

The Endocrine System
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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
- The pancreas and gonads produce both hormones and exocrine products

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

Autocrines and Paracrines

- Autocrines – chemicals that exert their effects on the same cells that secrete them
- Paracrines – locally acting chemicals that affect cells other than those that secrete them
- These are not considered hormones since hormones are long-distance chemical signals

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
 - True Hormones 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 – (Hormone like substances) 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 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: cAMP Second Messenger

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 PIP₂ into diacylglycerol (DAG) and IP₃ (both act as second messengers)

- DAG activates protein kinases; IP₃ triggers release of Ca²⁺ stores
- Ca²⁺ (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 produce mRNA
- The mRNA is translated into proteins, which bring about a cellular effect

Steroid Hormones

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 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

- Hormones circulate in the blood in two forms – free or bound
 - Steroids and thyroid hormone are attached to plasma proteins
 - All others are unencumbered

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

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
 - Antagonism – one or more hormones opposes the action of another hormone

Control of Hormone 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, neural, and 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

Humoral Stimuli

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

Hormonal Stimuli

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

Major Endocrine Organs: Pituitary (Hypophysis)

Pituitary-Hypothalamic Relationships:

Posterior Lobe

- The posterior lobe is 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

Pituitary-Hypothalamic Relationships:

Anterior Lobe

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

Pituitary-Hypothalamic Relationships:

Anterior Lobe

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 Adenophypophysis

- 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 Adenophypophysis

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

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 encourage the use of fats for fuel
- Most effects are mediated indirectly by somatomedins

Growth Hormone (GH)

- 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

Metabolic Action of Growth Hormone

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

Adrenocorticotrophic 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

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