Endocrine System: Overview

• With nervous system, coordinates and integrates activity of body cells
• Influences metabolic activities via hormones transported in blood
• Response slower but longer lasting than nervous system
• Examples of control and integration
  – Reproduction
  – Growth and development
  – Maintenance of electrolyte, water, and nutrient balance of blood
  – Regulation of cellular metabolism and energy balance
  – Mobilization of body defenses

Endocrine System: Overview

• Endocrine glands:
  – pituitary, thyroid, parathyroid, adrenal, and pineal glands
• Hypothalamus is neuroendocrine organ
• Mixed glands:
  – Pancreas, gonads, placenta
• Other tissues and organs that produce hormones
  – Adipose cells, thymus, and cells in walls of small intestine, stomach, kidneys, and heart

Figure 16.1 Location of selected endocrine organs of the body.
Chemistry of Hormones

• Two main classes
  – **Amino acid-based hormones**
    • Amino acid derivatives, peptides, and proteins
    • Many are at least partially water soluble and travel through blood without need of stabilizing ‘binding’ protein
    • Often short-lived, existing for seconds or minutes
  – **Steroids**
    • Synthesized from cholesterol
    • Gonadal and adrenocortical hormones
    • Most are lipophilic and poorly water soluble; need ‘binding’ during blood transport
    • Often long-lived, existing for minutes to hours

Mechanisms of Hormone Action

• Though hormones circulate systemically only cells with receptors for that hormone affected
  – Target cells - must have specific receptors to which hormone binds
  – Hormones alter target cell activity
    • Alter plasma membrane permeability and/or membrane potential by opening or closing ion channels
    • Stimulate synthesis of enzymes or other proteins
    • Activate or deactivate enzymes
    • Induce secretory activity
    • Stimulate mitosis

Mechanisms of Hormone Action

• Hormones act at receptors in one of two ways, depending on their chemical nature and receptor location
  1. Plasma membrane receptors respond to water-soluble hormones (all amino acid–based hormones except thyroid hormone)
  2. Intracellular/nuclear receptors respond to lipid-soluble hormones (steroid and thyroid hormones)
Plasma Membrane Receptors and Second-messenger Systems

cAMP signaling mechanism:
1. Hormone (first messenger) binds to receptor
2. Receptor activates G protein
3. G protein activates adenylate cyclase
4. Adenylate cyclase converts ATP to cAMP (second messenger)
5. cAMP activates protein kinases that phosphorylate proteins
6. Activated kinases phosphorylate various proteins, activating some and inactivating others
7. cAMP is rapidly degraded by enzyme phosphodiesterase
8. Intracellular enzymatic cascades have huge amplification effect

Recall from Chapter 3 that G protein signaling mechanisms are like a molecular relay race.

Hormone (1st messenger) → Receptor → G protein → Adenylate cyclase → cAMP (2nd messenger)

Inactive protein kinase

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

Active protein kinase

Intracellular Receptors and Direct Gene Activation

• Steroid hormones and thyroid hormone
  1. Diffuse into target cells and bind with intracellular receptors
  2. Receptor-hormone complex enters nucleus; binds to specific region of DNA
  3. Prompts DNA transcription to produce mRNA
  4. mRNA directs protein synthesis
  5. Promote metabolic activities, or promote synthesis of structural proteins or proteins for export from cell
Target Cell Specificity

- Target cells must have specific receptors to which hormone binds, for example
  - ACTH receptors found only on certain cells of adrenal cortex
  - Thyroxin receptors are found on nearly all cells of body

Target Cell Activation

- Target cell activation depends on three factors
  - Blood levels of hormone
  - Relative number of receptors on or in target cell
    - Up-regulation
    - Down-regulation
  - Affinity of binding between receptor and hormone
Control of Hormone Release

- Blood levels of hormones
  - Controlled by negative feedback systems
  - Vary only within narrow, desirable range
- Endocrine gland stimulated to synthesize and release hormones in response to
  - Humoral stimuli
  - Neural stimuli
  - Hormonal stimuli

Figure 16.4a  Three types of endocrine gland stimuli.

(a) Humoral Stimulus
Hormone release caused by altered levels of certain critical ions or nutrients.
Stimulus: Low concentration of Ca\(^{2+}\) in capillary blood.
Parathyroid glands
Parathyroid hormone (PTH), which increases blood Ca\(^{2+}\).

Figure 16.4b  Three types of endocrine gland stimuli.

(b) Neural Stimulus
Hormone release caused by neural input.
CNS (spinal cord)
Preganglionic sympathetic fibers
Medulla of adrenal gland
Stimulus: Action potentials in preganglionic sympathetic fibers to adrenal medulla.
Response: Adrenal medulla cells secrete epinephrine and norepinephrine.
Figure 16.4c  Three types of endocrine gland stimuli.

**Hormonal Stimulus**

Hormone release caused by another hormone (a tropic hormone). Hypothalamus

- **Stimulus:** Hormones from hypothalamus.
- **Response:** Anterior pituitary gland secretes hormones that stimulate other endocrine glands to secrete hormones.

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**Hormones in the Blood**

- Hormones circulate in blood either free or bound
  - Steroids and thyroid hormone are attached to plasma proteins
  - All others circulate without carriers
- Concentration of circulating hormone reflects
  - Rate of release
  - Speed of inactivation and removal from body

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**Hormones in the Blood**

- Hormones removed from blood by
  - Degrading enzymes
  - Kidneys
    - Excretion based on water solubility, size
  - Liver
    - **Half-life**—time required for hormone’s blood level to decrease by half
      - Varies from fraction of minute to a week
Onset of Hormone Activity

• Some responses ~ immediate
• Some, especially steroid, hours to days
• Some must be activated in target cells

Duration of Hormone Activity

• Limited
  – Ranges from 10 seconds to several hours
  – Effects may disappear as blood levels drop
  – Some persist at low blood levels

The Pituitary Gland and Hypothalamus

• Pituitary gland (hypophysis) has two major lobes
  – Posterior pituitary (lobe)
    • Neural tissue
  – Anterior pituitary (lobe)
    (adenohypophysis)
    • Glandular tissue
Posterior Pituitary and Hypothalamic Hormones

- **Oxytocin** and ADH
  - Each composed of nine amino acids
  - Almost identical – differ in two amino acids

**Oxytocin**

- Strong stimulant of uterine contraction
- Released during childbirth
- Hormonal trigger for milk ejection
- Acts as neurotransmitter in brain
ADH (Vasopressin)

- Inhibits or prevents urine formation
- Regulates water balance
- Targets kidney tubules → reabsorb more water
- Release also triggered by pain, low blood pressure, and drugs
- Inhibited by alcohol, diuretics
- High concentrations → vasoconstriction

Anterior Pituitary Hormones

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

Anterior Pituitary Hormones

- All are proteins
- All except GH activate cyclic AMP second-messenger systems at their targets
- TSH, ACTH, FSH, and LH are all tropic hormones (regulate secretory action of other endocrine glands)
Growth Hormone (GH)

- GH release chiefly regulated by hypothalamic hormones
  - Growth hormone–releasing hormone (GHRH)
    - Stimulates release
  - Growth hormone–inhibiting hormone (GHIH) (somatostatin)
    - Inhibits release

Growth Hormone (GH, or Somatotropin)

- Produced by somatotropic cells
- Direct actions on metabolism
  - Increases blood levels of fatty acids; encourages use of fatty acids for fuel; protein synthesis
  - Decreases rate of glucose uptake and metabolism – conserving glucose
  - Glycogen breakdown and glucose release to blood (anti-insulin effect)
Growth Hormone (GH, or Somatotropin)

- Indirect actions on growth
- Mediates growth via growth-promoting proteins – insulin-like growth factors (IGFs)
- IGFs stimulate
  - Uptake of nutrients → DNA and proteins
  - Formation of collagen and deposition of bone matrix
- Major targets—bone and skeletal muscle

Thyroid-stimulating Hormone (Thyrotropin)

- Produced by thyrotropic cells of anterior pituitary
- Stimulates normal development and secretory activity of thyroid
- Release triggered by thyrotropin-releasing hormone from hypothalamus
- Inhibited by rising blood levels of thyroid hormones that act on pituitary and hypothalamus

Figure 16.8 Regulation of thyroid hormone secretion.
Gonadotropins

• Follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
• Secreted by gonadotropic cells of anterior pituitary
• FSH stimulates gamete (egg or sperm) production
• LH promotes production of gonadal hormones
• Absent from the blood in prepubertal boys and girls

Gonadotropins

• Regulation of gonadotropin release
  – Triggered by gonadotropin-releasing hormone (GnRH) during and after puberty
  – Suppressed by gonadal hormones (feedback)

Adrenocorticotropic Hormone (Corticotropin)

• Secreted by corticotropic cells of anterior pituitary
• Stimulates adrenal cortex to release corticosteroids
Adrenocorticotropic Hormone (Corticotropin)

- Regulation of ACTH release
  - Triggered by hypothalamic corticotropin-releasing hormone (CRH) in daily rhythm
  - Internal and external factors such as fever, hypoglycemia, and stressors can alter release of CRH

Glucocorticoids

- Keep blood glucose levels relatively constant
- Maintain blood pressure by increasing action of vasoconstrictors
- **Cortisol (hydrocortisone)**
  - Only one in significant amounts in humans
- Cortisone
- Corticosterone

Glucocorticoids: Cortisol

- Released in response to ACTH, patterns of eating and activity, and stress
- Prime metabolic effect is gluconeogenesis—formation of glucose from fats and proteins
  - Promotes rises in blood glucose, fatty acids, and amino acids
- "Saves" glucose for brain
- Enhances vasoconstriction → rise in blood pressure to quickly distribute nutrients to cells