The Endocrine System
Imagine that you are in a clinic examining a 12-year-old female patient. Her parents are concerned about her excessive facial hair and the deepening of her voice. Further conversation with the parents brings out the fact that the girl started developing pubic hair at age 7 years. Examination of the patient confirmed the parents’ observations, plus showed that the girl was well above average height for her age. She also has unusually large amounts of acne on her face and the back of her neck. A vaginal tract examination indicates swelling of her external genitals. The girl started losing weight rapidly last year, and leg and thigh muscles became well developed. This was attributed to the girl starting intensive gymnastics practices for an upcoming competition. Everything else about the girl appears normal.
Case Study Investigation (cont.)

By reading this chapter, you will eventually conclude that this girl’s conditions are due to an abnormality of the endocrine system. It is the job of the examiner to determine what part of the endocrine system is being affected and figure out what is causing the abnormality. At the end of this chapter, you will be asked to determine the possible problem that is causing this set of conditions.
The Endocrine System

- Second-messenger system of the body
- Uses chemical messengers (hormones) that are released into the blood
- Hormones control several major processes
  - Reproduction
  - Growth and development
  - Mobilization of body defenses
  - Maintenance of much of homeostasis
  - Regulation of metabolism
Hormone Overview

- Hormones are produced by specialized cells
- Cells secrete hormones into extracellular fluids
- Blood transfers hormones to target sites
- These hormones regulate the activity of other cells
The Chemistry of Hormones

- Hormones are classified chemically as
  - Amino acid–based, which includes
    - Proteins
    - Peptides
    - Amines
  - Steroids—made from cholesterol
  - Prostaglandins—made from highly active lipids
Mechanisms of Hormone Action

- Hormones affect only certain tissues or organs (target cells or target organs)
- Target cells must have specific protein receptors
- Hormone-binding alters cellular activity
Effects Caused by Hormones

- Changes in plasma membrane permeability or electrical state
- Synthesis of proteins, such as enzymes
- Activation or inactivation of enzymes
- Stimulation of mitosis
- Promotion of secretory activity
The Chemistry of Hormones

- Two mechanisms in which hormones act
  - Direct gene activation
  - Second-messenger system
Direct Gene Activation
(Steroid Hormone Action)

- Diffuse through the plasma membrane of target cells
- Enter the nucleus
- Bind to a specific protein within the nucleus
- Bind to specific sites on the cell’s DNA
- Activate genes that result in synthesis of new proteins
Figure 9.1a

Steroid hormone

1. Cytoplasm
2. Receptor protein
3. Hormone-receptor complex
4. DNA
5. mRNA
6. New protein

Plasma membrane of target cell

Nucleus
Figure 9.1a, step 1

1. Steroid hormone enters the cell through the plasma membrane of the target cell.

Nucleus
Cytoplasm
Plasma membrane of target cell
Steroid hormone

Cytoplasm

Nucleus

Plasma membrane of target cell
Figure 9.1a, step 3

Steroid hormone

Cytoplasm

Nucleus

Receptor protein

Hormone-receptor complex

Plasma membrane of target cell
Steroid hormone

Cytoplasm

Nucleus

Receptor protein

Hormone-receptor complex

DNA

Plasma membrane of target cell

Figure 9.1a, step 4
Figure 9.1a, step 5

1. Steroid hormone enters the cell
2. Steroid hormone-receptor complex forms in the cytoplasm
3. Steroid hormone-receptor complex enters the nucleus
4. Steroid hormone-receptor complex binds to DNA
5. Steroid hormone-receptor complex activates gene expression, resulting in the production of mRNA

Plasma membrane of target cell

Cytoplasm

Nucleus

Receptor protein

Hormone-receptor complex

DNA

mRNA
Figure 9.1a, step 6

1. Steroid hormone

2. Cytoplasm

3. Nucleus

4. Receptor protein

5. Hormone-receptor complex

6. DNA

7. mRNA

8. New protein

9. Plasma membrane of target cell
Second-Messenger System (Nonsteroid Hormone Action)

- Hormone binds to a membrane receptor
- Hormone does not enter the cell
- Sets off a series of reactions that activates an enzyme
- Catalyzes a reaction that produces a second-messenger molecule
- Oversees additional intracellular changes to promote a specific response
Nonsteroid hormone (first messenger)

Enzyme

Receptor protein

Plasma membrane of target cell

Cytoplasm

ATP

cAMP

Second messenger

Effect on cellular function, such as glycogen breakdown

Figure 9.1b
Nonsteroid hormone (first messenger)

Receptor protein

Plasma membrane of target cell

Cytoplasm

Figure 9.1b, step 1
Nonsteroid hormone (first messenger)

Cytoplasm

Enzyme

Receptor protein

Plasma membrane of target cell

Figure 9.1b, step 2
Figure 9.1b, step 3

Nonsteroid hormone (first messenger)

Enzyme

ATP

cAMP

Second messenger

Plasma membrane of target cell

Receptor protein

Cytoplasm
Cytoplasm

Nonsteroid hormone (first messenger)

Receptor protein

Plasma membrane of target cell

Enzyme

ATP

Second messenger

cAMP

Effect on cellular function, such as glycogen breakdown
# Major Endocrine Glands and Hormones

## Table 9.1

<table>
<thead>
<tr>
<th>Gland</th>
<th>Hormone</th>
<th>Chemical class</th>
<th>Representative actions</th>
<th>Regulated by</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pineal body</td>
<td>Melatonin</td>
<td>Amine</td>
<td>Involved in biological rhythms (daily and seasonal)</td>
<td>Light/dark cycles</td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>Hormones released by the posterior pituitary; releasing and inhibiting hormones that regulate the anterior pituitary (see below)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pituitary gland</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Posterior lobe</td>
<td>Oxytocin</td>
<td>Peptide</td>
<td>Stimulates contraction of uterus and the milk “let-down” reflex</td>
<td>Nervous system (hypothalamus) in response to uterine stretching and/or suckling of a baby</td>
</tr>
<tr>
<td>(releases hormones made by the hypothalamus)</td>
<td>Antidiuretic hormone (ADH)</td>
<td>Peptide</td>
<td>Promotes retention of water by kidneys</td>
<td>Hypothalamus in response to water/salt imbalance</td>
</tr>
</tbody>
</table>

Table 9.1 (1 of 4)
### Table 9.1 (2 of 4)

<table>
<thead>
<tr>
<th>Gland</th>
<th>Hormone</th>
<th>Chemical class</th>
<th>Representative actions</th>
<th>Regulated by</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior lobe</td>
<td>Growth hormone (GHI)</td>
<td>Protein</td>
<td>Stimulates growth (especially of bones and muscles) and metabolism</td>
<td>Hypothalamic releasing and inhibiting hormones</td>
</tr>
<tr>
<td></td>
<td>Prolactin (PRL)</td>
<td>Protein</td>
<td>Stimulates milk production</td>
<td>Hypothalamic hormones</td>
</tr>
<tr>
<td></td>
<td>Follicle-stimulating hormone (FSH)</td>
<td>Protein</td>
<td>Stimulates production of ova and sperm</td>
<td>Hypothalamic hormones</td>
</tr>
<tr>
<td></td>
<td>Luteinizing hormone (LH)</td>
<td>Protein</td>
<td>Stimulates ovaries and testes</td>
<td>Hypothalamic hormones</td>
</tr>
<tr>
<td></td>
<td>Thyroid-stimulating hormone (TSH)</td>
<td>Protein</td>
<td>Stimulates thyroid gland</td>
<td>Thyroxine in blood; hypothalamic hormones</td>
</tr>
<tr>
<td></td>
<td>Adrenocorticotropic hormone (ACTH)</td>
<td>Protein</td>
<td>Stimulates adrenal cortex to secrete glucocorticoids</td>
<td>Glucocorticoids; hypothalamic hormones</td>
</tr>
<tr>
<td>Thyroid gland</td>
<td>Thyroxine ($T_4$) and triiodothyronine ($T_3$)</td>
<td>Amine</td>
<td>Stimulates metabolism</td>
<td>TSH</td>
</tr>
</tbody>
</table>

Table 9.1 (2 of 4)
# Major Endocrine Glands and Hormones

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<th>Hormone</th>
<th>Chemical class</th>
<th>Representative actions</th>
<th>Regulated by</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid gland</td>
<td>Calcitonin</td>
<td>Peptide</td>
<td>Reduces blood calcium level</td>
<td>Calcium level in blood</td>
</tr>
<tr>
<td>Parathyroid glands</td>
<td>Parathyroid hormone (PTH)</td>
<td>Peptide</td>
<td>Raises blood calcium level</td>
<td>Calcium level in blood</td>
</tr>
<tr>
<td>Thymus gland</td>
<td>Thymosin</td>
<td>Peptide</td>
<td>“Programs” T lymphocytes</td>
<td>Not known</td>
</tr>
<tr>
<td>Adrenal glands</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrenal medulla</td>
<td>Epinephrine and norepinephrine</td>
<td>Amines</td>
<td>Raise blood glucose level; increase rate of metabolism; constrict certain blood vessels</td>
<td>Nervous system (sympathetic division)</td>
</tr>
<tr>
<td>Adrenal cortex</td>
<td>Glucocorticoids</td>
<td>Steroids</td>
<td>Increase blood glucose</td>
<td>ACTH</td>
</tr>
<tr>
<td></td>
<td>Mineralocorticoids</td>
<td>Steroids</td>
<td>Promote reabsorption of Na(^{+}) and excretion of K(^{+}) in kidneys</td>
<td>Changes in blood volume or blood pressure; K(^{+}) (potassium) or Na(^{+}) levels in blood</td>
</tr>
</tbody>
</table>

Table 9.1 (3 of 4)
### Table 9.1: Major Endocrine Glands and Some of Their Hormones (continued)

<table>
<thead>
<tr>
<th>Gland</th>
<th>Hormone</th>
<th>Chemical class</th>
<th>Representative actions</th>
<th>Regulated by</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreas</td>
<td>Insulin</td>
<td>Protein</td>
<td>Reduces blood glucose</td>
<td>Glucose level in blood</td>
</tr>
<tr>
<td></td>
<td>Glucagon</td>
<td>Protein</td>
<td>Raises blood glucose</td>
<td>Glucose level in blood</td>
</tr>
<tr>
<td>Gonads</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Testes</td>
<td>Androgens</td>
<td>Steroids</td>
<td>Support sperm formation; development and maintenance of male secondary sex characteristics</td>
<td>FSH and LH</td>
</tr>
<tr>
<td>• Ovaries</td>
<td>Estrogens</td>
<td>Steroids</td>
<td>Stimulate uterine lining growth; development and maintenance of female secondary sex characteristics</td>
<td>FSH and LH</td>
</tr>
<tr>
<td></td>
<td>Progesterone</td>
<td>Steroids</td>
<td>Promotes growth of uterine lining</td>
<td>FSH and LH</td>
</tr>
</tbody>
</table>
Control of Hormone Release

- Hormone levels in the blood are mostly maintained by negative feedback
- A stimulus or low hormone levels in the blood triggers the release of more hormone
- Hormone release stops once an appropriate level in the blood is reached
Hormonal Stimuli of Endocrine Glands

- Most common stimuli
- Endocrine glands are activated by other hormones

**Examples:**
- Anterior pituitary hormones
Hormonal Stimuli of Endocrine Glands

1. The hypothalamus secretes hormones that...

2. ...stimulate the anterior pituitary gland to secrete hormones that...

3. ...stimulate other endocrine glands to secrete hormones (a) Hormonal

Figure 9.2a
Humoral Stimuli of Endocrine Glands

- Changing blood levels of certain ions stimulate hormone release

- *Humoral* indicates various body fluids such as blood and bile

- **Examples:**
  - Parathyroid hormone
  - Calcitonin
  - Insulin
Humoral Stimuli of Endocrine Glands

Figure 9.2b

① Capillary blood contains low concentration of Ca^{2+}, which stimulates...

Capillary (low Ca^{2+} in blood)

Thyroid gland (posterior view)

Parathyroid glands

② ...secretion of parathyroid hormone (PTH) by parathyroid glands

(b) Humoral
Neural Stimuli of Endocrine Glands

- Nerve impulses stimulate hormone release
- Most are under the control of the sympathetic nervous system
- Examples include the release of norepinephrine and epinephrine by the adrenal medulla
Neural Stimuli of Endocrine Glands

1. Preganglionic SNS fiber stimulates adrenal medulla cells...

2. ...to secrete catecholamines
(c) Neural

Figure 9.2c
Major Endocrine Organs

- Pituitary gland
- Thyroid gland
- Parathyroid glands
- Adrenal glands
- Pineal gland
- Thymus gland
- Pancreas
- Gonads (Ovaries and Testes)
- Hypothalamus
Location of Major Endocrine Organs

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

Figure 9.3
Pituitary Gland

- Size of a pea
- Hangs by a stalk from the hypothalamus in the brain
- Protected by the sphenoid bone
- Has two functional lobes
  - Anterior pituitary—glandular tissue
  - Posterior pituitary—nervous tissue
- Often called the “master endocrine gland”
Hormones of the Anterior Pituitary

- Six anterior pituitary hormones
  - Two affect non-endocrine targets
    - Growth hormone
    - Prolactin
  - Four stimulate other endocrine glands (tropic hormones)
    - Thyroid-stimulating hormone (thyrotropic hormone)
    - Adrenocorticotropic hormone
    - Two gonadotropic hormones
Hormones of the Anterior Pituitary

- Characteristics of all anterior pituitary hormones
  - Proteins (or peptides)
  - Act through second-messenger systems
  - Regulated by hormonal stimuli, mostly negative feedback
Hormones of the Anterior Pituitary

- Hypothalamus
  - Releasing hormones in portal circulation
  - Anterior pituitary
    - Growth hormone (GH)
      - Bones and muscles
    - Prolactin (PRL)
      - Mammary glands
    - Follicle-stimulating hormone (FSH)
      - and luteinizing hormone (LH)
      - Testes or ovaries
    - Thyrotropic hormone (TSH)
      - Thyroid
    - Adrenocorticotropic hormone (ACTH)
      - Adrenal cortex

Figure 9.4
Hormones of the Anterior Pituitary

- Growth hormone
  - General metabolic hormone
  - Major effects are directed to growth of skeletal muscles and long bones
  - Plays a role in determining final body size
  - Causes amino acids to be built into proteins
  - Causes fats to be broken down for a source of energy
Hormones of the Anterior Pituitary

- Growth hormone (GH) disorders
  - Pituitary dwarfism results from hyposcretion of GH during childhood
  - Gigantism results from hypersecretion of GH during childhood
  - Acromegaly results from hypersecretion of GH during adulthood
Hormones of the Anterior Pituitary

Gigantism

(a) At age 12

Figure 9.5a
Hormones of the Anterior Pituitary

- Gigantism

Robert Pershing Wadlow (February 22, 1918 - July 15, 1940)

On June 27, 1940 (eighteen days before his death), he was measured at 8 ft 11.1 in (2.72 m) by doctors at Washington University in St. Louis.

Robert Wadlow compared to his father, Harold Franklin Wadlow, whose height was 1.82 m (5 ft 11 1/2 in)
Hormones of the Anterior Pituitary

- Gigantism
Hormones of the Anterior Pituitary

Dwarfism

Figure 9.5b
Hormones of the Anterior Pituitary

- Dwarfism
Hormones of the Anterior Pituitary

- Acromegaly
Hormones of the Anterior Pituitary

Acromegaly

Pituitary adenoma (CT scan or MRI)

High blood - Growth Hormone

Visual field defects

Prominent supraorbital ridge

Large nose and jaw
Teeth are separated or lacking

Galactorrhoea (prolactin)

Abnormal glucose tolerance test
Glucosuria/polyuria

Cardiomegaly

Spade-shaped hands and feet

Hypertension

Arthrosis

Sexual dysfunction

Peripheral neuropathy

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Hormones of the Anterior Pituitary

- **Prolactin (PRL)**
  - Stimulates and maintains milk production following childbirth
  - Function in males is unknown

- **Adrenocorticotrophic hormone (ACTH)**
  - Regulates endocrine activity of the adrenal cortex

- **Thyroid-stimulating hormone (TSH)**
  - Influences growth and activity of the thyroid gland
Hormones of the Anterior Pituitary

- **Gonadotropic hormones**
  - Regulate hormonal activity of the gonads
    - **Follicle-stimulating hormone (FSH)**
      - Stimulates follicle development in ovaries
      - Stimulates sperm development in testes
    - **Luteinizing hormone (LH)**
      - Triggers ovulation of an egg in females
      - Stimulates testosterone production in males
Pituitary–Hypothalamus Relationship

- Hormonal release is regulated by releasing and inhibiting hormones produced by the hypothalamus

- Hypothalamus produces two hormones
  - These hormones are transported to neurosecretory cells of the posterior pituitary
    - Oxytocin
    - Antidiuretic hormone

- The posterior pituitary is not strictly an endocrine gland, but does release hormones
Hormones of the Posterior Pituitary

- Oxytocin
  - Stimulates contractions of the uterus during labor, sexual relations, and breastfeeding
  - Causes milk ejection in a nursing woman
Hormones of the Posterior Pituitary

- Antidiuretic hormone (ADH)
  - Inhibits urine production by promoting water reabsorption by the kidneys
  - In large amounts, causes vasoconstriction leading to increased blood pressure
  - Also known as vasopressin
Hormones of the Posterior Pituitary

- Antidiuretic hormone disorders
  - Diabetes insipidus
    - Excessive urine output

CAUTION Next photo is not pretty
Hormones of the Posterior Pituitary

- Diabetes insipidus (or any form of diabetes)
Hormones of the Posterior Pituitary

- Diabetes insipidus (or any form of diabetes)
Hormones of the Posterior Pituitary

Figure 9.6

- Hypothalamic neurosecretory cells
- Optic chiasma
- Axon terminals
- Arterial blood supply
- Posterior lobe
- Capillary bed
- Venous drainage
- Anterior lobe of the pituitary

- ADH
  - Kidney tubules
- Oxytocin
  - Mammary glands
  - Uterine muscles