Chapter 45

Hormones and the Endocrine System
Overview: 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
• Insect metamorphosis is regulated by hormones
Two systems coordinate communication throughout the body: the endocrine system and the nervous system.

The **endocrine system** secretes hormones that coordinate slower but longer-acting responses including reproduction, development, energy metabolism, growth, and behavior.

The **nervous system** conveys high-speed electrical signals along specialized cells called neurons; these signals regulate other cells.
Concept 45.1: Hormones and other signaling molecules bind to target receptors, triggering specific response pathways

- Endocrine signaling is just one of several ways that information is transmitted between animal cells
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
Endocrine Signaling

- Hormones secreted into extracellular fluids by endocrine cells reach their targets via the bloodstream
- Endocrine signaling maintains homeostasis, mediates responses to stimuli, regulates growth and development
Figure 45.2

(a) Endocrine signaling

(b) Paracrine signaling

(c) Autocrine signaling

(d) Synaptic signaling

(e) Neuroendocrine signaling
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
(a) Endocrine signaling

(b) Paracrine signaling

(c) Autocrine signaling
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.
(d) Synaptic signaling

(e) Neuroendocrine signaling
Signaling by Pheromones

• Members of the same 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.
Endocrine Tissues and Organs

- In some tissues, endocrine cells are grouped together in ductless organs called endocrine glands.
- Endocrine glands secrete hormones directly into surrounding fluid.
- These contrast with exocrine glands, which have ducts and which secrete substances onto body surfaces or into cavities.
Major endocrine glands:

- Hypothalamus
- Pineal gland
- Pituitary gland
- Thyroid gland
- Parathyroid glands (behind thyroid)
- Adrenal glands (atop kidneys)
- Pancreas
- Ovaries (female)
- Testes (male)

Organs containing endocrine cells:

- Thymus
- Heart
- Liver
- Stomach
- Kidneys
- Small intestine
Chemical Classes of Hormones

• Three major classes of molecules function as hormones in vertebrates
  – Polypeptides (proteins and peptides)
  – Amines derived from amino acids
  – Steroid hormones
• Lipid-soluble hormones (steroid hormones) pass easily through cell membranes, while water-soluble hormones (polypeptides and amines) do not.

• The solubility of a hormone correlates with the location of receptors inside or on the surface of target cells.
Cellular Response Pathways

- Water- and lipid-soluble hormones differ in their paths through a body.
- 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.
Figure 45.6-2

(a) Lipid-soluble hormone
- Signal receptor
- Cytoplasmic response
- Gene regulation
- Target cell or nucleus

(b) Water-soluble hormone
- Signal receptor
- Cytoplasmic response
- Gene regulation
- Target cell or nucleus
Pathway for Water-Soluble Hormones

- Binding of a hormone to its receptor initiates a signal transduction pathway leading to responses in the cytoplasm, enzyme activation, or a change in gene expression.
• 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 45.7-2

Epinephrine

G protein

G protein-coupled receptor

GTP

ATP

Adenylyl cyclase

cAMP Second messenger

Inhibition of glycogen synthesis

Promotion of glycogen breakdown

Protein kinase A
Pathway for Lipid-Soluble Hormones

- The response to a lipid-soluble hormone is usually a change in gene expression.
- Steroids, thyroid hormones, and the hormonal form of vitamin D enter target cells and bind to protein receptors in the cytoplasm or nucleus.
- Protein-receptor complexes then act as transcription factors in the nucleus, regulating transcription of specific genes.
Figure 45.8-2

**EXTRACELLULAR FLUID**

- **Hormone (estradiol)**
- **Estradiol (estrogen) receptor**
  - **Plasma membrane**
  - **Hormone-receptor complex**

**NUCLEUS**

- **DNA**
- **mRNA for vitellogenin**
- **Vitellogenin**

**CYTOPLASM**
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
Figure 45.9  

**Same receptors but different intracellular proteins (not shown)**

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<tr>
<th>Different cellular responses</th>
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<td>Different receptors</td>
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**Different cellular responses**

1. **Epinephrine**
   - **β receptor**
   - Glycogen deposits
   - Glycogen breaks down and glucose is released from cell.

2. **Epinephrine**
   - **β receptor**
   - Vessel dilates.

3. **Epinephrine**
   - **α receptor**
   - Vessel constricts.

(a) Liver cell  
(b) Skeletal muscle blood vessel  
(c) Intestinal blood vessel
Signaling by Local Regulators

- Local regulators are secreted molecules that link neighboring cells or directly regulate the secreting cell.
- Types of local regulators:
  - Cytokines and growth factors
  - Nitric oxide (NO)
  - Prostaglandins
• In the immune system, prostaglandins promote fever and inflammation and intensify the sensation of pain

• Prostaglandins help regulate aggregation of platelets, an early step in formation of blood clots
Coordination of Neuroendocrine and Endocrine Signaling

• The endocrine and nervous systems generally act coordinately to control reproduction and development
• For example, in larvae of butterflies and moths, the signals that direct molting originate in the brain
In insects, molting and development are controlled by a combination of hormones
- A brain hormone (PTTH) stimulates release of ecdysteroid from the prothoracic glands
- Juvenile hormone promotes retention of larval characteristics
- Ecdysone promotes molting (in the presence of juvenile hormone) and development (in the absence of juvenile hormone) of adult characteristics
Brain

Neurosecretory cells

Corpora cardiaca

Corpora allata

Prothoracic gland

Ecdysteroid

PTTH

Juvenile hormone (JH)

Low JH

EARLY LARVA

LATER LARVA

PUPA

ADULT

Figure 45.10-3
Concept 45.2: Feedback regulation and antagonistic hormone pairs are common in endocrine systems

- Hormones are assembled into regulatory pathways
Simple Hormone Pathways

- Hormones are released from an endocrine cell, travel through the bloodstream, and interact with specific receptors within a target cell to cause a physiological response.
• 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
Pathway Example

Stimulus Low pH in duodenum

Endocrine cell S cells of duodenum secrete the hormone secretin (•).

Blood vessel Target cells Pancreas

Response Bicarbonate release
• In a simple neuroendocrine pathway, the stimulus is received by a sensory neuron, which stimulates a neurosecretory cell
• The neurosecretory cell secretes a neurohormone, which enters the bloodstream and travels to target cells
**Pathway**

- **Stimulus**
  - Sensory neuron
  - Hypothalamus/posterior pituitary
  - Neurosecretory cell
  - Neurohormone
  - Blood vessel
  - Target cells

**Example**

- Suckling
  - Posterior pituitary secretes the neurohormone oxytocin.
  - Smooth muscle in breasts
  - Milk release

Figure 45.12
Feedback Regulation

- A **negative feedback** loop inhibits a response by reducing the initial stimulus, thus preventing excessive pathway activity.
- **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.
Insulin and Glucagon: Control of Blood Glucose

- **Insulin** (decreases blood glucose) and **glucagon** (increases blood glucose) are antagonistic hormones that help maintain glucose homeostasis.

- The pancreas has clusters of endocrine cells called pancreatic islets with alpha cells that produce glucagon and beta cells that produce insulin.
Body cells take up more glucose.

Beta cells of pancreas release insulin into the blood.

Liver takes up glucose and stores it as glycogen. Blood glucose level declines. Blood glucose level rises.

Homeostasis: Blood glucose level (70–110 mg/mL)

STIMULUS: Blood glucose level rises (for instance, after eating a carbohydrate-rich meal).

Liver breaks down glycogen and releases glucose into the blood.

STIMULUS: Blood glucose level falls (for instance, after skipping a meal).

Alpha cells of pancreas release glucagon into the blood.

STIMULUS: Blood glucose level rises (for instance, after eating a carbohydrate-rich meal).
Target Tissues for Insulin and Glucagon

• Insulin reduces blood glucose levels by
  – Promoting the cellular uptake of glucose
  – Slowing glycogen breakdown in the liver
  – Promoting fat storage, not breakdown
• Glucagon increases blood glucose levels by
  – Stimulating conversion of glycogen to glucose in the liver
  – Stimulating breakdown of fat and protein into glucose
Diabetes Mellitus

- **Diabetes mellitus** is perhaps the best-known endocrine disorder
- It is caused by a deficiency of insulin or a decreased response to insulin in target tissues
- It is marked by elevated blood glucose levels
• *Type 1 diabetes mellitus* (insulin-dependent) is an autoimmune disorder in which the immune system destroys pancreatic beta cells

• *Type 2 diabetes mellitus* (non-insulin-dependent) involves insulin deficiency or reduced response of target cells due to change in insulin receptors
Concept 45.3: The hypothalamus and pituitary are central to endocrine regulation

- Endocrine pathways are subject to regulation by the nervous system, including the brain
Coordination of Endocrine and Nervous Systems in 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 45.14

Pineal gland

Cerebellum

Spinal cord

Cerebrum

Thalamus

Hypothalamus

Pituitary gland

Posterior pituitary

Anterior pituitary

Hypothalamus
Posterior Pituitary Hormones

- The two hormones released from the posterior pituitary act directly on nonendocrine tissues
  - Oxytocin regulates milk secretion by the mammary glands
  - Antidiuretic hormone (ADH) regulates physiology and behavior
Neurosecretory cells of the hypothalamus

Neurohormone

Axons

Posterior pituitary

Anterior pituitary

Hormone

ADH

Oxytocin

Target

Kidney tubules

Mammary glands, uterine muscles

Figure 45.15
Anterior Pituitary Hormones

- Hormone production in the anterior pituitary is controlled by releasing and inhibiting hormones from 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.
Tropic effects only: FSH, LH, TSH, ACTH

Nontropic effects only: Prolactin, MSH

Nontropic and tropic effects: GH

Hormones:
- FSH and LH
- TSH
- ACTH
- Prolactin
- MSH
- GH

Targets:
- Testes or ovaries
- Thyroid
- Adrenal cortex
- Mammary glands
- Melanocytes
- Liver, bones, other tissues

Figure 45.16
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### Table 45.1a Major Human Endocrine Glands and Some of Their Hormones

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Thyroid Regulation: A Hormone Cascade Pathway

- A hormone can stimulate the release of a series of other hormones, the last of which activates a nonendocrine target cell; this is called a hormone cascade pathway.
- The release of thyroid hormone results from a hormone cascade pathway involving the hypothalamus, anterior pituitary, and thyroid gland.
- Hormone cascade pathways typically involve negative feedback.
Hypothalamus secretes thyrotropin-releasing hormone (TRH).  
Anterior pituitary secretes thyroid-stimulating hormone (TSH, also known as thyrotropin).
Thyroid gland secretes thyroid hormone ($T_3$ and $T_4$).
Body tissues
Increased cellular metabolism
Hypothalamus secretes thyrotropin-releasing hormone (TRH).

Anterior pituitary secretes thyroid-stimulating hormone (TSH, also known as thyrotropin).
The anterior pituitary secretes thyroid-stimulating hormone (TSH, also known as thyrotropin). Thyroid gland secretes thyroid hormone (T₃ and T₄). Body tissues respond with increased cellular metabolism. This process involves negative feedback to the hypothalamus.
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.
Figure 45.18

Low level of iodine uptake

High level of iodine uptake
Evolution of Hormone Function

• Over the course of evolution the function of a given hormone may diverge between species
• For example, thyroid hormone plays a role in metabolism across many lineages, but in frogs has taken on a unique function: stimulating the resorption of the tadpole tail during metamorphosis
• Prolactin also has a broad range of activities in vertebrates
Figure 45.19

▲ Tadpole

▲ Adult frog
• **Melanocyte-stimulating hormone (MSH)** regulates skin color in amphibians, fish, and reptiles by controlling pigment distribution in melanocytes

• In mammals, MSH plays additional roles in hunger and metabolism in addition to coloration
Tropic and Nontropic Hormones

• A tropic hormone regulates the function of endocrine cells or glands

• Three primarily tropic hormones are
  – Follicle-stimulating hormone (FSH)
  – Luteinizing hormone (LH)
  – Adrenocorticotropin hormone (ACTH)
• **Growth hormone (GH)** is secreted by the anterior pituitary gland and has tropic and nontropic actions
  • 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
Concept 45.4: Endocrine glands respond to diverse stimuli in regulating homeostasis, development, and behavior

- Endocrine signaling regulates homeostasis, development, and behavior
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
Active vitamin D increases Ca\(^{2+}\) uptake in intestines. Stimulates Ca\(^{2+}\) uptake in kidneys. Stimulates Ca\(^{2+}\) release from bones. Parathyroid gland (behind thyroid).

Blood Ca\(^{2+}\) level rises. STIMULUS: Falling blood Ca\(^{2+}\) level

Homeostasis: Blood Ca\(^{2+}\) level (about 10 mg/100 mL)
• PTH increases the level of blood Ca\(^{2+}\)
  – It releases Ca\(^{2+}\) from bone and stimulates reabsorption of Ca\(^{2+}\) in the kidneys
  – It also has an indirect effect, stimulating the kidneys to activate vitamin D, which promotes intestinal uptake of Ca\(^{2+}\) from food

• Calcitonin decreases the level of blood Ca\(^{2+}\)
  – It stimulates Ca\(^{2+}\) deposition in bones and secretion by kidneys
Adrenal Hormones: Response to Stress

- The adrenal glands are adjacent to 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
- They mediate various fight-or-flight responses
• 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

• The release of epinephrine and norepinephrine occurs in response to involuntary nerve signals
Figure 45.21

(a) Short-term stress response and the adrenal medulla

- Spinal cord (cross section)
- Nerve signals
- Nerve cell
- Adrenal medulla secretes epinephrine and norepinephrine.

(b) Long-term stress response and the adrenal cortex

- Stress
- Hypothalamus
- Releasing hormone
- Anterior pituitary
- Blood vessel
- Adrenal cortex secretes mineralocorticoids and glucocorticoids.

Effects of epinephrine and norepinephrine:
- Glycogen broken down to glucose; increased blood glucose
- Increased blood pressure
- Increased breathing rate
- Increased metabolic rate
- Change in blood flow patterns, leading to increased alertness and decreased digestive, excretory, and reproductive system activity

Effects of mineralocorticoids:
- Retention of sodium ions and water by kidneys

Effects of glucocorticoids:
- Proteins and fats broken down and converted to glucose, leading to increased blood glucose
- Increased blood volume and blood pressure
- Partial suppression of immune system
(a) Short-term stress response and the adrenal medulla

Stress

Nerve signals

Spinal cord (cross section)

Nerve cell

Adrenal medulla secretes epinephrine and norepinephrine.

Effects of epinephrine and norepinephrine:

- Glycogen broken down to glucose; increased blood glucose
- Increased blood pressure
- Increased breathing rate
- Increased metabolic rate
- Change in blood flow patterns, leading to increased alertness and decreased digestive, excretory, and reproductive system activity
Steroid Hormones from the Adrenal Cortex

- The adrenal cortex 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 (ACTH).
- Humans produce two types of corticosteroids: glucocorticoids and mineralocorticoids.
(b) Long-term stress response and the adrenal cortex

Stress

Hypothalamus

Releasing hormone

Anterior pituitary

ACTH

Blood vessel

Adrenal gland

Adrenal cortex secretes mineralocorticoids and glucocorticoids.

Kidney

Effects of mineralocorticoids:
- Retention of sodium ions and water by kidneys
- Increased blood volume and blood pressure

Effects of glucocorticoids:
- Proteins and fats broken down and converted to glucose, leading to increased blood glucose
- Partial suppression of immune system
• **Glucocorticoids**, such as cortisol, influence glucose metabolism and the immune system

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

• The adrenal cortex also produces small amounts of steroid hormones that function as sex hormones
Gonadal 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
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.
### RESULTS

<table>
<thead>
<tr>
<th>Chromosome Set</th>
<th>Appearance of Genitalia</th>
<th>Embryonic gonad removed</th>
</tr>
</thead>
<tbody>
<tr>
<td>XY (male)</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>XX (female)</td>
<td>Female</td>
<td>Female</td>
</tr>
</tbody>
</table>
• **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 FSH and LH from the anterior pituitary
Endocrine Disruptors

- Between 1938 and 1971 some pregnant women at risk for complications were prescribed a synthetic estrogen called diethylstilbestrol (DES)
- Daughters of women treated with DES are at higher risk for reproductive abnormalities, including miscarriage, structural changes, and cervical and vaginal cancers
DES is an endocrine disruptor, a molecule that interrupts the normal function of a hormone pathway, in this case, that of estrogen.
Melatonin and Biorhythms

- The **pineal gland**, located in the brain, secretes **melatonin**
- Light/dark cycles control release of melatonin
- Primary functions of melatonin appear to relate to biological rhythms associated with reproduction
Pathway

Example

Negative feedback

Stimulus

Low blood glucose

Endocrine cell

Pancreas secretes glucagon ( ).

Hormone

Liver

Target cells

Glycogen breakdown, glucose release into blood

Blood vessel

Response
Figure 45.UN03

- **Drug administered**
  - None
  - Dexamethasone

- **Cortisol level in blood**
  - Normal
  - Patient X
Milk production

Anterior pituitary secretes prolactin()

Blood vessel

Hypothalamus

Neurosecretory cell

Hypothalamus secretes prolactin-releasing hormone[ ]

Stimulus

Blood vessel

Mammary glands

Blood vessel