Endocrine System: Overview

- The hypothalamus has both neural functions and releases hormones
- Other tissues and organs that produce hormones—adipose cells, pockets of cells in the walls of the small intestine, stomach, kidneys, and heart

Major Endocrine Organs

Hormones

- Hormones—chemical substances secreted by cells into the extracellular fluids
  - Regulate the metabolic function of other cells
  - Have lag times ranging from seconds to hours
  - Tend to have prolonged effects
  - Are classified as amino acid-based hormones, or steroids
  - Eicosanoids—biologically active lipids with local hormone–like activity
### Types of Hormones

- **Amino acid based** – most hormones belong to this class, including:
  - Amines, thyroxine, peptide, and protein hormones
  - Steroids – gonadal and adrenocortical hormones
  - Eicosanoids – leukotrienes and prostaglandins

### Hormone Action

- Hormones alter target cell activity by one of two mechanisms:
  - Second messengers involving:
    - Regulatory G proteins
    - Amino acid–based hormones
    - Direct gene activation involving steroid hormones
  - The precise response depends on the type of the target cell

### Mechanism of Hormone Action

- Hormones produce one or more of the following cellular changes in target cells:
  - Alter plasma membrane permeability
  - Stimulate protein synthesis
  - Activate or deactivate enzyme systems
  - Induce secretory activity
  - Stimulate mitosis

### Amino Acid-Based Hormone Action: cAMP

- **cAMP Second Messenger**
  - Hormone (first messenger) binds to its receptor, which then binds to a G protein
  - The G protein is then activated as it binds GTP, displacing GDP
  - Activated G protein activates the effector enzyme adenylate cyclase
  - Adenylate cyclase generates cAMP (second messenger) from ATP
  - cAMP activates protein kinases, which then cause cellular effects

### Amino Acid-Based Hormone Action: PIP-Calcium

- **PIP-Calcium**
  - Hormone binds to the receptor and activates G protein
  - G protein binds and activates a phospholipase enzyme
  - Phospholipase splits the phospholipid PIP$_2$ into diacylglycerol (DAG) and IP$_3$ (both act as second messengers)
  - DAG activates protein kinases; IP$_3$ triggers release of Ca$^{2+}$ stores
  - Ca$^{2+}$ (third messenger) alters cellular responses
Steroid Hormones

- Steroid hormones and thyroid hormone diffuse easily into their target cells
- Once inside, they bind and activate a specific intracellular receptor
- The hormone-receptor complex travels to the nucleus and binds a DNA-associated receptor protein
- This interaction prompts DNA transcription to produce mRNA
- The mRNA is translated into proteins, which bring about a cellular effect

Target Cell Specificity

- Hormones circulate to all tissues but only activate cells referred to as target cells
- Target cells must have specific receptors to which the hormone binds
- These receptors may be intracellular or located on the plasma membrane

Target Cell Specificity

- Examples of hormone activity
  - ACTH receptors are only found on certain cells of the adrenal cortex
  - Thyroxin receptors are found on nearly all cells of the body

Target Cell Activation

- Target cell activation depends on three factors
  - Blood levels of the hormone
  - Relative number of receptors on the target cell
  - The affinity of those receptors for the hormone
  - Up-regulation – target cells form more receptors in response to the hormone
  - Down-regulation – target cells lose receptors in response to the hormone
Hormones circulate in the blood in two forms – free or bound.
- Steroids and thyroid hormone are attached to plasma proteins.
- All others are unencumbered.

Concentrations of circulating hormone reflect:
- Rate of release
- Speed of inactivation and removal from the body
- Hormones are removed from the blood by:
  - Degrading enzymes
  - The kidneys
  - Liver enzyme systems

Hormone Concentrations in the Blood

Three types of hormone interaction:
- Permissiveness – one hormone cannot exert its effects without another hormone being present.
- Synergism – more than one hormone produces the same effects on a target cell.
- Antagonism – one or more hormones opposes the action of another hormone.

Blood levels of hormones:
- Are controlled by negative feedback systems.
- Vary only within a narrow desirable range.
- Hormones are synthesized and released in response to:
  - Humoral stimuli
  - Neural stimuli
  - Hormonal stimuli

Humoral stimuli – secretion of hormones in direct response to changing blood levels of ions and nutrients.
- Example: concentration of calcium ions in the blood.
  - Declining blood Ca²⁺ concentration stimulates the parathyroid glands to secrete PTH (parathyroid hormone).
  - PTH causes Ca²⁺ concentrations to rise and the stimulus is removed.

Figure 16.4a
Neural Stimuli

- Neural stimuli – nerve fibers stimulate hormone release
  - Preganglionic sympathetic nervous system (SNS) fibers stimulate the adrenal medulla to secrete catecholamines

Hormonal Stimuli

- Hormonal stimuli – release of hormones in response to hormones produced by other endocrine organs
  - The hypothalamic hormones stimulate the anterior pituitary
  - In turn, pituitary hormones stimulate targets to secrete still more hormones

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Nervous System Modulation

- The nervous system modifies the stimulation of endocrine glands and their negative feedback mechanisms
- The nervous system can override normal endocrine controls
  - For example, control of blood glucose levels
    - Normally the endocrine system maintains blood glucose
    - Under stress, the body needs more glucose
    - The hypothalamus and the sympathetic nervous system are activated to supply ample glucose

Major Endocrine Organs: Pituitary (Hypophysis)

- Pituitary gland – two-lobed organ that secretes nine major hormones
- Neurohypophysis – posterior lobe (neural tissue) and the infundibulum
  - Receives, stores, and releases hormones from the hypothalamus
- Adenohypophysis – anterior lobe, made up of glandular tissue
  - Synthesizes and secretes a number of hormones
The posterior lobe is a downgrowth of hypothalamic neural tissue. It has a neural connection with the hypothalamus (hypothalamic-hypophyseal tract). Nuclei of the hypothalamus synthesize oxytocin and antidiuretic hormone (ADH). These hormones are transported to the posterior pituitary.

The anterior lobe of the pituitary is an outpocketing of the oral mucosa. There is no direct neural contact with the hypothalamus.

There is a vascular connection, the hypophyseal portal system, consisting of:
- The primary capillary plexus
- The hypophyseal portal veins
- The secondary capillary plexus

The six hormones of the adenohypophysis:
- Are abbreviated as GH, TSH, ACTH, FSH, LH, and PRL
- Regulate the activity of other endocrine glands
- In addition, pro-opiomelanocortin (POMC):
  - Has been isolated from the pituitary
  - Is enzymatically split into ACTH, opiates, and MSH

The hypothalamus sends a chemical stimulus to the anterior pituitary. Releasing hormones stimulate the synthesis and release of hormones. Inhibiting hormones shut off the synthesis and release of hormones.
### Activity of the Adenohypophysis

- The tropic hormones that are released are:
  - Thyroid-stimulating hormone (TSH)
  - Adrenocorticotropic hormone (ACTH)
  - Follicle-stimulating hormone (FSH)
  - Luteinizing hormone (LH)

### Growth Hormone (GH)

- Produced by somatotropic cells of the anterior lobe that:
  - Stimulate most cells, but target bone and skeletal muscle
  - Promote protein synthesis and encourage the use of fats for fuel
  - Most effects are mediated indirectly by somatomedins

### Metabolic Action of Growth Hormone

- GH stimulates liver, skeletal muscle, bone, and cartilage to produce insulin-like growth factors
- Direct action promotes lipolysis and inhibits glucose uptake

### Thyroid Stimulating Hormone (Thyrotropin)

- Tropic hormone that stimulates the normal development and secretory activity of the thyroid gland
- Triggered by hypothalamic peptide thyrotropin-releasing hormone (TRH)
- Rising blood levels of thyroid hormones act on the pituitary and hypothalamus to block the release of TSH
### Adrenocorticotropic Hormone (Corticotropin)
- Stimulates the adrenal cortex to release corticosteroids
- Triggered by hypothalamic corticotropin-releasing hormone (CRH) in a daily rhythm
- Internal and external factors such as fever, hypoglycemia, and stressors can trigger the release of CRH

### Gonadotropins
- Gonadotropins – follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
  - Regulate the function of the ovaries and testes
  - FSH stimulates gamete (egg or sperm) production
  - Absent from the blood in prepubertal boys and girls
  - Triggered by the hypothalamic gonadotropin-releasing hormone (GnRH) during and after puberty

### Functions of Gonadotropins
- In females
  - LH works with FSH to cause maturation of the ovarian follicle
  - LH works alone to trigger ovulation (expulsion of the egg from the follicle)
  - LH promotes synthesis and release of estrogens and progesterone

### Functions of Gonadotropins
- In males
  - LH stimulates interstitial cells of the testes to produce testosterone
  - LH is also referred to as interstitial cell-stimulating hormone (ICSH)

### Prolactin (PRL)
- In females, stimulates milk production by the breasts
- Triggered by the hypothalamic prolactin-releasing hormone (PRH)
- Inhibited by prolactin-inhibiting hormone (PIH)
- Blood levels rise toward the end of pregnancy
- Suckling stimulates PRH release and encourages continued milk production

### The Posterior Pituitary and Hypothalamic Hormones
- Posterior pituitary – made of axons of hypothalamic neurons, stores antidiuretic hormone (ADH) and oxytocin
- ADH and oxytocin are synthesized in the hypothalamus
- ADH influences water balance
- Oxytocin stimulates smooth muscle contraction in breasts and uterus
- Both use PIP-calcium second-messenger mechanism