CHAPTER 16

The Endocrine System
Endocrine System: Overview

- The **Endocrine system** and the **Nervous system** are the two main control systems of the body
  - Nervous system **quick** - nerve impulses to effectors
  - Endocrine system is much **slower** - carried out via **Hormones**
Major Endocrine Organs

- Pineal gland
- Hypothalamus
- Pituitary gland
- Thyroid gland
- Parathyroid glands (on dorsal aspect of thyroid gland)
- Thymus
- Adrenal glands
- Pancreas
- Ovary (female)
- Testis (male)
Chemical Messengers

- **Hormones**
  - Long distance chemical signals that 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

- Not always classified as Hormones since hormones mostly act long distance
Endocrine Glands

- Hormones are produced by **Endocrine glands**
  - ductless glands
  - hormones enter blood stream or lymph fluid

- There are several types of endocrine glands:
  - pituitary, thyroid, parathyroid, adrenal, pineal and thymus glands
  - pancreas, gonads (ovaries & testes)
    - Also have exocrine functions – non-hormonal secretions (sweat, saliva, etc)

- Hypothalamus – Neuroendocrine; for control

- Special regions of small intestine, stomach, kidneys, heart with endocrine functions
Chemistry of Hormones

- **Hormones**: chemical substances secreted by cells into extracellular fluid to regulate a metabolic function
  - **Amino acid based**
    - Makes up the majority of all the hormones & includes amines, thyroxine, peptide, and protein hormones
  - **Steroids**
    - Made from cholesterol & includes gonadal and adrenocortical hormones
  - **Eicosanoids** (generally act as paracrines or autocrines)
    - lipids made from arachidonic acid
      - Leukotrienes - inflammation & allergic reactions
      - Prostaglandins - blood pressure, uterine contraction, pain, blood clotting, inflammation
Hormone Actions

- Hormones can produce one or more of the following cellular changes in target cells:
  - Alter plasma membrane permeability by opening/closing ion channels
  - Stimulate protein synthesis
  - Activate or deactivate enzyme systems
  - Induce secretory activity
  - Stimulate mitosis
Mechanism of Hormone Action

- Hormones alter target cell activity by one of two mechanisms

  - **Second messengers system** (signal cascade)
    - For water-soluble hormones (Amino acid–based)
      - Cannot enter target cells alone
    - Use G protein coupled receptors on plasma membrane of cell to transmit intracellular response
      - Cyclic AMP (cAMP) signaling & PIP-Calcium Signaling (main 2 ways)

  - **Direct gene activation**
    - for lipid-soluble hormones (steroid & thyroid)
    - act directly on intracellular receptors which activates genes
Amino Acid-Based Hormone Action: cAMP Second Messenger

1. **Hormone (1st messenger)** binds receptor.

2. **Receptor** activates **G protein (Gₘ)**.

3. **G protein** activates **adenylate cyclase**.

4. **Adenylate cyclase** converts **ATP** to **cAMP** (2nd messenger).

5. **cAMP** activates **protein kinases**.

**Hormones that act via cAMP mechanisms:**
- Epinephrine
- ACTH
- FSH
- LH
- Glucagon
- PTH
- TSH
- Calcitonin

**Cytoplasm**

*Copyright © 2010 Pearson Education, Inc.*
Amino Acid-Based Hormone Action: cAMP Second Messenger

- Amino Acid-based hormones are large and water soluble — they cannot cross the plasma membrane.
  - **Hormone (first messenger)** binds to its receptor, which then binds to a **G protein = signal transducer**.
  - The G protein is then activated as it binds GTP, displacing GDP.
  - Activated G protein activates the **effector enzyme adenylate cyclase**.
  - Adenylate cyclase generates **cAMP (second messenger)** from **ATP**.
  - cAMP activates protein kinases → add phosphate groups to enzymes → **activation or inactivation** of the enzyme (triggers response of target cell).
cAMP signal termination

- Effects of hormones are amplified by second messenger systems

- cAMP present = more amplification of signal

- cAMP is degraded quickly enzyme by phosphodiesterase
Amino Acid-Based Hormone Action: cAMP Second Messenger

1. **Hormone (1st messenger) binds receptor.**
2. **Receptor activates G protein (G_s).**
3. **G protein activates adenylate cyclase.**
4. **Adenylate cyclase converts ATP to cAMP (2nd messenger).**
5. **cAMP activates protein kinases.**

Hormones that act via cAMP mechanisms:
- Epinephrine
- ACTH
- FSH
- LH
- Glucagon
- PTH
- TSH
- Calcitonin

Triggers responses of target cell (activates enzymes, stimulates cellular secretion, opens ion channel, etc.)

Copyright © 2010 Pearson Education, Inc.

Animation
Amino Acid-Based Hormone Action: PIP Mechanism

1. **Extracellular fluid**
   - Hormone

2. **Receptor**
   - Gq
   - GTP
   - GDP

3. **Phospholipase C**
   - PIP₂
   - GTP

4. **Inactive protein kinase C**
   - IP₃
   - DAG

5. **Active protein kinase C**
   - Triggers responses of target cell

6. **Endoplasmic reticulum**
   - Ca²⁺
   - Ca²⁺-calmodulin

**Hormones**:
- Catecholamines
- TRH
- ADH
- GnRH
- Oxytocin

**Animation**
Amino Acid-Based Hormone Action: PIP-Calcium Signaling

- Used by some amino acid-based hormones
  - Hormone binds to the receptor and activates **G protein**
  - G protein binds and activates **phospholipase**
  - **Phospholipase** splits the phospholipid **PIP₂** (Phosphatidyl inositol bisphosphate) into **diacylglycerol (DAG)** and **Inositol triphosphate (IP₃)** (both act as **second messengers**)
  - DAG activates protein kinases; IP₃ triggers release of Ca²⁺ stores
  - Ca²⁺ can bind to **calmodulin** and activate enzymes or directly regulate cellular responses
Amino Acid-Based Hormone Action: PIP-Calcium Mechanism

1. Hormone binds to the receptor, activating Gq.
2. GTP activates the receptor, leading to GDP release.
3. PIP2 is cleaved by phospholipase C, forming DAG and IP3.
4. IP3 triggers the release of Ca2+ from the endoplasmic reticulum.
5. Ca2+ and Ca2+-calmodulin activate protein kinase C.
6. Protein kinase C triggers the responses of the target cell.
Other signaling mechanisms by amino acid based hormones

- Insulin and other growth factors work without second messengers

- **Insulin** binds to a receptor that is a **tyrosine kinase**—insulin binding activates this kinase
Steroid hormones are fat (lipid) soluble and can freely cross the plasma membrane.

- Bind to an internal **steroid hormone receptor**

- Complex binds to a specific region of DNA

**Animation**
- DNA transcription is initiated to produce mRNA
- The mRNA is translated into proteins, which bring about a cellular effect

Figure 16.4

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 hormone response-element (a specific DNA sequence).
4. Binding initiates transcription of the gene to mRNA.
5. The mRNA directs protein synthesis.
Figure 16.4

- Hormone response elements
- Chromatin
- Transcription
- mRNA
- Nucleus
- New protein
- Ribosome
- Translation
Hormones only activate cells referred to as **target cells**

**Target cells** must have **specific receptors** to which the hormone can bind

These receptors may be intracellular or located on the plasma membrane

Examples of specific hormone activity

- ACTH (adrenocorticotropic hormone) receptors are only found on certain cells of the adrenal cortex
- Thyroxin—which is the major hormone stimulating metabolism—has receptors on nearly all cells of the body
Target Cell Activation

- Target cell activation depends on three factors
  - Blood levels of the hormone
  - Relative number of receptors on the target cell
  - The affinity (strength) of those receptors for the hormone

- **Up-regulation** – positive feedback
  - Target cells form more receptors in response to hormone

- **Down-regulation** – negative feedback
  - Target cells lose receptors in response to prolonged hormone exposure (usually preventative)
Hormone Activity: Half-life, Onset & Duration

- **Half-life**
  - Time required for a hormone’s blood level to decrease by half
  - Usually short and removal is facilitated by:
    - Enzymes which degrade hormone or second messenger
    - Liver & kidneys
    - Excretion from body via urine & feces

- **Onset – varies with hormone**
  - Can be immediate if hormone is already in active form OR
  - Slower if the hormone is a prohormone (must be activated)

- **Duration – varies with hormone**
Hormone Interactions

- Multiple hormones may act on the same target cells
- 3 Types of Interactions
  - **Permissiveness**: one hormone cannot exert its effects without another hormone being present
    - Thyroid & growth hormone for reproductive development
  - **Synergism**: multiple hormones with same effect
    - glucagon and epinephrine both cause the liver to release glucose
  - **Antagonism**: multiple hormones with opposing effects
    - calcitonin and PTH for blood calcium
Control of Hormone Release

- Blood levels of hormones:
  - controlled by **negative feedback** systems
  - vary within a narrow desirable range

- Hormones are synthesized and released in response to:
  - Humoral (fluid) stimuli
  - Neural stimuli
  - Hormonal stimuli
Control of Hormone Release: Humoral Stimuli

- Fluid stimuli
- secretion of hormones in direct response to changing blood levels of ions and nutrients

- Exs: concentration of calcium ions in the blood; pancreas - insulin response to blood sugar levels
Control of Hormone Release: Neural Stimuli

- nerve fibers stimulate hormone release

- Ex: sympathetic nervous system (SNS) stimulate the adrenal medulla to secrete norepinephrine, and epinephrine
Control of Hormone Release: Hormonal Stimuli

- release of hormones in response to hormones (tropic hormones)
  - Hypothalamic-pituitary-target feedback loop
    - hypothalamic hormones → anterior pituitary
    - pituitary hormones → targets to secrete more hormones
  - Animation TRH → TSH
Control of Hormone Release: Nervous System Modulation

- Any mechanism turning “on” or “off” hormone release may be modified by the nervous system
  - Nervous system can override all other mechanisms
  - Ex. Thermostat regulating household temperature OR you change temp on thermostat
  - Ex: Blood glucose
    - Normally the endocrine system maintains blood glucose
    - Under stress, the body needs more glucose
    - The hypothalamus and the sympathetic nervous system are activated to supply more glucose
Major Endocrine Organs

- Pituitary gland (Hypophysis)
- Thyroid gland
- Parathyroid glands
- Adrenal glands
- Pancreas
- Gonads
- Pineal gland
- Thymus
Major Endocrine Organs: Pituitary (Hypophysis)

- Pea-like organ (peas on a stalk) seated in sella turcica
- Secretes nine major hormones
- Has two lobes:
  - **Posterior pituitary (Neurohypophysis)**
    - Made of neural tissue and the *infundibulum* (stalk of attachment to hypothalamus)
    - Receives, stores, and releases hormones from the hypothalamus
  - **Anterior pituitary (Adenohypophysis)**
    - Made up of glandular tissue
    - Synthesizes and secretes a number of hormones
Major Endocrine Organs: Pituitary (Hypophysis)
Pituitary-Hypothalamic Relationships: Anterior Lobe (adenohypophysis)

- The anterior lobe is an extension of oral mucosa
- There is no direct neural contact with the hypothalamus
- It is controlled by the hypothalamic hormones via the Hypophyseal portal system
Control of the Adenohypophysis

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

- Hypothalamic hormones travel through portal veins to the anterior pituitary where they stimulate or inhibit release of hormones made in the anterior pituitary.
- In response to releasing hormones, the anterior pituitary secretes hormones into the secondary capillary plexus. This in turn empties into the general circulation.
- When appropriately stimulated, hypothalamic neurons secrete releasing or inhibiting hormones into the primary capillary plexus.

Hypophyseal portal system:
- Primary capillary plexus
- Hypophyseal portal veins
- Secondary capillary plexus

A portal system is two capillary plexuses (beds) connected by veins.

GH, TSH, ACTH, FSH, LH, PRL
Pituitary-Hypothalamic Relationships: Anterior Lobe

- The **hypophyseal portal system**: 
  - Capillary system that begins at the hypothalamus and drains into capillaries at the adenohypophysis
  - This is the pathway by which inhibiting or releasing hormones from the hypothalamus control the adenohypophysis (anterior lobe)
Pituitary-Hypothalamic Relationships: Anterior Lobe

Figure 16.6

- Hypothalamic neurons in the paraventricular nuclei
- Neurons in the ventral hypothalamus
- Infundibulum (connecting stalk)
- Hypothalamic-hypophyseal tract
- Neurohypophysis (storage area for hypothalamic hormones)
- Posterior lobe
- Venule

Hypophyseal portal system:
- Primary capillary plexus
- Hypophyseal portal veins
- Secondary capillary plexus

Anterior lobe
- Secretory cells of adenohypophysis
- TSH, FSH, LH, ACTH, GH, PRL
- Inferior hypophyseal artery
- Oxytocin ADH
Anterior Pituitary Hormones

- The six hormones of the adenohypophysis:
  - Growth hormone (GH)
  - Thyroid-stimulating hormone (TSH)
  - Adrenocorticotropic hormone (ACTH)
  - Follicle-stimulating hormone (FSH)
  - Lutenizing hormone (LH)
  - Prolactin (PRL)

- In addition, pro-opiomelanocortin (POMC):
  - Prohormone
  - Is split into ACTH, opiates, and MSH (melanin stimulating hormone)
Anterior Pituitary Hormones

- All are proteins
- All except GH & PRL activate second-messenger systems at their targets

- TSH, ACTH, LH, FSH are all tropic hormones
  - hormones that regulate the secretory action of other endocrine glands (regulate the release/production of other hormones)
Anterior Pituitary Hormones: Growth Hormone (GH)

- Produced in the **anterior lobe of the pituitary** by the **somatotropic** cells
  - Also called somatotropin
- Promotes protein synthesis & encourages use of fats for fuel
- Direct Gene Action of GH
  - Stimulates liver, sk. Muscle, bone & cartilage to produce insulin-like growth factors > inc growth & protein synthesis
  - Release inc breakdown of fats and glycogen stores
- GH is regulated by GHRH (releasing) and GHIH (inhibiting – somatostatin)
Metabolic Action of Growth Hormone

- Hypothalamus secretes growth hormone–releasing hormone (GHRH), and somatostatin (GHIH)
- Anterior pituitary
- Feedback
- Inhibits GHRH release
- Stimulates GHIH release
- Inhibits GH synthesis and release
- Growth hormone

Indirect actions (growth-promoting)

- Liver and other tissues
  - Insulin-like growth factors (IGFs)
    - Produce
    - Effects

- Skeletal
  - Increased cartilage formation and skeletal growth

- Extraskeletal
  - Increased protein synthesis, and cell growth and proliferation

- Fat
  - Increased fat breakdown and release

- Carbohydrate metabolism
  - Increased blood glucose and other anti-insulin effects

Increases, stimulates
Reduces, inhibits

Initial stimulus
Physiological response
Result
Homeostatic Imbalances of GH

- **Hypersecretion**: secreting more than normal amounts
  - in children results in **Gigantism**
  - in adults results in **Acromegaly** (enlarged extremities)
    - Excessive GH secreted after epiphseal plate closure
- **Hyposecretion**: secreting less than normal amounts
  - In adults usually does not cause major problems
  - In children results in **pituitary dwarfism**
    - can be treated with GH injections
      - Taking supplemental GH >> fluid retention, joint & muscle pain, diabetes, possibly cancer
Anterior Pituitary Hormones: Thyroid Stimulating Hormone (TSH)

- Tropic hormone; also called thyrotropin
- Stimulates normal development & secretory activity of thyroid gland
- Regulation of TSH release
  - Released in response to thyrotropin releasing hormone - TRH
  - Inhibited by rising blood levels of thyroid hormones $\rightarrow$ block the release of TSH $\Rightarrow$ negative feedback
- Stimulates the production of thyroid hormones via second messenger system
Anterior Pituitary Hormones: Adrenocorticotropic Hormone (ACTH)

- Tropic hormone; Also called Corticotropin
- Stimulates adrenal cortex to release corticosteroids via 2\textsuperscript{nd} messenger
- Regulation of ACTH release:
  - triggered by corticotropin releasing hormone (CRH) in a daily rhythm
    - internal & external factors (hypoglycemia, fever and stressors) can alter CRH
  - Inhibited by increased levels of glucocorticoids
- Negative feedback
Anterior Pituitary Hormones:

Gonadotropins: FSH & LH

- Follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
  - also called gonadotropins
  - Tropic hormones (direct in females)

- Regulate function of gonads via cAMP 2nd messenger
  - ovaries & testes

- FSH stimulates gametes (egg or sperm)

- LH promotes production of gonadal hormones

- Absent from the blood in prepubertal boys and girls
Anterior Pituitary Hormones: Gonadotropins: FSH & LH

- Regulation of gonadotropin release:
  - Triggered by gonadotropin releasing hormone (GnRH) during and after puberty
  - Suppressed by gonadal hormones (negative feedback)
    - increasing levels of gonadal hormones (testosterone, estrogen, progesterone) shuts off production of Gonadotropins via Negative feedback
Gonadotropins:

Functions of FSH & LH

- **FSH**
  - targets ovaries and testes to stimulate gamete production
    - sperm in males, egg in females

- **LH**
  - in women works to trigger ovulation (release of egg), promotes synthesis and release of estrogen and progesterone from ovaries.
  - In males LH stimulates interstitial cells of the testes to produce testosterone.

- **FSH and LH in women** act together for maturation of ovarian follicle
Anterior Pituitary Hormones: Prolactin (PRL)

- Stimulates milk production
- Regulation of PRL release
  - Primarily controlled by prolactin-inhibiting hormone (PIH; dopamine)
  - In females, stimulated by estrogen & prolactin releasing hormone (PRH)
    - Blood levels rise toward the end of pregnancy
    - Suckling stimulates PRH
- Works through direct gene activation
- Role in males not well understood
  - Possible basis for erectile dysfunction
    - High PRL can suppress FSH and GnRH >> hypogonadism
Pituitary-Hypothalamic Relationships: Posterior Pituitary (Neurohypophysis)

- Contains axons of hypothalamic neurons

- Stores oxytocin and antidiuretic hormone (ADH)
  - Released in response to nerve impulses
  - Both use second-messenger mechanisms at their targets
  - These hormones are transported to the posterior pituitary where they are stored until neuronal stimulation from the hypothalamus for their release
Pituitary-Hypothalamic Relationships: Posterior Pituitary (Neurohypophysis)

Paraventricular nuclei ↓ Oxytocin

Supraoptic nuclei ↓ ADH
**Control of Neurohypophyphysis**

**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).
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.
Posterior Pituitary Hormones: 
Oxytocin “cuddle hormone”

- Stimulates uterine contractions during childbirth
- Triggers milk ejection (“letdown” reflex) in women producing milk
- Plays a role in sexual arousal and orgasm in males & females
- Promotes nurturing, affectionate behavior
- Uses PIP-Ca 2nd messenger system
  - Can also be Direct acting for lactation
- Made by paraventricular nuclei of the Hypothal. but STORED in the posterior pituitary
- Regulated by positive feedback until birth or suckling stops
- PITOCIN is the artificial form
Posterior Pituitary Hormones: Antidiuretic Hormone (ADH; Vasopressin)

- Hypothalamic osmoreceptors respond to changes in the solute conc. of the blood

- If solute conc. is high:
  - Osmoreceptors depolarize & transmit impulses to hypothalamic neurons
  - ADH is synthesized and released, inhibiting urine formation

- If solute conc. is low:
  - ADH is not released, allowing water loss

- Alcohol inhibits ADH release and causes increased urine output
Posterior Pituitary Hormones: Antidiuretic Hormone (ADH; Vasopressin)

- Produced by **supraoptic nuclei** of the hypothalamus and stored in the posterior pituitary gland
- Targets renal tubules of the kidneys through cAMP 2nd messenger, specifically the collecting ducts
  - it causes these collecting ducts to reabsorb more water during times of high blood solute levels
- As solute levels return to normal the osmoreceptors turn off the production of ADH = Negative Feedback
- **Diuretics** inhibit ADH > used to treat edema, High BP etc.
- ADH is also known as **vasopressin** because it is also a vasoconstrictor of visceral blood vessels >> inc BP – through PIP-Ca
Hormonal Imbalances of ADH

- ADH deficiency can result in diabetes insipidus
  - Huge urine output; intense thirst
  - Diabetes “overflow”; insipidus “tasteless”

- ADH hypersecretion
  - In children with meningitis
  - Following neurosurgery, trauma, or secreted by cancer cells
  - After general anesthesia
    - All can lead to SIADH (syndrome of inappropriate ADH secretion) – fluid retention, headache and disorientation
Major Endocrine Organs: Thyroid Gland

- Consists of 2 lateral lobes in the anterior neck connected by a median mass called the **isthmus**

- Composed of **follicles** (chambers with cells) that produce the glycoprotein **thyroglobulin**
  - **Colloid** (thyroglobulin + iodine) fills the lumen of the follicles and is the precursor of **thyroid hormone (TH)**
  - **Parafollicular cells** are on the outer edges of the follicles; produce the hormone **calcitonin**
Thyroid gland anatomy

(a) Gross anatomy of the thyroid gland, anterior view

(b) Photomicrograph of thyroid gland follicles (125x)
Figure 16.9 *Synthesis of thyroid hormone.* Only a few tyrosines of the thyroglobulins in the colloid are illustrated. The colloid is represented by the unstructured yellow substance outside of the cells.
Thyroid Gland Hormones: Thyroid Hormone (TH)

- Thyroid hormone – major metabolic hormone
  - Works via direct gene activation
- Actually 2 iodine-containing compounds
  - $T_4$ – thyroxine;
  - $T_3$ – triiodothyronine;
- Increases the metabolic rate & body heat production by stimulating enzymes used in glucose metabolism
- Plays a role in:
  - Maintenance of blood pressure, Regulation of tissue growth,
  - Development of skeletal & muscle systems, Reproductive capabilities
Negative feedback
Homeostatic Imbalances of TH

- **Hyposecretion of TH (hypothyroidism)**
  - **In adults**
    - Myxedema “mucous swelling”
      - Low metabolic rate, chilled, constipation, thick, dry skin, puffy eyes, edema, lethargy, mental sluggishness
    - Enlarged thyroid > Goiter (if myxedema is due to lack of iodine)
  - **In infants**
    - Cretinism
      - Mental retardation, short, disproportionate body, thick tongue & neck

- **Hypersecretion of TH (hyperthyroidism)**
  - **Grave’s disease:** autoimmune disease; overproduction of TSH-like antibodies > continuously stimulate TH production
    - Elevated metabolic rate, sweating, rapid irregular heartbeat, nervousness, weightloss, exophthalmos (bulging eyes)
# Homeostatic Imbalances of TH

- **Symptoms of hyper vs hypothyroidism**

<table>
<thead>
<tr>
<th>Hyperthyroidism</th>
<th>Hypothyroidism</th>
</tr>
</thead>
<tbody>
<tr>
<td>High metabolic rate</td>
<td>Low metabolic rate</td>
</tr>
<tr>
<td>Weight loss</td>
<td>Weight gain</td>
</tr>
<tr>
<td>Sweating</td>
<td>Chilled</td>
</tr>
<tr>
<td>Nervous/ irritated-difficulty sleeping</td>
<td>Lethargy (sleepy/tired)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Constipation</td>
</tr>
<tr>
<td>Rapid irregular heart rate</td>
<td>Dry skin</td>
</tr>
<tr>
<td>Exophtalmos (extreme=bulging eyes)</td>
<td></td>
</tr>
</tbody>
</table>
Goiter and exophthalomos
Thyroid Gland Hormones: Calcitonin

- Produced by parafollicular cells in the thyroid gland
- Works through cAMP 2nd messenger system
- Released in response to high calcium levels
  - Targets the skeleton (inhibits osteoclasts)
  - Stimulates calcium uptake and deposition into bone (lowers blood calcium levels)
- Inhibited by low blood calcium (Ca) levels via humoral Negative feedback
- Antagonist to parathyroid hormone (PTH)
Calcitonin and PTH

Calcitonin stimulates calcium salt deposit in bone.

Parathyroid glands release parathyroid hormone (PTH).

Rising blood Ca^{2+} levels

Osteoclasts degrade bone matrix and release Ca^{2+} into blood.

Falling blood Ca^{2+} levels

Calcium homeostasis of blood: 9–11 mg/100 ml

PTH;
calcitonin

Secreted

Parathyroid glands release parathyroid hormone (PTH).

Calcitonin stimulates calcium salt deposit in bone.

Thyroid gland

Thyroid gland

Osteoclasts degrade bone matrix and release Ca^{2+} into blood.

Falling blood Ca^{2+} levels

Rising blood Ca^{2+} levels

Parathyroid glands release parathyroid hormone (PTH).

Calcium homeostasis of blood: 9–11 mg/100 ml
Major Endocrine Organs: Parathyroid Glands

Pharynx (posterior aspect)
Thyroid gland
Parathyroid glands
Esophagus
Trachea

Chief cells (secrete parathyroid hormone)
Oxyphil cells
Capillary

Copyright © 2010 Pearson Education, Inc.
Major Endocrine Organs:

Parathyroid Glands

- Four to eight tiny glands embedded in the posterior thyroid
- Contain oxyphil cells (unknown function) and chief cells that secrete parathyroid hormone (PTH)
- PTH – most important hormone in Calcium homeostasis
- Works via cAMP 2nd messenger system
Parathyroid Hormone

- Functions:
  - Stimulates osteoclasts to digest bone matrix
  - Enhances reabsorption of Ca
  - Promotes activation of Vit D >> inc absorption of Ca by intestinal mucosa
- released in response to low blood calcium levels
- Increase blood calcium levels inhibits release of PTH via Negative feedback
Effects of Parathyroid Hormone

Hypocalcemia (low blood Ca\(^{2+}\)) stimulates parathyroid glands to release PTH.

1. PTH activates osteoclasts: Ca\(^{2+}\) and PO\(_4\)\(^{3-}\) released into blood.
2. PTH increases Ca\(^{2+}\) reabsorption in kidney tubules.
3. PTH promotes kidney’s activation of vitamin D, which increases Ca\(^{2+}\) absorption from food.
Homeostatic Imbalances of PTH

- Hyperparathyroidism (rare) due to tumor
  - Bones soften & deform (*osteitis fibrosa cystica*)
  - Elevated blood calcium depresses nervous system and contributes to formation of kidney stones (calculi) & calcification of soft tissues

- Hypoparathyroidism following gland trauma or removal (also prolonged Mg deficiency – req’d for PTH secretion)
  - Increases excitability of muscles
    - Results in tetany, respiratory paralysis, and possibly death
osteitis fibrosa cystica
Hyperparathyroidism: calculi
Major Endocrine Organs:
Adrenal (Suprarenal) Glands

- **Adrenal glands** *(ad=near renal=kidney)*
  - Triangular gland
  - Adrenal hormones help body cope with **stressful situations**

- Structurally & functionally two glands in one
  - **Adrenal medulla**
    - Nervous tissue
    - Part of sympathetic nervous system
    - Hormones produced here work via G-protein 2\textsuperscript{nd} messengers
  - **Adrenal cortex**
    - Three layers of glandular tissue that synthesize & secrete corticosteroids (from cholesterol)
    - All hormones produced here work via direct gene activation
Adrenal Glands: Adrenal Cortex Hormones

- 3 layers of adrenal cortex & the corticosteroids produced within (superficial to deep)
  - **Zona glomerulosa**
    - Mineralocorticoids
      - main one is aldosterone
  - **Zona fasciculata**
    - Glucocorticoids
      - main one is cortisol/hydrocortisone
  - **Zona reticularis**
    - Gonadocorticoids (sex hormones)
      - main ones are androgens
Adrenal Cortex

(a) Drawing of the histology of the adrenal cortex and a portion of the adrenal medulla

(b) Photomicrograph (160x)

Capsule
Zona glomerulosa
Zona fasciculata
Zona reticularis
Adrenal medulla

Hormones secreted
- Aldosterone
- Cortisol and androgens
- Epinephrine and NE

Copyright © 2010 Pearson Education, Inc.
Adrenal Cortex Hormones:
Mineralocorticoids

- Regulate electrolytes (primarily Na+ and K+) in ECF
  - Importance of Na+: affects ECF volume, blood volume, blood pressure, levels of other ions
  - Importance of K+: sets RMP of cells
- Aldosterone is the most potent mineralcorticoid
  - stimulates Na+ reabsorption and water retention by kidneys
    - Considered an antidiuretic
- Direct acting; Produced in the Zona glomerulosa
- Inhibited by various negative feedback loops
Homeostatic Imbalances of Aldosterone

- **Aldosteronism**
  - Hypersecretion of aldosterone due to adrenal tumors
    - Hypertension and edema due to excessive Na+
    - Excretion of K+ leads to abnormal function of neurons & muscle, possibly coma and death

- **Addison’s Disease**
  - Hyposecretion of aldosterone (usually along with hyposecretion of glucocorticoids)
    - Weight loss, glucose and Na levels drop, K levels rise
    - Dehydration and hypotension
    - Treated with replacement therapy
Adrenal Cortex Hormones:

Glucocorticoids (Cortisol/hydrocortisone)

- Keep blood sugar levels relatively constant
- Maintain BP by inc the action of vasoconstrictors
- Cortisol is most significant
  - Released in response to ACTH, patterns of eating and activity, stress
  - Promotes gluconeogenesis (formation of glucose from non-carb sources)
  - Promotes rises in blood glucose, fatty acids, and amino acids
- Produced in the adrenal cortex—Zona fasciculata
- inhibited by increased levels of cortisol—Negative feedback
- Glucocorticoids are major group released in stress
Homeostatic Imbalances of Glucocorticoids

- Hypersecretion - Cushing’s syndrome
  - Depresses cartilage & bone formation
  - Inhibits inflammation
  - Depresses the immune system
  - Promotes changes in cardiovasc., neural and GI function
    - Symptoms of Cushing’s: persistent hyperglycemia, loss in muscle and bone protein, water and salt retention leading to higher BP and edema

- Hyposecretion - Addison’s disease
  - Also involved deficits in mineralcorticoids
Cushing’s symptoms

Swollen “moon” face

Buffalo hump on back of neck
Adrenal Cortex Hormones: 
Gonadocorticoids (Sex Hormones)

- Most are **androgens** (male sex hormones) that are converted to testosterone in tissue cells or estrogens in females.

- Androgens contribute to:
  - The onset of puberty
  - The appearance of secondary sex characteristics
  - Sex drive in females

- Their production is not significant in comparison with sex hormones released from the gonads during puberty.
Homeostatic Imbalances in Androgens

- Hypersecretion of androgens
  - Adrenogenital syndrome (masculinization)
    - Males: rapid maturation of the reproductive organs and secondary sex characteristics in young males; generally not visible
    - Females: **masculinization**—hair growth in areas associated with males and clitoris can elongate to resemble a small penis
Adrenal Glands: Adrenal Medulla

- Made up of **chromaffin cells** that secrete **catecholamines** (epinephrine & norepinephrine)
- Production stimulated by the sympathetic nervous system in response to short term stress
- Targets lots of organ systems
- These hormones cause:
  - Rise in blood glucose, blood vessels constriction (> inc in BP), inc heart rate, blood diversion from digestive system to the brain, heart and skeletal muscle etc. .....prep for fight or flight
- Inhibited by parasympathetic nervous system
Stress and the Adrenal Gland

**Short-term stress response**
1. Increased heart rate
2. Increased blood pressure
3. Liver converts glycogen to glucose and releases glucose to blood
4. Dilation of bronchioles
5. Changes in blood flow patterns leading to decreased digestive system activity and reduced urine output
6. Increased metabolic rate

**Long-term stress response**
1. Retention of sodium and water by kidneys
2. Increased blood volume and blood pressure
3. Suppression of immune system

**More prolonged**
- Hypothalamus
- CRH (corticotropin-releasing hormone)
- ACTH
- Adrenal cortex
- To target in blood

**Corticotroph cells of anterior pituitary**

**Nerve impulses**
- Spinal cord
- Preganglionic sympathetic fibers

**Catecholamines** (epinephrine and norepinephrine)

**Adrenal medulla**
Major Endocrine Organs: Pancreas

- A triangular gland located behind the stomach
- Has both exocrine and endocrine cells

  - **Acinar cells** (exocrine) produce an enzyme-rich juice used for digestion
  - Pancreatic islets (islets of Langerhans) contain endocrine cells
    - The islets contain two major cell types:
      - Alpha (α) cells that produce **glucagon** (a hyperglycemic hormone)
      - Beta (β) cells that produce **insulin** (a hypoglycemic hormone)
Major Endocrine Organs: Pancreas
Pancreas Hormones: Glucagon

- Hyperglycemic agent = raises blood glucose (sugar) levels
- Released in response to low blood glucose
  - i.e. when you have not eaten in awhile
- Its major target is the liver (via cAMP second messenger, where it promotes:
  - Glycogenolysis – the breakdown of glycogen to glucose
  - Gluconeogenesis – synthesis of glucose from non-carbohydrates
  - Release of glucose to the blood from liver cells
- Antagonist to insulin – works in opposition to insulin
Pancreas Hormones:

Insulin

- hypoglycemic agent = lowers blood glucose
- released in response to high blood glucose levels
- Synthesized as part of proinsulin and then excised by enzymes, releasing functional insulin

Effects of insulin:
- Lowers blood glucose levels
- Enhances membrane transport of glucose into fat & muscle cells
- Participates in neuronal development, learning & memory
- Inhibits glycogenolysis & gluconeogenesis
Insulin Action on Cells

- After glucose enters a cell, insulin binding triggers enzymatic activity that:
  - Triggers glucose metabolism to make ATP
  - Forms glycogen
  - Stores glucose as fat

- Stimulation is directly based on elevated blood sugar levels and indirectly by any hyperglycemic hormone (glucagon, epinephrine, GH, glucocorticoids)
Both glucagon and insulin are controlled by Negative feedback
Hormonal Imbalances of Insulin

- Diabetes mellitus (DM): “overflow of honey”
  - Due to hypossecretion or hypoactivity of insulin
  - The three cardinal signs of DM are:
    - **Polyuria**: huge urine output - excess glucose by osmosis pulls out water
    - **Polydipsia**: excessive thirst
    - **Polyphagia**: excessive hunger and food consumption

- Hyperinsulinism:
  - Excessive insulin secretion; results in hypoglycemia, disorientation, unconsciousness
Diabetes Mellitus continued

- Hyperglycemia can lead to nausea and output of glucose in urine = glycosuria
- The lack of glucose uptake requires tissues to use fatty acids for energy. This can result in higher than normal levels of fatty acids and their metabolites also called ketone bodies in the blood
- Rapid collection of Ketone bodies can cause acidic conditions called **Ketoacidosis** (late stage; serious) – kidney damage/failure, coma and death
  - Nervous system responds by initiating deep breathing to remove CO2 from blood (increases blood pH)
Types of Diabetes Mellitus

- **Type I**: Insulin dependent (IDDM)
  - early onset, total lack of insulin production
  - Usually have long term vascular and neural problems. Vascular problems related usually to high cholesterol levels in blood—increases risk of vascular diseases, arteriosclerosis, stroke, heart attack (MI) leads to other problems like blindness, gangrene

- **Type II**: non-insulin dependent (DM)
  - late onset, inadequate amount or inefficient (resistant) insulin receptors, 90% characterized by overweight

- [Animation type I](#)
- [Animation type II](#)
The gonads produce **steroidal** sex hormones via **ovaries** in females and **testes** in males.
Major Endocrine Organs:

Female Gonads

- Paired ovaries in the abdominopelvic cavity produce:
  - Estrogens
    - Maturation of the reproductive organs
    - Appearance of secondary sexual characteristics
    - Thickening of the uterus in preparation for pregnancy
  - Progesterone (and estrogens)
    - Breast development
    - Menstrual cycle
Major Endocrine Organs:

Male Gonads

- Testes located in an extra-abdominal sac (scrotum)
- Produce testosterone for:
  - Initiates maturation of male reproductive organs
  - Causes appearance of secondary sexual characteristics and sex drive
  - Is necessary for sperm production
  - Maintains reproductive organs in their functional state
Major Endocrine Organs:

Pineal Gland (body)

- Small gland hanging from the roof of the third ventricle of the brain
- Produces melatonin
- Melatonin is involved with:
  - Timing of sexual maturation & puberty
  - Day/night cycles like sleep wake
  - Physiological processes that show rhythmic variations (body temperature, sleep, appetite)
Major Endocrine Organs:

Thymus

- Lobulated gland located deep to the sternum
- Large in children, but shrinks with age
- Major hormonal products are thymopoietins and thymosins
  - These hormones are essential for the development of the T lymphocytes (T cells) of the immune system
  - Part of immune response
    - More in Chapter 21
Other hormone-producing structures

- Heart
  - Atrial Naturetic Peptide – decreases blood pressure (more in Ch 19)

- GI tract enteroendocrine cells
  - Gastrin – HCl release in response to food
  - Secretin – stimulates pancreas to secrete digestive enzymes
  - Cholecystokinin (CKK) – stimulates pancreas, gallbladder

- Kidneys
  - Erythropoetin – stimulates red blood cell production
  - Renin – returns blood pressure to normal
Other hormone-producing structures

- **Skin**
  - Cholecalciferol – converts to Vit D; aids in transport of calcium

- **Adipose tissue**
  - Leptin – suppresses appetite; inc energy use

- **Skeleton**
  - Osteocalcin – increases insulin production