Endocrine System

Endocrine System: Overview

- 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
- Other tissues and organs that produce hormones – adipose cells, pockets of cells in the walls of the small intestine, stomach, kidneys, and heart

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 adrenocoritcal 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

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

Amino Acid–Based Hormone 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 *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

- 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

Amino Acid–Based Hormone Action:
PIP-Calcium

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 producing mRNA
- The mRNA is translated into proteins, which bring about a cellular effect

Steroid Hormones

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

Target Cell Activation

- Target cell activation depends upon 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

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 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

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

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

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

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

Pituitary-Hypothalamic Relationships: Posterior Lobe

- Posterior lobe – a downgrowth of hypothalamic neural tissue
- 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

Pituitary-Hypothalamic Relationships: Anterior Lobe

- 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

Adenohypophyseal Hormones

- 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

Activity of the Adenohypophysis

- The hypothalamus sends 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
- 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

- Antagonistic hypothalamic hormones regulate GH
- Growth hormone–releasing hormone (GHRH) stimulates GH release
- Growth hormone–inhibiting hormone (GHIH) inhibits GH release

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 (eggs 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
- 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 second-messenger mechanisms