Why This Matters

• Understanding the endocrine system enables you to monitor and advise patients with diseases such as diabetes mellitus
Video: Why This Matters
15.1 Endocrine System Overview

- **Endocrine system** acts with nervous system to coordinate and integrate activity of body cells.
- Influences metabolic activities via **hormones** transported in blood.
- Responses slower but longer lasting than nervous system responses.
- **Endocrinology**: study of hormones and endocrine organs.
15.1 Endocrine System Overview

• Endocrine system controls and integrates:
  – Reproduction
  – Growth and development
  – Maintenance of electrolyte, water, and nutrient balance of blood
  – Regulation of cellular metabolism and energy balance
  – Mobilization of body defenses
15.1 Endocrine System Overview

- **Exocrine glands**
  - Produce nonhormonal substances (examples: sweat, saliva)
  - Have ducts to carry secretion to membrane surface

- **Endocrine glands**
  - Produce hormones
  - Lack ducts
15.1 Endocrine System Overview

- Endocrine glands: pituitary, thyroid, parathyroid, adrenal, and pineal glands
- Hypothalamus is **neuroendocrine** organ
- Some have exocrine and endocrine functions
  - Pancreas, gonads, placenta
- Other tissues and organs that produce hormones
  - Adipose cells, thymus, and cells in walls of small intestine, stomach, kidneys, and heart
Figure 15.1 Location of selected endocrine organs of the body.

- Pineal gland
- Hypothalamus
- Pituitary gland
- Thyroid gland
- Parathyroid glands (on dorsal aspect of thyroid gland)
- Thymus
- Adrenal glands
- Pancreas
- Gonads
  - Ovary (female)
  - Testis (male)
• Chemical messengers of endocrine system:
  – **Hormones**: long-distance chemical signals; travel in blood or lymph
  – **Autocrines**: chemicals that exert effects on same cells that secrete them
  – **Paracrines**: locally acting chemicals that affect cells other than those that secrete them
  – Autocrines and paracrines are local chemical messengers; not considered part of endocrine system
15.2 Hormone Chemical Structure

- Two main classes of hormones:
  - **Amino acid–based hormones**
    - Amino acid derivatives, peptides, and proteins
  - **Steroids**
    - Synthesized from cholesterol
    - Gonadal and adrenocortical hormones
- A possible third class, **eicosanoids**, is considered a hormone by some scientists, but most classify it as a paracrine
15.3 Action of Hormones

• Though hormones circulate systemically, only cells with receptors for that hormone are affected

• **Target cells**: tissues with receptors for a specific hormone

• Hormones alter target cell activity
• Hormone action on target cells may be to:
  – Alter plasma membrane permeability and/or membrane potential by opening or closing ion channels
  – Stimulate synthesis of enzymes or other proteins
  – Activate or deactivate enzymes
  – Induce secretory activity
  – Stimulate mitosis
15.3 Action of Hormones

- Hormones act in one of two ways, depending on their chemical nature and receptor location
  1. *Water-soluble hormones* (all amino acid–based hormones except thyroid hormone)
     - Act on plasma membrane receptors
     - Act via G protein second messengers
     - Cannot enter cell
  2. *Lipid-soluble hormones* (steroid and thyroid hormones)
     - Act on intracellular receptors that directly activate genes
     - Can enter cell

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Plasma Membrane Receptors and Second-Messenger Systems

• Amino acid–based hormones, except thyroid hormone, exert effects through second-messenger systems

• Two main second-messenger systems:
  – Cyclic AMP
  – PIP$_2$-calcium
Plasma Membrane Receptors and Second-Messenger Systems (cont.)

• Cyclic AMP (cAMP) signaling mechanism
  1. Hormone (first messenger) binds to receptor
  2. Receptor activates a G protein
  3. G protein activates or inhibits effector enzyme adenylate cyclase
  4. Adenylate cyclase then converts ATP to cAMP (second messenger)
  5. cAMP activates protein kinases that phosphorylate (add a phosphate) other proteins
Cyclic AMP (cAMP) signaling mechanism (cont.)

- Phosphorylated proteins are then either activated or inactivated
- cAMP is rapidly degraded by enzyme phosphodiesterase, stopping cascade
- Cascades have huge amplification effect
Figure 15.2 Cyclic AMP second-messenger mechanism of water-soluble hormones.

G protein signaling mechanisms are like a molecular relay race.

1. Hormone (1st messenger) binds receptor.

Hormone (1st messenger) → Receptor → G protein $\rightarrow$ Enzyme → 2nd messenger

Extracellular fluid → Cytoplasm

G protein ($G_s$) → GDP → GTP → ATP → cAMP

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G protein signaling mechanisms are like a molecular relay race.

1. Hormone (1st messenger) binds receptor.

2. Receptor activates G protein (Gs).

Hormone (1st messenger) → Receptor → G protein → Enzyme → 2nd messenger

Extracellular fluid

Cytoplasm
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Hormone (1st messenger)
Receptor
G protein
Enzyme
2nd messenger

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4. Adenylate cyclase converts ATP to cAMP (2nd messenger).
5. cAMP activates protein kinases.

Hormone (1st messenger) → Receptor → G protein → Enzyme → 2nd messenger

- Extracellular fluid
- Cytoplasm

Triggers responses of target cell (activates enzymes, stimulates cellular secretion, opens ion channel, etc.)
• PIP$_2$-calcium signaling mechanism
  – Hormone-activated G protein activates a different effector enzyme: **phospholipase C**
  – Activated phospholipase C splits membrane protein, PIP$_2$, into two second messengers:
    • Diacylglycerol (DAG) activates protein kinases
    • Inositol trisphosphate (IP$_3$) causes Ca$^{2+}$ release from intracellular storage sites
Plasma Membrane Receptors and Second-Messenger Systems (cont.)

- **PIP$_2$-calcium signaling mechanism (cont.)**
  - Calcium ions act as another second messenger
    - $\text{Ca}^{2+}$ alters enzyme activity and channels, or binds to regulatory protein **calmodulin**
    - Calcium-bound calmodulin activates enzymes that amplify cellular response
• Other signaling mechanisms
  – cGMP (cyclic guanosine monophosphate) is second messenger for selected hormones
  – Other hormones work without second messenger system
    • Example: insulin receptor is a tyrosine kinase enzyme that autophosphorylates upon insulin binding
      – Activated tyrosine kinases provide docking sites for relay proteins that trigger cell responses
Intracellular Receptors and Direct Gene Activation

• Lipid-soluble steroid hormones and thyroid hormone can diffuse into target cells and bind with intracellular receptors
• Receptor-hormone complex enters nucleus and binds to specific region of DNA
• Helps initiate DNA transcription to produce mRNA
• mRNA is then translated into specific protein
  – Proteins synthesized have various functions
  – Examples: metabolic activities, structural purposes, or exported from cell
The steroid hormone diffuses through the plasma membrane and binds an intracellular receptor.
Figure 15.3 Direct gene activation mechanism of lipid-soluble hormones.

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2. The receptor-hormone complex enters the nucleus.
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Figure 15.3 Direct gene activation mechanism of lipid-soluble hormones.

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4. Binding initiates transcription of the gene to mRNA.
Figure 15.3 Direct gene activation mechanism of lipid-soluble hormones.

1. The steroid hormone diffuses through the plasma membrane and binds an intracellular receptor.

2. The receptor-hormone complex enters the nucleus.

3. The receptor-hormone complex binds a specific DNA region.

4. Binding initiates transcription of the gene to mRNA.

5. The mRNA directs protein synthesis.
A&P Flix™: Mechanism of Hormone Action: Second Messenger cAMP
15.4 Hormone Release

• Blood levels of hormones
  – Controlled by **negative feedback systems**
    • Increased hormone effects on target organs can inhibit further hormone release
  – Levels vary only within narrow, desirable range
  – Hormone release is triggered by:
    • Endocrine gland stimuli
    • Nervous system modulation
Endocrine Gland Stimuli

- Endocrine glands are stimulated to synthesize and release hormones in response to one of three stimuli:
  - Humoral stimuli
  - Neural stimuli
  - Hormonal stimuli
Endocrine Gland Stimuli (cont.)

• Humoral stimuli
  – Changing blood levels of ions and nutrients directly stimulate secretion of hormones
  – Example: Ca$^{2+}$ in blood
  • Declining blood Ca$^{2+}$ concentration stimulates parathyroid glands to secrete PTH (parathyroid hormone)
  • PTH causes Ca$^{2+}$ concentrations to rise, and stimulus is removed
Hormone release caused by altered levels of certain critical ions or nutrients.

**Stimulus:** Low concentration of Ca$^{2+}$ in capillary blood.

**Response:** Parathyroid glands secrete parathyroid hormone (PTH), which increases blood Ca$^{2+}$. 
Endocrine Gland Stimuli (cont.)

• Neural stimuli
  – Nerve fibers stimulate hormone release
    • Sympathetic nervous system fibers stimulate adrenal medulla to secrete catecholamines
Hormone release caused by neural input.

**Stimulus:** Action potentials in preganglionic sympathetic fibers to adrenal medulla.

**Response:** Adrenal medulla cells secrete epinephrine and norepinephrine.
• **Hormonal stimuli**
  – Hormones stimulate other endocrine organs to release their hormones
    • Hypothalamic hormones stimulate release of most anterior pituitary hormones
    • Anterior pituitary hormones stimulate targets to secrete still more hormones
    • Hypothalamic–pituitary–target endocrine organ feedback loop
      – Hormones from final target organs inhibit release of anterior pituitary hormones
Hormone release caused by another hormone (a tropic hormone).

**Stimulus:** Hormones from hypothalamus.

**Response:** Anterior pituitary gland secretes hormones that stimulate other endocrine glands to secrete hormones.
Nervous System Modulation

- Nervous system can make adjustments to hormone levels when needed
  - Can modify stimulation or inhibition of endocrine glands
- Nervous system can override normal endocrine controls
  - Example: under severe stress, hypothalamus and sympathetic nervous system override insulin to allow blood glucose levels to increase
    - Prepare body for “fight or flight”
15.5 Target Cell Specificity

• Target cells must have specific receptors to which hormone binds
  – Example: ACTH receptors are found only on certain cells of adrenal cortex, but thyroxin receptors are found on nearly all cells of body

• Target cell activation depends on three factors:
  1. Blood levels of hormone
  2. Relative number of receptors on/in target cell
  3. Affinity (strength) of binding between receptor and hormone
• Amount of hormone can influence number of receptors for that hormone
  – **Up-regulation**: target cells form more receptors in response to low hormone levels
  – **Down-regulation**: target cells lose receptors in response to high hormone levels

  • Desensitizes the target cells to prevent them from overreacting to persistently high levels of hormone
Half-Life, Onset, and Duration of Hormone Activity

• Hormones circulate in blood either free or bound
  – Steroids and thyroid hormone are attached to plasma proteins
  – All others circulate without carriers
• Concentration of circulating hormone reflects:
  1. Rate of release
  2. Speed at which it is inactivated and removed from body
Half-Life, Onset, and Duration of Hormone Activity (cont.)

• Hormones can be removed from blood by:
  – Degrading enzymes or
  – Kidneys or
  – Liver

  • **Half-life**: time required for level of hormone in blood level to decrease by half
    – Varies anywhere from fraction of a minute to a week, depending on hormone
Half-Life, Onset, and Duration of Hormone Activity (cont.)

- Hormones have different response times:
  - Some responses are immediate
  - Some, especially steroid, can take hours to days
  - Some are inactive until they enter target cells
- The duration of response is usually limited
  - Ranges from 10 seconds to several hours
  - Effects may disappear rapidly as blood levels drop, but some may persist for hours at low blood levels
Half-life, onset, and duration of hormone activity are dependent on whether the hormone is water or lipid soluble.
### Table 15.1 Comparison between Lipid- and Water-Soluble Hormones

<table>
<thead>
<tr>
<th></th>
<th>LIPID-SOLUBLE HORMONES</th>
<th>WATER-SOLUBLE HORMONES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Examples</td>
<td>All steroid hormones and thyroid hormone</td>
<td>All amino acid-based hormones except thyroid hormone</td>
</tr>
<tr>
<td>Sources</td>
<td>Adrenal cortex, gonads, and thyroid gland*</td>
<td>All other endocrine glands</td>
</tr>
<tr>
<td>Can be stored in secretory vesicles</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Transport in blood</td>
<td>Bound to plasma proteins</td>
<td>Usually free in plasma</td>
</tr>
<tr>
<td>Half-life in blood</td>
<td>Long (most need to be metabolized by liver)</td>
<td>Short (most can be removed by kidneys)</td>
</tr>
<tr>
<td>Location of receptors</td>
<td>Usually inside cell</td>
<td>On plasma membrane</td>
</tr>
<tr>
<td>Mechanism of action at target cell</td>
<td>Activate genes, causing synthesis of new proteins</td>
<td>Usually act through second-messenger systems</td>
</tr>
</tbody>
</table>

*Skin is a source of cholecalciferol (an inactive form of vitamin D).*
Interaction of Hormones at Target Cells

• Multiple hormones may act on same target at same time
  – **Permissiveness**: one hormone cannot exert its effects without another hormone being present
    • Example: reproductive hormones need thyroid hormone to have effect
  – **Synergism**: more than one hormone produces same effects on target cell, causing amplification
    • Example: glucagon and epinephrine both cause liver to release glucose

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Interaction of Hormones at Target Cells (cont.)

– **Antagonism**: one or more hormones oppose(s) action of another hormone
  
  • Example: insulin and glucagon
Hypothalamus is connected to pituitary gland (hypophysis) via stalk called infundibulum.

Pituitary secretes at least eight major hormones.

It has two major lobes:
- **Posterior pituitary**: composed of neural tissue that secretes neurohormones.
  - Posterior lobe, along with infundibulum make up the neurohypophysis.
- **Anterior pituitary**: (adenohypophysis) consists of glandular tissue.
Pituitary-Hypothalamic Relationships

- Posterior lobe is neural tissue derived from a downgrowth of brain
  - Maintains neural connection to hypothalamus via hypothalamic-hypophyseal tract
    - Tract arises from neurons in paraventricular and supraoptic nuclei in hypothalamus
    - Runs through infundibulum
  - Secretes two neurohormones (oxytocin and ADH)
    - Hormones are stored in axon terminals in posterior pituitary and are released into blood when neurons fire
Focus Figure 15.1-1 The hypothalamus controls release of hormones from the pituitary gland in two different ways.

**Posterior Pituitary:** Action potentials travel down the axons of hypothalamic neurons, causing hormone release from their axon terminals in the posterior pituitary.

1. Hypothalamic neurons synthesize oxytocin or antidiuretic hormone (ADH).
Focus Figure 15.1-1 The hypothalamus controls release of hormones from the pituitary gland in two different ways.

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3. Oxytocin and ADH are stored in axon terminals in the posterior pituitary.

- Posterior lobe of pituitary
- optic chiasma
- Supraoptic nucleus
- Paraventricular nucleus
- Infundibulum (connecting stalk)
- Hypothalamic-hypophyseal tract
- Inferior hypophyseal artery
- Axon terminals
- Oxytocin
- Antidiuretic hormone (ADH)
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2. Oxytocin and ADH are transported down the axons of the hypothalamic-hypophyseal tract to the posterior pituitary.
3. Oxytocin and ADH are stored in axon terminals in the posterior pituitary.
4. When associated hypothalamic neurons fire, action potentials arriving at the axon terminals cause oxytocin or ADH to be released into the blood.
Pituitary-Hypothalamic Relationships (cont.)

- Anterior lobe is glandular tissue derived from an outpocketing of oral mucosa
  - Vascularly connected to hypothalamus via hypophyseal portal system consisting of:
    - Primary capillary plexus
    - Hypophyseal portal veins
    - Secondary capillary plexus
- Hypothalamus secretes releasing and inhibiting hormones to anterior pituitary to regulate hormone secretion
The hypothalamus controls release of hormones from the pituitary gland in two different ways (continued).

**Anterior Pituitary:** Hypothalamic hormones released into special blood vessels (the hypophyseal portal system) control the release of anterior pituitary hormones.

1. When appropriately stimulated, hypothalamic neurons secrete releasing or inhibiting hormones into the primary capillary plexus.

2. Hypothalamic hormones travel through portal veins to the anterior pituitary where they stimulate or inhibit release of hormones made in the anterior pituitary.

3. In response to releasing hormones, the anterior pituitary secretes hormones into the secondary capillary plexus. This in turn empties into the general circulation.

- **Growth hormone (GH)**
- **Thyroid-stimulating hormone (TSH)**
- **Adrenocorticotropic hormone (ACTH)**
- **Follicle-stimulating hormone (FSH)**
- **Luteinizing hormone (LH)**
- **Prolactin (PRL)**

A portal system is two capillary plexuses (beds) connected by veins.
Posterior Pituitary and Hypothalamic Hormones

- Posterior pituitary consists of axon terminals of neurons from hypothalamic neurons:
  - Paraventricular neurons produce oxytocin
  - Supraoptic neurons produce antidiuretic hormone (ADH)

- **Oxytocin** and **ADH**
  - Each composed of nine amino acids
  - Almost identical but differ in two amino acids
Posterior Pituitary and Hypothalamic Hormones (cont.)

• **Oxytocin**
  – Strong stimulant of uterine contractions released during childbirth
  – Also acts as hormonal trigger for milk ejection
  – Both are *positive feedback* mechanisms
  – Acts as neurotransmitter in brain
    • Uses PIP$_2$-calcium second messenger system
• **Antidiuretic hormone (ADH)**
  – Hypothalamus contains *osmoreceptors* that monitor solute concentrations
  – If concentration too high, posterior pituitary triggered to secrete ADH
  – Targets kidney tubules to reabsorb more water to inhibit or prevent urine formation
  – Release also triggered by pain, low blood pressure, and drugs
Posterior Pituitary and Hypothalamic Hormones (cont.)

- **Antidiuretic hormone (ADH) (cont.)**
  - Inhibited by alcohol, diuretics
  - High concentrations cause vasoconstriction, so also called *vasopressin*
<table>
<thead>
<tr>
<th>HORMONE (CHEMICAL STRUCTURE AND CELL TYPE)</th>
<th>REGULATION OF RELEASE</th>
<th>TARGET ORGAN AND EFFECTS</th>
<th>EFFECTS OF HYPOSECRETION ↓ AND HYPERSECRETION ↑</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oxytocin</strong> (Peptide, mostly from neurons in paraventricular nucleus of hypothalamus)</td>
<td>Stimulated by impulses from hypothalamic neurons in response to cervical/uterine stretching and suckling of infant at breast</td>
<td>Uterus: stimulates uterine contractions; initiates labor&lt;br&gt;Breast: initiates milk ejection</td>
<td>Unknown</td>
</tr>
<tr>
<td><strong>Antidiuretic hormone (ADH)</strong> or vasopressin (Peptide, mostly from neurons in supraoptic nucleus of hypothalamus)</td>
<td>Stimulated by impulses from hypothalamic neurons in response to increased blood solute concentration or decreased blood volume; also stimulated by pain, some drugs, low blood pressure</td>
<td>Kidneys: stimulate kidney tubule cells to reabsorb water</td>
<td>↓ Diabetes insipidus&lt;br&gt;↑ Syndrome of inappropriate ADH secretion (SIADH)</td>
</tr>
<tr>
<td></td>
<td>Inhibited by lack of appropriate neural stimuli</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inhibited by adequate hydration of the body and by alcohol</td>
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</tbody>
</table>
• Diabetes insipidus
  – ADH deficiency due to damage to hypothalamus or posterior pituitary
  – Must keep well hydrated

• Syndrome of inappropriate ADH secretion (SIADH)
  – Retention of fluid, headache, disorientation
  – Fluid restriction; blood sodium level monitoring
Anterior Pituitary Hormones

- All six hormones are peptide hormones
- All but growth hormone (GH) activate target cells via cAMP second-messenger system
- All but two are **tropic hormones** (tropins) that regulate secretion of other hormones
  - Growth hormone (GH)
  - Thyroid-stimulating hormone (TSH) (tropic)
  - Adrenocorticotropic hormone (ACTH) (tropic)
  - Follicle-stimulating hormone (FSH) (tropic)
  - Luteinizing hormone (LH) (tropic)
  - Prolactin (PRL)
Anterior Pituitary Hormones (cont.)

- Growth hormone (GH)
  - Also called somatotropin as it is produced by somatotropic cells
  - Has direct actions on metabolism and indirect growth-promoting actions
    - Direct actions on metabolism
      - *Glucose-sparing* actions decrease rate of cellular glucose uptake and metabolism (*anti-insulin effects*)
      - Triggers liver to break down glycogen into glucose
      - Increases blood levels of fatty acids for use as fuel and encourages cellular protein synthesis
Indirect actions on growth:

• GH triggers liver, skeletal muscle, and bone to produce insulin-like growth factors (IGFs)
• IGFs then stimulate:
  – Cellular uptake of nutrients used to synthesize DNA and proteins needed for cell division
  – Formation of collagen and deposition of bone matrix
• GH stimulates most cells to enlarge and divide, but major targets are bone and skeletal muscle
Anterior Pituitary Hormones (cont.)

– Regulation of secretion
  • GH release or inhibition chiefly regulated by hypothalamic hormones on somatotropic cells
    – Growth hormone–releasing hormone (GHRH) stimulates GH release
      » Triggered by low blood GH or glucose, or high amino acid levels
    – Growth hormone–inhibiting hormone (GHIH) (somatostatin) inhibits release
      » Triggered by increase in GH and IGF levels
  • Ghrelin (hunger hormone) also stimulates GH release
Figure 15.5 Growth-promoting and metabolic actions of growth hormone (GH).

Hypothalamus secretes growth hormone–releasing hormone (GHRH), and GHIH (somatostatin) 

Anterior pituitary

Hypothalamus

Feedback

Inhibits GHRH release

Stimulates GHIH release

Inhibits GH synthesis and release

Growth hormone (GH)

Indirect actions (growth-promoting)

Liver and other tissues

Produce

Insulin-like growth factors (IGFs)

Effects

Direct actions (metabolic, anti-insulin)

Skeletal

Increased cartilage formation and skeletal growth

Extraskeletal

Increased protein synthesis, and cell growth and proliferation

Fat metabolism

Increased fat breakdown and release

Carbohydrate metabolism

Increased blood glucose and other anti-insulin effects

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• Hypersecretion of GH is usually caused by anterior pituitary tumor
  – In children results in **gigantism**
    • Can reach heights of 8 feet
  – In adults results in **acromegaly**
    • Overgrowth of hands, feet, and face

• Hyposecretion of GH
  – In children results in **pituitary dwarfism**
    • May reach height of only 4 feet
  – In adults usually causes no problems
Figure 15.6 Disorders of pituitary growth hormone.
• Thyroid-stimulating hormone
  – Tropic hormone that is also called thyrotropin as it is produced by thyrotropic cells
  – Stimulates normal development and secretory activity of thyroid
  – Release triggered by thyrotropin-releasing hormone from hypothalamus
  – Inhibited by rising blood levels of thyroid hormones that act on both pituitary and hypothalamus
    • Also inhibited by GHIH
Figure 15.7 Regulation of thyroid hormone secretion.
Anterior Pituitary Hormones (cont.)

• **Adrenocorticotropic hormone (ACTH)**
  – Also called **corticotropin** as it is secreted by **corticotropic cells**
    • Precursor to corticotropin is **pro-opiomelanocortin**
  – ACTH stimulates adrenal cortex to release corticosteroids
  – Regulation of ACTH release
    • Triggered by hypothalamic **corticotropin-releasing hormone (CRH)** in daily rhythm
      – Highest levels in morning
    • Internal and external factors that alter release of CRH include fever, hypoglycemia, and stressors
Anterior Pituitary Hormones (cont.)

• Gonadotropins (FSH and LH)
  – Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) are secreted by gonadotropic cells of anterior pituitary
  – FSH stimulates production of gametes (egg or sperm)
  – LH promotes production of gonadal hormones
    • In females, LH helps mature follicles of egg, triggers ovulation and release of estrogen and progesterone
    • In males, LH stimulates production of testosterone
Anterior Pituitary Hormones (cont.)

- **Gonadotropins (FSH and LH) (cont.)**
  - LH and FSH both are absent from blood in prepubertal boys and girls
  - Regulation of gonadotropin release
    - Triggered by **gonadotropin-releasing hormone (GnRH)** during and after puberty
    - Suppressed by gonadal hormones (feedback)
Anterior Pituitary Hormones (cont.)

• Prolactin (PRL)
  – Secreted by prolactin cells of anterior pituitary
  – Stimulates milk production in females; role in males not well understood
  – Regulation primarily controlled by prolactin-inhibiting hormone (PIH), which is dopamine
  – PIH prevents release of PRL until needed, with decreased levels leading to lactation
Anterior Pituitary Hormones (cont.)

- Prolactin (PRL) (cont.)
  - Increased estrogen levels stimulate PRL
    - Reason behind breast swelling and tenderness during menstrual cycle
  - Blood levels rise toward end of pregnancy
  - Suckling stimulates PRL release and promotes continued milk production
• Hypersecretion of prolactin is more common than hyposecretion
  – Hyposecretion not a problem in anyone except women who choose to nurse
• *Hyperprolactinemia* is the most frequent abnormality of anterior pituitary tumors
• Clinical signs include inappropriate lactation, lack of menses, infertility in females, and impotence in males
### Table 15.2  Pituitary Hormones: Summary of Regulation and Effects (continued)

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<tr>
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<tbody>
<tr>
<td><strong>Anterior Pituitary Hormones</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Growth hormone (GH)</strong> (Protein, somatotropic cells)</td>
<td>Stimulated by GHRH* release, which is triggered by low blood levels of GH as well as by a number of secondary triggers including hypoglycemia, increases in blood levels of amino acids, low levels of fatty acids, exercise, and other types of stressors</td>
<td>Liver, muscle, bone, cartilage, and other tissues: anabolic hormone; stimulates somatic growth; mobilizes fats; spares glucose</td>
<td>↓ Pituitary dwarfism in children; ↑ Gigantism in children; acromegaly in adults</td>
</tr>
<tr>
<td></td>
<td>Inhibited by feedback inhibition exerted by GH and IGFs, and by hyperglycemia, hyperlipidemia, obesity, and emotional deprivation via either increased GHIH* (somatostatin) or decreased GHRH* release</td>
<td>Growth-promoting effects mediated indirectly by IGFs</td>
<td></td>
</tr>
</tbody>
</table>

*Indicates hypothalamic releasing and inhibiting hormones: GHRH = growth hormone–releasing hormone; GHIH = growth hormone–inhibiting hormone; TRH = thyrotropin-releasing hormone; CRH = corticotropin-releasing hormone; GnRH = gonadotropin-releasing hormone; PIH = prolactin-inhibiting hormone
<table>
<thead>
<tr>
<th>HORMONE (CHEMICAL STRUCTURE AND CELL TYPE)</th>
<th>REGULATION OF RELEASE</th>
<th>TARGET ORGAN AND EFFECTS</th>
<th>EFFECTS OF HYPOSECRETION ↓ AND HYPERSECRETION ↑</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid-stimulating hormone (TSH) (Glycoprotein, thyrotropic cells)</td>
<td>Stimulated by TRH* and in infants indirectly by cold temperature; Inhibited by feedback inhibition exerted by thyroid hormones on anterior pituitary and hypothalamus and by GHIH*</td>
<td>Thyroid gland: stimulates thyroid gland to release thyroid hormones</td>
<td>↓ Cretinism in children; myxedema in adults; ↑ Hyperthyroidism; effects similar to those of Graves' disease, in which antibodies mimic TSH</td>
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<tr>
<td>Adrenocorticotropic hormone (ACTH) (Peptide, corticotropic cells)</td>
<td>Stimulated by CRH*; stimuli that increase CRH release include fever, hypoglycemia, and other stressors; Inhibited by feedback inhibition exerted by glucocorticoids</td>
<td>Adrenal cortex: promotes release of glucocorticoids and androgens (mineralocorticoids to a lesser extent)</td>
<td>↓ Rare; ↑ Cushing's disease</td>
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<tr>
<td>Follicle-stimulating hormone (FSH) (Glycoprotein, gonadotropic cells)</td>
<td>Stimulated by GnRH*; Inhibited by feedback inhibition exerted by inhibin, and estrogens in females and testosterone in males</td>
<td>Ovaries and testes: in females, stimulates ovarian follicle maturation and production of estrogens; in males, stimulates sperm production</td>
<td>↓ Failure of sexual maturation; ↑ No important effects</td>
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<tr>
<td>Luteinizing hormone (LH) (Glycoprotein, gonadotropic cells)</td>
<td>Stimulated by GnRH*; Inhibited by feedback inhibition exerted by estrogens and progesterone in females and testosterone in males</td>
<td>Ovaries and testes: in females, triggers ovulation and stimulates ovarian production of estrogens and progesterone; in males, promotes testosterone production</td>
<td>As for FSH</td>
</tr>
<tr>
<td>Prolactin (PRL) (Protein, prolactin cells)</td>
<td>Stimulated by decreased PIH*; release enhanced by estrogens, birth control pills, breast-feeding, and dopamine-blocking drugs; Inhibited by PIH* (dopamine)</td>
<td>Breast secretory tissue: promotes lactation</td>
<td>↓ Poor milk production in nursing women; ↑ Inappropriate milk production (galactorrhea); cessation of menses in females; impotence in males</td>
</tr>
</tbody>
</table>

*Indicates hypothalamic releasing and inhibiting hormones: GHRH = growth hormone-releasing hormone; GHIH = growth hormone-inhibiting hormone; TRH = thyrotropin-releasing hormone; CRH = corticotropin-releasing hormone; GnRH = gonadotropin-releasing hormone; PIH = prolactin-inhibiting hormone.