Bio-organic chemistry

Lecture #2

The key role of hormones in the body, their classification, methods of isolation and identification. Amino acids and peptides related to hormones and used in hormone therapy.

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Endocrine System Components

- endocrine system – glands, tissues, and cells that are spread in other organs and tissues (nervous system, digestive tract, pancreas, kidneys, heart, thyroid, etc.) that secrete hormones
- endocrinology – is the science that studies the endocrine system's structure and function, and the hormone's physiological and pathological biosynthesis, actions and metabolism, the diagnosis and treatment of its disorders
- endocrine glands – organs that produce hormones
- hormones – are the endocrine system's information messengers, chemical messengers transported by the bloodstream that stimulate responses in another tissue or organ, often far away

Hormones - Overview of functions

- regulate chemical composition and volume of internal environment: water and electrolytes
- regulate metabolism and energy balance
- regulate contraction of smooth and cardiac muscle fibers
- regulate homeostasis despite disruptions
- regulate activities of immune system
- integration of growth and development
- contribute to basic processes of reproduction

What Are Hormones?

Definition

Hormones are chemical messengers produced by glands in the body that travel through the bloodstream to regulate and control various functions, including growth, metabolism, and reproduction. They work by sending signals to specific cells and organs, much like a lock and key, to coordinate processes like sleep, mood, and development.

- ✓ Biologically active compounds produced by endocrine glands
- ✓ Regulate metabolism, growth, development, reproduction
- ✓ Act at extremely low concentrations
- ✓ High specificity due to receptor interaction

Key Properties

Signal molecules

Transported via bloodstream

Rapid and long-term effects

Hormone Action

- Hormones alter target cell activity by one of two mechanisms

– Second messengers involving:

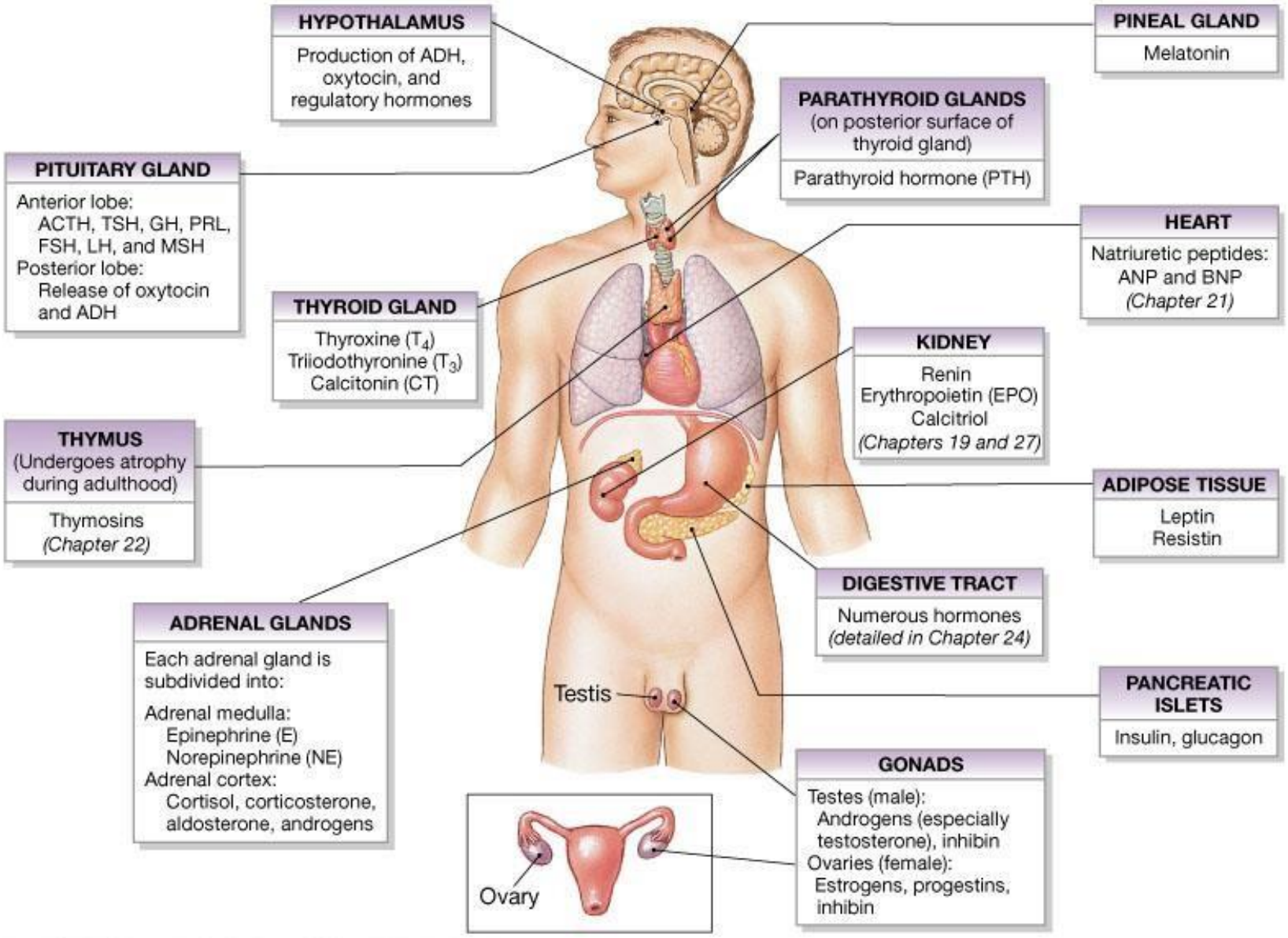
- Amino acid–based hormones cannot pass through the membrane.

– They attach to a specific regulatory G protein on surface of cell membrane.

– This sets off a series of steps that can activate or inhibit numerous functioning enzymes in the cell.

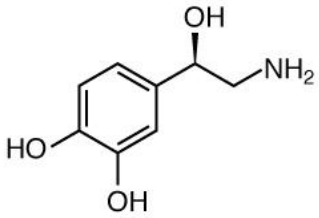
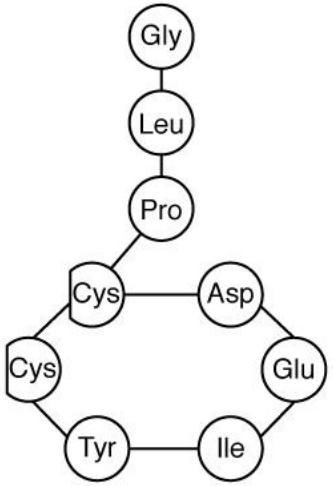
– Direct gene activation involving steroid hormones

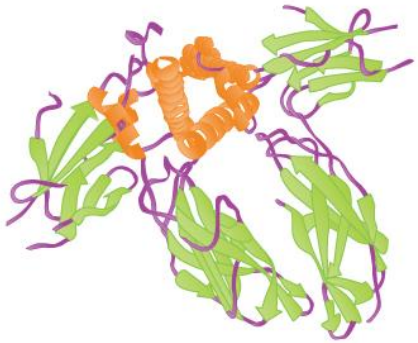
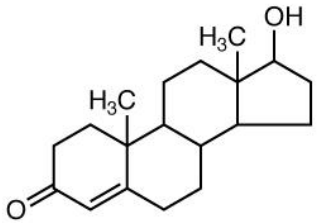
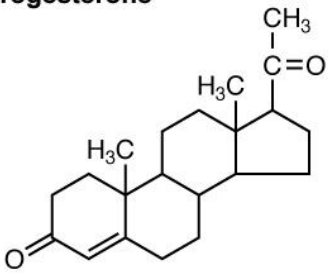
- Since steroid based hormones are lipophillic they can diffuse through the cell membrane and enter the nucleus where they can alter gene expression and alter the rate of protein synthesis.


HYPOTHALAMUS
Production of ADH, oxytocin, and regulatory hormones
PINEAL GLAND
Melatonin
PARATHYROID GLANDS
(on posterior surface of thyroid gland)
Parathyroid hormone (PTH)
PITUITARY GLAND
Anterior lobe:
ACTH, TSH, GH, PRL, FSH, LH, and MSH
Posterior lobe:
Release of oxytocin and ADH
HEART
Natriuretic peptides: ANP and BNP
(Chapter 21)
THYROID GLAND
Thyroxine (T_4)
Triiodothyronine (T_3)
Calcitonin (CT)
KIDNEY
Renin
Erythropoietin (EPO)
Calcitriol
(Chapters 19 and 27)
THYMUS
(Undergoes atrophy during adulthood)
Thymosins
(Chapter 22)
ADIPOSE TISSUE
Leptin
Resistin
DIGESTIVE TRACT
Numerous hormones
(detailed in Chapter 24)
ADRENAL GLANDS
Each adrenal gland is subdivided into:
Adrenal medulla:
Epinephrine (E)
Norepinephrine (NE)
Adrenal cortex:
Cortisol, corticosterone, aldosterone, androgens
Testis
PANCREATIC ISLETS
Insulin, glucagon
GONADS
Testes (male):
Androgens (especially testosterone), inhibin
Ovaries (female):
Estrogens, progestins, inhibin
Ovary

Types of Hormones

The hormones of the human body can be divided into two major groups on the basis of their chemical structure. Hormones derived from amino acids include amines, peptides, and proteins. Those derived from lipids include steroids (Figure 1). These chemical groups affect a hormone's distribution, the type of receptors it binds to, and other aspects of its function.

Hormone Class	Components	Example(s)
Amine Hormone	Amino acids with modified groups (e.g. norepinephrine's carboxyl group is replaced with a benzene ring)	**Norepinephrine** 
Peptide Hormone	Short chains of linked amino acids	**Oxytocin** 

Protein Hormone	Long chains of linked amino acids	**Human Growth Hormone** 
Steroid Hormones	Derived from the lipid cholesterol	**Testosterone**  **Progesterone** 

Amine Hormones

Hormones derived from the modification of amino acids are referred to as amine hormones. Typically, the original structure of the amino acid is modified such that a −COOH, or carboxyl, group is removed, whereas the NH+3, or amine, group remains.

Amine hormones are synthesized from the amino acids tryptophan or tyrosine. An example of a hormone derived from tryptophan is melatonin, which is secreted by the pineal gland and helps regulate circadian rhythm. Tyrosine derivatives include the metabolism-regulating thyroid hormones, as well as the catecholamines, such as epinephrine, norepinephrine, and dopamine. Epinephrine and norepinephrine are secreted by the adrenal medulla and play a role in the fight-or-flight response, whereas dopamine is secreted by the hypothalamus and inhibits the release of certain anterior pituitary hormones.

Peptide and Protein Hormones

Whereas the amine hormones are derived from a single amino acid, peptide and protein hormones consist of multiple amino acids that link to form an amino acid chain. Peptide hormones consist of short chains of amino acids, whereas protein hormones are longer polypeptides. Both types are synthesized like other body proteins: DNA is transcribed into mRNA, which is translated into an amino acid chain.

Examples of peptide hormones include antidiuretic hormone (ADH), a pituitary hormone important in fluid balance, and atrial-natriuretic peptide, which is produced by the heart and helps to decrease blood pressure. Some examples of protein hormones include growth hormone, which is produced by the pituitary gland, and follicle-stimulating hormone (FSH), which has an attached carbohydrate group and is thus classified as a glycoprotein. FSH helps stimulate the maturation of eggs in the ovaries and sperm in the testes.

Steroid Hormones

The primary hormones derived from lipids are steroids. Steroid hormones are derived from the lipid cholesterol. For example, the reproductive hormones testosterone and the estrogens—which are produced by the gonads (testes and ovaries)—are steroid hormones. The adrenal glands produce the steroid hormone aldosterone, which is involved in osmoregulation, and cortisol, which plays a role in metabolism.

Like cholesterol, steroid hormones are not soluble in water (they are hydrophobic). Because blood is water-based, lipid-derived hormones must travel to their target cell bound to a transport protein. This more complex structure extends the half-life of steroid hormones much longer than that of hormones derived from amino acids. A hormone's half-life is the time required for half the concentration of the hormone to be degraded. For example, the lipid-derived hormone cortisol has a half-life of approximately 60 to 90 minutes. In contrast, the amino acid–derived hormone epinephrine has a half-life of approximately one minute.

Hormones can be isolated using methods like chromatography and SPE (solid-phase extraction), which separate them from a complex mixture based on their properties. Identification and measurement are then often performed using bioassays (measuring biological effects), immunoassays (using antibodies), or biochemical/physical techniques like gas chromatography-mass spectrometry (GC-MS), which compares their physical properties and mass-to-charge ratio to known standards.

Isolation methods

Chromatography: A general technique that separates compounds based on how they move through a medium. It can be used on small or large scales to purify hormones.

Solid-Phase Extraction (SPE): A commonly used method that uses sorbent-coated particles in cartridges or syringes to capture and separate hormones from a liquid sample.

Electrophoresis: Techniques like SDS-PAGE can be used to separate proteins and hormones based on size and charge.

Identification and quantification methods

Bioassays: The oldest method, which measures the specific physiological or cellular response to the presence of the hormone.

Immunoassays: Uses antibodies that specifically bind to a hormone. Examples include radioimmunoassays (RIA) and enzyme-linked immunosorbent assays (ELISA).

Gas Chromatography-Mass Spectrometry (GC-MS):

Hormones are identified by comparing their retention time (how long they take to pass through the column) and ion-abundance ratio with a known standard.

Identification is confirmed when both the retention time and the ratio match the standard.

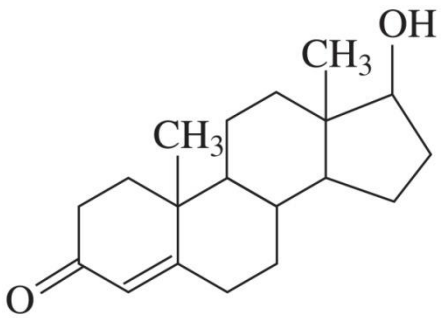
Mass Spectrometry (MS): Provides structural information and can be used for quantification. By comparing the resulting mass-to-charge ratio to known standards, the hormone can be identified.

Receptor assays: Measures the hormone's ability to bind to its specific receptor.

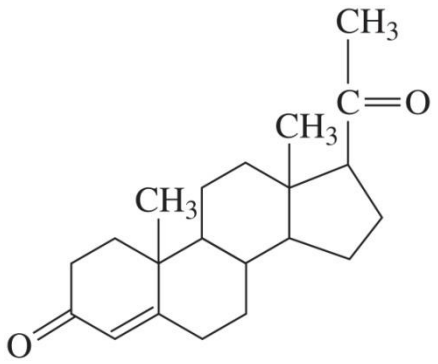
Affinity chromatography: Can be used for purification by using a binding molecule, such as an antibody or a receptor, attached to a solid support to "capture" the target hormone.

Steroid hormones

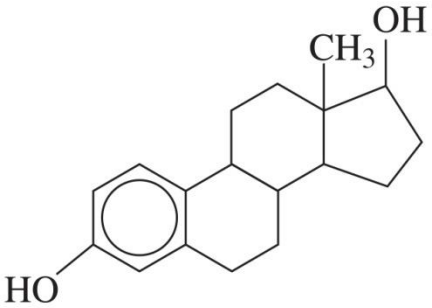
- are chemical messengers in cells.
- are produced from cholesterol.
- include sex hormones, such as androgens (testosterone) in males and estrogens (estradiol) in females.



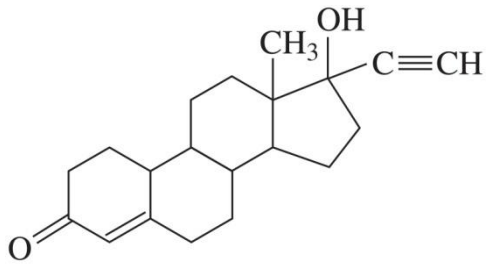
Testosterone (androgen)
(produced in testes)



Progesterone
(produced in ovaries)



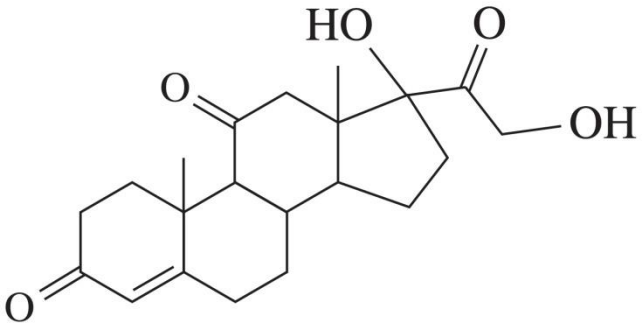
Estradiol (estrogen)
(produced in ovaries)



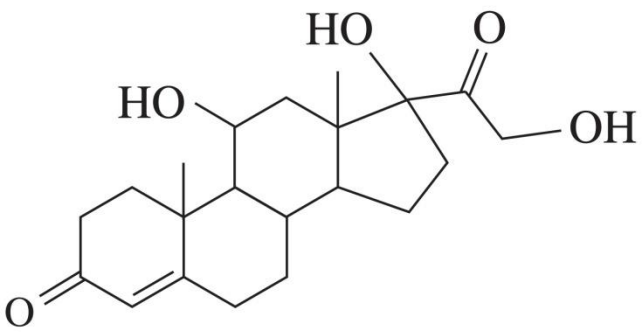
Norethindrone
(synthetic progestin)

Adrenal corticosteroids are steroid hormones produced by the adrenal glands located on the top of each kidney and include

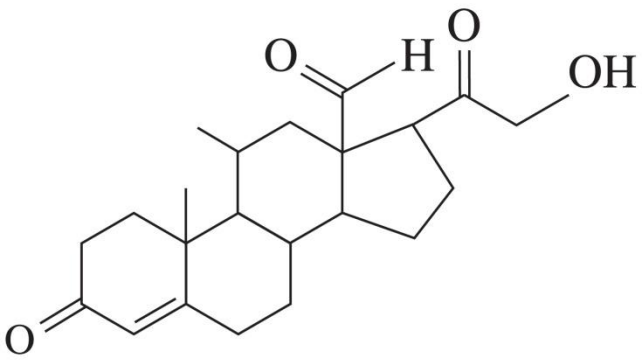
- *aldosterone*, which regulates electrolytes and water balance by the kidneys;
- *cortisol,* released under stress to increase blood sugar and regulate carbohydrate, fat, and protein metabolism; and
- *prednisone,* a synthetic corticosteroid, derived from cortisone, used for reducing inflammation, treating asthma and rheumatoid arthritis.



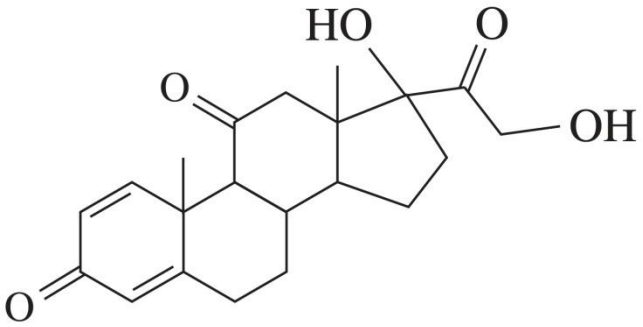
Cortisone



Cortisol



Aldosterone (mineralocorticoid)



Prednisone