Hormones and the Endocrine System
1. Overview of Endocrine Hormone Signaling
The Body’s Long-Distance Regulators

- Animal **hormones** are chemical signals that are secreted into the circulatory system and communicate regulatory messages within the body.

- Hormones reach all parts of the body, but only target cells have receptors for that hormone.
Intercellular Communication

- The ways that signals are transmitted between animal cells are classified by two criteria
  - The type of secreting cell
  - The route taken by the signal in reaching its target
Paracrine and Autocrine Signaling

- **Local regulators** are molecules that act over short distances, reaching target cells solely by diffusion.

- In **paracrine signaling**, the target cells lie near the secreting cells.

- In **autocrine signaling**, the target cell is also the secreting cell.
Figure 45.2a

(a) Endocrine signaling

(b) Paracrine signaling

(c) Autocrine signaling
- Paracrine and autocrine signaling play roles in processes such as blood pressure regulation, nervous system function, and reproduction

- Local regulators that mediate such signaling include the **prostaglandins**
  - Prostaglandins function in reproduction, the immune system, and blood clotting
Synaptic and Neuroendocrine Signaling

- In synaptic signaling, neurons form specialized junctions with target cells, called **synapses**.

- At synapses, neurons secrete molecules called **neurotransmitters** that diffuse short distances and bind to receptors on target cells.

- In neuroendocrine signaling, specialized neurosecretory cells secrete molecules called **neurohormones** that travel to target cells via the bloodstream.
Figure 45.2b

(d) Synaptic signaling

(e) Neuroendocrine signaling
Signaling by Pheromones

- Members of an animal species sometimes communicate with **pheromones**, chemicals that are released into the environment.

- Pheromones serve many functions, including marking trails leading to food, defining territories, warning of predators, and attracting potential mates.
Classes of Local Regulators

- Local regulators such as the prostaglandins are modified fatty acids
- Others are polypeptides and some are gases
  - Nitric oxide (NO) is a gas that functions in the body as both a local regulator and a neurotransmitter
    - When the level of oxygen in blood falls, NO activates an enzyme that results in vasodilation, increasing blood flow to tissues
## Classes of Hormones

- Hormones fall into three major classes: **polypeptides**, **steroids**, and **amines**

- Polypeptides and amines are water-soluble whereas steroid hormones and other largely nonpolar hormones are lipid-soluble

<table>
<thead>
<tr>
<th>Water-soluble (hydrophilic)</th>
<th>Lipid-soluble (hydrophobic)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Polypeptides</strong></td>
<td><strong>Steroids</strong></td>
</tr>
<tr>
<td><img src="image" alt="Insulin" /></td>
<td><img src="image" alt="Cortisol" /></td>
</tr>
<tr>
<td><img src="image" alt="Epinephrine" /></td>
<td><img src="image" alt="Thyroxine" /></td>
</tr>
</tbody>
</table>

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Cellular Response Pathways

- Water-soluble hormones are secreted by exocytosis, travel freely in the bloodstream, and bind to cell-surface receptors.

- Lipid-soluble hormones diffuse across cell membranes, travel in the bloodstream bound to transport proteins, and diffuse through the membrane of target cells.

- They bind to receptors in the cytoplasm or nucleus of the target cells.
Figure 45.5

(a) Water-soluble hormone; receptor in plasma membrane

SECRETORY CELL

Water-soluble hormone

Blood vessel

Receptor protein

TARGET CELL

OR

Cytoplasmic response

Gene regulation

NUCLEUS

(b) Lipid-soluble hormone; receptor in nucleus or cytoplasm

SECRETORY CELL

Lipid-soluble hormone

Blood vessel

Transport protein

TARGET CELL

Receptor protein

Cytoplasmic response

Gene regulation

NUCLEUS
Water-Soluble Hormones require Signal Transduction

For example:

- The hormone **epinephrine** has multiple effects in mediating the body’s response to short-term stress.
- Epinephrine binds to receptors on the plasma membrane of liver cells.
- This triggers the release of messenger molecules that activate enzymes and result in the release of glucose into the bloodstream.
Figure 45.6

An Example of Signal Transduction

EXTRACELLULAR FLUID

Hormone (epinephrine)

G protein

GTP

ATP

cAMP

G protein-coupled receptor

Adenylyl cyclase

CYTOPLASM

Protein kinase A

Inhibition of glycogen synthesis

Promotion of glycogen breakdown

Second messenger
Signaling with Lipid-Soluble Hormones

- When a steroid hormone binds to its cytosolic receptor, a hormone-receptor complex forms that moves into the nucleus.
- There, the receptor part of the complex acts as a transcriptional regulator of specific target genes.
Multiple Effects of Hormones

- The same hormone may have different effects on target cells that have
  - Different receptors for the hormone
  - Different signal transduction pathways
- For example, the hormone epinephrine can increase blood flow to major skeletal muscles, but decrease blood flow to the digestive tract
Figure 45.8

Same receptors but different intracellular proteins (not shown)

Different receptors

(a) Liver cell

- Epinephrine
- β receptor
- Glycogen deposits
- Glucose

Glycogen breaks down and glucose is released from cell.

Blood glucose level increases.

(b) Smooth muscle cell in wall of blood vessel that supplies skeletal muscle

- Epinephrine
- β receptor

Cell relaxes.

Blood vessel dilates, increasing flow to skeletal muscle.

(c) Smooth muscle cell in wall of blood vessel that supplies intestines

- Epinephrine
- α receptor

Cell contracts.

Blood vessel constricts, decreasing flow to intestines.
Feedback Regulation

- A **negative feedback** loop inhibits a response by reducing the initial stimulus, thus preventing excessive pathway activity

- For example, the release of acidic contents of the stomach into the duodenum stimulates endocrine cells there to secrete secretin

- This causes target cells in the pancreas, a gland behind the stomach, to raise the pH in the duodenum
Simple endocrine pathway

STIMULUS

Endocrine cell

Hormone

Target cells

RESPONSE

Negative feedback

Example: secretin signaling

Low pH in duodenum

S cells of duodenum

Secretin (•)

Pancreatic cells

Bicarbonate release
 Positive feedback reinforces a stimulus to produce an even greater response

For example, in mammals oxytocin causes the release of milk, causing greater suckling by offspring, which stimulates the release of more oxytocin
Figure 45.11

Simple neuroendocrine pathway

<table>
<thead>
<tr>
<th>STIMULUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensory neuron</td>
</tr>
<tr>
<td>Hypothalamus/posterior pituitary</td>
</tr>
<tr>
<td>Neurosecretory cell</td>
</tr>
<tr>
<td>Neurohormone</td>
</tr>
</tbody>
</table>

Positive feedback

Target cells

RESPONSE

Example: oxytocin signaling

Suckling

Oxytocin (▪)

Smooth muscle in mammary glands

Milk release
Endocrine Tissues and Organs

- Endocrine cells are often grouped in ductless organs called **endocrine glands**, such as the thyroid and parathyroid glands, testes, and ovaries.

- In contrast, **exocrine glands**, such as salivary glands have ducts to carry secreted substances onto body surfaces or into body cavities.
Figure 45.9

<table>
<thead>
<tr>
<th>Endocrine gland</th>
<th>Hormones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pineal gland</td>
<td>• Melatonin: Participates in regulation of biological rhythms.</td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>• Hormones released from posterior pituitary (oxytocin and vasopressin)</td>
</tr>
<tr>
<td></td>
<td>• Releasing and inhibiting hormones: Regulate anterior pituitary</td>
</tr>
<tr>
<td>Pituitary gland</td>
<td></td>
</tr>
<tr>
<td>Anterior pituitary</td>
<td>• Follicle-stimulating hormone (FSH) and luteinizing hormone (LH): Stimulate ovaries and testes</td>
</tr>
<tr>
<td></td>
<td>• Thyroid-stimulating hormone (TSH): Stimulates thyroid gland</td>
</tr>
<tr>
<td></td>
<td>• Adrenocorticotropic hormone (ACTH): Stimulates adrenal cortex</td>
</tr>
<tr>
<td></td>
<td>• Prolactin: Stimulates mammary gland cells</td>
</tr>
<tr>
<td></td>
<td>• Growth hormone (GH): Stimulates growth and metabolic functions</td>
</tr>
<tr>
<td>Posterior pituitary</td>
<td>• Oxytocin: Stimulates contraction of smooth muscle cells in uterus and mammary glands</td>
</tr>
<tr>
<td></td>
<td>• Vasopressin: (also called antidiuretic hormone, ADH): Promotes retention of water by kidneys; influences social behavior and bonding</td>
</tr>
<tr>
<td>Thyroid gland</td>
<td>• Thyroid hormone (T&lt;sub&gt;3&lt;/sub&gt; and T&lt;sub&gt;4&lt;/sub&gt;): Stimulates and maintains metabolic processes</td>
</tr>
<tr>
<td></td>
<td>• Calcitonin: Lowers blood calcium level</td>
</tr>
<tr>
<td>Parathyroid glands</td>
<td>• Parathyroid hormone (PTH): Raises blood calcium level</td>
</tr>
<tr>
<td>Adrenal glands</td>
<td></td>
</tr>
<tr>
<td>Adrenal medulla</td>
<td>• Epinephrine and norepinephrine: Raise blood glucose level; increase metabolic activities; constrict certain blood vessels.</td>
</tr>
<tr>
<td>Adrenal cortex</td>
<td>• Glucocorticoids: Raise blood glucose level</td>
</tr>
<tr>
<td></td>
<td>• Mineralocorticoids: Promote reabsorption of Na&lt;sup&gt;+&lt;/sup&gt; and excretion of K&lt;sup&gt;+&lt;/sup&gt; in kidneys</td>
</tr>
<tr>
<td>Pancreas</td>
<td>• Insulin: Lowers blood glucose level</td>
</tr>
<tr>
<td></td>
<td>• Glucagon: Raises blood glucose level</td>
</tr>
<tr>
<td>Ovaries (female)</td>
<td>• Estrogens*: Stimulate uterine lining growth; promote development and maintenance of female secondary sex characteristics</td>
</tr>
<tr>
<td></td>
<td>• Progestins*: Promote uterine lining growth</td>
</tr>
<tr>
<td>Testes (male)</td>
<td>• Androgens*: Support sperm formation; promote development and maintenance of male secondary sex characteristics</td>
</tr>
</tbody>
</table>

*Found in both males and females, but with a major role in one sex
2. Coordination of the Endocrine and Nervous Systems
Invertebrates

- The endocrine pathway that controls the molting of larva originates in the larval brain where neurosecretory cells produce PTTH.

- In the prothoracic gland, PTTH directs the release of ecdysteroid.

- Bursts of ecdysteroid trigger each successive molt as well as metamorphosis.

- Metamorphosis is not triggered until the level of another hormone, JH (juvenile hormone), drops.
Vertebrates

- The **hypothalamus** receives information from the nervous system and initiates responses through the endocrine system.

- Attached to the hypothalamus is the **pituitary gland**, composed of the posterior pituitary and anterior pituitary.

- The **posterior pituitary** stores and secretes hormones that are made in the hypothalamus.

- The **anterior pituitary** makes and releases hormones under regulation of the hypothalamus.
Figure 45.13

- Pineal gland
- Cerebellum
- Spinal cord
- Cerebrum
- Thalamus
- Hypothalamus
- Pituitary gland
- Posterior pituitary
- Anterior pituitary

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Neurosecretory cells of the hypothalamus synthesize the two posterior pituitary hormones:

- **Antidiuretic hormone (ADH)** regulates physiology and behavior.
- **Oxytocin** regulates milk secretion by the mammary glands.
Figure 45.14

Hypothalamus

Neurosecretory cells of the hypothalamus

Neurohormone

Posterior pituitary

Axons

Hormone

ADH

Oxytocin

Target

Kidney tubules

Mammary glands, uterine muscles
Anterior Pituitary Hormones

- Hormone production in the anterior pituitary is controlled by releasing hormones and inhibiting hormones secreted by the hypothalamus.

- For example, prolactin-releasing hormone from the hypothalamus stimulates the anterior pituitary to secrete prolactin (PRL), which has a role in milk production.
Figure 45.15

Neurosecretory cells of the hypothalamus

Portal vessels

Endocrine cells of the anterior pituitary

Anterior pituitary hormones

Hypothalamic releasing and inhibiting hormones

Posterior pituitary

HORMONE

TARGET

FSH and LH

Testes or ovaries

Tropic effects only

TSH

Thyroid

Tropic effects only

ACTH

Adrenal cortex

Nontropic effects only

Prolactin

Mammary glands

Nontropic effects only

MSH

Melanocytes

Tropic and nontropic effects

GH

Liver, bones, other tissues
Hormone Cascades

- Sets of hormones from the hypothalamus, anterior pituitary, and a target endocrine gland are often organized into a hormone cascade pathway.

- The anterior pituitary hormones in these pathways are called *tropic hormones* – hormones that target other endocrine glands.

  - **Non-tropic hormones** stimulate targets other than endocrine glands.
Thyroid Regulation: A Hormone Cascade Pathway

- In humans and other mammals, thyroid hormone regulates many functions.
- If thyroid hormone level drops in the blood, the hypothalamus secretes thyrotropin-releasing hormone (TRH) causing the anterior pituitary to secrete thyroid-stimulating hormone (TSH).
- TSH stimulates release of thyroid hormone by the thyroid gland.
The hypothalamus secretes TRH into the blood. Portal vessels carry TRH to anterior pituitary. Thyroid hormone levels drop. TRH causes anterior pituitary to secrete TSH.
Figure 45.16b

- **TSH**
  - TSH circulation throughout body via blood

- **Thyroid gland**
  - TSH stimulates endocrine cells in thyroid gland to secrete $T_3$ and $T_4$.

- **Thyroid hormone**
  - Circulation throughout body via blood

- **RESPONSE**
  - 5. Thyroid hormone levels return to normal range.
  - 6. Thyroid hormone blocks TRH release and TSH release preventing over-production of thyroid hormone.

- **4.** TSH stimulates endocrine cells in thyroid gland to secrete $T_3$ and $T_4$. 
Disorders of Thyroid Function and Regulation

- Hypothyroidism, too little thyroid function, can produce symptoms such as
  - Weight gain, lethargy, cold intolerance
- Hyperthyroidism, excessive production of thyroid hormone, can lead to
  - High temperature, sweating, weight loss, irritability, and high blood pressure
- Malnutrition can alter thyroid function
Graves’ disease, a form of hyperthyroidism caused by autoimmunity, is typified by protruding eyes.

*Thyroid hormone* refers to a pair of hormones:

- Triiodothyronin ($T_3$), with three iodine atoms
- Thyroxine ($T_4$), with four iodine atoms

Insufficient dietary iodine leads to an enlarged thyroid gland, called a goiter.

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Hormonal Regulation of Growth

- Growth hormone (GH) is secreted by the anterior pituitary gland and has tropic and nontropic effects.
- It promotes growth directly and has diverse metabolic effects.
- It stimulates production of growth factors.
- An excess of GH can cause gigantism, while a lack of GH can cause dwarfism.
3. Other Endocrine Hormones
Parathyroid Hormone and Vitamin D: Control of Blood Calcium

- Two antagonistic hormones regulate the homeostasis of calcium (Ca\(^{2+}\)) in the blood of mammals
  - **Parathyroid hormone** *(PTH)* is released by the parathyroid glands
  - **Calcitonin** is released by the thyroid gland
Blood Ca\(^{2+}\) level rises.

Active vitamin D increases Ca\(^{2+}\).

Blood Ca\(^{2+}\) level falls.

PTH stimulates Ca\(^{2+}\) uptake and promotes activation of vitamin D.

PTH stimulates Ca\(^{2+}\) release.

Parathyroid glands release PTH.

NORMAL BLOOD Ca\(^{2+}\) LEVEL
(about 10 mg/100 mL)
- PTH increases the level of blood $\text{Ca}^{2+}$
  - It releases $\text{Ca}^{2+}$ from bone and stimulates reabsorption of $\text{Ca}^{2+}$ in the kidneys
  - It also has an indirect effect, stimulating the kidneys to activate vitamin D, which promotes intestinal uptake of $\text{Ca}^{2+}$ from food
- Calcitonin decreases the level of blood $\text{Ca}^{2+}$
  - It stimulates $\text{Ca}^{2+}$ deposition in bones and secretion by kidneys
Adrenal Hormones: Response to Stress

- The adrenal glands are associated with the kidneys.
- Each *adrenal gland* actually consists of two glands: the *adrenal medulla* (inner portion) and *adrenal cortex* (outer portion).
Catecholamines from the Adrenal Medulla

- The adrenal medulla secretes epinephrine (adrenaline) and norepinephrine (noradrenaline)
- These hormones are members of a class of compounds called catecholamines
- They are secreted in response to stress-activated impulses from the nervous system
Figure 45.20a

(a) Short-term stress response
- Spinal cord (cross section)
- Nerve impulses
- Neuron
- Adrenal medulla

(b) Long-term stress response
- Hypothalamus
- Releasing hormone
- Anterior pituitary
- Blood vessel
- ACTH
- Adrenal cortex

Secretion of epinephrine and norepinephrine
- Kidney
- Adrenal gland

Secretion of mineralo- and glucocorticoids
Epinephrine and Norepinephrine

- Trigger the release of glucose and fatty acids into the blood
- Increase oxygen delivery to body cells
- Direct blood toward heart, brain, and skeletal muscles and away from skin, digestive system, and kidneys

<table>
<thead>
<tr>
<th>(a) Short-term stress response and the adrenal medulla</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects of epinephrine and norepinephrine:</td>
</tr>
<tr>
<td>• Glycogen broken down to glucose;</td>
</tr>
<tr>
<td>increased blood glucose</td>
</tr>
<tr>
<td>• Increased blood pressure</td>
</tr>
<tr>
<td>• Increased breathing rate</td>
</tr>
<tr>
<td>• Increased metabolic rate</td>
</tr>
<tr>
<td>• Change in blood flow patterns, leading to</td>
</tr>
<tr>
<td>increased alertness and decreased digestive,</td>
</tr>
<tr>
<td>excretory, and reproductive system activity</td>
</tr>
</tbody>
</table>
Steroid Hormones from the Adrenal Cortex

- The adrenal cortex reacts to endocrine signals.
- It releases a family of steroids called corticosteroids in response to stress.
- These hormones are triggered by a hormone cascade pathway via the hypothalamus and anterior pituitary.
- Humans produce two types of corticosteroids: glucocorticoids and mineralocorticoids.
• **Glucocorticoids**, such as cortisol, influence glucose metabolism and the immune system

• **Mineralocorticoids**, such as aldosterone, affect salt and water balance

<table>
<thead>
<tr>
<th>(b) Long-term stress response and the adrenal cortex</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Effects of mineralocorticoids:</strong></td>
</tr>
<tr>
<td>• Retention of sodium ions and water by kidneys</td>
</tr>
<tr>
<td>• Increased blood volume and blood pressure</td>
</tr>
<tr>
<td><strong>Effects of glucocorticoids:</strong></td>
</tr>
<tr>
<td>• Proteins and fats broken down and converted to glucose, leading to increased blood glucose</td>
</tr>
<tr>
<td>• Partial suppression of immune system</td>
</tr>
</tbody>
</table>
Sex Hormones

- The gonads, testes and ovaries, produce most of the sex hormones: **androgens**, **estrogens**, and **progestins**

- All three sex hormones are found in both males and females, but in significantly different proportions

**Androgens**

- The testes primarily synthesize **androgens**, mainly **testosterone**, which stimulate development and maintenance of the male reproductive system

- Testosterone causes an increase in muscle and bone mass and is often taken as a supplement to cause muscle growth, which carries health risks
Estrogens & Progestins

- **Estrogens**, most importantly **estradiol**, are responsible for maintenance of the female reproductive system and the development of female secondary sex characteristics.

- In mammals, **progestins**, which include **progesterone**, are primarily involved in preparing and maintaining the uterus.

- Synthesis of the sex hormones is controlled by follicle-stimulating hormone and luteinizing hormone from the anterior pituitary.
Figure 45.21

Bipotential gonad

Male duct (Wolffian)

Female duct (Müllerian)

Embryo (XY or XX)

Testosterone

Absence of male hormones

AMH

Testis

Vas deferens

Seminal vesicle

Bladder

Male (XY) fetus

Ovary

Uterus

Oviduct

Bladder

Female (XX) fetus

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Hormones and Biological Rhythms

- The **pineal gland**, located in the brain, secretes **melatonin**

- Primary functions of melatonin appear to relate to biological rhythms associated with reproduction and with daily activity levels

- The release of melatonin by the pineal gland is controlled by a group of neurons in the hypothalamus called the suprachiasmatic nucleus (SCN)