Impacts, Issues
Hormones in Balance

- Many chemicals we release into the environment (such as the herbicide atrazine) have disruptive hormonal effects
35.1 Introducing the Vertebrate Endocrine System

- Animal cells communicate with one another by way of a variety of short-range and long-range chemical signals.

- Animal cells communicate with adjacent cells through gap junctions and by releasing molecules that bind to receptors in or on other cells.
Shot-Distance Signaling

- **Neurotransmitters** secreted by neurons diffuse across the synaptic cleft to the target cell

- **Local signaling molecules**, such as prostaglandins released by injured cells, affect only neighboring cells
Long-Distance Signaling

- **Animal hormones** secreted into interstitial fluid enter capillaries, are distributed throughout the body, and have wide-reaching effects.

- **Pheromones** diffuse through water or air and bind to target cells in other individuals (help integrate social behavior).
Overview of the Endocrine System

- **Hormones**
  - Internal secretions carried by the blood that influence the activities of specific body organs

- **Endocrine system**
  - Glands and other hormone-secreting sources
Nervous and endocrine systems interact
- Both respond to the hypothalamus, a command center in the forebrain

Most organs receive and respond to both nervous signals and hormones
The Human Endocrine System

Hypothalamus
- Makes and secretes releasing and inhibiting hormones that act in the anterior lobe of the pituitary.
- Also makes antidiuretic hormone and oxytocin, which are stored in and released from the posterior lobe of the pituitary.

Pituitary gland
- Anterior lobe makes and secretes: ACTH, TSH, LH, FSH (stimulates secretion by other endocrine glands), prolactin (acts on mammary glands) and growth hormone (affects overall growth).
- Posterior lobe secretes antidiuretic hormone (acts on kidney) and oxytocin (acts on uterus and mammary glands), both are made in hypothalamus.

Adrenal glands (one pair)
- Adrenal cortex makes and secretes corticosteroids (catabolism, immunity response), aldosterone (acts in kidney), small amount of sex hormones.
- Adrenal medulla makes and secretes norepinephrine and epinephrine, which prepare body for exciting or dangerous situations.

Ovaries (one pair of female gonads)
- Make and secrete estrogen and progesterone, which control primary sex organs and influence secondary sexual traits.

Testes (one pair of male gonads)
- Make and secrete testosterone and other androgens, which control primary sex organs and influence secondary sexual traits.

Pineal gland
- Makes and secretes melatonin (affects sleep-wake cycle, crest of puberty).

Thyroid gland
- Makes and secretes thyroid hormone (metabolism and developmental effects) and calcitonin (lowers blood calcium).

Parathyroid glands (four)
- Make and secrete parathyroid hormone (raises blood calcium level).

Thymus gland
- Makes and secretes thymosins (act in maturation of T cells, a type of white blood cell).

Pancreas
- Makes and secretes insulin (lowers blood glucose level) and glucagon (raises blood glucose level).
<table>
<thead>
<tr>
<th>Location of clinic</th>
<th>Columbia, Missouri</th>
<th>Los Angeles, California</th>
<th>Minneapolis, Minnesota</th>
<th>New York, New York</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age</td>
<td>30.7</td>
<td>29.8</td>
<td>32.2</td>
<td>36.1</td>
</tr>
<tr>
<td>Percent nonsmokers</td>
<td>79.5</td>
<td>70.5</td>
<td>85.8</td>
<td>81.6</td>
</tr>
<tr>
<td>Percent with history of STD</td>
<td>11.4</td>
<td>12.9</td>
<td>13.6</td>
<td>15.8</td>
</tr>
<tr>
<td>Sperm count (million/ml)</td>
<td>58.7</td>
<td>80.8</td>
<td>98.6</td>
<td>102.9</td>
</tr>
<tr>
<td>Percent motile sperm</td>
<td>48.2</td>
<td>54.5</td>
<td>52.1</td>
<td>56.4</td>
</tr>
</tbody>
</table>
35.2 The Nature of Hormone Action

- Cell communication involves three steps.

- For a hormone to have an effect, it must bind to protein receptors on or inside a target cell.
## Categories and Examples of Hormones

<table>
<thead>
<tr>
<th>Categories</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroids</td>
<td>Testosterone and other androgens, estrogens, progesterone, aldosterone, cortisol</td>
</tr>
<tr>
<td>Amines</td>
<td>Melatonin, epinephrine, thyroid hormone</td>
</tr>
<tr>
<td>Peptides</td>
<td>Glucagon, oxytocin, antidiuretic hormone, calcitonin, parathyroid hormone</td>
</tr>
<tr>
<td>Proteins</td>
<td>Growth hormone, insulin, prolactin, follicle-stimulating hormone, luteinizing hormone</td>
</tr>
</tbody>
</table>
Intracellular Receptors

- Steroid hormones are made from cholesterol and can diffuse across the plasma membrane.

- Most steroid hormones form a hormone-receptor complex that binds to a promoter inside the nucleus and alters the expression of specific genes.
Receptors at the Plasma Membrane

- Large amine, peptide and protein hormones bind to a receptor at the plasma membrane

- Binding triggers formation of a second messenger (molecule that relays signal into cell)
  - Enzyme converts ATP to cAMP
  - cAMP activates a cascading series of reactions
Hormone Actions

**Step 1.** A steroid hormone molecule is moved from blood into interstitial fluid bathing a target cell.

**Step 2.** Being lipid soluble, the hormone easily diffuses across the cell’s plasma membrane.

**Step 3.** The hormone diffuses through the cytoplasm and nuclear envelope. It binds with its receptor in the nucleus.

**Step 4.** The hormone–receptor complex triggers transcription of a specific gene.

**Step 5.** The resulting mRNA moves into the cytoplasm and is transcribed into a protein.

**Gene Product**

---

**Step 1.** A peptide hormone molecule, glucagon, diffuses from blood into interstitial fluid bathing the plasma membrane of a liver cell.

**Step 2.** Glucagon binds with a receptor. Binding activates an enzyme that catalyzes the formation of cyclic AMP from ATP inside the cell.

**Step 3.** Cyclic AMP activates another enzyme in the cell.

**Step 4.** The enzyme activated by cyclic AMP activates another enzyme, which in turn activates another kind that catalyzes the breakdown of glycogen to its glucose monomers.

**Step 5.** The enzyme activated by cyclic AMP also inhibits glycogen synthesis.
Hypothalamus

GnRH

Anterior Pituitary

FSH, LH

Gonads

Sex hormones
Receptor Function and Diversity

- Only cells with appropriate and functional receptor proteins can respond to a hormone.

- Gene mutations that alter receptor structure can prevent or change cell response to a hormone.
  - *Examples:* Androgen insensitivity syndrome, variations in ADH receptors.
35.1-35.2 Key Concepts

Signaling Mechanisms

- *Hormones and other signaling molecules function in communication among body cells*

- *A hormone travels through the blood and acts on any cell that has receptors for it*

- *The receptor may be at a target cell’s surface or inside the cell*
35.3 The Hypothalamus and Pituitary Gland

- Hypothalamus and pituitary gland deep inside the brain interact as a central command center.
Hypothalamus

- **Hypothalamus**
  - Main center for control of internal environment
  - Lies deep inside the forebrain and interacts, structurally and functionally, with the pituitary gland
Pituitary Gland

- **Pituitary gland**
  - Posterior lobe secretes hormones made in the hypothalamus
  - Anterior lobe synthesizes its own hormones

- The hypothalamus signals the pituitary by way of secretory neurons that make hormones
Some secretory neurons of the hypothalamus make hormones that move through axons into the posterior pituitary, which releases them

- Antidiuretic hormone (ADH)
- Oxytocin (OT)
Interactions of Hypothalamus and Posterior Pituitary

A. Cell bodies of secretory neurons in hypothalamus synthesize ADH or oxytocin.

B. The ADH or oxytocin moves downward inside the axons of the secretory neurons and accumulates in the axon terminals.

C. Action potentials trigger the release of these hormones, which enter blood capillaries in the posterior lobe of the pituitary.

D. Blood vessels carry hormones to the general circulation.
Anterior Pituitary Function

- Other hypothalamus neurons produce **releasers** and **inhibitors** carried by blood that regulate secretion of anterior pituitary hormones
  - Adrenocorticotropic hormone (ACTH)
  - Thyroid-stimulating hormone (TSH)
  - Follicle stimulating hormone (FSH)
  - Luteinizing hormone (LH)
  - Prolactin (PRL)
  - Growth hormone (GH)
Interactions of Hypothalamus and Anterior Pituitary

A. Cell bodies of secretory neurons in hypothalamus synthesize inhibitors or releasers that are secreted into the stalk that connects to the pituitary.

B. The inhibitors or releasers picked up by capillaries in the stalk get carried in blood to the anterior pituitary.

C. The inhibitors or releasers diffuse out of capillaries in the anterior pituitary and bind to their target cells.

D. When encouraged by a releaser, anterior pituitary cells secrete hormone that enters blood vessels that lead into the general circulation.
# Primary Actions of Pituitary Hormones

<table>
<thead>
<tr>
<th>Pituitary Lobe</th>
<th>Secretions</th>
<th>Designation</th>
<th>Main Targets</th>
<th>Primary Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Posterior</strong></td>
<td>Antidiuretic hormone</td>
<td>ADH</td>
<td>Kidneys</td>
<td>Induces water conservation as required to maintain extracellular fluid volume and solute concentrations</td>
</tr>
<tr>
<td>Nervous tissue (extension of hypothalamus)</td>
<td>(vasopressin)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxytocin</td>
<td>OT</td>
<td>Mammary glands</td>
<td></td>
<td>Induces milk movement into secretory ducts</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Uterus</td>
<td></td>
<td>Induces uterine contractions during childbirth</td>
</tr>
<tr>
<td><strong>Anterior</strong></td>
<td>Adrenocorticotropic hormone</td>
<td>ACTH</td>
<td>Adrenal glands</td>
<td>Stimulates release of cortisol, an adrenal steroid hormone</td>
</tr>
<tr>
<td>Glandular tissue, mostly</td>
<td>Thyroid-stimulating hormone</td>
<td>TSH</td>
<td>Thyroid gland</td>
<td>Stimulates release of thyroid hormones</td>
</tr>
<tr>
<td></td>
<td>Follicle-stimulating hormone</td>
<td>FSH</td>
<td>Ovaries, testes</td>
<td>In females, stimulates estrogen secretion, egg maturation; in males, helps stimulate sperm formation</td>
</tr>
<tr>
<td></td>
<td>Luteinizing hormone</td>
<td>LH</td>
<td>Ovaries, testes</td>
<td>In females, stimulates progesterone secretion, ovulation, corpus luteum formation; in males, stimulates testosterone secretion, sperm release</td>
</tr>
<tr>
<td></td>
<td>Prolactin</td>
<td>PRL</td>
<td>Mammary glands</td>
<td>Stimulates and sustains milk production</td>
</tr>
<tr>
<td></td>
<td>Growth hormone (somatotropin)</td>
<td>GH</td>
<td>Most cells</td>
<td>Promotes growth in young; induces protein synthesis, cell division; roles in glucose, protein metabolism in adults</td>
</tr>
</tbody>
</table>

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Feedback Controls of Hormone Secretion

- Positive feedback mechanisms
  - Response increases the intensity of the stimulus
  - *Example*: Oxytocin and childbirth contractions

- Negative feedback mechanisms
  - Response decreases the stimulus
Excessive growth hormone (GH) causes faster than normal bone growth
  • Occurrence in childhood results in gigantism
  • Occurrence in adulthood results in acromegaly

A deficiency of GH during childhood can cause dwarfism
Examples of Disrupted GH Function
35.3-35.4 Key Concepts
A Master Integrating Center

- *In vertebrates, the hypothalamus and pituitary gland are connected structurally and functionally.*

- *Together, they coordinate activities of many other glands.*

- *Pituitary hormones affect growth, reproductive functions, and composition of extracellular fluid.*
In addition to the hypothalamus and pituitary gland, endocrine glands and endocrine cells secrete hormones.

The gut, kidneys, and heart are among the organs that are not glands, but include hormone-secreting cells.
## Sources and Actions of Vertebrate Hormones

<table>
<thead>
<tr>
<th>Source</th>
<th>Examples of Secretion(s)</th>
<th>Main Target(s)</th>
<th>Primary Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thyroid</strong></td>
<td>Thyroid hormone</td>
<td>Most cells</td>
<td>Regulates metabolism; has roles in growth, development</td>
</tr>
<tr>
<td></td>
<td>Calcitonin</td>
<td>Bone</td>
<td>Lowers calcium level in blood</td>
</tr>
<tr>
<td><strong>Parathyroids</strong></td>
<td>Parathyroid hormone</td>
<td>Bone, kidney</td>
<td>Elevates calcium level in blood</td>
</tr>
<tr>
<td><strong>Pancreatic islets</strong></td>
<td>Insulin</td>
<td>Liver, muscle, adipose tissue</td>
<td>Promotes cell uptake of glucose; thus lowers glucose level in blood</td>
</tr>
<tr>
<td></td>
<td>Glucagon</td>
<td>Liver</td>
<td>Promotes glycogen breakdown; raises glucose level in blood</td>
</tr>
<tr>
<td></td>
<td>Somatostatin</td>
<td>Insulin-secreting cells</td>
<td>Inhibits digestion of nutrients, hence their absorption from gut</td>
</tr>
<tr>
<td><strong>Adrenal cortex</strong></td>
<td>Glucocorticoids (including cortisol)</td>
<td>Most cells</td>
<td>Promotes breakdown of glycogen, fats, and proteins as energy sources; thus help raise blood level of glucose</td>
</tr>
<tr>
<td></td>
<td>Mineralocorticoids (including aldosterone)</td>
<td>Kidney</td>
<td>Promotes sodium reabsorption (sodium conservation); help control the body’s salt-water balance</td>
</tr>
<tr>
<td><strong>Adrenal medulla</strong></td>
<td>Epinephrine (adrenaline)</td>
<td>Liver, muscle, adipose tissue</td>
<td>Raises blood level of sugar, fatty acids; increases heart rate and force of contraction</td>
</tr>
<tr>
<td></td>
<td>Norepinephrine</td>
<td>Smooth muscle of blood vessels</td>
<td>Promotes constriction or dilation of certain blood vessels; thus affects distribution of blood volume to different body regions</td>
</tr>
<tr>
<td><strong>Gonads</strong></td>
<td><strong>Testes</strong> (in males)</td>
<td>Androgens (including testosterone)</td>
<td>Required in sperm formation; development of genitals; maintenance of sexual traits; growth, development</td>
</tr>
<tr>
<td></td>
<td><strong>Ovaries</strong> (in females)</td>
<td>Estrogens</td>
<td>Required for egg maturation and release; preparation of uterine lining for pregnancy and its maintenance in pregnancy; genital development; maintenance of sexual traits; growth, development</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Progesterone</td>
<td>Prepares, maintains uterine lining for pregnancy; stimulates development of breast tissues</td>
</tr>
<tr>
<td><strong>Pineal gland</strong></td>
<td><strong>Melatonin</strong></td>
<td>Brain</td>
<td>Influences daily biorhythms, seasonal sexual activity</td>
</tr>
<tr>
<td><strong>Thymus</strong></td>
<td><strong>Thymosins</strong></td>
<td>T lymphocytes</td>
<td>Poorly understood regulatory effect on T lymphocytes</td>
</tr>
</tbody>
</table>
Most cells have receptors for multiple hormones, and the effect of one hormone can be enhanced or opposed by another one.

*Example*: Skeletal muscle hormone receptors

- Glucagon, insulin, cortisol, epinephrine, estrogen, testosterone, growth hormone, somatostatin, thyroid hormone and others.
35.6 Thyroid and Parathyroid Glands

- The thyroid regulates metabolic rate, and the adjacent parathyroids regulate calcium levels.
The Thyroid Gland

- **Thyroid gland**
  - Located at the base of the neck; secretes iodine-containing thyroid hormones and calcitonin
  - Regulated by a negative feedback loop

- **Hypothyroidism**
  - Low levels of thyroid hormone, caused by iodine deficiency or Graves’ disease, causes goiter
Negative Feedback Control of Thyroid

Blood level of thyroid hormone falls below a set point.

Hypothalamus

TRH

Anterior Pituitary

TSH

Thyroid Gland

Thyroid hormone is secreted.

Rise of thyroid hormone level in blood inhibits the secretion of TRH and TSH.
The Parathyroid Glands

- **Parathyroid glands**
  - Release parathyroid hormone (PTH) in response to low blood calcium levels
  - Targets bone cells and kidney cells
  - Stimulates conversion of vitamin D to calcitriol
Thyroid and Parathyroid Diseases
35.7 Twisted Tadpoles

- Impaired thyroid function in frogs: An example of hormone-disruptor pollution in the environment
  - Includes pesticides, perchlorates
35.8 Pancreatic Hormones

- Pancreas
  - Exocrine cells secrete digestive enzymes
  - Endocrine cells clustered in pancreatic islets
Insulin and Glucagon

- Two pancreatic hormones with opposing effects work together to regulate blood sugar levels

- **Insulin**
  - Increases cell uptake and storage of glucose
  - Secreted in response to high blood glucose

- **Glucagon**
  - Increases breakdown of glycogen to glucose
  - Secreted in response to low blood glucose
Responses to Changes in Blood Glucose

A Stimulus
Increase in blood glucose

B alpha cells

- glucagon

C beta cells

+ insulin

D Body cells, especially those muscle and adipose tissue, take up and use more glucose.
Cells in skeletal muscle and liver store glucose in the form of glycogen.

E Response
Decrease in blood glucose

F Stimulus
Decrease in blood glucose

G alpha cells

+ glucagon

H beta cells

- insulin

I Cells in liver break down glycogen faster. The released glucose monomers enter blood.

J Response
Increase in blood glucose
35.9 Blood Sugar Disorders

- Glucose is the main energy source for brain cells and the only energy source for red blood cells.

- Having too much or too little glucose in blood causes problems throughout the body.
Diabetes

- Diabetes mellitus is a metabolic disorder in which cells do not take up glucose properly
  - Results in complications throughout the body

- **Type 1 diabetes** (juvenile-onset diabetes)
  - Autoimmune disease that destroys insulin-producing cells; requires insulin injections

- **Type 2 diabetes** (adult onset diabetes)
  - Target cells do not respond to insulin
Some Complications of Diabetes

<table>
<thead>
<tr>
<th>Table 35.4</th>
<th>Some Complications of Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes</td>
<td>Changes in lens shape and vision; damage to blood vessels in retina; blindness</td>
</tr>
<tr>
<td>Skin</td>
<td>Increased susceptibility to bacterial and fungal infections; patches of discoloration; thickening of skin on the back of hands</td>
</tr>
<tr>
<td>Digestive system</td>
<td>Gum disease; delayed stomach emptying that causes heartburn, nausea, vomiting</td>
</tr>
<tr>
<td>Kidneys</td>
<td>Increased risk of kidney disease and failure</td>
</tr>
<tr>
<td>Heart and blood vessels</td>
<td>Increased risk of heart attack, stroke, high blood pressure, and atherosclerosis</td>
</tr>
<tr>
<td>Hands and feet</td>
<td>Impaired sensations of pain; formation of calluses, foot ulcers; poor circulation in feet especially sometimes leads to tissue death that can only be treated by amputation</td>
</tr>
</tbody>
</table>
Controlling Diabetes
Hypoglycemia

- Hypoglycemia
  - Blood glucose levels low enough to disrupt normal body functions
  - Caused by excess insulin production or overdose of injected insulin in diabetics
  - Can cause dizziness, confusion, and shock
35.10 The Adrenal Glands

- **Adrenal glands**
  - Sit atop kidneys
  - Have two parts (adrenal cortex and adrenal medulla) that are controlled by different mechanisms and release different hormones
Hormonal Control of Adrenal Cortex

- The adrenal cortex secretes steroid hormones
  - Small amounts of sex hormones
  - **Aldosterone** controls sodium and water reabsorption in the kidneys
  - **Cortisol** affects metabolism and the stress response; controlled by negative feedback
Cortisol: Negative Feedback Control

**STIMULUS**

A Blood level of cortisol falls below a set point.

B CRH

**RESPONSE**

D Hypothalamus and pituitary detect rise in blood level of cortisol and slow its secretion.

Arenal Cortex

C Cortisol is secreted and has the following effects:

- Cellular uptake of glucose from blood slows in many tissues, especially muscles (but not in the brain).
- Protein breakdown accelerates, especially in muscles. Some of the amino acids freed by this process get converted to glucose.
- Fats in adipose tissue are degraded to fatty acids and enter blood as an alternative energy source, indirectly conserving glucose for the brain.
Nervous Control of the Adrenal Medulla

- The *adrenal medulla* contains specialized nerves of the sympathetic division that release epinephrine and norepinephrine, which stimulate the fight-flight response
Cortisol has many functions

- Induces liver cells to break down glycogen
- Suppresses uptake of glucose by other cells
- Causes adipose cells to degrade fats, and skeletal muscles to degrade proteins
- Suppresses immune responses
- Suppresses inflammatory response
Chronic Stress and Elevated Cortisol

- Chronic stress can produce high cortisol levels
  - Impairs growth, healing, sexual function, memory
  - High blood pressure and blood sugar
Low Cortisol Level

- Hypocortisolism (Addison’s disease) results from adrenal gland damage
  - Blood pressure and blood sugar fall
  - Symptoms include fatigue, weakness, depression, weight loss, darkening of skin
35.12 Other Endocrine Glands

- Outputs from gonads, pineal gland, and thymus all change as an individual enters **puberty** (a stage of development when reproductive organs and structures mature)
The Gonads

- Gonads are the primary reproductive organs that produce gametes (eggs and sperm)
  - Testes produce testosterone
  - Ovaries produce estrogens and progesterone
Control of Sex Hormone Secretion

- The hypothalamus and anterior pituitary control secretion of sex hormones by gonads.
Pineal Gland and Thymus

- **Pineal gland** secretes **melatonin**
  - Part of an internal biological clock
  - Secretion declines when the retina detects light

- **Thymus** secretes thymosins
  - Helps infection-fighting T cells mature
Other Hormone Sources

- Negative feedback loops to the hypothalamus and pituitary control secretions from many glands

- Signals from the nervous system and internal solute concentrations also influence hormone secretion
• Genes for hormone receptors and enzymes involved in hormone synthesis evolved over time

• We can trace the evolutionary roots of the vertebrate endocrine system in invertebrates
Cnidarians (e.g. sea anemones) and mollusks (e.g. sea slugs) have receptors that resemble those that bind vertebrate hormones.
Hormones and Molting

- Some hormones are unique to invertebrates

Example: **ecdysone**, a steroid hormone that controls molting in arthropods
  - Hormone-secreting neurons in the brain respond to signals such as light and temperature
  - Mechanisms differ in crustaceans and insects
Molting:
Hormonal Control in Crustaceans

Absence of suitable stimuli

X organ releases molt-inhibiting hormone (MIH)

MIH prevents Y organ from making ecdysone

No molting

Presence of suitable stimuli

Signals from brain inhibit release of MIH

Y organ makes and releases ecdysone

Molting

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Hormones control molting and other events in invertebrate life cycles

Vertebrate hormones and receptors for them first evolved in ancestral lineages of invertebrates