An Introduction to the Endocrine System

• Learning Outcomes
  • 18-1 Explain the importance of intercellular communication, describe the mechanisms involved, and compare the modes of intercellular communication that occur in the endocrine and nervous systems.
  • 18-2 Compare the cellular components of the endocrine system with those of other systems, contrast the major structural classes of hormones, and explain the general mechanisms of hormonal action on target organs.
An Introduction to the Endocrine System

• Learning Outcomes
  • 18-3 Describe the location, hormones, and functions of the pituitary gland, and discuss the effects of abnormal pituitary hormone production.
  • 18-4 Describe the location, hormones, and functions of the thyroid gland, and discuss the effects of abnormal thyroid hormone production.
  • 18-5 Describe the location, hormones, and functions of the parathyroid glands, and discuss the effects of abnormal parathyroid hormone production.
An Introduction to the Endocrine System

• Learning Outcomes
  • 18-6 Describe the location, structure, hormones, and general functions of the adrenal glands, and discuss the effects of abnormal adrenal hormone production.
  • 18-7 Describe the location of the pineal gland, and discuss the functions of the hormone it produces.
  • 18-8 Describe the location, structure, hormones, and functions of the pancreas, and discuss the effects of abnormal pancreatic hormone production.
An Introduction to the Endocrine System

• Learning Outcomes
  • 18-9 Describe the functions of the hormones produced by the kidneys, heart, thymus, testes, ovaries, and adipose tissue.
  • 18-10 Explain how hormones interact to produce coordinated physiological responses and influence behavior, describe the role of hormones in the general adaptation syndrome, and discuss how aging affects hormone production and give examples of interactions between the endocrine system and other organ systems.
An Introduction to the Endocrine System

- The Endocrine System
  - Regulates long-term processes
    - Growth
    - Development
    - Reproduction
  - Uses chemical messengers to relay information and instructions between cells
Figure 18-1 Organs and Tissues of the Endocrine System (Part 1 of 2).

**Hypothalamus**
- Production of ADH, OXT, and regulatory hormones

**Pituitary Gland**
- **Anterior lobe**
  - ACTH, TSH, GH, PRL, FSH, LH, and MSH
- **Posterior lobe**
  - Release of oxytocin (OXT) and antidiuretic hormone (ADH)

**Pineal Gland**
- Melatonin

**Parathyroid Glands**
- (located on the posterior surface of the thyroid gland)
- Parathyroid hormone (PTH)
Figure 18-1 Organs and Tissues of the Endocrine System (Part 2 of 2).

<table>
<thead>
<tr>
<th>Organ/Region</th>
<th>Key Hormones/Functions</th>
<th>See Chapter</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Thyroid Gland</strong></td>
<td>Thyroxine (T₄), Triiodothyronine (T₃), Calcitonin (CT)</td>
<td></td>
</tr>
<tr>
<td><strong>Adrenal Gland</strong></td>
<td>Medulla: Epinephrine (E), Norepinephrine (NE)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cortex: Cortisol, corticosterone, aldosterone, androgens</td>
<td></td>
</tr>
<tr>
<td><strong>Pancreatic Islets</strong></td>
<td>Insulin, glucagon</td>
<td></td>
</tr>
<tr>
<td><strong>Organs with Secondary Endocrine Functions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Heart</strong></td>
<td>• Atrial natriuretic peptide (ANP)</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>• Brain natriuretic peptide (BNP)</td>
<td></td>
</tr>
<tr>
<td><strong>Thymus</strong></td>
<td>(Undergoes atrophy during adulthood)</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>• Thymosins</td>
<td></td>
</tr>
<tr>
<td><strong>Adipose Tissue</strong></td>
<td>• Leptin</td>
<td></td>
</tr>
<tr>
<td><strong>Digestive Tract</strong></td>
<td>Secretes numerous hormones involved in the coordination of system functions, glucose metabolism, and appetite</td>
<td>25</td>
</tr>
<tr>
<td><strong>Kidneys</strong></td>
<td>• Erythropoietin (EPO)</td>
<td>19, 26</td>
</tr>
<tr>
<td></td>
<td>• Calcitriol</td>
<td></td>
</tr>
<tr>
<td><strong>Gonads</strong></td>
<td>Testes (male)</td>
<td>28, 29</td>
</tr>
<tr>
<td></td>
<td>Androgens (especially testosterone), inhibin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ovaries (female)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Estrogens, progesterone, inhibin</td>
<td></td>
</tr>
</tbody>
</table>

**KEY TO PITUITARY HORMONES**

- ACTH: Adrenocorticotropic hormone
- TSH: Thyroid-stimulating hormone
- GH: Growth hormone
- PRL: Prolactin
- FSH: Follicle-stimulating hormone
- LH: Luteinizing hormone
- MSH: Melanocyte-stimulating hormone
18-1 Homeostasis and Intercellular Communication

• **Direct Communication**
  • Exchange of ions and molecules between adjacent cells across gap junctions
  • Occurs between two cells of same type
  • Highly specialized and relatively rare

• **Paracrine Communication**
  • Uses chemical signals to transfer information from cell to cell within single tissue
  • Most common form of intercellular communication
• **Endocrine Communication**
  - Endocrine cells release chemicals (hormones) into bloodstream
  - Alters metabolic activities of many tissues and organs simultaneously

18-1 Homeostasis and Intercellular Communication
18-1 Homeostasis and Intercellular Communication

• **Target Cells**
  • Are specific cells that possess receptors needed to bind and “read” hormonal messages

• **Hormones**
  • Stimulate synthesis of enzymes or structural proteins
  • Increase or decrease rate of synthesis
  • Turn existing enzyme or membrane channel “on” or “off”
18-1 Homeostasis and Intercellular Communication

- **Synaptic Communication**
  - Ideal for crisis management
  - Occurs across synaptic clefts
  - Chemical message is “neurotransmitter”
  - Limited to a very specific area
Table 18-1: Mechanisms of Intercellular Communication

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Transmission</th>
<th>Chemical Mediators</th>
<th>Distribution of Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct communication</td>
<td>Through gap junctions</td>
<td>Ions, small solutes, lipid-soluble materials</td>
<td>Usually limited to adjacent cells of the same type that are interconnected by connexons</td>
</tr>
<tr>
<td>Paracrine communication</td>
<td>Through extracellular fluid</td>
<td>Paracrine factors</td>
<td>Primarily limited to a local area, where paracrine factor concentrations are relatively high. Target cells must have appropriate receptors</td>
</tr>
<tr>
<td>Endocrine communication</td>
<td>Through the bloodstream</td>
<td>Hormones</td>
<td>Target cells are primarily in other tissues and organs and must have appropriate receptors</td>
</tr>
<tr>
<td>Synaptic communication</td>
<td>Across synapses</td>
<td>Neurotransmitters</td>
<td>Limited to very specific area; target cells must have appropriate receptors</td>
</tr>
</tbody>
</table>
• Classes of Hormones
  • Hormones can be divided into three groups
    1. Amino acid derivatives
    2. Peptide hormones
    3. Lipid derivatives

• Secretion and Distribution of Hormones
  • Hormones circulate freely or travel bound to special carrier proteins
18-2 Hormones

• Amino Acid Derivatives
  • Are small molecules structurally related to amino acids
    • Derivatives of tyrosine
      • Thyroid hormones
      • Catecholamines
        • Epinephrine, norepinephrine
    • Derivatives of tryptophan
      • Dopamine, serotonin, melatonin
18-2 Hormones

- **Peptide Hormones**
  - Are chains of amino acids
  - Most are synthesized as prohormones
    - Inactive molecules converted to active hormones before or after they are secreted
- **Glycoproteins**
  - Proteins are more than 200 amino acids long and have carbohydrate side chains
    - *Thyroid-stimulating hormone* (TSH)
    - *Luteinizing hormone* (LH)
    - *Follicle-stimulating hormone* (FSH)
18-2 Hormones

- Peptide Hormones
  - Short polypeptides/small proteins
    - Short chain polypeptides
      - Antidiuretic hormone (ADH) and oxytocin (OXT) (each 9 amino acids long)
    - Small proteins
      - Growth hormone (GH; 191 amino acids) and prolactin (PRL; 198 amino acids)
  - Includes all hormones secreted by:
    - Hypothalamus, heart, thymus, digestive tract, pancreas, and posterior lobe of the pituitary gland, as well as several hormones produced in other organs
18-2 Hormones

• Lipid Derivatives
  • **Eicosanoids** – derived from arachidonic acid, a 20-carbon fatty acid
    • Paracrine factors that coordinate cellular activities and affect enzymatic processes (such as blood clotting) in extracellular fluids
    • Some eicosanoids (such as **leukotrienes**) have secondary roles as hormones
    • A second group of eicosanoids – **prostaglandins** – involved primarily in coordinating local cellular activities
    • In some tissues, prostaglandins are converted to **thromboxanes** and **prostacyclins**, which also have strong paracrine effects
18-2 Hormones

- Lipid Derivatives
  - **Steroid hormones** – derived from cholesterol
    - Released by:
      - The reproductive organs (androgens by the testes in males, estrogens and progestins by the ovaries in females)
      - The cortex of the adrenal glands (corticosteroids)
      - The kidneys (calcitriol)
    - Because circulating steroid hormones are bound to specific transport proteins in the plasma:
      - They remain in circulation longer than secreted peptide hormones
18-2 Hormones

• Secretion and Distribution of Hormones
  • Free Hormones
    • Remain functional for less than 1 hour
      1. Diffuse out of bloodstream and bind to receptors on target cells
      2. Are broken down and absorbed by cells of liver or kidneys
      3. Are broken down by enzymes in plasma or interstitial fluids
18-2 Hormones

• Secretion and Distribution of Hormones
  • Thyroid and Steroid Hormones
    • Remain in circulation much longer because most are “bound”
    • Enter bloodstream
      • More than 99 percent become attached to special transport proteins
      • Bloodstream contains substantial reserve of bound hormones
18-2 Hormones

• Mechanisms of Hormone Action
  • Hormone Receptor
    • Is a protein molecule to which a particular molecule binds strongly
    • Responds to several different hormones
    • Different tissues have different combinations of receptors
    • Presence or absence of specific receptor determines hormonal sensitivity
18-2 Hormones

- Hormones and Plasma Membrane Receptors
  - Catecholamines and Peptide Hormones
    - Are not lipid soluble
    - Unable to penetrate plasma membrane
    - Bind to receptor proteins at *outer* surface of plasma membrane (extracellular receptors)
  - Eicosanoids
    - Are lipid soluble
    - Diffuse across plasma membrane to reach receptor proteins on *inner* surface of plasma membrane (intracellular receptors)
18-2 Hormones

• Hormones and Plasma Membrane Receptors
  • First and Second Messengers
    • Bind to receptors in plasma membrane
    • Cannot have direct effect on activities inside target cell
    • Use intracellular intermediary to exert effects
18-2 Hormones

• First Messenger
  • Leads to second messenger
  • May act as enzyme activator, inhibitor, or cofactor
  • Results in change in rates of metabolic reactions
18-2 Hormones

- Important **Second Messengers**
  1. *Cyclic-AMP* (cAMP)
     - Derivative of ATP
  2. *Cyclic-GMP* (cGMP)
     - Derivative of GTP
  3. Calcium ions
18-2 Hormones

• The Process of Amplification
  • Is the binding of a small number of hormone molecules to membrane receptors
  • Leads to thousands of second messengers in cell
  • Magnifies effect of hormone on target cell
• **Down-regulation**
  • Presence of a hormone triggers decrease in number of hormone receptors
  • When levels of particular hormone are high, cells become *less* sensitive to it

• **Up-regulation**
  • Absence of a hormone triggers increase in number of hormone receptors
  • When levels of particular hormone are low, cells become *more* sensitive to it
18-2 Hormones

- **G Protein**
  - Enzyme complex coupled to membrane receptor
  - Involved in link between first messenger and second messenger

- **G Proteins and cAMP**
  - *Adenylate cyclase* is activated when hormone binds to receptor at membrane surface and changes concentration of second messenger cyclic-AMP (cAMP) within cell
    - Increased cAMP level accelerates metabolic activity within cell
The first messenger (a peptide hormone, catecholamine, or eicosanoid) binds to a membrane receptor and activates a G protein. A G protein is an enzyme complex coupled to a membrane receptor that serves as a link between the first and second messenger.

**Effects on cAMP Levels**

Many G proteins, once activated, exert their effects by changing the concentration of cyclic AMP, which acts as the second messenger within the cell.

If levels of cAMP increase, enzymes may be activated or ion channels may be opened, accelerating the metabolic activity of the cell.

In some instances, G protein activation results in decreased levels of cAMP in the cytoplasm. This decrease has an inhibitory effect on the cell.

**First Messenger Examples**

- Epinephrine and norepinephrine (β receptors)
- Calcitonin
- Parathyroid hormone
- ADH, ACTH, FSH, LH, TSH

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A&P Flix Animation: Mechanism of Hormone Action: Second Messenger cAMP
Hormones

- G Proteins and Calcium Ions
  - Activated G proteins trigger:
    - Opening of calcium ion channels in membrane
    - Release of calcium ions from intracellular stores
    - G protein activates enzyme *phospholipase C* (*PLC*)
    - Enzyme triggers receptor cascade
      - Production of *diacylglycerol* (*DAG*) and *inositol triphosphate* (*IP₃*) from membrane phospholipids
      - May further activate more calcium ion channels through *protein kinase C* (*PKC*)
      - Calcium ions may activate *calmodulin*, which causes further cellular changes
The first messenger (a peptide hormone, catecholamine, or eicosanoid) binds to a membrane receptor and activates a G protein. A G protein is an enzyme complex coupled to a membrane receptor that serves as a link between the first and second messenger.

**Effects on Ca\(^{2+}\) Levels**

Some G proteins use Ca\(^{2+}\) as a second messenger.

- **First Messenger Examples**
  - Epinephrine and norepinephrine (α\(_1\) receptors)
  - Oxytocin
  - Regulatory hormones of hypothalamus
  - Several eicosanoids
18-2 Hormones

• Hormones and Intracellular Receptors
  • Alter rate of DNA transcription in nucleus
    • Change patterns of protein synthesis
  • Directly affect metabolic activity and structure of target cell
  • Include steroids and thyroid hormones
Steroid hormones diffuse through the plasma membrane and bind to receptors in the cytoplasm or nucleus. The complex then binds to DNA in the nucleus, activating specific genes.
Thyroid hormones enter the cytoplasm and bind to receptors in the nucleus to activate specific genes. They also bind to receptors on mitochondria and accelerate ATP production.
18-2 Hormones

• Control of Endocrine Activity by Endocrine Reflexes
  • Endocrine Reflexes
    • Functional counterparts of neural reflexes
    • In most cases, controlled by negative feedback mechanisms
      • Stimulus triggers production of hormone; the direct or indirect effects of the hormone reduce intensity of the stimulus
18-2 Hormones

- Endocrine Reflexes
  - Can be triggered by:
    1. *Humoral stimuli*
       - Changes in composition of extracellular fluid
    2. *Hormonal stimuli*
       - Arrival or removal of specific hormone
    3. *Neural stimuli*
       - Arrival of neurotransmitters at neuroglandular junctions
18-2 Hormones

• Endocrine Reflexes
  • Simple Endocrine Reflex
    • Involves only one hormone
    • Controls hormone secretion by the heart, pancreas, parathyroid gland, and digestive tract
  • Complex Endocrine Reflex
    • One or more intermediary steps
    • Two or more hormones
  • The hypothalamus provides highest level of endocrine control
Figure 18-5 Three Mechanisms of Hypothalamic Control over Endocrine Function.

1. Production of antidiuretic hormone (ADH) and oxytocin (OXT)
2. Secretion of regulatory hormones to control activity of the anterior lobe of pituitary gland
3. Control of sympathetic output to adrenal medullae

Hormones secreted by the anterior pituitary control other endocrine organs
Release of antidiuretic hormone (ADH) and oxytocin (OXT)
Secretion of epinephrine (E) and norepinephrine (NE)
18-2 Hormones

• Neuroendocrine Reflexes
  • Pathways include both neural and endocrine components

• Complex Commands
  • Issued by changing:
    • Amount of hormone secreted
    • Pattern of hormone release
      • Hypothalamic and pituitary hormones released in sudden bursts
      • Frequency changes response of target cells
18-3 The Pituitary Gland

• The **Pituitary Gland**
  • Also called **hypophysis**
  • Lies within **sella turcica**
    • **Sellar diaphragm**
      • A dural sheet that locks pituitary in position
      • Isolates it from cranial cavity
  • Hangs inferior to hypothalamus
    • Connected by **infundibulum**
18-3 The Pituitary Gland

- The Pituitary Gland
  - Releases nine important peptide hormones
  - Hormones bind to membrane receptors
    - Use cAMP as second messenger
Figure 18-6a The Anatomy and Orientation of the Pituitary Gland.

- Posterior pituitary lobe
- Sphenoid (sella turcica)
- Mammillary body
- Third ventricle
- Hypothalamus
- Optic chiasm
- Infundibulum
- Sellar diaphragm
- Anterior pituitary lobe
  - Pars tuberalis
  - Pars distalis
  - Pars intermedia
- Posterior pituitary lobe
- Sphenoid (sella turcica)
- Median eminence
- Relationship of the pituitary gland to the hypothalamus
Figure 18-6b The Anatomy and Orientation of the Pituitary Gland.

**Histology of the pituitary gland showing the anterior and posterior lobes**

**Anterior pituitary lobe**
- Pars distalis
- Pars intermedia

**Posterior pituitary lobe**
- Secretes other pituitary hormones
- Secretes MSH
- Releases ADH and OXT

**Pituitary gland**

LM × 77

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18-3 The Pituitary Gland

• The **Anterior Lobe** of the Pituitary Gland
  • Also called **adenohypophysis**
  • Hormones “turn on” endocrine glands or support other organs
  • Has three regions
    1. **Pars distalis**
    2. **Pars tuberalis**
    3. **Pars intermedia**
• The Hypophyseal Portal System
  • *Median eminence*
    • Swelling near attachment of infundibulum
    • Where hypothalamic neurons release regulatory factors
      • Into interstitial fluids
      • Through *fenestrated capillaries*
18-3 The Pituitary Gland

• Portal Vessels
  • Blood vessels link two capillary networks
  • Entire complex is portal system
    • Ensures that regulatory factors reach intended target cells before entering general circulation
Figure 18-7 The Hypophyseal Portal System and the Blood Supply to the Pituitary Gland.

- **Supraoptic nuclei**
- **Paraventricular nuclei**
- **Neurosecretory neurons**
- **Mammillary body**
- **Optic chiasm**
- **Capillary network in the median eminence**
- **Infundibulum**
- **Anterior lobe of the pituitary gland**
- **Capillary network in the anterior lobe**
- **Posterior lobe of the pituitary gland**
- **Endocrine cells**

- The superior hypophyseal artery delivers blood to the capillary network in the median eminence.
- The portal vessels deliver blood containing regulatory factors to the capillary network within the anterior lobe of the pituitary gland.
- The inferior hypophyseal artery delivers blood to the posterior lobe of the pituitary gland.
- Hypophyseal veins carry blood containing the pituitary hormones to the cardiovascular system for delivery to the rest of the body.
• Hypothalamic Control of the Anterior Lobe
  • Two classes of hypothalamic regulatory hormones
    1. **Releasing hormones (RH)**
       • Stimulate synthesis and secretion of one or more hormones at anterior lobe
    2. **Inhibiting hormones (IH)**
       • Prevent synthesis and secretion of hormones from the anterior lobe
  • Rate of secretion is controlled by negative feedback
The hypothalamus produces a releasing hormone (RH) to stimulate hormone production by other glands. Control occurs by negative feedback.
<table>
<thead>
<tr>
<th>Releasing hormone (RH)</th>
<th>Hormone 1 (from pituitary)</th>
<th>Endocrine target organ</th>
<th>Hormone 2 (from target organ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRH</td>
<td>TSH</td>
<td>Thyroid gland</td>
<td>Thyroid hormones</td>
</tr>
<tr>
<td>CRH</td>
<td>ACTH</td>
<td>Adrenal cortex</td>
<td>Glucocorticoids</td>
</tr>
<tr>
<td>GnRH</td>
<td>FSH</td>
<td>Testes</td>
<td>Inhibin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Estrogens</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inhibin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Estrogens</td>
</tr>
<tr>
<td></td>
<td>LH</td>
<td>Testes</td>
<td>Androgens</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Progesterone</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Estrogens</td>
</tr>
</tbody>
</table>

Table showing the hypothalamic releasing hormones that follow the typical pattern of regulation shown in Figure 18-8d above.
The regulation of prolactin (PRL) production by the anterior lobe. In this case, the hypothalamus produces both a releasing factor (PRF) and an inhibiting hormone (PIH). When one is stimulated, the other is inhibited.
Feedback Control of Endocrine Secretion at the Hypothalamus

Variations on the Typical Pattern of Regulation of Endocrine Organs by the Hypothalamus and Anterior Pituitary Lobe

The regulation of growth hormone (GH) production by the anterior lobe. When GH–RH release is inhibited, GH–IH release is stimulated.

- Stimulates growth of skeletal muscle, cartilage, and many other tissues
- Stimulation
- Inhibition
Figure 18-9 Pituitary Hormones and Their Targets (Part 1 of 2).

**Hypothalamus**

- **Direct Control by Nervous System**
- **Indirect Control through Release of Regulatory Hormones**

   Regulatory hormones are released into the hypophyseal portal system for delivery to the anterior lobe of the pituitary gland.

**KEY TO PITUITARY HORMONES:**

- **ACTH** Adrenocorticotropic hormone
- **TSH** Thyroid-stimulating hormone
- **GH** Growth hormone
- **PRL** Prolactin
- **FSH** Follicle-stimulating hormone
- **LH** Luteinizing hormone
- **MSH** Melanocyte-stimulating hormone
- **ADH** Antidiuretic hormone
- **OXT** Oxytocin

**Adrenal medulla**

- Epinephrine and norepinephrine

**Adrenal cortex**

- Glucocorticoids (cortisol, corticosterone)

**Thyroid gland**

- Thyroid hormones ($T_3$, $T_4$)

**LIVER**

- PRL, FSH, LH

**Somatomedins**

**Bone, muscle, other tissues**

**Mammary glands**

**Testes of male**

- Inhibin, Testosterone

**Ovaries of female**

- Estrogen, Progesterone, Inhibin

**Melanocytes (uncertain significance in healthy adults)**

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Table 18-2 The Pituitary Hormones (Part 1 of 2).

<table>
<thead>
<tr>
<th>ANTERIOR LOBE</th>
<th>Hormone</th>
<th>Target</th>
<th>Hormonal Effect</th>
<th>Hypothalamic Regulatory Hormone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pars distalis</td>
<td>Thyroid-stimulating hormone (TSH)</td>
<td>Thyroid gland</td>
<td>Secretion of thyroid hormones</td>
<td>Thyrotropin-releasing hormone (TRH)</td>
</tr>
<tr>
<td>Adrenocorticotropic hormone (ACTH)</td>
<td>Adrenal cortex (zona fasciculata)</td>
<td></td>
<td>Secretion of glucocorticoids (cortisol, corticosterone)</td>
<td>Corticotropin-releasing hormone (CRH)</td>
</tr>
<tr>
<td>Gonadotropins:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follicle-stimulating hormone (FSH)</td>
<td>Follicle cells of ovaries</td>
<td></td>
<td>Secretion of estrogen, follicle development</td>
<td>Gonadotropin-releasing hormone (GnRH)</td>
</tr>
<tr>
<td></td>
<td>Nurse cells of testes</td>
<td></td>
<td>Stimulation of sperm maturation</td>
<td>Gonadotropin-releasing hormone (GnRH)</td>
</tr>
<tr>
<td>Luteinizing hormone (LH)</td>
<td>Follicle cells of ovaries</td>
<td></td>
<td>Ovulation, formation of corpus luteum, secretion of progesterone</td>
<td>Gonadotropin-releasing hormone (GnRH)</td>
</tr>
<tr>
<td></td>
<td>Interstitial cells of testes</td>
<td></td>
<td>Secretion of testosterone</td>
<td>Gonadotropin-releasing hormone (GnRH)</td>
</tr>
<tr>
<td>Prolactin (PRL)</td>
<td>Mammary glands</td>
<td></td>
<td>Production of milk</td>
<td>Prolactin-releasing factor (PRF) Prolactin-inhibiting hormone (PIH)</td>
</tr>
<tr>
<td>Growth hormone (GH)</td>
<td>All cells</td>
<td></td>
<td>Growth, protein synthesis, lipid mobilization and catabolism</td>
<td>Growth hormone--releasing hormone (GH-RH) Growth hormone--inhibiting hormone (GH-IH)</td>
</tr>
<tr>
<td>Pars intermedia (not active in normal adults)</td>
<td>Melanocyte-stimulating hormone (MSH)</td>
<td>Melanocytes</td>
<td>Increased melanin synthesis in epidermis</td>
<td>Melanocyte-stimulating hormone--inhibiting hormone (MSH-IH)</td>
</tr>
</tbody>
</table>
18-3 The Pituitary Gland

• The **Posterior Lobe** of the Pituitary Gland
  • Also called **neurohypophysis**
    • Contains unmyelinated axons of hypothalamic neurons
  • **Supraoptic** and **paraventricular nuclei** manufacture:
    • **Antidiuretic hormone** (ADH)
    • **Oxytocin** (OXT)
Figure 18-9 Pituitary Hormones and Their Targets (Part 2 of 2).

**KEY TO PITUITARY HORMONES:**
- ACTH: Adrenocorticotropic hormone
- TSH: Thyroid-stimulating hormone
- GH: Growth hormone
- PRL: Prolactin
- FSH: Follicle-stimulating hormone
- LH: Luteinizing hormone
- MSH: Melanocyte-stimulating hormone
- ADH: Antidiuretic hormone
- OXT: Oxytocin

**Hypothalamus**

**Direct Release of Hormones**
- Sensory stimulation
- Osmoreceptor stimulation

**Posterior lobe of pituitary gland**

**ADH**

**Kidneys**

**Males:** Smooth muscle in ductus deferens and prostate gland

**Females:** Uterine smooth muscle and mammary glands
Table 18-2 The Pituitary Hormones (Part 2 of 2).

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Target</th>
<th>Hormonal Effect</th>
<th>Hypothalamic Regulatory Hormone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>POSTERIOR LOBE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidiuretic hormone (ADH)</td>
<td>Kidneys</td>
<td>Reabsorption of water, elevation of blood volume and pressure</td>
<td>None: Transported along axons from supraoptic nucleus to the posterior lobe of the pituitary gland</td>
</tr>
<tr>
<td>Oxytocin (OXT)</td>
<td>Uterus, mammary glands (females)</td>
<td>Labor contractions, milk ejection</td>
<td>None: Transported along axons from paraventricular nucleus to the posterior lobe of the pituitary gland</td>
</tr>
<tr>
<td></td>
<td>Ductus deferens and prostate gland (males)</td>
<td>Contraction of ductus deferens and prostate gland</td>
<td></td>
</tr>
</tbody>
</table>
18-4 The Thyroid Gland

- The **Thyroid Gland**
  - Lies inferior to thyroid cartilage of larynx
  - Consists of two **lobes** connected by narrow **isthmus**

- **Thyroid follicles**
  - Hollow spheres lined by cuboidal epithelium
  - Cells surround **follicle cavity** that contains viscous colloid
  - Surrounded by network of capillaries that:
    - Deliver nutrients and regulatory hormones
    - Accept secretory products and metabolic wastes
• **Thyroglobulin** (Globular Protein)
  - Synthesized by follicle cells
  - Secreted into colloid of thyroid follicles
  - Molecules contain the amino acid *tyrosine*

• **Thyroxine** ($T_4$)
  - Also called *tetraiodothyronine*
  - Contains four iodide ions

• **Triiodothyronine** ($T_3$)
  - Contains three iodide ions
Figure 18-10a The Thyroid Gland.

- Hyoid bone
- Superior thyroid artery
- Thyroid cartilage of larynx
- Superior thyroid vein
- Common carotid artery
- Right lobe of thyroid gland
- Middle thyroid vein
- Thyrocervical trunk
- Trachea
- Outline of clavicle
- Outline of sternum

Location and anatomy of the thyroid gland
Figure 18-10b The Thyroid Gland.

Thyroid gland

Histological organization of the thyroid

Thyroid follicles

LM × 122
Figure 18-10c The Thyroid Gland.

Histological details of the thyroid gland showing thyroid follicles and both cell types in the follicular epithelium. 

ATLAS: Plate 18c
The synthesis, storage, and secretion of thyroid hormones. The numbered events are explained in the text.
The regulation of thyroid secretion.

**Homeostasis Disturbed**
- Decreased $T_3$ and $T_4$ concentrations in blood or low body temperature

**Homeostasis Restored**
- Increased $T_3$ and $T_4$ concentrations, normal body temperature

**HOMEOSTASIS**
- Normal $T_3$ and $T_4$ concentrations, normal body temperature

**Thyroid follicles release $T_3$ and $T_4$**

- Hypothalamus releases TRH
- Anterior lobe of the pituitary gland releases TSH

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18-4 The Thyroid Gland

- **Thyroid-binding Globulins (TBGs)**
  - Plasma proteins that bind about 75 percent of $T_4$ and 70 percent of $T_3$ entering the bloodstream

- **Transthyretin** (*thyroid-binding prealbumin – TBPA*) and *albumin*
  - Bind most of the remaining thyroid hormones

- About 0.3 percent of $T_3$ and 0.03 percent of $T_4$ are unbound
18-4 The Thyroid Gland

- Thyroid-Stimulating Hormone (TSH)
  - Absence causes thyroid follicles to become inactive
    - Neither synthesis nor secretion occurs
  - Binds to membrane receptors
  - Activates key enzymes in thyroid hormone production
The Thyroid Gland

 Functions of Thyroid Hormones
  Thyroid Hormones
   Enter target cells by transport system
   Affect most cells in body
   Bind to receptors in:
     1. Cytoplasm
     2. Surfaces of mitochondria
     3. Nucleus
  In children, essential to normal development of:
    Skeletal, muscular, and nervous systems
18-4 The Thyroid Gland

- Calorigenic Effect
  - Cell consumes more energy resulting in increased heat generation
  - Is responsible for strong, immediate, and short-lived increase in rate of cellular metabolism
18-4 The Thyroid Gland

- Effects of Thyroid Hormones on Peripheral Tissues
  1. Elevates rates of oxygen consumption and energy consumption; in children, may cause a rise in body temperature
  2. Increases heart rate and force of contraction; generally results in a rise in blood pressure
  3. Increases sensitivity to sympathetic stimulation
  4. Maintains normal sensitivity of respiratory centers to changes in oxygen and carbon dioxide concentrations
  5. Stimulates red blood cell formation and thus enhances oxygen delivery
  6. Stimulates activity in other endocrine tissues
  7. Accelerates turnover of minerals in bone
• The C Cells of the Thyroid Gland and Calcitonin
  • C (clear) cells also called parafollicular cells
  • Produce calcitonin (CT)
    • Helps regulate concentrations of Ca\(^{2+}\) in body fluids
      1. Inhibits osteoclasts, which slows the rate of Ca\(^{2+}\) release from bone
      2. Stimulates Ca\(^{2+}\) excretion by the kidneys
• Four Parathyroid Glands
  • Embedded in the posterior surface of the thyroid gland
  • Altogether, the four glands weigh 1.6 g

• Parathyroid Hormone (PTH) or parathormone
  • Produced by parathyroid (chief) cells in response to low concentrations of Ca$^{2+}$
  • Antagonist for calcitonin
The Parathyroid Glands.

Thyroid gland, posterior view. The location of the parathyroid glands on the posterior surface of the thyroid lobes. (The thyroid lobes are located anterior to the trachea.)
Figure 18-12b The Parathyroid Glands.

- **Both parathyroid and thyroid tissues.**
- **Connective tissue capsule of parathyroid gland**
- **Blood vessel**
- **Thyroid follicle**
- **Parathyroid gland**

LM × 94
Figure 18-12c The Parathyroid Glands.

Parathyroid cells and oxyphil cells

- **Parathyroid (chief) cells**
- **Oxyphil cells**

Parathyroid gland cells.
18-5 Parathyroid Glands

• Three Effects of PTH

1. It stimulates osteoclasts and inhibits osteoblasts
   • Accelerates mineral turnover and releases Ca\(^{2+}\) from bone
   • Reduces rate of calcium deposition in bone

2. It enhances reabsorption of Ca\(^{2+}\) at kidneys, reducing urinary losses

3. It stimulates formation and secretion of calcitriol by the kidneys
   • Effects complement or enhance PTH
   • Also enhances Ca\(^{2+}\), PO\(_4\)\(^{3–}\) absorption by digestive tract
Thyroid gland produces calcitonin

Increased excretion of calcium by kidneys

Calcium deposition in bone

HOMEOSTASIS DISTURBED
Increasing calcium levels in blood

HOMEOSTASIS RESTORED
Blood calcium levels decrease

HOMEOSTASIS
Normal blood calcium levels (8.5–11 mg/dL)
Figure 18-13 The Homeostatic Regulation of Calcium Ion Concentrations (Part 2 of 2).

HOMEOSTASIS
Normal blood calcium levels (8.5–11 mg/dL)

HOMEOSTASIS DISTURBED
Decreasing calcium levels in blood

Parathyroid glands secrete parathyroid hormone (PTH)

Increased reabsorption of calcium by kidneys
Calcium release from bone
Increased calcitriol production causes Ca\(^{2+}\) absorption by digestive tract

HOMEOSTASIS RESTORED
Blood calcium levels increase

Decreasing levels of blood calcium
### Table 18–4  Hormones of the Thyroid Gland and Parathyroid Glands

<table>
<thead>
<tr>
<th>Gland/Cells</th>
<th>Hormone</th>
<th>Target</th>
<th>Hormonal Effect</th>
<th>Regulatory Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>THYROID GLAND</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follicular epithelium</td>
<td>Thyroxine (T&lt;sub&gt;4&lt;/sub&gt;)</td>
<td>Most cells</td>
<td>Increases energy utilization, oxygen consumption,</td>
<td>Stimulated by TSH from the anterior lobe of the pituitary gland</td>
</tr>
<tr>
<td></td>
<td>Triiodothyronine (T&lt;sub&gt;3&lt;/sub&gt;)</td>
<td></td>
<td>growth, and development</td>
<td></td>
</tr>
<tr>
<td>C cells</td>
<td>Calcitonin (CT)</td>
<td>Bone, kidneys</td>
<td>Decreases Ca&lt;sup&gt;2+&lt;/sup&gt; concentrations in body fluids</td>
<td>Stimulated by elevated blood Ca&lt;sup&gt;2+&lt;/sup&gt; levels; actions opposed by PTH</td>
</tr>
<tr>
<td><strong>PARATHYROID GLANDS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parathyroid (chief) cells</td>
<td>Parathyroid hormone (PTH)</td>
<td>Bone, kidneys</td>
<td>Increases Ca&lt;sup&gt;2+&lt;/sup&gt; concentrations in body fluids</td>
<td>Stimulated by low blood Ca&lt;sup&gt;2+&lt;/sup&gt; levels; PTH effects enhanced by calcitriol and opposed by calcitonin</td>
</tr>
</tbody>
</table>
18-6 Adrenal Glands

• The **Adrenal Glands**
  • Lie along superior border of each kidney
  • Subdivided into:
    • Superficial **adrenal cortex**
      • Stores lipids, especially cholesterol and fatty acids
      • Manufactures steroid hormones (**corticosteroids**)
    • Inner **adrenal medulla**
      • Secretory activities controlled by sympathetic division of ANS
      • Produces epinephrine (adrenaline) and norepinephrine
      • Metabolic changes persist for several minutes
18-6 Adrenal Glands

• Adrenal Cortex
  • Subdivided into three regions
    1. Zona glomerulosa
    2. Zona fasciculata
    3. Zona reticularis
18-6 Adrenal Glands

- **Zona Glomerulosa**
  - Outer region of adrenal cortex
  - Produces *mineralocorticoids*
    - For example, *aldosterone*
• **Aldosterone**
  - Stimulates conservation of sodium ions and elimination of potassium ions
  - Increases sensitivity of salt receptors in taste buds
  - Secretion responds to:
    - Drop in blood Na⁺, blood volume, or blood pressure
    - Rise in blood K⁺ concentration
18-6 Adrenal Glands

• Zona Fasciculata
  • Produces glucocorticoids
  • For example, cortisol (hydrocortisone) with corticosterone
    • Liver converts cortisol to cortisone
  • Secretion regulated by negative feedback
  • Has inhibitory effect on production of:
    • Corticotropin-releasing hormone (CRH) in hypothalamus
    • ACTH in adenohypophysis
18-6 Adrenal Glands

- **Glucocorticoids**
  - Accelerate glucose synthesis and glycogen formation
  - Show *anti-inflammatory* effects
    - Inhibit activities of white blood cells and other components of immune system
18-6 Adrenal Glands

- **Zona Reticularis**
  - Network of endocrine cells
  - Forms narrow band bordering each adrenal medulla
  - Produces androgens under stimulation by ACTH
Figure 18-14a The Adrenal Gland.

A superficial view of the kidneys and adrenal glands.
Figure 18-14b The Adrenal Gland.

An adrenal gland in section

- Capsule
- Cortex
- Medulla
Figure 18-14c The Adrenal Gland.

The Adrenal Hormones

<table>
<thead>
<tr>
<th>Region/Zone</th>
<th>Hormones</th>
<th>Primary Target</th>
<th>Hormonal Effects</th>
<th>Regulatory Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADRENAL CAPSULE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ADRENAL CORTEX</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zona glomerulosa</td>
<td>Mineralocorticoids, primarily aldosterone</td>
<td>Kidneys</td>
<td>Increase renal reabsorption of Na(^+) and water (especially in the presence of ADH), and accelerate urinary loss of K(^+)</td>
<td>Stimulated by angiotensin II, elevated blood K(^+) or fall in blood Na(^+); inhibited by ANP and BNP</td>
</tr>
<tr>
<td>Zona fasciculata</td>
<td>Glucocorticoids (cortisol [hydrocortisone], corticosterone)</td>
<td>Most cells</td>
<td>Increase rates of glucose and glycogen formation by the liver; release of amino acids from skeletal muscles, and lipids from adipose tissues; promote peripheral utilization of lipids; anti-inflammatory effects</td>
<td>Stimulated by ACTH from the anterior lobe of the pituitary gland</td>
</tr>
<tr>
<td>Zona reticularis</td>
<td>Androgens</td>
<td>Most cells</td>
<td>Adrenal androgens stimulate the development of pubic hair in boys and girls before puberty.</td>
<td>Androgen secretion is stimulated by ACTH.</td>
</tr>
<tr>
<td>ADRENAL MEDULLA</td>
<td>Epinephrine (E), norepinephrine (NE)</td>
<td>Most cells</td>
<td>Increases cardiac activity, blood pressure, glycogen breakdown, blood glucose levels; releases lipids by adipose tissue</td>
<td>Stimulated by sympathetic preganglionic fibers</td>
</tr>
</tbody>
</table>

The major regions and zones of an adrenal gland and the hormones they produce
• The Adrenal Medulla
  • Contains two types of secretory cells
    • One produces epinephrine (adrenaline)
      • 75 to 80 percent of medullary secretions
    • The other produces norepinephrine (noradrenaline)
      • 20 to 25 percent of medullary secretions
18-6 Adrenal Glands

- Epinephrine and Norepinephrine
  - Activation of the adrenal medullae has the following effects:
    - In skeletal muscles, epinephrine and norepinephrine trigger mobilization of glycogen reserves
    - And accelerate the breakdown of glucose to provide ATP
      - This combination increases both muscular strength and endurance
    - In adipose tissue, stored fats are broken down into fatty acids
      - Which are released into the bloodstream for other tissues to use for ATP production
• Epinephrine and Norepinephrine
  • Activation of the adrenal medullae has the following effects:
    • In the liver, glycogen molecules are broken down
    • The resulting glucose molecules are released into the bloodstream
      • Primarily for use by neural tissue, which cannot shift to fatty acid metabolism
    • In the heart, the stimulation of beta 1 receptors triggers an increase in the rate and force of cardiac muscle contraction
18-7 Pineal Gland

- The **Pineal Gland**
  - Lies in posterior portion of roof of third ventricle
  - Contains **pinealocytes**
    - Synthesize hormone **melatonin**
Functions of Melatonin:

- *Inhibits reproductive functions*
- *Protects against damage by free radicals*
- *Influences circadian rhythms*
Figure 18-15 The Pineal Gland.
The Pancreas

- Lies between:
  - Inferior border of stomach
  - And proximal portion of small intestine
- Contains exocrine and endocrine cells
18-8 Pancreas

- **Exocrine Pancreas**
  - Consists of clusters of gland cells called *pancreatic acini* and their attached ducts
  - Takes up roughly 99 percent of pancreatic volume
  - Gland and duct cells secrete alkaline, enzyme-rich fluid
    - That reaches the lumen of the digestive tract through a network of secretory ducts
18-8 Pancreas

• Endocrine Pancreas
  • Consists of cells that form clusters known as **pancreatic islets**, or **islets of Langerhans**
    1. **Alpha cells** produce glucagon
    2. **Beta cells** produce insulin
    3. **Delta cells** produce peptide hormone identical to GH–IH
    4. **F cells** secrete pancreatic polypeptide (PP)
The gross anatomy of the pancreas

- Common bile duct
- Accessory pancreatic duct
- Head of pancreas
- Small intestine (duodenum)
- Pancreatic duct
- Body of pancreas
- Lobule
- Tail

The pancreas is a gland located behind the stomach that produces enzymes and hormones.
Figure 18-16b The Pancreas.

A pancreatic islet surrounded by exocrine cells

Pancreatic acini (clusters of exocrine cells)

Pancreatic islet (islet of Langerhans)

Capillary

b A pancreatic islet surrounded by exocrine cells
• Blood Glucose Levels
  • When levels rise:
    • Beta cells secrete insulin, stimulating transport of glucose across plasma membranes
  • When levels decline:
    • Alpha cells release glucagon, stimulating glucose release by liver
Figure 18-17 The Regulation of Blood Glucose Concentrations (Part 1 of 2).

- Increased rate of glucose transport into target cells
- Increased rate of glucose utilization and ATP generation
- Increased conversion of glucose to glycogen
- Increased amino acid absorption and protein synthesis
- Increased triglyceride synthesis in adipose tissue

HOMEOSTASIS

Normal blood glucose levels (70–110 mg/dL)

HOMEOSTASIS RESTORED

Blood glucose levels decrease

Beta cells secrete insulin

HOMEOSTASIS DISTURBED

Increasing blood glucose levels

Increasing blood glucose levels
Figure 18-17 The Regulation of Blood Glucose Concentrations (Part 2 of 2).

HOMEOSTASIS

Normal blood glucose levels (70–110 mg/dL)

HOMEOSTASIS DISTURBED
Decreasing blood glucose levels

Alpha cells secrete glucagon

Increased breakdown of glycogen to glucose (in liver, skeletal muscle)

Increased breakdown of fat to fatty acids (in adipose tissue)

Increased synthesis and release of glucose (by the liver)

HOMEOSTASIS RESTORED
Blood glucose levels increase

Decreasing blood glucose levels
• **Insulin**
  • Is a peptide hormone released by beta cells
  • Affects target cells
    • *Accelerates glucose uptake*
    • *Accelerates glucose utilization and enhances ATP production*
    • *Stimulates glycogen formation*
    • *Stimulates amino acid absorption and protein synthesis*
    • *Stimulates triglyceride formation in adipose tissue*
18-8 Pancreas

- **Glucagon**
  - Released by alpha cells
  - Mobilizes energy reserves
  - Affects target cells
    - Stimulates breakdown of glycogen in skeletal muscle and liver cells
    - Stimulates breakdown of triglycerides in adipose tissue
    - Stimulates production of glucose in liver (gluconeogenesis)
Table 18-5 Hormones Produced by the Pancreatic Islets.

<table>
<thead>
<tr>
<th>Structure/Cells</th>
<th>Hormone</th>
<th>Primary Targets</th>
<th>Hormonal Effect</th>
<th>Regulatory Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PANCREATIC ISLETS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alpha cells</td>
<td>Glucagon</td>
<td>Liver, adipose tissue</td>
<td>Mobilizes lipid reserves; promotes glucose synthesis and glycogen breakdown in liver; elevates blood glucose concentrations</td>
<td>Stimulated by low blood glucose concentrations; inhibited by GH–IH from delta cells</td>
</tr>
<tr>
<td>Beta cells</td>
<td>Insulin</td>
<td>Most cells</td>
<td>Facilitates uptake of glucose by target cells; stimulates formation and storage of lipids and glycogen</td>
<td>Stimulated by high blood glucose concentrations, parasympathetic stimulation, and high levels of some amino acids; inhibited by GH–IH from delta cells and by sympathetic activation</td>
</tr>
<tr>
<td>Delta cells</td>
<td>GH–IH (somatostatin)</td>
<td>Other islet cells, digestive epithelium</td>
<td>Inhibits insulin and glucagon secretion; slows rates of nutrient absorption and enzyme secretion along digestive tract</td>
<td>Stimulated by protein-rich meal; mechanism unclear</td>
</tr>
<tr>
<td>F cells</td>
<td>Pancreatic polypeptide (PP)</td>
<td>Digestive organs</td>
<td>Inhibits gallbladder contraction; regulates production of pancreatic enzymes; influences rate of nutrient absorption by digestive tract</td>
<td>Stimulated by protein-rich meal and by parasympathetic stimulation</td>
</tr>
</tbody>
</table>
18-8 Pancreas

- **Diabetes Mellitus**
  - Is characterized by glucose concentrations high enough to overwhelm the reabsorption capabilities of the kidneys
    - **Hyperglycemia** = abnormally high glucose levels in the blood in general
    - **Glucose** appears in the urine, and urine volume generally becomes excessive (**polyuria**)
Diabetes Mellitus

**Type 1 (insulin dependent) diabetes**

- Is characterized by inadequate insulin production by the pancreatic beta cells
- Persons with type 1 diabetes require insulin to live and usually require multiple injections daily, or continuous infusion through an insulin pump or other device
- This form of diabetes accounts for only around 5–10 percent of cases; it often develops in childhood
18-8 Pancreas

• Diabetes Mellitus
  • **Type 2 (non-insulin dependent) diabetes**
    • Is the most common form of diabetes mellitus
    • Most people with this form of diabetes produce normal amounts of insulin, at least initially, but their tissues do not respond properly, a condition known as **insulin resistance**
  • Type 2 diabetes is associated with obesity
    • Weight loss through diet and exercise can be an effective treatment
• Diabetes Mellitus
  • Complications of untreated, or poorly managed diabetes mellitus include:
    • Kidney degeneration
    • Retinal damage
    • Early heart attacks
    • Peripheral nerve problems
    • Peripheral tissue damage
18-8 Pancreas

• Kidney Degeneration
  • **Diabetic nephropathy**
    • Degenerative changes in the kidneys can lead to kidney failure

• Retinal Damage
  • **Diabetic retinopathy**
    • The proliferation of capillaries and hemorrhaging at the retina may cause partial or complete blindness
Early Heart Attacks
- Degenerative blockages in cardiac circulation can lead to early heart attacks
  - For a given age group, heart attacks are three to five times more likely in diabetic individuals than in nondiabetic people

Peripheral Nerve Problems
- Abnormal blood flow to neural tissues is probably responsible for a variety of neural problems with peripheral nerves, including abnormal autonomic function
  - These disorders are collectively termed diabetic neuropathy
Peripheral Tissue Damage

Blood flow to the distal portions of the limbs is reduced, and peripheral tissues may suffer as a result.

For example, a reduction in blood flow to the feet can lead to tissue death, ulceration, infection, and loss of toes or a major portion of one or both feet.
18-9 Endocrine Tissues of Other Systems

- Many Organs of Other Body Systems Have Secondary Endocrine Functions
  - Intestines (digestive system)
  - Kidneys (urinary system)
  - Heart (cardiovascular system)
  - Thymus (lymphatic system and immunity)
  - Gonads (reproductive system)
18-9 Endocrine Tissues of Other Systems

- The Intestines
  - Produce hormones important to coordination of digestive activities

- The Kidneys
  - Produce the hormones **calcitriol** and **erythropoietin** (EPO)
  - Produce the enzyme **renin**
Figure 18-19a Endocrine Functions of the Kidneys.

The production of calcitriol

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The release of renin and erythropoietin, and an overview of the renin-angiotensin-aldosterone system beginning with the activation of angiotensinogen by renin.
18-9 Endocrine Tissues of Other Systems

• The Heart
  • Produces natriuretic peptides (*ANP* and *BNP*)
    • When blood volume becomes excessive
    • Action opposes angiotensin II
    • Resulting in reduction in blood volume and blood pressure
The **Thymus**
- Produces **thymosins** (blend of thymic hormones)
- That help develop and maintain normal immune defenses
18-9 Endocrine Tissues of Other Systems

• The Gonads
  • Testes
    • Produce androgens in interstitial cells
      • Testosterone is the most important male hormone
    • Secrete inhibin in nurse cells
      • Support differentiation and physical maturation of sperm
The Gonads

• Ovaries
  • Produce estrogens
    • Principal estrogen is estradiol
  • After ovulation, follicle cells:
    • Reorganize into corpus luteum
    • Release estrogens and progestins, especially progesterone
<table>
<thead>
<tr>
<th>Structure/Cells</th>
<th>Hormone</th>
<th>Primary Target</th>
<th>Hormonal Effect</th>
<th>Regulatory Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TESTES</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interstitial cells</td>
<td>Androgens</td>
<td>Most cells</td>
<td>Support functional maturation of sperm, protein synthesis in skeletal muscles,</td>
<td>Stimulated by LH from the anterior lobe of the pituitary gland</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>male secondary sex characteristics, and associated behaviors</td>
<td></td>
</tr>
<tr>
<td>Nurse cells</td>
<td>Inhibin</td>
<td>Pituitary gland</td>
<td>Inhibits secretion of FSH</td>
<td>Stimulated by FSH from the anterior lobe</td>
</tr>
<tr>
<td><strong>OVARIES</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follicular cells</td>
<td>Estrogens</td>
<td>Most cells</td>
<td>Support follicle maturation, female secondary sex characteristics, and</td>
<td>Stimulated by FSH and LH from the anterior lobe of the pituitary gland</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>associated behaviors</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inhibin</td>
<td>Pituitary gland</td>
<td>Inhibits secretion of FSH</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corpus luteum</td>
<td>Progesterone</td>
<td>Uterus, mammary glands</td>
<td>Prepares uterus for implantation; prepares mammary glands for secretory activity</td>
<td>Stimulated by LH from the anterior lobe of the pituitary gland</td>
</tr>
</tbody>
</table>
18-9 Endocrine Tissues of Other Systems

- Adipose Tissue Secretions
  - Leptin
    - Feedback control for appetite
    - Controls normal levels of GnRH, gonadotropin synthesis
<table>
<thead>
<tr>
<th>Organ</th>
<th>Hormone</th>
<th>Primary Target</th>
<th>Hormonal Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestines</td>
<td>Many (secretin, gastrin,</td>
<td>Other regions and organs of the</td>
<td>Coordinate digestive activities</td>
</tr>
<tr>
<td></td>
<td>cholecystokinin, etc.)</td>
<td>digestive system</td>
<td></td>
</tr>
<tr>
<td>Kidneys</td>
<td>Erythropoietin (EPO)</td>
<td>Red bone marrow</td>
<td>Stimulates red blood cell production</td>
</tr>
<tr>
<td></td>
<td>Calcitriol</td>
<td>Intestinal lining, bone, kidneys</td>
<td>Stimulates calcium and phosphate absorption; stimulates Ca^{2+} release from</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>bone; inhibits PTH secretion</td>
</tr>
<tr>
<td>Heart</td>
<td>Natriuretic peptides (ANP</td>
<td>Kidneys, hypothalamus, adrenal gland</td>
<td>Increase water and salt loss at kidneys; decrease thirst; suppress secretion of</td>
</tr>
<tr>
<td></td>
<td>and BNP)</td>
<td></td>
<td>ADH and aldosterone</td>
</tr>
<tr>
<td>Thymus</td>
<td>Thymosins (many)</td>
<td>Lymphocytes and other cells of the</td>
<td>Coordinate and regulate immune response</td>
</tr>
<tr>
<td></td>
<td></td>
<td>immune response</td>
<td></td>
</tr>
<tr>
<td>Gonads</td>
<td>See Table 18–7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adipose tissues</td>
<td>Leptin</td>
<td>Hypothalamus</td>
<td>Suppression of appetite; permissive effects on GnRH and gonadotropin synthesis</td>
</tr>
</tbody>
</table>

Table 18–6 Representative Hormones Produced by Organs of Other Systems.
• Hormones Interact to Produce Coordinated Physiological Responses
  • When a cell receives instructions from two hormones at the same time, four outcomes are possible
    1. **Antagonistic effects** – opposing
    2. **Synergistic effects** – additive
    3. **Permissive effects** – one hormone is necessary for another to produce effect
    4. **Integrative effects** – hormones produce different and complementary results
18-10 Hormone Interactions

- Hormones Important to Growth
  - *Growth hormone* (GH)
  - *Thyroid hormones*
  - *Insulin*
  - *PTH and calcitriol*
  - *Reproductive hormones*
18-10 Hormone Interactions

• Growth Hormone (GH)
  • In children:
    • Supports muscular and skeletal development
  • In adults:
    • Maintains normal blood glucose concentrations
    • Mobilizes lipid reserves
18-10 Hormone Interactions

• Thyroid Hormones
  • If absent during fetal development or for first year:
    • Nervous system fails to develop normally
    • Mental retardation results
  • If $T_4$ concentrations decline before puberty:
    • Normal skeletal development will not continue
18-10 Hormone Interactions

- Insulin
  - Allows passage of glucose and amino acids across plasma membranes

- Parathyroid Hormone (PTH) and Calcitriol
  - Promote absorption of calcium salts for deposition in bone
  - Inadequate levels cause weak and flexible bones
18-10 Hormone Interactions

• Reproductive Hormones
  • Androgens in males, estrogens in females
  • Stimulate cell growth and differentiation in target tissues
  • Produce gender-related differences in:
    • Skeletal proportions
    • Secondary sex characteristics
Table 18-8 Clinical Implications of Endocrine Malfunctions (Part 1 of 2).

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Underproduction or Tissue Insensitivity</th>
<th>Principal Signs and Symptoms</th>
<th>Overproduction or Tissue Hypersensitivity</th>
<th>Principal Signs and Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Growth hormone (GH)</td>
<td>Pituitary growth failure</td>
<td>Retarded growth, abnormal fat distribution, low blood glucose hours after a meal</td>
<td>Gigantism, acromegaly</td>
<td>Excessive growth</td>
</tr>
<tr>
<td>Antidiuretic hormone (ADH)</td>
<td>Diabetes insipidus</td>
<td>Polyuria, dehydration, thirst</td>
<td>SIADH (syndrome of inappropriate ADH secretion)</td>
<td>Increased body weight and water content</td>
</tr>
<tr>
<td>or vasopressin (VP)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroxine (T₄), triiodothyronine (T₃)</td>
<td>Hypothyroidism, infantile hypothyroidism, myxedema</td>
<td>Low metabolic rate; low body temperature; impaired physical and mental development</td>
<td>Hyperthyroidism, Graves disease</td>
<td>High metabolic rate and body temperature</td>
</tr>
<tr>
<td>Parathyroid hormone (PTH)</td>
<td>Hypoparathyroidism</td>
<td>Muscular weakness, neurological problems, formation of dense bones, tetany due to low blood Ca²⁺ concentrations</td>
<td>Hyperparathyroidism</td>
<td>Neurological, mental, muscular problems due to high blood Ca²⁺ concentrations; weak and brittle bones</td>
</tr>
<tr>
<td>Insulin</td>
<td>Diabetes mellitus (Type 1)</td>
<td>High blood glucose, impaired glucose utilization, dependence on lipids for energy; glycosuria</td>
<td>Excess insulin production or administration</td>
<td>Low blood glucose levels, possibly causing coma</td>
</tr>
<tr>
<td>Hormone</td>
<td>Underproduction or Tissue Insensitivity</td>
<td>Principal Signs and Symptoms</td>
<td>Overproduction or Tissue Hypersensitivity</td>
<td>Principal Signs and Symptoms</td>
</tr>
<tr>
<td>------------------</td>
<td>----------------------------------------</td>
<td>------------------------------------------------------------------</td>
<td>------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Mineralocorticoids (MCs)</td>
<td>Hypoaldosteronism</td>
<td>Polyuria, low blood volume, high blood K⁺, low blood Na⁺ concentrations</td>
<td>Aldosteronism</td>
<td>Increased body weight due to Na⁺ and water retention; low blood K⁺ concentration</td>
</tr>
<tr>
<td>Glucocorticoids (GCs)</td>
<td>Addison’s disease</td>
<td>Inability to tolerate stress, mobilize energy reserves, or maintain normal blood glucose concentrations</td>
<td>Cushing’s disease</td>
<td>Excessive breakdown of tissue proteins and lipid reserves; impaired glucose metabolism</td>
</tr>
<tr>
<td>Epinephrine (E), norepinephrine (NE)</td>
<td>None identified</td>
<td></td>
<td>Pheochromocytoma</td>
<td>High metabolic rate, body temperature, and heart rate; elevated blood glucose levels</td>
</tr>
<tr>
<td>Estrogens (females)</td>
<td>Hypogonadism</td>
<td>Sterility, lack of secondary sex characteristics</td>
<td>Adrenogenital syndrome</td>
<td>Overproduction of androgens by zona reticularis of adrenal cortex leads to masculinization</td>
</tr>
<tr>
<td>Androgens (males)</td>
<td>Hypogonadism</td>
<td>Sterility, lack of secondary sex characteristics</td>
<td>Adrenogenital syndrome (gynecomastia)</td>
<td>Abnormal production of estrogen, sometimes due to adrenal or interstitial cell tumors; leads to breast enlargement</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Precocious puberty</td>
<td>Premature sexual maturation and related behavioral changes</td>
</tr>
</tbody>
</table>
18-10 Hormone Interactions

• The Hormonal Responses to Stress
  • **General Adaptation Syndrome (GAS)**
    • Also called *stress response*
    • How body responds to stress-causing factors
    • Is divided into three phases
      1. *Alarm phase*
      2. *Resistance phase*
      3. *Exhaustion phase*
During the **alarm phase**, an immediate response to the stress occurs. The sympathetic division of the autonomic nervous system directs this response. In the alarm phase, (1) energy reserves are mobilized, mainly in the form of glucose, and (2) the body prepares to deal with the stress-causing factor by “fight or flight” responses. Epinephrine is the dominant hormone of the alarm phase. Its secretion is part of a generalized sympathetic activation.

### Immediate Short-Term Responses to Crises
- Increased mental alertness
- Increased energy use by all cells
- Mobilization of glycogen and lipid reserves
- Changes in circulation
- Decreased digestive activity and urine production
- Increased sweat gland secretion
- Increased heart rate and respiratory rate
If a stress lasts longer than a few hours, the person enters the **resistance phase** of GAS. Glucocorticoids are the dominant hormones of the resistance phase. Epinephrine, GH, and thyroid hormones are also involved. Energy demands in the resistance phase remain higher than normal, due to the combined effects of these hormones. Neural tissue has a high demand for energy, and requires a reliable supply of glucose. If blood glucose levels fall too low, neural function deteriorates. Glycogen reserves can meet neural demand during the alarm phase, but become depleted after several hours. Hormones of the resistance phase mobilize lipids and amino acids as energy sources to conserve glucose for use by neural tissue.

**Long-Term Metabolic Adjustments**

- Mobilization of remaining energy reserves: Lipids are released by adipose tissue; amino acids are released by skeletal muscle
- Conservation of glucose: Peripheral tissues (except neural) break down lipids to obtain energy
- Elevation of blood glucose concentrations: Liver synthesizes glucose from other carbohydrates, amino acids, and lipids
- Conservation of salts and water, loss of $K^+$ and $H^+$
Exhaustion Phase

The body's lipid reserves are sufficient to maintain the resistance phase for weeks or even months. But when the resistance phase ends, homeostatic regulation breaks down and the exhaustion phase begins. Unless corrective actions are taken almost immediately, the failure of one or more organ systems will prove fatal. The production of aldosterone throughout the resistance phase results in a conservation of Na⁺ at the expense of K⁺. As the body's K⁺ content decreases, a variety of cells begin to malfunction. The underlying problem of the exhaustion phase is the body's inability to sustain the endocrine and metabolic adjustments of the resistance phase.

Collapse of Vital Systems

- Exhaustion of lipid reserves
- Cumulative structural or functional damage to vital organs
- Inability to produce glucocorticoids
- Failure of electrolyte balance
18-10 Hormone Interactions

• The Effects of Hormones on Behavior
  • Hormone changes
    • Can alter intellectual capabilities, memory, learning, and emotional states
    • Affect behavior when endocrine glands are oversecreting or undersecreting
18-10 Hormone Interactions

- Aging and Hormone Production
  - Causes few functional changes
  - Decline in concentration of:
    - Growth hormone
    - Reproductive hormones
Figure 18-21 diagrams the functional relationships between the endocrine system and other body systems we have studied so far.

**SYSTEM INTEGRATOR**

<table>
<thead>
<tr>
<th>Body System</th>
<th>Endocrine System</th>
<th>Body System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Integumentary</td>
<td>Protects superficial endocrine organs; epidermis synthesizes vitamin D</td>
<td>Endocrine System</td>
</tr>
<tr>
<td>Skeletal</td>
<td>Protects endocrine organs, especially in brain, chest, and pelvic cavity</td>
<td></td>
</tr>
<tr>
<td>Muscular</td>
<td>Skeletal muscles provide protection for some endocrine organs</td>
<td></td>
</tr>
<tr>
<td>Nervous</td>
<td>Hypothalamic hormones directly control pituitary secretions and indirectly control secretions of other endocrine organs; controls adrenal medulla; secretes ADH and OXT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sex hormones stimulate sebaceous gland activity, influence hair growth, fat distribution, and apocrine sweat gland activity; PRL stimulates development of mammary glands; adrenal hormones alter dermal blood flow; MSH stimulates melanocyte activity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Skeletal growth regulated by several hormones; calcium mobilization regulated by parathyroid hormone and calcitonin; sex hormones speed growth and closure of epiphyseal cartilages at puberty and help maintain bone mass in adults</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hormones adjust muscle metabolism, energy production, and growth; regulate calcium and phosphate levels in body fluids; speed skeletal muscle growth</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Several hormones affect neural metabolism and brain development; hormones help regulate fluid and electrolyte balance; reproductive hormones influence CNS development and behaviors</td>
<td></td>
</tr>
</tbody>
</table>

**The ENDOCRINE System**

The endocrine system provides long-term regulation and adjustments of homeostatic mechanisms that affect many body functions. For example, the endocrine system regulates fluid and electrolyte balance, cell and tissue metabolism, growth and development, and reproductive functions. It also works with the nervous system in responding to stressful stimuli through the general adaptation syndrome.

Gonads—ovaries in females and testes in males—are organs that produce gametes (sex cells). LH and FSH, hormones secreted by the anterior lobe of the pituitary gland, affect these organs. The ovaries and testes are discussed further in Chapter 28.