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.

![Diagram of hormone signaling](image)
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
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.
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.
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.

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)

Adenylyl cyclase

G protein

GTP

ATP

cAMP

Second messenger

Protein kinase A

Inhibition of glycogen synthesis

Promotion of glycogen breakdown

Cytoplasm

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
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.
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.

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.
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.
**Posterior Pituitary Hormones**

- 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

**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
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.
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 (T₃), with three iodine atoms
- Thyroxine (T₄), with four iodine atoms

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

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

**Figure 45.19**

<table>
<thead>
<tr>
<th>NORMAL BLOOD Ca(^{2+}) LEVEL (about 10 mg/100 mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Ca(^{2+}) level rises.</td>
</tr>
<tr>
<td>Active vitamin D increases Ca(^{2+}).</td>
</tr>
<tr>
<td>PTH stimulates Ca(^{2+}) uptake and promotes activation of vitamin D.</td>
</tr>
<tr>
<td>PTH stimulates Ca(^{2+}) release.</td>
</tr>
<tr>
<td>Blood Ca(^{2+}) level falls.</td>
</tr>
<tr>
<td>Parathyroid glands release PTH.</td>
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- 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 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
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

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

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 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

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

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
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
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).