**ENDOCRINE SYSTEM**

- Endocrine system – the body’s second great controlling system which influences metabolic activities of cells by means of hormones
- Endocrine glands – pituitary, thyroid, parathyroid, adrenal, pineal, and thymus glands
- The pancreas and gonads produce both hormones and exocrine products
- The hypothalamus has both neural functions and releases hormones

**Location of the Major Endocrine Glands**

- The major endocrine glands include:
  - Pineal gland, hypothalamus, and pituitary
  - Thyroid, parathyroid, and thymus
  - Adrenal glands and pancreas
  - Gonads – male testes and female ovaries

**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

**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 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
Homeostatic Control Mechanisms

Negative Feedback
- In negative feedback systems, the output shuts off the original stimulus
- Example: Regulation of blood glucose levels

Positive Feedback
- In positive feedback systems, the output enhances or exaggerates the original stimulus
- Example: Regulation of blood clotting

Mechanism of Action of Hormones

MECHANISM OF HORMONE ACTION
- Hormones produce one or more of the following cellular changes
  - Alter plasma membrane permeability
  - Stimulate protein synthesis
  - Activate or deactivate enzyme systems
  - Induce secretory activity
  - Stimulate mitosis

Action: 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 adenylyl cyclase
- Adenylyl cyclase generates cyclic AMP (cAMP) (second messenger) from ATP
- cAMP activates protein
**Action:**

**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

**Hormones with Cell Surface Receptors**

<table>
<thead>
<tr>
<th>Second</th>
<th>Examples of Hormones Which Utilize This System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein kinase activity</td>
<td>Epinephrine and norepinephrine, glucagon, luteinizing hormone, follicle-stimulating hormone, thyroid-stimulating hormone, calcitonin, parathyroid hormone, antidiuretic hormone</td>
</tr>
<tr>
<td>Protein kinase activity</td>
<td>Insulin, growth hormone, prolactin, oxytocin, erythropoietin, several growth factors</td>
</tr>
<tr>
<td>Calcium and/or phosphoinositides</td>
<td>Epinephrine and norepinephrine, angiotensin II, antidiuretic hormone, gonadotropin-releasing hormone, thyroid-releasing hormone</td>
</tr>
<tr>
<td>Cyclic GMP</td>
<td>Atrial natriuretic hormone, nitric oxide</td>
</tr>
</tbody>
</table>

**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

**Hormone–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
- 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

**Hormone Concentrations in the Blood**

- 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
CONTROL OF HORMONE SYNTHESIS AND RELEASE

- 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

- 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⁺

Neural 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⁺

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

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