

Lecture One: Principles of Endocrinology

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Endocrine System

Hormones

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Mechanism of Hormone Action

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Amino Acid–Based Hormone Action: IP₃–Calcium

Steroid and Thyroid Hormones

Hormone–Target Cell Specificity and Target Cell Activation

Control of Hormone Synthesis and Release

Nervous System Modulation



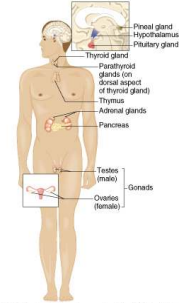
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Location of the Major Endocrine Glands

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The major endocrine glands include:

- Pineal gland, hypothalamus, and pituitary
- Thyroid, parathyroid, and thymus
- Adrenal glands and pancreas
- Gonads – male testes and female ovaries



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

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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

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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

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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

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Mechanism of Action of Hormones

Location of Receptor	Classes of Hormones	Principle Mechanism of Action
Cell surface receptors (plasma membrane)	Proteins and peptides, catecholamines and eicosanoids	Generation of <i>second messengers</i> which alter the activity of other molecules - usually enzymes - within the cell
Intracellular receptors (cytoplasm and/or nucleus)	Steroids and thyroid hormones	Alter transcriptional activity of responsive genes

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MECHANISM OF HORMONE ACTION

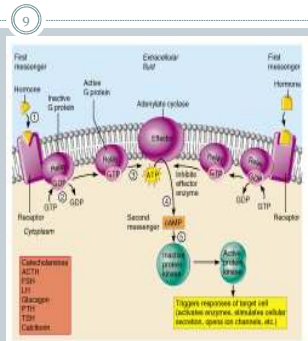
- Hormones produce one or more of the following cellular changes
 - Alter plasma membrane permeability
 - Stimulate protein synthesis
 - Activate or deactivate enzyme systems
 - Induce secretory activity
 - Stimulate mitosis

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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 cyclic AMP (cAMP) (second messenger) from ATP
- cAMP activates protein kinases, which then cause cellular effects

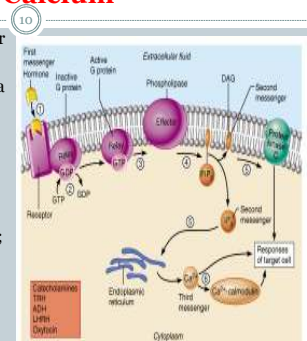


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Amino Acid–Based Hormone Action: IP₃–Calcium

- 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



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Hormones with Cell Surface Receptors

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

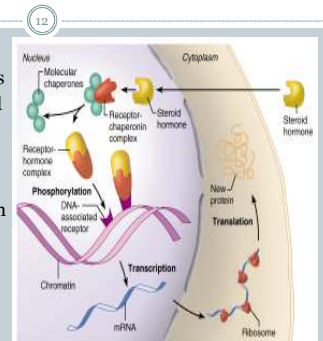
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Steroid and Thyroid Hormones

- 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



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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

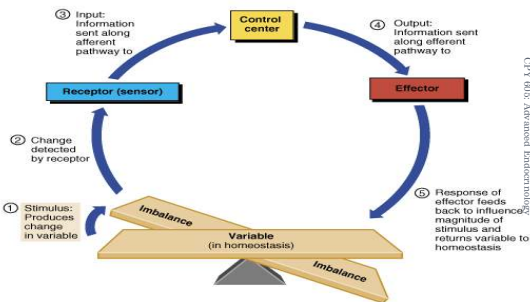
Hormone Concentrations in the Blood

- 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

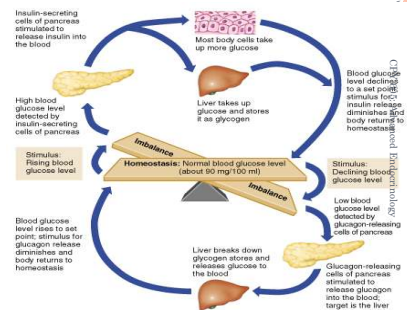
- Blood levels of hormones:
 - Are controlled by negative feedback systems
 - Vary only within a narrow desirable range
- Hormones are synthesized and released in response to:
 - Humoral stimuli
 - Neural stimuli
 - Hormonal stimuli

HOMEOSTATIC CONTROL MECHANISMS



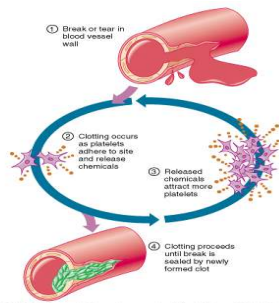
NEGATIVE FEEDBACK

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



POSITIVE FEEDBACK

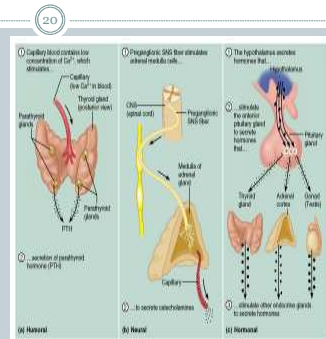
- In positive feedback systems, the output enhances or exaggerates the original stimulus
- Example: Regulation of blood clotting



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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

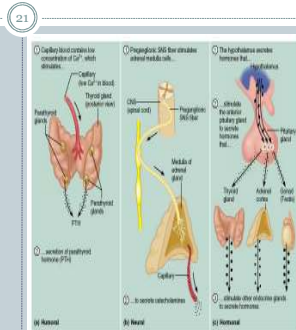


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Neural Stimuli

- Humoral stimuli – secretion of hormones in direct response to changing blood levels of ions and nutrients
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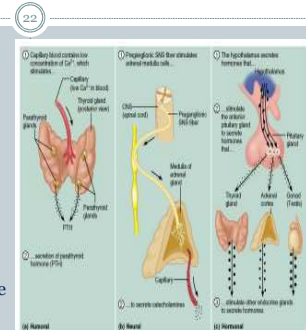


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Hormonal Stimuli

- 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

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