

Hormones

BCH 358

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Introduction to Hormones

Lecture 1

Syllabus:

- Introduction: Chemical natures of hormones
- Molecular basis of hormone action
- Pituitary gland and hypothalamus
- Thyroid and parathyroid glands
- Pancreas
- Adrenal gland (cortex and medulla)
- Gonads (male and female hormones)

Glands

Presence or absence of ducts

- Exocrine – ducted
- Endocrine – ductless

- 1) Exocrine - glands that excrete their secretions into a ductule system. Have two parts, acinous = secretory bulb and ductule.
- 2) Endocrine - glands excrete their secretions directly into body fluids, ultimately blood.

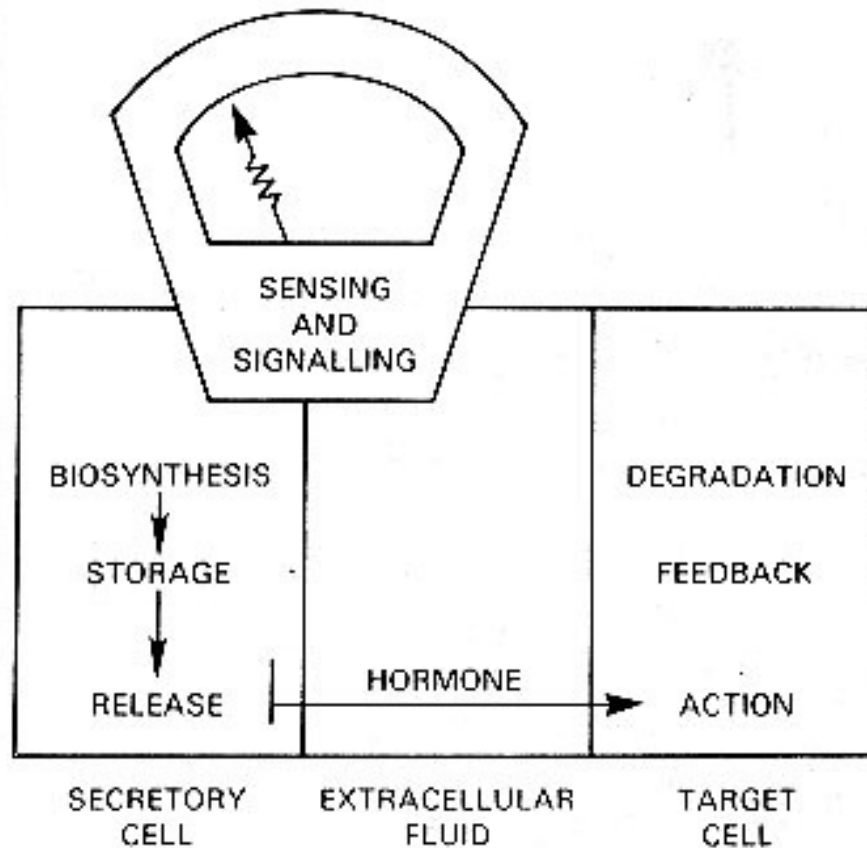
Each hormone :

- Structure
- Biosynthesis
- Regulation of secretion
- Transport
- Mechanism of action
- Metabolism
- Effects (action)
- pathphysiology

References

- Harper's biochemistry
- Basic and clinical endocrinology (Lange medical book)
Francis S. Greenspan
- Zubay (hormones)

Sensing and signaling



Endocrine “glands” synthesize and store hormones. These glands have a sensing and signaling system which regulate the duration and magnitude of hormone release via feedback from the target cell.

Principal functions of the endocrine system

- Maintenance of the internal environment in the body (maintaining the optimum biochemical environment). Maintain homeostasis.
- Regulate growth and development
- Promote sexual maturation and facilitate reproduction
- Regulate energy production
- Adapt/adjust body to stressful/emergency situations
- Promote/inhibit production or release of other hormones

Terms

- Endocrinology
 - Science that deals with a group of ductless glands and the action of their secretions which are transported via the blood stream
- Hormones
 - **Hormones - chemical messengers carried by the blood from endocrine glands to the cell upon which they act. (Affect distal targets.)**
- **The word “hormone” is derived from a Greek term that means to arouse to activity.**

Endocrine versus Nervous System

- Major communication systems in the body
- Integrate stimuli and responses to changes in external and internal environment
- Unlike the nervous system, the endocrine system is anatomically discontinuous.

Types of hormones according to actions

Endocrine action: hormones that travel via blood stream and binds to distant target cells.

Paracrine action: hormones act on adjacent cells.

Autocrine action: the hormone acts on the same cell that produced it.

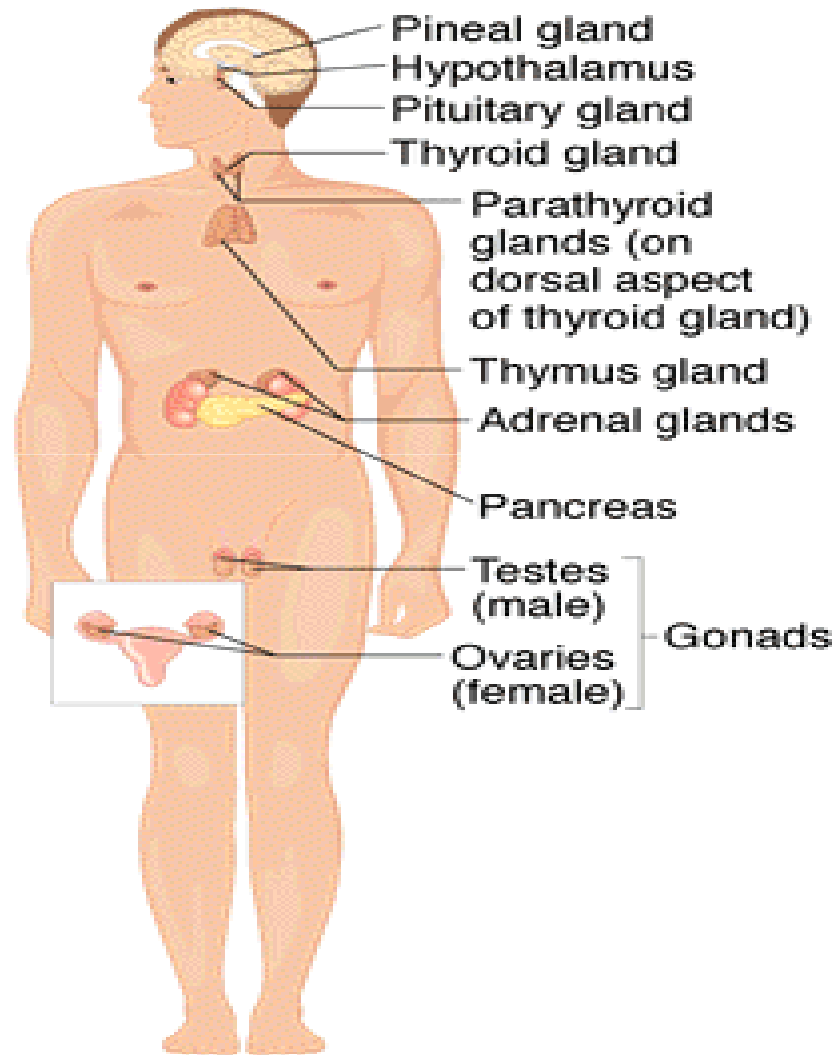


Endocrine System

–Endocrine glands - release their substances into the surrounding fluid (*ductless glands*). They include the **pituitary, thyroid, parathyroid, adrenal, pineal, and the thymus glands**. Also included are the **pancreas** and **gonads**. The **hypothalamus** is called a *neuroendocrine organ*.

–Figure

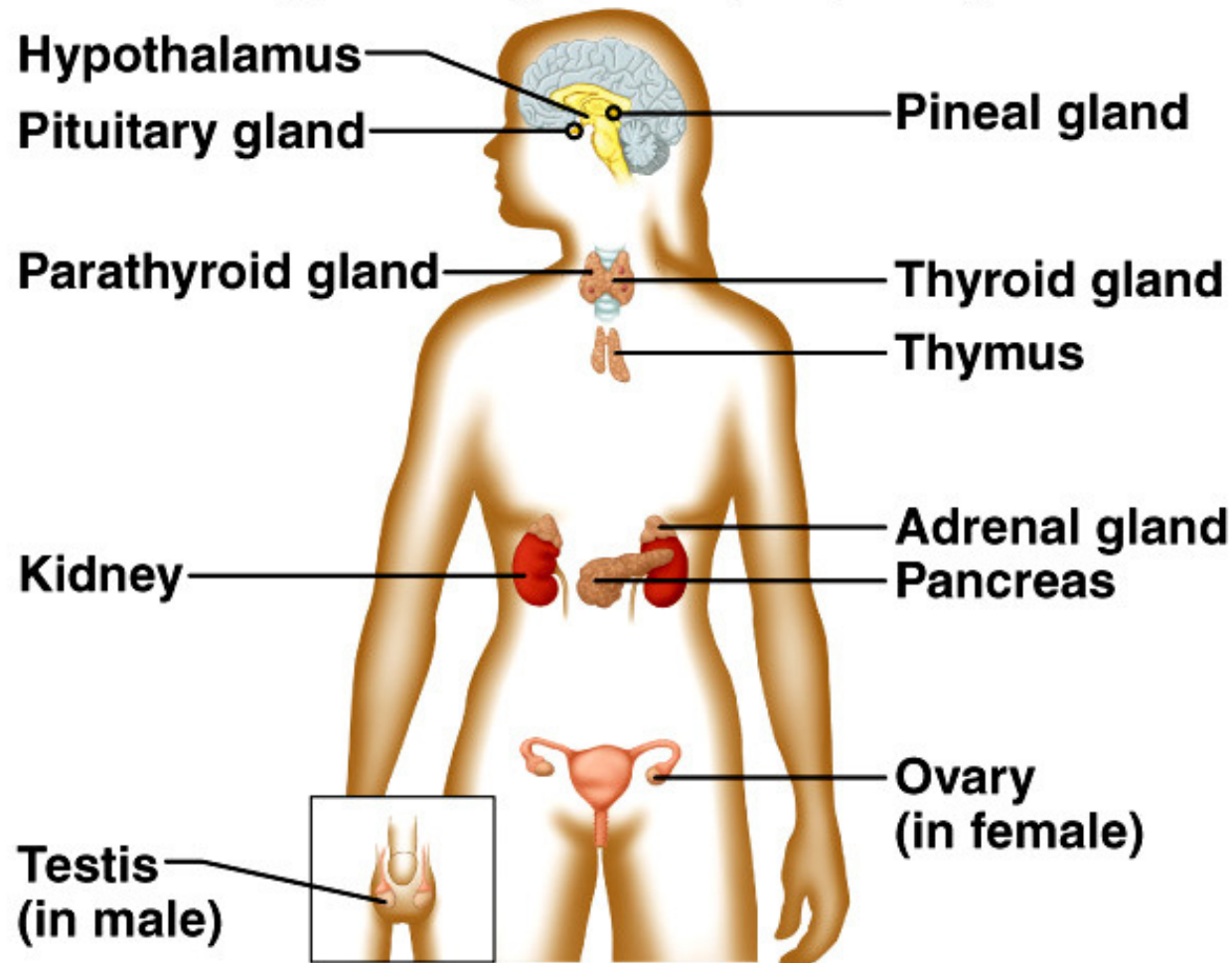
Endocrine System



Fig

Major Endocrine Glands

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Endocrine Glands

Hypothalamus

The hypothalamus makes hormones that control the pituitary gland. In addition, it makes hormones that are stored in the pituitary gland.

Pineal gland

The pineal gland releases melatonin, which is involved in rhythmic activities, such as daily sleep-wake cycles.

Pituitary gland

The pituitary gland produces hormones that regulate many of the other endocrine glands.

Thyroid

The thyroid produces thyroxine, which regulates metabolism.

Parathyroid glands

These four glands release parathyroid hormone, which regulate the level of calcium in the blood.

Pancreas

The pancreas produces insulin and glucagon, which regulate the level of glucose in the blood.

Thymus

During childhood, the thymus releases thymosin, which stimulates Tcell development.

Ovary

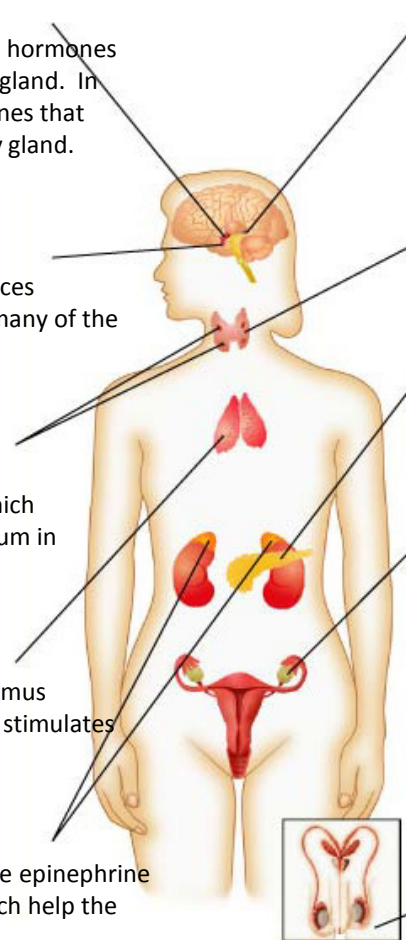
The ovaries produce estrogen and progesterone. Estrogen is required for the development of secondary sex characteristics and for the development of eggs. Progesterone prepares the uterus for a fertilized egg.

Adrenal glands

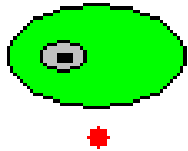
The adrenal glands release epinephrine and nonepinephrine, which help the body deal with stress.

Testis

The testis produce testosterone, which is responsible for sperm production and the development of male secondary sex characteristics



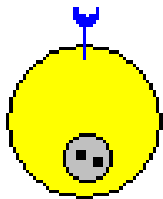
Hormones travel via the blood stream to target cells



- **The endocrine system**

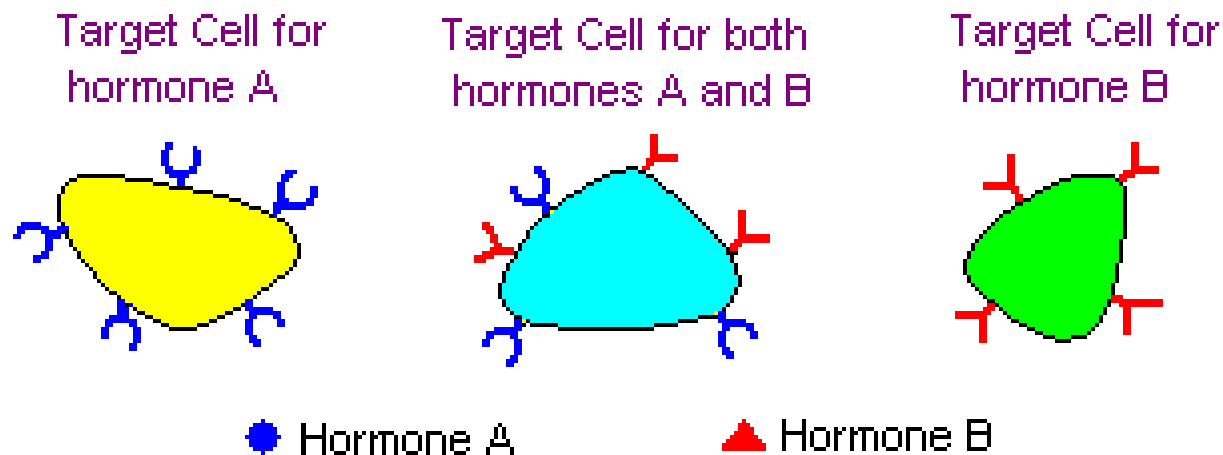
- send its hormonal messages to essentially all cells by secretion into blood and extracellular fluid.

- cells must have a *receptor* for the hormone in order to respond.



A cell is a target because it has a specific receptor for the hormone

Most hormones circulate in blood, coming into contact with essentially all cells. However, a given hormone usually affects only a limited number of cells, which are called **target cells**. A target cell responds to a hormone because it has **receptors** for the hormone.



Classification and Properties of Hormone

A. Site of Production

B. Type of action

1. Primary hormone of reproduction

2. Metabolic hormone

C. Chemical Structure

1. General structure

- Proteins and polypeptides
- Steroids
- Fatty acids
- Modified amino acid

2. Size

Classification and Properties of Hormone

A. Site of Production

B. Type of action

1. Primary hormone of reproduction

follicle stimulating hormone (FSH)

luteinizing hormone (LH),

estrogen, progesterone

testosterone

2. Metabolic hormone

thyroxin,

insulin

| | | | |
|-------------|--|--------------|---|
| ACTH | Adrenocorticotrophic hormone | GH | Growth hormone |
| ANF | Atrial natriuretic factor | IGF-I | Insulin-like growth factor-I |
| cAMP | Cyclic adenosine monophosphate | LH | Luteotropic hormone |
| CBG | Corticosteroid-binding globulin | LPH | Lipotropin |
| CG | Chorionic gonadotropin | MIT | Monoiodotyrosine |
| cGMP | Cyclic guanosine monophosphate | MSH | Melanocyte-stimulating hormone |
| CLIP | Corticotropin-like intermediate lobe peptide | OHSD | Hydroxysteroid dehydrogenase |
| DBH | Dopamine β -hydroxylase | PNMT | Phenylethanolamine- <i>N</i> -methyltransferase |
| DHEA | Dehydroepiandrosterone | POMC | Pro-opiomelanocortin |
| DHT | Dihydrotestosterone | SHBG | Sex hormone-binding globulin |
| DIT | Diiodotyrosine | StAR | Steroidogenic acute regulatory (protein) |
| DOC | Deoxycorticosterone | TBG | Thyroxine-binding globulin |
| EGF | Epidermal growth factor | TEBG | Testosterone-estrogen-binding globulin |
| FSH | Follicle-stimulating hormone | TRH | Thyrotropin-releasing hormone |
| | | TSH | Thyrotropin-stimulating hormone |

- **Chemical Classification**

- **Hormones are categorized into four structural groups, with members of each group having many properties in common:**

- **Peptide hormones and proteins** - 3 or more amino acids
- **Steroid hormones** - derived from cholesterol
- **Amine hormones** - single amino acids
- **Fatty acid derivatives** - Eicosanoids

Classification and Properties of Hormone

- Chemical Structure
 - Polypeptides - hypothalamic
 - Protein - pituitary
 - Steroids - gonad, adrenal
 - Fatty acid - prostaglandins
 - Modified amino acid - pineal

Chemical Structure of Hormones

Molecular size of hormones that regulate reproduction

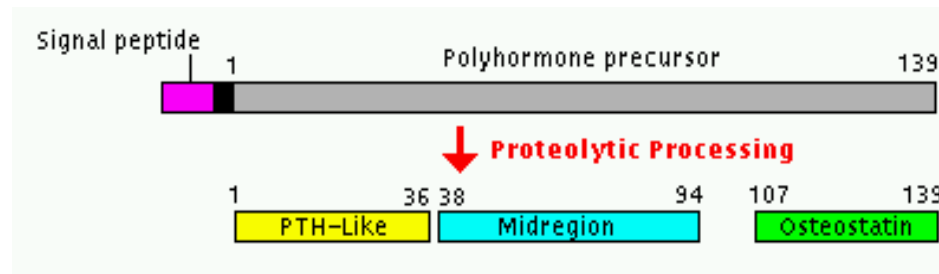
| Hormone | Molecular Weight |
|--------------|------------------|
| FSH | 30,000 to 37,000 |
| LH | 26,000 to 32,000 |
| Prolactin | 23,000 to 25,000 |
| HCG | 37,70 |
| ACTH | 4,500 |
| Oxytocin | 1,007 |
| GnRH | 1,200 |
| Estradiol | 300 |
| Testosterone | 300 |
| Progesterone | 300 |

Chemical Types of Hormones

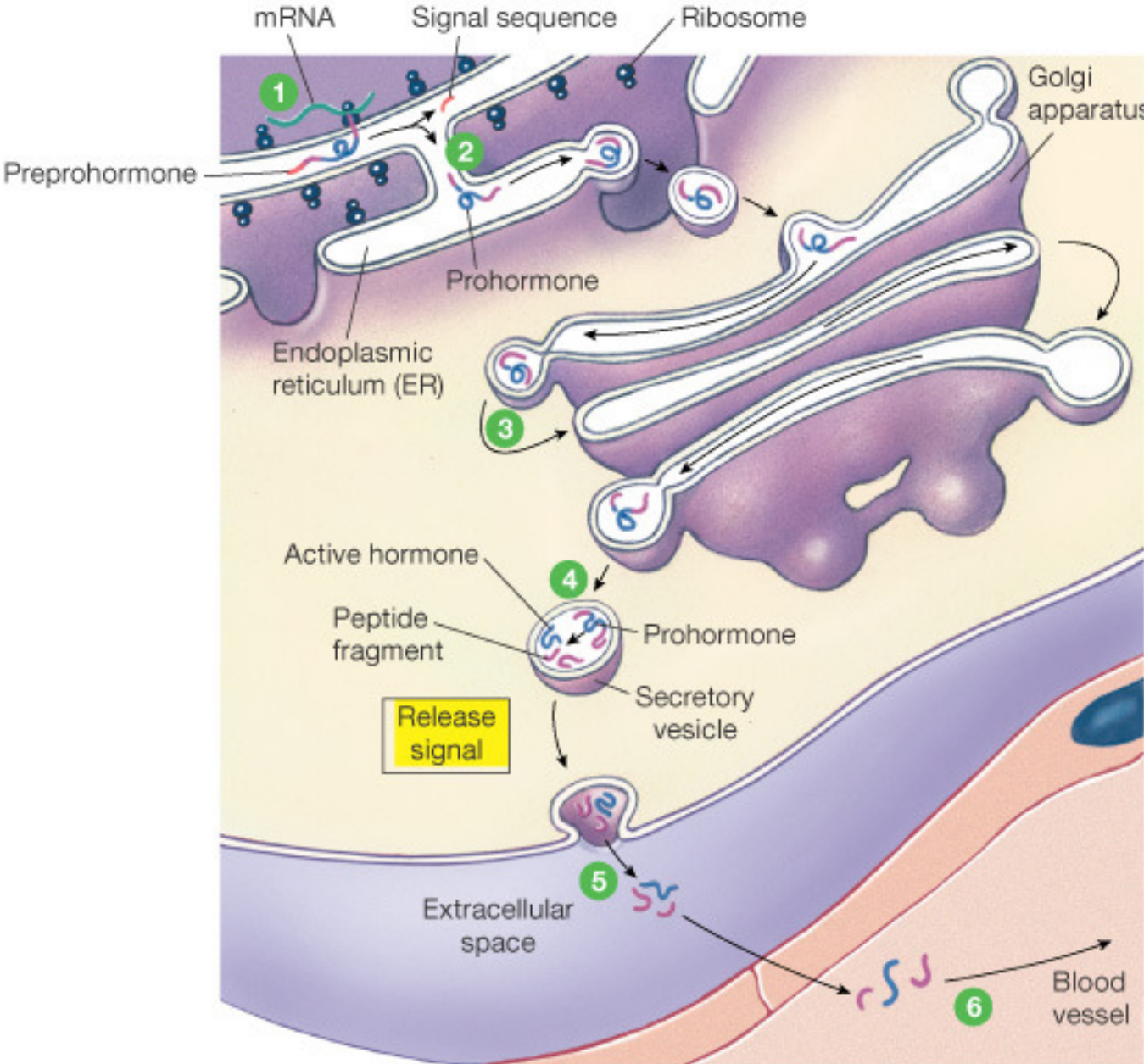
Peptide/protein hormones

- Range from 3 amino acids to hundreds of amino acids in size.
- Often produced as larger molecular weight precursors that are proteolytically cleaved to the active form of the hormone.
- Peptide/protein hormones are water soluble.
- Comprise the largest number of hormones—perhaps in thousands

- Classification, Peptide hormone - eg: Insulin, parathyroid hormone (PTH)
 - Synthesis - RER, preprohormone is converted to prohormone by peptidase.
 - The prohormone is directed to Golgi apparatus.
 - In Golgi apparatus, pro hormone is converted to hormone and fragments by proteolytic cleavage.
 - Packaged in vesicles
 - Preprohormones contain **signal peptides (leader sequence)** (hydrophobic amino acids which targets them to the golgi) where signal sequence is removed).



Peptide hormone synthesis, packaging, and release



-Released into ECF when cell is signaled to do so.

-Transported in blood, half-life – minutes (Short term effects.)

- Soluble in plasma

- Mechanism of action - bind to cell surface receptors to trigger the activation of adenylyl cyclase resulting in the production of cyclic-AMP and some use tyrosine kinase

- Action - open or close membrane channels or modulate metabolic enzymatic activity or transport proteins

- **Classification, Steroid hormones, eg: estradiol**
 - Synthesis - SER, lipophilic, synthesized as needed
 - Produced by the adrenal cortex, the gonads, and the placenta
 - Precursor is cholesterol
 - Found bound (inactive) to protein carriers in blood
 - Half-life - hours
 - Mechanism - diffuses across cell membrane to cytoplasmic and nuclear receptors. Interact with DNA
 - Slow response by cells - hours

Steroid hormones

- Are not packaged, but synthesized and immediately released
- Are all derived from the same parent compound: Cholesterol
- Enzymes which produce steroid hormones from cholesterol are located in mitochondria and smooth ER
- Steroids are lipid soluble and thus are freely permeable to membranes so are not stored in cells

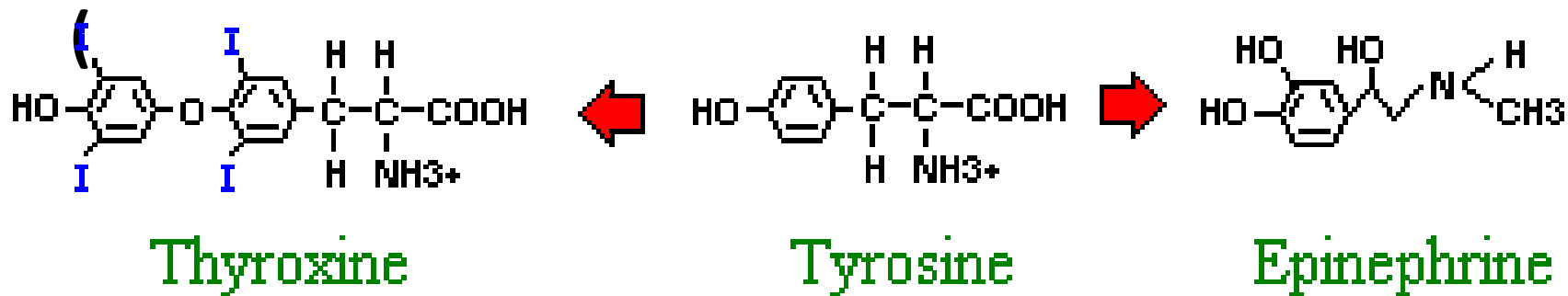
Steroid hormones

- Steroid hormones are not water soluble so have to be carried in the blood complexed to **specific binding globulins**.
 - * Corticosteroid binding globulin (**CBG**) carries cortisol
 - * Sex steroid binding globulin (**SHBG**) carries testosterone and estrogen.
- In some cases a steroid is secreted by one cell and is converted to the active steroid by the target cell:
an example **is androgen which secreted by the gonad and converted into estrogen in the brain**

Amine hormones

There are two groups of hormones derived from the amino acid **tyrosine**.

Thyroid hormones and **Catecholamines** (These include epinephrine, and norepinephrine)



- Poorly soluble in plasma
- Enter the target cell, penetrate the nuclei, react with the DNA to promote or suppress gene action
- Provide long term effects

- **Classification, Amine hormones**

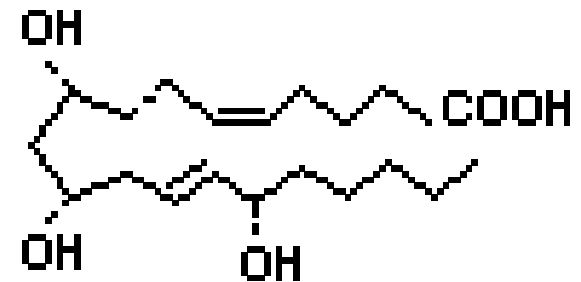
- Nitrogen-containing.
- They behave like peptide hormones (**catecholamines**) or **like steroid hormones (Thyroid hormones)**
- Thyroid hormones: produced by thyroid gland found in the lower part of the neck. It secretes 3 hormones:
 - Thyroxine - T_4
 - Triiodothyromine - T_3
 - Calcitonin
- The first two are collectively known as thyroid hormones (TH) and contain iodine
- Every tissue in the body is affected by TH

Amine Hormones

- **Two other amino acids are used for synthesis of hormones:**
- **Tryptophan** is the precursor **to serotonin** and the pineal hormone melatonin
- **Histidine** is converted to **histamine**

Fatty Acid Derivatives-Eicosanoids

- Arachadonic acid is the most abundant precursor for these hormones.
- Stores of arachadonic acid are present in membrane lipids and released through the action of various lipases.
- These hormones are rapidly inactivated by being metabolized, and are typically active for only a few seconds.
- **Eicosanoids** are a large group of molecules derived from polyunsaturated fatty acids.
- For examples: prostaglandins



Prostaglandin F₂α