the four-ring backbone.

Figure 17.15
Hormone Synthesis - Peptides

• Synthesized in same way as any protein
  – Gene is transcribed to mRNA
  – Peptide is assembled from amino acids at ribosome
  – Rough ER and Golgi may modify peptide to form mature hormone
    • Example: Proinsulin has connecting peptide removed to form insulin (two peptide chains connected by disulfide bridges)

Figure 17.17a
Hormone Synthesis - Monoamines

- **Melatonin** is synthesized from the amino acid **tryptophan**
- **Other monoamines** come from the amino acid **tyrosine**
- **Thyroid hormone** is composed of two tyrosines
  - Follicular cells absorb **iodide (I\(^-\)) ions** from blood and oxidize them to a reactive form
  - The cells also synthesize the large protein **thyroglobulin (Tg)** and store it in follicle lumen
  - Iodine (one or two atoms) is added to tyrosines within Tg
  - When two tyrosines within Tg meet, they link to each other forming forerunners of \(T_3\) (three iodines) and \(T_4\) (four iodines)
  - When follicle cell receives TSH, it absorbs Tg and employs lysosomal enzymes to split Tg and free thyroid hormone (TH)
  - TH (mostly as \(T_4\)) is released from basal side of follicle cell into blood capillary
Thyroid Hormone Synthesis and Secretion

Figure 17.17
Hormone Transport

• Most monoamines and peptides are **hydrophilic**
  – Mix easily with blood plasma

• Steroids and thyroid hormone are **hydrophobic**
  – Bind to **transport proteins** (albumins and globulins synthesized by the liver)
  – **Bound hormones** have longer half-life
    - Protected from liver enzymes and kidney filtration
  – Only **unbound hormone** leaves capillaries to reach target cell
  – Transport proteins protect circulating hormones from being broken down by enzymes in the plasma and liver, and from being filtered out of the blood by the kidneys
Hormone Transport

• Thyroid hormone binds to three transport proteins in the plasma
  – Albumin, thyretin, thyroxine-binding globulin (TGB)
  – More than 99% of circulating TH is protein bound

• Steroid hormones bind to globulins
  – Transcortin: the transport protein for cortisol

• Aldosterone—short half-life; 85% unbound, 15% binds weakly to albumin and others
Hormone Receptors and Mode of Action

• Hormones stimulate only those cells that have receptors for them

• **Receptors** are protein or glycoprotein molecules
  – On plasma membrane, in the cytoplasm, or in the nucleus

• **Receptors** act like switches turning on metabolic pathways when hormone binds to them
Hormone Receptors and Mode of Action

• Usually each target cell has a few thousand receptors for a given hormone

• Receptor–hormone interactions exhibit specificity and saturation
  – Specific receptor for each hormone
  – Saturated when all receptor molecules are occupied by hormone molecules
Hormone Receptors and Mode of Action

- **Peptide hormones**
  - Cannot penetrate target cell
  - Bind to surface receptors and activate intracellular processes through second messengers

- **Steroid hormones**
  - Penetrate plasma membrane and bind to internal receptors (usually in nucleus)
  - Influence expression of genes of target cell
  - Take several hours to days to show effect due to lag for protein synthesis

Figure 17.18
Steroids and Thyroid Hormone

• **Estrogen binds to nuclear receptors in cells of uterus**
  – It activates the gene for the progesterone receptor
  – Progesterone comes later in the menstrual cycle and binds to
    these receptors stimulating transcription of a gene for a nutrient
    synthesizing enzyme

• **Thyroid hormone enters target cell by means of an
  ATP-dependent transport protein**
  – Within target cell, $T_4$ is converted to more potent $T_3$
  – $T_3$ binds to nuclear receptors and activates gene for the sodium-
    potassium pump
Peptides and Catecholamines

- Hormone binds to cell-surface receptor
- Activates G protein
- Activates adenylate cyclase
- Produces cAMP
- Activates or inhibits enzymes
- Metabolic reactions
  - Synthesis
  - Secretion
  - Change membrane potentials
- Phosphodiesterase breaks down cAMP
Membrane receptors can alter metabolism through other second messenger systems causing varied effects.

- Diacylglycerol (diglyceride) activates a protein kinase.
- Inositol triphosphate system increases Ca^{++}.

**Figure 17.20**

- Hormones: ADH, TRH, OT, LHRH, Catecholamines.
- Various metabolic effects: Smooth muscle contraction, Protein synthesis, Secretion, Mitosis, etc.
Signal Amplification

- Hormones are extraordinarily potent chemicals
- One hormone molecule can activate many enzyme molecules
- Very small stimulus can produce very large effect
- Hormone concentrations in blood are low

Figure 17.21
Modulation of Target-Cell Sensitivity

- Target-cell sensitivity adjusted by changing the number of receptors

- **Up-regulation** means number of receptors is increased
  - Sensitivity is increased

- **Down-regulation** reduces number of receptors
  - Cell less sensitive to hormone
  - Happens with long-term exposure to high hormone concentrations

Figure 17.22
Hormone Interactions

• Most cells sensitive to more than one hormone and exhibit interactive effects

• Synergistic effects
  – Multiple hormones act together for greater effect
    • Synergism between FSH and testosterone on sperm production

• Permissive effects
  – One hormone enhances the target organ’s response to a second later hormone
    • Estrogen prepares uterus for action of progesterone

• Antagonistic effects
  – One hormone opposes the action of another
    • Insulin lowers blood glucose and glycogen raises it
Hormone Interactions

Figure 17.23
Hormone Clearance

• Hormone signals must be turned off when they have served their purpose

• Most hormones are taken up and degraded by liver and kidney
  – Excreted in bile or urine

• Metabolic clearance rate (MCR)
  – Rate of hormone removal from the blood
  – **Half-life:** time required to clear 50% of hormone from the blood
  – The faster the MCF, the shorter the half-life
Stress and Adaptation

• **Expected Learning Outcomes**
  – Give a physiological definition of stress.
  – Discuss how the body adapts to stress through its endocrine and sympathetic nervous systems.
Stress and Adaptation

- **Stress**—situation that upsets homeostasis and threatens one’s physical or emotional well-being
  - Injury, surgery, infection, intense exercise, pain, grief, depression, anger, etc.

- **General adaptation syndrome (GAS)**
  - Consistent way the body reacts to stress; typically involves elevated levels of epinephrine and glucocorticoids (especially cortisol)
  - Occurs in three stages
    - Alarm reaction
    - Stage of resistance
    - Stage of exhaustion
The Alarm Reaction

• Initial response
  – Mediated by norepinephrine from the sympathetic nervous system and epinephrine from the adrenal medulla
  – Prepares body for fight or flight
  – Stored glycogen is consumed
  – Increases aldosterone and angiotensin levels
    • Angiotensin helps raise blood pressure
    • Aldosterone promotes sodium and water conservation
The Stage of Resistance

- After a few hours, glycogen reserves gone, but brain still needs glucose
- Provide alternate fuels for metabolism
- Stage dominated by cortisol
- Hypothalamus secretes corticotropin-releasing hormone (CRH)
- Pituitary secretes ACTH
  - Stimulates the adrenal cortex to secrete cortisol and other glucocorticoids
  - Promotes breakdown of fat and protein into glycerol, fatty acids, and amino acids, for gluconeogenesis
The Stage of Resistance

- Cortisol has **glucose-sparing effect**—inhibits protein synthesis leaving free amino acids for gluconeogenesis
  - Adverse effects of excessive cortisol:
    - Depresses immune function
    - Increases susceptibility to infection and ulcers
    - Lymphoid tissues atrophy, antibody levels drop, and wounds heal poorly
The Stage of Exhaustion

- When stress continues for several months, and fat reserves are gone, homeostasis is overwhelmed
  - Often marked by rapid decline and death
- Protein breakdown and muscle wasting
- Loss of glucose homeostasis because adrenal cortex stops producing glucocorticoids
- Aldosterone promotes water retention and hypertension
  - Conserves sodium and hastens elimination of $K^+$ and $H^+$
  - Hypokalemia and alkalosis leads to death
- Death results from heart and kidney infection or overwhelming infection
Eicosanoids and Paracrine Signaling

• Expected Learning Outcomes
  – Explain what eicosanoids are and how they are produced.
  – Identify some classes and functions of eicosanoids.
  – Describe several physiological roles of prostaglandins.
Eicosanoids and Paracrine Signaling

- **Paracrines**—chemical messengers that diffuse short distances and stimulate nearby cells
  - Histamine
    - From mast cells in connective tissue
    - Causes relaxation of blood vessel
  - Nitric oxide
    - From endothelium of blood vessels, causes vasodilation
  - Catecholamines
    - Diffuse from adrenal medulla to cortex

- A single chemical can act as a hormone, paracrine, or even neurotransmitter in different locations
Eicosanoids and Paracrine Signaling

• **Eicosanoids**—important family of paracrines
  – Derived from fatty acid called **arachidonic acid**

• **Lipoxygenase** converts arachidonic acid into leukotrienes
  – **Leukotrienes**
    • Mediate allergic and inflammatory reactions
Eicosanoids and Paracrine Signaling (Continued)

• Cyclooxygenase converts arachidonic acid to three other types of eicosanoids
  – Prostacyclin
    • Inhibits blood clotting and vasoconstriction
  – Thromboxanes
    • Produced by blood platelets after injury
    • Overrides prostacyclin
    • Stimulates vasoconstriction and clotting
  – Prostaglandins
    • PGE—relaxes smooth muscle in bladder, intestines, bronchioles, uterus; stimulates contraction of blood vessels
    • PGF—causes opposite effects
Eicosanoid Synthesis

Figure 17.24

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Anti-Inflammatory Drugs

- **Cortisol and corticosterone**
  - Steroidal anti-inflammatory drugs (SAIDs)
  - Inhibit inflammation by blocking release of arachidonic acid from plasma membrane and inhibit synthesis of eicosanoids
    - Disadvantage—produce symptoms of Cushing syndrome

- **Aspirin, ibuprofen, and celecoxib (Celebrex)**
  - Nonsteroidal anti-inflammatory drugs (NSAIDs)
    - **COX inhibitors** since block cyclooxygenase (COX)
    - Do not affect lipoxygenase function or leukotriene production
    - Useful in treatment of fever and thrombosis
      - Inhibit prostaglandin and thromboxane synthesis
Endocrine Disorders

• **Expected Learning Outcomes**
  – Explain some general causes and examples of hormone hyposecretion and hypersecretion.
  – Briefly describe some common disorders of pituitary, thyroid, parathyroid, and adrenal function.
  – In more detail, describe the causes and pathology of diabetes mellitus.
Endocrine Disorders

- Variations in hormone concentration and target-cell sensitivity have noticeable effects on body

- **Hyposecretion**—inadequate hormone release
  - Tumor or lesion destroys gland or interferes with its ability to receive signals from another gland
    - Head trauma affects pituitary gland’s ability to secrete ADH
      - **Diabetes insipidus**: chronic polyuria
    - Autoantibodies fail to distinguish person’s own gland from foreign matter
      - One cause of diabetes mellitus
Endocrine Disorders

• Hypersecretion—excessive hormone release
  – Tumors or autoimmune disorder
    • Pheochromocytoma—tumor of adrenal medulla secretes excessive epinephrine and norepinephrine
    • Toxic goiter (Graves disease)—autoantibodies mimic effect of TSH on the thyroid (bind and activate TSH recetor), causing thyroid hypersecretion
Pituitary Disorders

- Hypersecretion of growth hormone (GH)
  - **Acromegaly**: thickening of bones and soft tissues in adults
    - Especially hands, feet, and face
  - Problems in childhood or adolescence (before growth plates are depleted)
    - **Gigantism** if hypersecretion
    - **Pituitary dwarfism** if hyposecretion—rare since growth hormone is now made by genetically engineered bacteria
Thyroid and Parathyroid Disorders

• **Congenital hypothyroidism (decreased TH)**
  – Hyposecretion present at birth
  – Treat with oral thyroid hormone

• **Myxedema (decreased TH)**
  – Adult hypothyroidism
  – Treat with oral thyroid hormone

• **Goiter**—any pathological enlargement of the thyroid gland
  – **Endemic goiter** (disease occurs in a geographic locality)
    • Dietary iodine deficiency, no TH, no feedback, increased TSH stimulates hypertrophy
Endemic Goiter

Figure 17.26

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Thyroid and Parathyroid Disorders

• **Hypoparathyroidism**
  – Surgical excision during thyroid surgery
  – Fatal tetany (spasms in larynx) in just a few days due to rapid decline in blood calcium level

• **Hyperparathyroidism:** excess PTH secretion
  – Parathyroid tumor
  – Bones become soft, fragile, and deformed
  – $\text{Ca}^{2+}$ and phosphate blood levels increase
  – Promotes renal calculi formation
Adrenal Disorders

• **Cushing syndrome**—excess cortisol secretion
  – Hyperglycemia, hypertension, weakness, edema
  – Rapid muscle and bone loss due to protein catabolism
  – Abnormal fat deposition
    • Moon face and buffalo hump

• **Adrenogenital syndrome (AGS)**
  – Adrenal androgen hypersecretion (accompanies Cushing)
  – Enlargement of external sexual organs in children and early onset of puberty
    • Newborn girls exhibit masculinized genitalia
  – Masculinizing effects on women
    • Increased body hair, deeper voice, beard growth
Cushing Syndrome

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Figure 17.27b
Diabetes Mellitus

- Most prevalent metabolic disease in the world
  - Disruption of metabolism due to hyposecretion or inaction of insulin
  - Symptoms
    - Polyuria (excess urine output), polydipsia (intense thirst), and polyphagia (hunger)
    - Revealed by elevated blood glucose, glucose in urine, and ketones in the urine
    - Polyuria (with thirst and dehydration) occurs because kidneys exhibit a **transport maximum**—limit to how fast the glucose transporters can work to reabsorb
      - Excess glucose enters urine and water follows it
Types and Treatment

• **Type 1 diabetes mellitus (IDDM)**—5% to 10% of cases in United States
  – **Insulin** is always used to treat type 1
    • Insulin injections, insulin pump, or dry insulin inhaler
    • Monitoring blood glucose levels and controlled diet
  – Hereditary susceptibility
  – If susceptible individual is infected with certain viruses (rubella, cytomegalovirus), autoantibodies attack and destroy pancreatic beta cells
Types and Treatment

• **Type 2 (NIDDM)**—90% to 95% of diabetics
  – Problem is **insulin resistance**
    • Failure of target cells to respond to insulin
  – Risk factors are heredity (36 genes so far known to increase risk), age (40+), obesity, and ethnicity (Native American, Hispanic, and Asian)
  – Treated with weight-loss program and exercise since:
    • Loss of muscle mass causes difficulty with regulation of glycemia
    • Adipose signals interfere with glucose uptake into most cells
  – If necessary, also use glycemia-lowering oral medications and, if still not enough, use insulin
Pathogenesis

- Pathogenesis—cells cannot absorb glucose, must rely on fat and proteins for energy needs, thus weight loss and weakness
  - Fat catabolism increases free fatty acids and ketones in blood
    - **Ketonuria** promotes osmotic diuresis, loss of Na\(^+\) and K\(^+\), irregular heartbeat, and neurological issues
    - **Ketoacidosis** occurs as ketones decrease blood pH
      - Deep, gasping breathing and diabetic coma are terminal result
Pathogenesis

• **Chronic pathology (chronic hyperglycemia)**
  – Leads to neuropathy and cardiovascular damage from atherosclerosis and microvascular disease
    • Arterial damage in retina and kidneys (common in type 1), atherosclerosis leads to heart failure (common in type 2)
    • **Diabetic neuropathy**—nerve damage from impoverished blood flow can lead to erectile dysfunction, incontinence, poor wound healing, and loss of sensation from area