Chapter 15  Part B

The Endocrine System

PowerPoint® Lecture Slides
prepared by
Karen Dunbar Kareiva
Ivy Tech Community College
15.7 Thyroid Gland

Location and Structure

- Butterfly-shaped gland in anterior neck on the trachea, just inferior to larynx, that consists of:
  - **Isthmus**: median mass connecting two lateral lobes
  - **Follicles**: hollow sphere of epithelial *follicular cells* that produce glycoprotein *thyroglobulin*
Location and Structure (cont.)

- **Colloid**: fluid of follicle lumen containing thyroglobulin plus iodine and is precursor to thyroid hormone
- **Parafollicular cells**: produce hormone calcitonin
Figure 15.8a The thyroid gland.

(a) Gross anatomy of the thyroid gland, anterior view
Figure 15.8b The thyroid gland.

(b) Photomicrograph of thyroid gland follicles (315×)

Parafollicular cells (secrete calcitonin)
Follicular cells (secrete thyroid hormone)
Colloid-filled follicles
Thyroid Hormone (TH)

• Body’s major metabolic hormone
• Found in two forms
  – $T_4$ (thyroxine): major form that consists of two tyrosine molecules with four bound iodine atoms
  – $T_3$ (triiodothyronine): form that has two tyrosines with three bound iodine atoms
    • Must be converted to $T_4$ at tissue level
• Both are iodine-containing amine hormones
Thyroid Hormone (TH) (cont.)

- TH affects virtually every cell in body
- Enters target cell and binds to intracellular receptors within nucleus
  - Triggers transcription of various metabolic genes
- Effects of thyroid hormone include:
  - Increases basal metabolic rate and heat production
    - Referred to as calorigenic effect
Thyroid Hormone (TH) (cont.)

– Regulates tissue growth and development
  • Critical for normal skeletal and nervous system development and reproductive capabilities

– Maintains blood pressure
  • Increases adrenergic receptors in blood vessels
Thyroid Hormone (TH)

• Synthesis
  – Thyroid gland stores hormone extracellularly in follicle lumen until triggered by TSH to release
  – Seven steps involved in synthesis of TH:
    1. Thyroglobulin is synthesized and discharged into follicle lumen
    2. Iodide is trapped: iodide ions (I⁻) are actively taken into cell and released into lumen
    3. Iodide oxidized: electrons are removed, converting it to iodine (I₂)
Thyroid Hormone (TH) (cont.)

• Synthesis (cont.)
  
  4. Iodine is attached to tyrosine: mediated by peroxidase enzymes
     – **Monoiodotyrosine (MIT)**: formed if only one iodine attaches
     – **Diiodotyrosine (DIT)**: formed if two iodines attach
  
  5. Iodinated tyrosines link together to form $T_3$ and $T_4$
     – If one MIT and one DIT link, $T_3$ is formed
     – If two DITs link, $T_4$ is formed
Thyroid Hormone (TH) (cont.)

• Synthesis (cont.)
  6. Colloid is endocytosed by follicular cells
     – Vesicle is then combined with a lysosome
  7. Lysosomal enzymes cleave $T_3$ and $T_4$ from thyroglobulin
     – Hormones are secreted into bloodstream
     – Mostly $T_4$ secreted, but $T_3$ is also secreted
     – $T_4$ must be converted to $T_3$ at tissue level
Thyroglobulin is synthesized and discharged into the follicle lumen.
Iodide (I<sup>-</sup>) is trapped (actively transported in).

1. Thyroglobulin is synthesized and discharged into the follicle lumen.

2. Iodide (I<sup>-</sup>) is trapped (actively transported in).
Figure 15.9 Synthesis of thyroid hormone.

1. Thyroglobulin is synthesized and discharged into the follicle lumen.
2. Iodide (I\(^{-}\)) is trapped (actively transported in).
3. Iodide is oxidized to iodine.

**Caption:**
- Capillary
- Rough ER
- Golgi apparatus
- Iodide (I\(^{-}\))
- Thyroid follicular cells
- Colloid
- Thyroglobulin
- Colloid in lumen of follicle
Figure 15.9 Synthesis of thyroid hormone.

1. Thyroglobulin is synthesized and discharged into the follicle lumen.
2. Iodide (I) is trapped (actively transported in).
3. Iodide is oxidized to iodine.
4. Iodine is attached to tyrosine in colloid, forming DIT and MIT.

Capillary

Thyroid follicular cells

Thyroid follicular cells

Tyrosines (part of thyroglobulin molecule)

Iodine (I) is trapped (actively transported in).

Thyroglobulin colloid

Colloid in lumen of follicle

Thyroglobulin is synthesized and discharged into the follicle lumen.

Iodide (I) is oxidized to iodine.

Iodine is attached to tyrosine in colloid, forming DIT and MIT.
Figure 15.9 Synthesis of thyroid hormone.

1. Thyroglobulin is synthesized and discharged into the follicle lumen.

2. Iodide (I \textsubscript{1}) is trapped (actively transported in).

3. Iodide is oxidized to iodine.

4. Iodine is attached to tyrosine in colloid, forming DIT and MIT.

5. Iodinated tyrosines are linked together to form T\textsubscript{3} and T\textsubscript{4}.

Capillary

Rough ER

Golgi apparatus

Iodide (I \textsubscript{1})

Tyrosines (part of thyroglobulin molecule)

Iodine

DIT

MIT

Thyroglobulin colloid

Thyroid follicular cells

Colloid

Colloid in lumen of follicle
Figure 15.9 Synthesis of thyroid hormone.

1. Thyroglobulin is synthesized and discharged into the follicle lumen.
2. Iodide (I\(_2\)) is trapped (actively transported in).
3. Iodide is oxidized to iodine.
4. Iodine is attached to tyrosine in colloid, forming DIT and MIT.
5. Iodinated tyrosines are linked together to form T\(_3\) and T\(_4\).
6. Thyroglobulin colloid is endocytosed and combined with a lysosome.

Capillary

Thyroid follicular cells

Colloid

Thyroglobulin colloid

Tyrosines (part of thyroglobulin molecule)

Iodide (I\(_2\)) is trapped (actively transported in).

Iodide

Iodine

DIT

MIT

T\(_4\)

T\(_3\)
Figure 15.9 Synthesis of thyroid hormone.

1. Thyroglobulin is synthesized and discharged into the follicle lumen.
2. Iodide (I) is trapped (actively transported in).
3. Iodide is oxidized to iodine.
4. Iodine is attached to tyrosine in colloid, forming DIT and MIT.
5. Iodinated tyrosines are linked together to form T₃ and T₄.
6. Thyroglobulin colloid is endocytosed and combined with a lysosome.
7. Lysosomal enzymes cleave T₄ and T₃ from thyroglobulin and hormones diffuse into bloodstream.

Thyroid follicular cells

Capillary

Rough ER

Golgi apparatus

Iodide (I)

Colloid

Tyrosines (part of thyroglobulin molecule)

MIT

DIT

Thyroglobulin colloid

To peripheral tissues
Thyroid Hormone (TH) (cont.)

- Transport and regulation
  - $T_4$ and $T_3$ transported by thyroxine-binding globulins (TBGs)
    - Both bind to target receptors, but $T_3$ is 10 times more active than $T_4$
    - Peripheral tissues have enzyme needed to convert $T_4$ to $T_3$
      - Enzyme removes one iodine
Thyroid Hormone (TH) (cont.)

- **Transport and regulation (cont.)**
  
  TH release is regulated by negative feedback
  
  - Falling TH levels stimulate release of *thyroid-stimulating hormone* (*TSH*)
    
    - Rising TH levels provide negative feedback inhibition on TSH
    
    - TSH can also be inhibited by GHIH, dopamine, and increased levels of cortisol and iodide
  
  - Hypothalamic *thyrotropin-releasing hormone* (*TRH*)
    
    can overcome negative feedback during pregnancy or exposure to cold, especially in infants
Figure 15.7 Regulation of thyroid hormone secretion.

- **Hypothalamus**
  - TRH
  - Stimulates

- **Anterior pituitary**
  - TSH
  - Inhibits
  - Stimulates

- **Thyroid gland**
  - Thyroid hormones

- **Target cells**
Table 15.3 Major Effects of Thyroid Hormone ($T_4$ and $T_3$) in the Body

<table>
<thead>
<tr>
<th>PROCESS OR SYSTEM AFFECTED</th>
<th>NORMAL PHYSIOLOGICAL EFFECTS</th>
<th>EFFECTS OF HYPOSECRETION</th>
<th>EFFECTS OF HYPERSECRETION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal metabolic rate (BMR)/</td>
<td>Promotes normal oxygen use and BMR; calorigensis; enhances effects of sympathetic nervous</td>
<td>BMR below normal; decreased body temperature, cold intolerance; decreased appetite; weight gain; reduced sensitivity to catecholamines</td>
<td>BMR above normal; increased body temperature, heat intolerance; increased appetite; weight loss</td>
</tr>
<tr>
<td>temperature regulation</td>
<td>system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbohydrate/lipid/protein</td>
<td>Promotes glucose catabolism; mobilizes fats; essential for protein synthesis; enhances liver's synthesis of cholesterol</td>
<td>Decreased glucose metabolism; elevated cholesterol/triglyceride levels in blood; decreased protein synthesis; edema</td>
<td>Enhanced catabolism of glucose, proteins, and fats; weight loss; loss of muscle mass</td>
</tr>
<tr>
<td>metabolism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervous system</td>
<td>Promotes normal development of nervous system in fetus and infant; promotes normal adult nervous system function</td>
<td>In infant, slowed/deficient brain development, intellectual disability; in adult, mental dulling, depression, paresthesias, memory impairment, hypoactive reflexes</td>
<td>Irritability, restlessness, insomnia, personality changes, exophthalmos (in Graves' disease)</td>
</tr>
<tr>
<td>Cardiovascular system</td>
<td>Promotes normal functioning of the heart</td>
<td>Decreased efficiency of heart's pumping action; low heart rate and blood pressure</td>
<td>Increased sensitivity to catecholamines can lead to rapid heart rate, palpitations, high blood pressure, and ultimately heart failure</td>
</tr>
<tr>
<td>Muscular system</td>
<td>Promotes normal muscular development and function</td>
<td>Sluggish muscle action; muscle cramps; myalgia</td>
<td>Muscle atrophy and weakness</td>
</tr>
<tr>
<td>Skeletal system</td>
<td>Promotes normal growth and maturation of the skeleton</td>
<td>In child, growth retardation, skeletal stunting and retention of child's body proportions; in adult, joint pain</td>
<td>In child, excessive skeletal growth initially, followed by early epiphyseal closure and short stature; in adult, demineralization of skeleton</td>
</tr>
<tr>
<td>Gastrointestinal (GI) system</td>
<td>Promotes normal GI motility and tone; increases secretion of digestive juices</td>
<td>Depressed GI motility, tone, and secretory activity; constipation</td>
<td>Excessive GI motility; diarrhea</td>
</tr>
<tr>
<td>Reproductive system</td>
<td>Promotes normal female reproductive ability and lactation</td>
<td>Depressed ovarian function; sterility; depressed lactation</td>
<td>In females, depressed ovarian function; in males, impotence</td>
</tr>
<tr>
<td>Integumentary system</td>
<td>Promotes normal hydration and secretory activity of skin</td>
<td>Skin pale, thick, and dry; facial edema; hair coarse and thick</td>
<td>Skin flushed, thin, and moist; hair fine and soft; nails soft and thin</td>
</tr>
</tbody>
</table>

© 2017 Pearson Education, Inc.
Clinical – Homeostatic Imbalance 15.4

• Hyposecretion of TH in adults can lead to myxedema
  – Symptoms include low metabolic rate, thick and/or dry skin, puffy eyes, feeling chilled, constipation, edema, mental sluggishness, lethargy
  – If due to lack of iodine, a goiter may develop
    • Lack of iodine decreases TH levels, which triggers increased TSH secretion, triggering thyroid to synthesize more and more unusable thyroglobulin
    • Thyroid enlarges
Hyposecretion in infants leads to **cretinism**

- Symptoms include intellectual disabilities, short and disproportionately sized body, thick tongue and neck
(a) An enlarged thyroid (goiter); due to iodine deficiency
• Hypersecretion of TH: most common type is **Graves’ disease**
  – Autoimmune disease: body makes abnormal antibodies directed against thyroid follicular cells
  – Antibodies mimic TSH, stimulating TH release
  – Symptoms include elevated metabolic rate, sweating, rapid and irregular heartbeats, nervousness, and weight loss despite adequate food
  • **Exophthalmos** may result: eyes protrude as tissue behind eyes becomes edematous and fibrous
• Hypersecretion of TH: most common type is **Graves’ disease (cont.)**
  – Treatments include surgical removal of thyroid or radioactive iodine to destroy active thyroid cells
(b) Bulging eyes (exophthalmos) of Graves’ disease
Calcitonin

- Produced by **parafollicular (C) cells** in response to high Ca\(^{2+}\) levels
- Antagonist to parathyroid hormone (PTH)
- No known physiological role in humans at normal physiological levels, but at higher-than-normal doses:
  - Inhibits osteoclast activity and prevents release of Ca\(^{2+}\) from bone matrix
  - Stimulates Ca\(^{2+}\) uptake and incorporation into bone matrix
Figure 15.8b The thyroid gland.

(b) Photomicrograph of thyroid gland follicles (315×)

- Parafollicular cells (secrete calcitonin)
- Follicular cells (secrete thyroid hormone)
- Colloid-filled follicles
15.8 Parathyroid Gland

• Four to eight tiny yellow-brown glands embedded in posterior aspect of thyroid

• Contain oxyphil cells (function not clear) and parathyroid cells that secrete parathyroid hormone (PTH), or parathormone

• PTH is most important hormone in Ca^{2+} homeostasis
  – Secreted in response to low blood levels of Ca^{2+}
  – Inhibited by rising levels of Ca^{2+}

• Target organs are skeleton, kidneys, and intestine
Figure 15.11 The parathyroid glands.

- Pharynx (posterior aspect)
- Thyroid gland
- Esophagus
- Trachea
- Parathyroid glands
- Capillary
- Parathyroid cells (secrete parathyroid hormone)
- Oxyphil cells
15.8 Parathyroid Gland

• Functions to:
  – Stimulate osteoclasts to digest bone matrix and release Ca\(^{2+}\) to blood
  – Enhances reabsorption of Ca\(^{2+}\) and secretion of phosphate (PO\(_4^{3-}\)) by kidneys
  – Promotes activation of vitamin D by kidneys, which leads to increased absorption of Ca\(^{2+}\) by intestinal mucosa
Figure 15.12 Effects of parathyroid hormone on bone, the kidneys, and the intestine.

Hypocalcemia (low blood Ca^{2+})

↑PTH release from parathyroid gland

↑Osteoclast activity in bone causes Ca^{2+} and PO_{4}^{3-} release into blood

↑Ca^{2+} reabsorption in kidney tubule

↑Activation of vitamin D by kidney

↑Ca^{2+} absorption from food in small intestine

↑Ca^{2+} in blood
• **Hyperparathyroidism** due to parathyroid gland tumor
  – Calcium leaches from bones, causing them to soften and deform
  – Elevated $\text{Ca}^{2+}$ depresses nervous system and contributes to formation of kidney stones
  – *Osteitis fibrosa cystica*: severe form resulting in easily fractured bones
Clinical – Homeostatic Imbalance 15.5

• **Hypoparathyroidism** following gland trauma or removal can cause hypocalcemia
  – Results in tetany, respiratory paralysis, and death
15.9 Adrenal Gland

- Paired, pyramid-shaped organs atop kidneys
  - Also referred to as suprarenal glands
- Structurally and functionally it is two glands in one
  - **Adrenal cortex**: three layers of glandular tissue that synthesize and secrete several different hormones
  - **Adrenal medulla**: nervous tissue that is part of sympathetic nervous system
Adrenal Cortex

- This area of adrenal gland produces over 24 different hormones collectively called **corticosteroids**
- Steroid hormones are not stored in cells
  - Rate of release depends on rate of synthesis
- Three layers of cortical cells produce the different corticosteroids
  - **Zona glomerulosa**—Mineralocorticoids
  - **Zona fasciculata**—Glucocorticoids
  - **Zona reticularis**—Gonadocorticoids
Figure 15.13 Microscopic structure of the adrenal gland.

Adrenal gland
- Medulla
- Cortex

Kidney

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

(b) Photomicrograph (115×)

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

Capsule
Zona glomerulosa
Zona fasciculata
Zona reticularis
Adrenal medulla
Mineralocorticoids

- Regulate electrolyte concentrations (primarily Na\(^+\) and K\(^+\)) in ECF
  - Importance of Na\(^+\): affects ECF volume, blood volume, blood pressure, and levels of other ions (K\(^+\), H\(^+\), HCO\(_3\)^\(-\) and Cl\(^-\))
  - Importance of K\(^+\): sets resting membrane potential of cells
- **Aldosterone**: most potent mineralocorticoid
  - Stimulates Na\(^+\) reabsorption by kidneys
    - Results in increased blood volume and blood pressure
  - Stimulates K\(^+\) elimination by kidneys
Mineralocorticoids (cont.)

- Effects of aldosterone are short lived
- Stimulates synthesis and activation of Na\(^+\)-K\(^+\) ATPase transport pumps
  - Pump exchanges Na\(^+\) for K\(^+\)
- Factors that regulate aldosterone secretion:
  - Renin-angiotensin-aldosterone mechanism
  - Plasma concentration of K\(^+\)
  - ACTH
  - Atrial natriuretic peptide
Mineralocorticoids (cont.)

- Renin-angiotensin-aldosterone mechanism
  1. Decreased blood pressure stimulates special cells in kidneys
  2. These cells release renin into blood
  3. Renin cleaves off part of plasma protein, **angiotensinogen**, that triggers enzyme cascade, resulting in conversion to angiotensin II
     - Angiotensin II is a potent stimulator of aldosterone release
Adrenal Cortex (cont.)

• Mineralocorticoids (cont.)
  – Plasma concentration of $K^+$
    • Increased $K^+$ directly influences zona glomerulosa cells to release aldosterone
      – Increased $K^+$ directly stimulates aldosterone release; low levels inhibit it
  – ACTH
    • Can cause small increases of aldosterone during periods of increased stress
  – Atrial natriuretic peptide (ANP)
    • Secreted by heart in response to high blood pressure
    • Blocks renin and aldosterone secretion to decrease blood pressure
Figure 15.14 Major mechanisms controlling aldosterone release.

<table>
<thead>
<tr>
<th>Primary regulators</th>
<th>Other factors</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Renin-angiotensin-aldosterone mechanism</strong></td>
<td><strong>Adrenocorticotropin hormone (ACTH)</strong></td>
</tr>
<tr>
<td>- Blood volume and/or blood pressure</td>
<td>- Stress</td>
</tr>
<tr>
<td>- Renin</td>
<td>- Blood pressure and/or blood volume</td>
</tr>
<tr>
<td>- Angiotensin II</td>
<td>- Hypothalamus</td>
</tr>
<tr>
<td>- Direct stimulating effect</td>
<td>- CRH</td>
</tr>
<tr>
<td>- Initiates cascade that produces Angiotensin II</td>
<td>- Anterior pituitary</td>
</tr>
<tr>
<td></td>
<td>- Atrial natriuretic peptide (ANP)</td>
</tr>
</tbody>
</table>

**Adrenal cortex** (zona glomerulosa)

- Targets kidney tubules
- Enhanced secretion of aldosterone
- Absorption of Na⁺ and water; increased K⁺ excretion
- Blood volume and/or blood pressure
Clinical – Homeostatic Imbalance 15.6

• **Aldosteronism**: hypersecretion usually due to adrenal tumors

• Results in two major problems:
  1. Hypertension and edema due to excessive Na$^+$
  2. Excretion of K$^+$, leading to abnormal nonresponsive neurons and muscle
Adrenal Cortex (cont.)

• **Glucocorticoids**
  – Influence metabolism of most cells and help us resist stressors
  – Keep blood glucose levels relatively constant
  – Maintain blood pressure by increasing action of vasoconstrictors
  – Glucocorticoid hormones include:
    • **Cortisol** *(hydrocortisone)*; only glucocorticoid in significant amounts in humans
    • Cortisone
    • Corticosterone
Adrenal Cortex (cont.)

– Regulation of secretion

• Cortisol is released in response to ACTH
  – ACTH released in response to corticotropin-releasing hormone (CRH)
  – CRH released in response to low cortisol levels
  – Increased cortisol levels inhibit ACTH and CRH through negative feedback

• Cortisol secretion cycles are governed by patterns of eating and activity

• Acute stress (infection, physical or emotional trauma) interrupts cortisol rhythm

• CNS can override cortisol inhibition of ACTH and CRH, leading to more cortisol secretion
Adrenal Cortex (cont.)

– **Actions**

- Cortisol causes increase in blood levels of glucose, fatty acids, and amino acids
- Prime metabolic effect is *gluconeogenesis*, formation of glucose from fats and proteins
  - Encourages cells to use fatty acids for fuel so glucose is “saved” for brain
- Other function is to enhance vasoconstriction
  - Causes rise in blood pressure to quickly distribute nutrients to cells
Adrenal Cortex (cont.)

– Actions (cont.)

• Excessive levels of glucocorticoids:
  – Depress cartilage and bone formation
  – Inhibit inflammation by decreasing release of inflammatory chemicals
  – Depress immune system
  – Disrupt normal cardiovascular, neural, and gastrointestinal functions

• Glucocorticoid drugs can control symptoms of many inflammatory diseases (arthritis, allergies) but can also cause undesirable effects
• Hypersecretion—Cushing’s syndrome/disease
  – Depresses cartilage/bone formation and immune system; inhibits inflammation; disrupts neural, cardiovascular, and gastrointestinal function
  – Causes: tumor on pituitary, lungs, pancreas, kidney, or adrenal cortex; overuse of corticosteroids
  – Cushingoid signs: “moon” face and “buffalo hump”
  – Treatment: removal of tumor, discontinuation of drugs
Clinical – Homeostatic Imbalance 15.7

• **Hyposecretion—Addison’s disease**
  – Also involves deficits in mineralocorticoids
  – Decrease in glucose and Na\(^+\) levels
  – Weight loss, severe dehydration, and hypotension
  – Treatment: corticosteroid replacement therapy
Figure 15.15 The effects of excess glucocorticoid.

(a) Patient before onset  
(b) Same patient with Cushing’s syndrome. The white arrow shows the characteristic “buffalo hump” of fat on the upper back.
Adrenal Cortex (cont.)

• **Gonadocorticoids (adrenal sex hormone)**
  – Weak androgens (male sex hormones) converted to *testosterone* in tissue cells, some to estrogens
    • Example: *androstenedione* and *dehydroepiandrosterone* (DHEA)
  – May contribute to:
    • Onset of puberty and appearance of secondary sex characteristics
    • Sex drive in women
    • Source of estrogens in postmenopausal women
Clinical – Homeostatic Imbalance 15.8

• Hypersecretion
  – **Adrenogenital syndrome** (masculinization)
  – Not noticeable in adult males
    • Already masculinized with testosterone, so no effect
  – Females and prepubertal males
    • Boys: reproductive organs mature; secondary sex characteristics emerge early
    • Females: beard, masculine pattern of body hair; clitoris resembles small penis
Adrenal Medulla

- **Medullary chromaffin cells** synthesize *catecholamines* **epinephrine** (80%) and **norepinephrine** (20%)

- Effects of catecholamines:
  - Vasoconstriction
  - Increased heart rate
  - Increased blood glucose levels
  - Blood diverted to brain, heart, and skeletal muscle
Both hormones have basically same effects, but:

- Epinephrine is more a stimulator of metabolic activities
  - Example: bronchial dilation, and blood flow to skeletal muscles and heart
- Norepinephrine has more of an influence on peripheral vasoconstriction and blood pressure

Responses to stressors are brief, unlike adrenal cortical hormones
Figure 15.16 Stress and the adrenal gland.

**Short-term stress**

- Nerve impulses from the spinal cord to the hypothalamus
- Hypothalamus secretes CRH (corticotropin-releasing hormone)
- CRH travels to the anterior pituitary to release ACTH
- ACTH stimulates the adrenal cortex to secrete steroid hormones
- Adrenal medulla secretes norepinephrine and epinephrine (catecholamines)

**Short-term stress response**
- Heart rate increases
- Blood pressure increases
- Bronchioles dilate
- Liver converts glycogen to glucose and releases glucose to blood
- Blood flow changes, reducing digestive system activity and urine output
- Metabolic rate increases

**Long-term stress response**
- Kidneys retain sodium and water
- Blood volume and blood pressure rise
- Proteins and fats converted to glucose or broken down for energy
- Blood glucose increases
- Immune system suppressed

**Prolonged stress**

- Corticotrophic cells of the anterior pituitary
- To target via blood
- Adrenal cortex secretes mineralocorticoids and glucocorticoids
• **Hyposcercetion**
  – Epinephrine and norepinephrine are not essential to life; therefore there are no problems associated with hyposcercetion

• **Hypersecretion**
  – Leads to symptoms of uncontrolled sympathetic nervous system, such as:
    • Hyperglycemia, increased metabolic rate, rapid heartbeat, palpitations, hypertension, intense nervousness, and sweating
  – Can be due to *pheochromocytoma*, tumor of medullary chromaffin cells
<table>
<thead>
<tr>
<th>HORMONE</th>
<th>REGULATION OF RELEASE</th>
<th>TARGET ORGAN AND EFFECTS</th>
<th>EFFECTS OF HYPERSECRETION AND HYPOSECRETION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenocortical Hormones</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mineralocorticoids (chiefly aldosterone)</td>
<td><strong>Stimulated</strong> by renin-angiotensin-aldosterone mechanism (activated by decreasing blood volume or blood pressure), elevated blood K⁺ levels, and ACTH (minor influence)</td>
<td>Kidneys: increase blood levels of Na⁺ and decrease blood levels of K⁺; since water reabsorption usually accompanies sodium retention, blood volume and blood pressure rise</td>
<td>↑ Aldosteronism, ↓ Addison's disease</td>
</tr>
<tr>
<td>Glucocorticoids (chiefly cortisol)</td>
<td><strong>Stimulated</strong> by ACTH, <strong>Inhibited</strong> by feedback inhibition exerted by cortisol</td>
<td>Body cells: promote gluconeogenesis and hyperglycemia; mobilize fats for energy metabolism; stimulate protein catabolism; assist body to resist stressors; depress inflammatory and immune responses</td>
<td>↑ Cushing's syndrome, ↓ Addison's disease</td>
</tr>
<tr>
<td>Gonadocorticoids (chiefly androgens, converted to testosterone or estrogens after release)</td>
<td><strong>Stimulated</strong> by ACTH; mechanism of inhibition incompletely understood, but feedback inhibition not seen</td>
<td>Insignificant effects in males; contributes to female libido; development of pubic and axillary hair in females; source of estrogens after menopause</td>
<td>↑ Masculinization of females (adrenogenital syndrome), ↓ No effects known</td>
</tr>
<tr>
<td>Adrenal Medullary Hormones</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catecholamines (epinephrine and norepinephrine)</td>
<td><strong>Stimulated</strong> by preganglionic fibers of the sympathetic nervous system</td>
<td>Sympathetic nervous system target organs: effects mimic sympathetic nervous system activation; increase heart rate and metabolic rate; increase blood pressure by promoting vasoconstriction</td>
<td>↑ Prolonged fight-or-flight response; hypertension, ↓ Unimportant</td>
</tr>
</tbody>
</table>
15.10 Pineal Gland

- Small gland hanging from roof of third ventricle
- **Pinealocytes** secrete **melatonin**, derived from serotonin
- Melatonin may affect:
  - Timing of sexual maturation and puberty
  - Day/night cycles
  - Physiological processes that show rhythmic variations (body temperature, sleep, appetite)
  - Production of antioxidant and detoxification molecules in cells
Figure 15.1 Location of selected endocrine organs of the body.

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

- Triangular gland located partially behind stomach
- Has both exocrine and endocrine cells
  - **Acinar cells** (exocrine) produce enzyme-rich juice for digestion
  - **Pancreatic islets (islets of Langerhans)** contain endocrine cells
    - **Alpha (α) cells** produce **glucagon** (hyperglycemic hormone)
    - **Beta (β) cells** produce **insulin** (hypoglycemic hormone)
Figure 15.17 Photomicrograph of differentially stained pancreatic tissue.

Pancreatic islet

- $\alpha$ (Glucagon-producing) cells
- $\beta$ (Insulin-producing) cells

Pancreatic acinar cells (exocrine)
Glucagon

- Extremely potent hyperglycemic agent
  - Triggered by decreased blood glucose levels, rising amino acid levels, or sympathetic nervous system
- Raises blood glucose levels by targeting liver to:
  - Break down glycogen into glucose
    - *Glycogenolysis*
  - Synthesize glucose from lactic acid and other noncarbohyrades
    - *Gluconeogenesis*
  - Release glucose into blood
Other Endocrine Organs

• Insulin
  – Secreted when blood glucose levels increase
  – Synthesized as proinsulin that is then modified
  – Insulin lowers blood glucose levels in three ways:
    • Enhances membrane transport of glucose into fat and muscle cells
    • Inhibits breakdown of glycogen to glucose
    • Inhibits conversion of amino acids or fats to glucose
15.11 Other Endocrine Organs

- Insulin (cont.)
  - Not needed for glucose uptake in liver, kidney, or brain
  - Plays a role in neuronal development, learning, and memory
  - Binding to tyrosine kinase enzyme receptor triggers cell to increase glucose uptake
  - Insulin also triggers cells to:
    - Catalyze oxidation of glucose for ATP production: first priority
    - Polymerize glucose to form glycogen
    - Convert glucose to fat (particularly in adipose tissue)
• Insulin (cont.)
  – Factors that influence insulin release
    • Elevated blood glucose levels: primary stimulus
    • Rising blood levels of amino acids and fatty acids
    • Release of acetylcholine by parasympathetic nerve fibers
    • Hormones glucagon, epinephrine, growth hormone, thyroxine, glucocorticoids
    • Somatostatin and sympathetic nervous system inhibit insulin release
Figure 15.18 Insulin and glucagon from the pancreas regulate blood glucose levels.

- Insulin stimulates glucose uptake by cells, which stimulates glycogen formation.
- Blood glucose falls to normal range.

- Pancreas secretes glucagon, which stimulates glycogen breakdown.
- Blood glucose rises to normal range.

**Stimulus**

- ↑ Blood glucose level
- ↓ Blood glucose level

**Balance:** Normal blood glucose level (about 90 mg/100 ml)
• Diabetes mellitus (DM) can be due to:
  – Hyposcretion of insulin: Type 1
  – Hypoactivity of insulin: Type 2
  – When blood glucose levels remain high, person feels nauseated, leading to sympathetic response
    • Fight-or-flight response acts to further increase blood glucose levels
  – Glycosuria: excess glucose is spilled into urine
Three cardinal signs of DM:

- **Polyuria**: huge urine output
  - Glucose acts as osmotic diuretic
- **Polydipsia**: excessive thirst
  - From water loss due to polyuria
- **Polyphagia**: excessive hunger and food consumption
  - Cells cannot take up glucose and are “starving”
– When sugars cannot be used as fuel, as in DM, fats are used, causing *lipidemia*: high levels of fatty acids in blood

– Fatty acid metabolism results in formation of **ketones (ketone bodies)**

– Ketones are acidic, and their build-up in blood can cause **ketoacidosis**
  • Also causes *ketonuria*: ketone bodies in urine

– Untreated ketoacidosis causes hyperpnea, disrupted heart activity and $O_2$ transport, and severe depression of nervous system that can possibly lead to coma and death
• Hyperinsulinism
  – Excessive insulin secretion
  – Causes hypoglycemia: low blood glucose levels
  – Symptoms: anxiety, nervousness, disorientation, unconsciousness, even death
  – Treatment: sugar ingestion
Figure 15.19 Consequences of insulin deficit (diabetes mellitus).

- **Blood**
  - All tissues
  - Liver breaks down glycogen to glucose (gluconeogenesis)
  - Skeletal muscle breaks down proteins
  - Adipocytes break down fat (lipolysis)
  - Liver converts fats to ketone bodies
  - Liver converts amino acids to glucose

- **Blood glucose** (hyperglycemia)

- **Urine**
  - Glucose in urine (glycosuria)
  - Glucose “pulls” water into kidney tubules
  - Osmotic diuresis
  - Ketones in urine (ketonuria)
  - Ketones “pull” cations into kidney tubules
  - Loss of Na⁺, K⁺, H⁺ in urine

- **Signs and symptoms**
  - **Polyuria** (↑ Urine output)
  - Dehydration
  - **Polydipsia** (↑ Water intake)
  - **Polyphagia** (↑ Appetite)
  - Heart rhythm abnormalities
  - Nausea, vomiting, abdominal pain
  - Central nervous system depression, coma
  - Acetone breath
  - ↑ Rate and depth of breathing
BioFlix Video: Homeostasis

BioFlix®
Homeostasis: Regulating Blood Sugar
The Gonads and Placenta

- Gonads produce same steroid sex hormones as those of adrenal cortex, just lesser amounts
- Ovaries produce **estrogens** and **progesterone**
  - Estrogen
    - Maturation of reproductive organs
    - Appearance of secondary sexual characteristics
    - With progesterone, causes breast development and cyclic changes in uterine mucosa
The Gonads and Placenta (cont.)

• Testes produce **testosterone**
  – Initiates maturation of male reproductive organs
  – Causes appearance of male secondary sexual characteristics and sex drive
  – Necessary for normal sperm production
  – Maintains reproductive organs in functional state

• **Placenta** secretes estrogens, progesterone, and human chorionic gonadotropin (hCG)
Hormone Secretion by Other Organs

• **Adipose tissue**
  – Adipose cells release:
    • **Leptin**: appetite control; stimulates increased energy expenditure
    • **Resistin**: insulin antagonist
    • **Adiponectin**: enhances sensitivity to insulin
Hormone Secretion by Other Organs (cont.)

• Gastrointestinal tract
  – Enteroendocrine cells secrete these hormones:
    • **Gastrin** stimulates release of HCl
    • **Ghrelin** from stomach stimulates food intake
    • **Secretin** stimulates liver and pancreas
    • **Cholecystokinin (CCK)** activates pancreas, gallbladder, and hepatopancreatic sphincter
    • **Incretins** enhance insulin release and inhibit glucagon
Hormone Secretion by Other Organs (cont.)

• Heart
  – Atrial natriuretic peptide (ANP) decreases blood Na\(^+\) concentration, therefore blood pressure and blood volume

• Kidneys
  – Erythropoietin signals production of red blood cells
  – Renin initiates the renin-angiotensin-aldosterone mechanism
Hormone Secretion by Other Organs (cont.)

• **Skeleton**
  – Osteoblasts in bone secrete **osteocalcin**
    • Prods pancreas to secrete more insulin; restricts fat storage; improves glucose handling; reduces body fat
    • Activated by insulin
    • Low levels of osteocalcin are present in type 2 diabetes: perhaps increasing levels may be new treatment
Hormone Secretion by Other Organs (cont.)

• Skin
  – **Cholecalciferol**, precursor of vitamin D
  – **Calcitriol**: active form of vitamin D that helps absorb calcium from intestine
  – Also modulates immunity, decreases inflammation, and may act as anticancer agent
Hormone Secretion by Other Organs (cont.)

• **Thymus**
  – Large in infants and children; shrinks with age
  – *Thymulin, thymopoietins, and thymosins* may be involved in normal development of T lymphocytes in immune response
  • Classified as hormones but act as paracrines