Endocrine System: Overview

- The endocrine system interacts with the nervous system to coordinate and integrate the activity of body cells.
- The e.s. influences metabolic activities by means of hormones.
- Binding of hormones to cellular receptors initiates responses that occur after a lag period of seconds to days.
- Once initiated, the responses tend to be much more prolonged than those initiated by the nervous system.
Endocrine System: Overview

- Major processes controlled by hormones are:
  - Reproduction
  - Growth & development
  - Body defenses
  - Balance humoral electrolyte levels, water & nutrients
  - Cellular metabolism & energy balance
Endocrine System: Overview

- Two types of glands: Exocrine & Endocrine
  - Exocrine glands: produce nonhumoral substances and have ducts
    - E.g. sweat and saliva glands
  - Endocrine glands: Ductless glands. Release hormone into surrounding tissue fluid. Have a rich vascular & lymphatic drainage that receives the hormones.
    - E.g. pituitary, thyroid, parathyroid, adrenal, pineal, thymus, hypothalamus (neuroendocrine organ)
Endocrine System: Overview

- Several organs contain areas of endocrine tissue and produce both hormones & exocrine products
  - E.g. pancreas and gonads
- 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
Endocrine System: Overview

- Autocrines: chemicals that exert their function on the same cell that secretes them.
  - E.g. prostaglandins released by smooth muscle cells cause those smooth muscle cells to contract

- Paracrines: act locally but affect cell types other than those that secrete them.
  - E.g. somatostatin released by one pancreatic cell inhibits the release of insulin by another type of pancreatic cell
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)
Hormones

- Chemistry of Hormones
  - Almost all hormones can be classified either as amino acid based or steroids.
  - Most hormones are amino acid based ranging from amine to peptides to proteins
  - Steroids are synthesized from cholesterol and include gonadal & adrenocortical hormones
  - Eicosanoids: e.g. leukotrienes and prostaglandins
    - These biologically active lipids are made from arachidonic acid and are released by almost all cell membranes
Hormone Action

- Hormones alter target cell activity by one of two mechanisms
  - Second messengers:
    - Regulatory G proteins
    - Amino acid–based hormones
  - Direct gene activation
    - 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 by altering the cell’s activity, e.g. increase or decrease the rate of their normal cellular processes
  - Alter plasma membrane permeability
  - Stimulate protein synthesis
  - Activate or deactivate enzyme systems
  - Induce secretory activity
  - Stimulate mitosis
Mechanisms of Cellular Transduction

- 1) Water soluble hormones (a.a. based) act on receptors in the plasma membrane, e.g GPCRs
- 2) Lipid soluble hormones (steroid & thyroid) act on intracellular receptors directly activating genes
Amino Acid-Based Hormone Action: cAMP Second Messenger

- Involves three components:
  - Hormone receptor
  - G-protein (signal transducer)
  - Effector enzyme (adenylate cyclase)

- The steps are:
  - 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: cAMP Second Messenger

**Extracellular fluid**

1. **Hormone A**
   - Receptor
   - $G_s$
   - Adenylate cyclase
   - Formation of cAMP
   - Activation of protein kinase A

2. **GTP**
   - Activation of protein kinase A

3. **ATP**
   - Phosphorylation of target proteins

4. **Inactive protein kinase A**
   - Phosphorylation
   - Activation

5. **Active protein kinase A**
   - Phosphorylation of target proteins
   - Triggers responses of target cell (activates enzymes, stimulates cellular secretion, opens ion channels, etc.)

**Cytoplasm**

- Catecholamines
- ACTH
- FSH
- LH
- Glucagon
- PTH
- TSH
- Calcitonin

**Figure 16.2**
Intracellular Receptors & Direct Gene Activation: Steroid Hormones

- Steroid hormones diffuse into their target cells where they bind to an intracellular receptor.
- Hormone-receptor complex travels to the nuclear chromatin where the hormone receptor binds to a region of the DNA (the hormone response element).
- This interaction prompts DNA transcription to produce mRNA (“turn on” the gene).
- The mRNA is translated into proteins, which bring about a cellular effect.
Steroid hormone

Cytoplasm

Receptor-chaperonin complex

Molecular chaperones

Receptor-hormone complex

Binding

Hormone response elements

Chromatin

Transcription

mRNA

Nucleus

Translation

Ribosome

mRNA

New protein

Figure 16.4
Hormone response elements

Binding

Chromatin

Transcription

mRNA

mRNA

Nucleus

Ribosome

Translation

New protein
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 Activation

- Target cell activation depends on three factors
  - Blood levels of the hormone
  - Relative number of receptors on, or in, 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 (to prevent overreaction of target cell to corresponding hormone.)
Hormone Concentrations in the Blood

- Hormones circulate in the blood in two forms – free or bound to a protein carrier
  - Steroids and thyroid hormones, which are lipid soluble, travel in blood attached to plasma proteins
  - All others are free circulating
Hormone Concentrations in the Blood

- Concentrations of circulating hormone reflect:
  - Rate of release
  - The rate that it is inactivated and removed.
  - Hormones are removed from the blood by:
    - Degrading enzymes
    - The kidneys
    - Liver enzyme systems

And are broken down & excreted in urine
Interaction of Hormones at Target Cells

- 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 and their combined effects are amplified
  - Antagonism – when one hormone opposes the action of another hormone
Control of Hormone Release

- Blood levels of hormones:
  - Are controlled by negative feedback systems
    - As hormone levels rise, they cause target organ effects and inhibit further hormone release
  - Vary only within a narrow desirable range
Control of Hormone Release

- Hormones are synthesized and released in response to:
  - Humoral stimuli
  - Neural stimuli
  - Hormonal stimuli
Humoral 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 Ca\(^{2+}\) concentration stimulates the parathyroid glands to secrete PTH (parathyroid hormone)
  - PTH causes Ca\(^{2+}\) concentrations to rise and the stimulus is removed
Neural Stimuli

- Neural stimuli – nerve fibers stimulate hormone release
  
  - Preganglionic sympathetic nervous system (SNS) fibers stimulate the adrenal medulla to secrete catecholamines (norepinephrine & epinephrine) during periods of stress
Hormonal Stimuli

- Hormonal stimuli – release of hormones in response to hormones produced by other endocrine organs
  - The hypothalamic hormones stimulate the anterior pituitary
Nervous System Modulation

- The nervous system can modify both “turn on” and “turn off” factors
- w/o nervous control, endocrine activity would act like a thermostat and be static
- The nervous system allows for dynamic control
Major Endocrine Organs: Pituitary (Hypophysis)

- Located in the sella turcica of the sphenoid bone, the two-lobed organ secretes nine major hormones

- Neurohypophysis – posterior lobe (neural tissue) and the infundibulum
  - Composed of pituicytes (supporting cells) & nerve fibers
  - Release neurohormones (hormones secreted by neurons) received by the hypothalamus
  - Hormone storage area, NOT a true endocrine gland

- Adenohypophysis – anterior lobe, made up of glandular tissue
  - Synthesizes and secretes a number of hormones
Major Endocrine Organs: Pituitary (Hypophysis)
Pituitary-Hypothalamic Relationships: Posterior Lobe

- The posterior lobe is a down-growth of hypothalamic neural tissue

- Has a neural connection with the hypothalamus (hypothalamic-hypophyseal tract)

- Neurosecretory cells synthesize two neurohormones & transport them via axons to the posterior pituitary
  - Oxytocin: made in the paraventricular neurons
  - ADH (antidiuretic hormone) made in the supraoptic neurons

- When the nerves fire, these hormones are released into a capillary bed and transported to the posterior pituitary
Pituitary-Hypothalamic Relationships: Anterior Lobe

- The anterior lobe of the pituitary is an out-pocketing of the oral mucosa
- There is no direct neural contact with the hypothalamus, only a vascular one
The primary capillary plexus in the infundibulum communicates inferiorly via the small hypophyseal portal veins with a secondary capillary plexus in the anterior lobe.
Adenohypophyseal Hormones

- The six hormones (all proteins) of the adenohypophysis:
  - Abbreviated as GH, TSH, ACTH, FSH, LH, and PRL
  - Regulate the activity of other endocrine glands
- In addition, pro-opiomelanocortin (POMC):
  - Prohormone that can be split enzymatically into one or more hormones
Activity of the Adenohypophysis

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

They regulate secretory action of other endocrine glands
Growth Hormone (GH)

- Produced by somatotrophic cells of the anterior lobe that:
  - Stimulate most cells, but target bone and skeletal muscle
  - Promote protein synthesis and use of fats for fuel
- Most effects are mediated indirectly by insulin-like growth factors (IGFs) like somatomedins
- GH releases fat from fat deposits increasing blood levels of fatty acids
Growth Hormone (GH): Insulin-like Growth Factors (IGFs)

- IGFs:
  - i) stimulate uptake of a.a. from the blood and their incorporation into cellular proteins
  - ii) stimulate uptake of sulfur into cartilage matrix (needed for the synthesis of chondroitin)
Growth Hormone (GH)

- Secretion of GH is regulated by two hypothalamic hormones with antagonistic effects
  - Growth hormone–releasing hormone (GHRH) stimulates GH release
  - Growth hormone–inhibiting hormone (GHIH, aka somatostatin) inhibits GH release

Secretion of GH is at its greatest during adolescence
Should Adults be taking GH as a supplement?

- Growth hormone plays a role in adults:
  - healthy muscle
  - how our bodies collect fat (especially around the stomach area)
  - the ratio of high density to low density lipoproteins in our cholesterol levels
  - bone density
  - In addition, growth hormone is needed for normal brain function.
Thyroid Stimulating Hormone (Thyrotropin)

- Stimulates the normal development and secretory activity of the thyroid
- Release from thyrotroph cells of the anterior pituitary is 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)

- Secreted by corticotroph cell of the adenohypophysis
- Stimulates the adrenal cortex to release corticosteroid hormones, most importantly glucocorticoid
- 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)

- Produced by lactotroph cells
- In females, stimulates milk production by the breasts
- Triggered by the hypothalamic prolactin-releasing hormone (PRH)
- Inhibited by prolactin-inhibiting hormone (PIH) aka dopamine. A decrease in PIH results in a surge of PRL
Prolactin (PRL)

- A brief rise in PRL levels just before the menstrual period accounts for some of the breast swelling and tenderness that some women experience.

- Because the PRL stimulus is relatively short, no milk is produced.

- Toward the end of pregnancy PRL levels rise dramatically and milk production becomes possible.