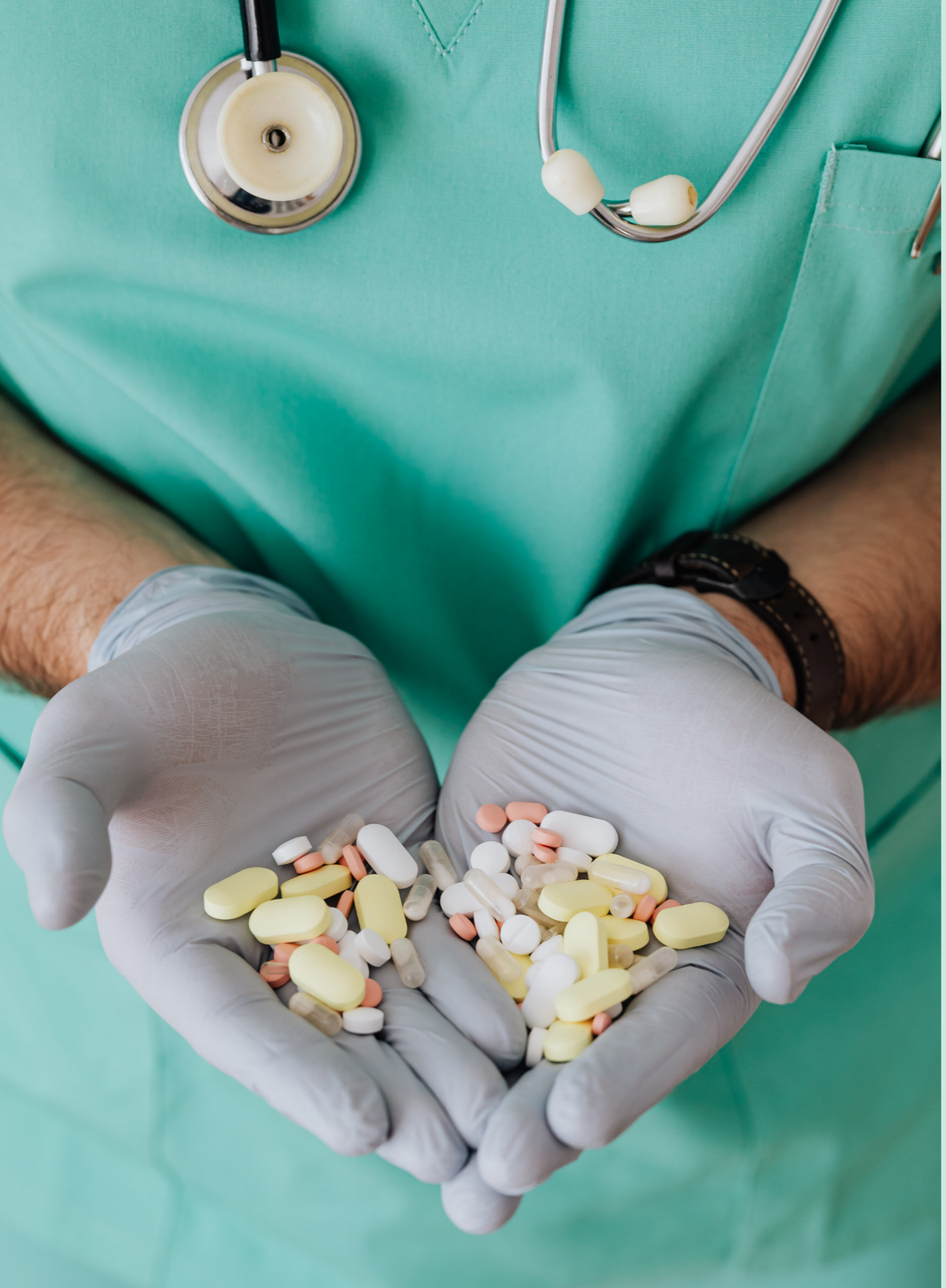

Sheet# 1

PASSION ACADEMIC TEAM YU - MEDICINE

Endocrine system

Lec. Title : Introduction to Endocrinology

Written By : Noor Hammouri

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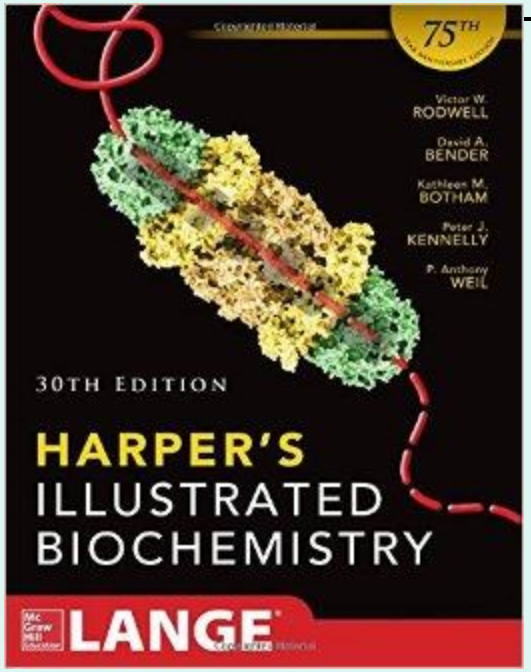


The Diversity of Endocrine System

Chapter 41

30th Ed

The word "hormone" is derived from a Greek term that means to arouse to activity
(stimulate something to do an action).

ABBREVIATIONS

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

The survival of multicellular organisms depends on their ability to adapt to a constantly changing environment.

Intercellular communication (communication between different types of the cells) mechanisms are necessary requirements for this adaptation.

The nervous system and the endocrine system provide this intercellular, organism-wide communication.

Neural regulation of the endocrine system is important in the production and secretion of some hormones(when and where to secret the products of endocrine cells)

A hormone is a substance that is synthesized in one organ and transported by the circulatory system to act on another tissue.

Autocrine and **paracrine** are also included

(Included in the hormone discription from the point of view of the action of the hormone)

Diverse hormones: each with distinctive mechanisms of action and properties of biosynthesis, storage, secretion, transport, and metabolism.

THE TARGET CELL CONCEPT

- There are about 200 types of differentiated cells in humans.

- Only a few produce hormones.

- 75 trillion cells in a human are targets of one or more of the over 50 known hormones.

(a Few hormones can affect trillions of cells in our bodies because of the diversity of the action of these hormones)

The response of a target cell to a hormone depends on:

1. The concentration of the hormone at the target cell.

2. Factors that affect the actual response of the target cell to the hormone. (certain other factors in the target cell itself)

1. factors that affect the concentration of the hormone at the target cell.

Table 41–1. Determinants of the Concentration of a Hormone at the Target Cell

The rate of synthesis and secretion of the hormones.
The proximity of the target cell to the hormone source (dilution effect).
The dissociation constants of the hormone with specific plasma transport proteins (if any).
The conversion of inactive or suboptimally active forms of the hormone into the fully active form.
The rate of clearance from plasma by other tissues or by digestion, metabolism, or excretion.

Regarding to the previous slide:

- Point 2: if the target cell is far away from secretory cell the hormone will be more diluted. Means the concentration of the hormone will decrease if the target cell is farther away.

- Point 3: some hormones have difficulty in moving through blood because they are hydrophobic and they need carriers to move easily (like albumin). Between this hormone and its carrier there is a dissociation constant that effect the releasing of it from the carrier and then the concentration of this hormone around the target cell.

- Some hormones are converted into its active form either by target cells or during transportation of them, so the more active form of concentrated hormones the greater the response.

Regarding to the previous slide:

- Point5:the rate of synthesis and the rate of clearance play the major rule in the concentration of the hormone, means how much do the cells produce of the hormones and how much the body metabolize from them (some hormones have long half-life and stay for hours and some have short half-life and metabolized after a few seconds)

2. factors that affect the actual response of the target cell to the hormone.

Depend on the target cells themselves and how do they response to the hormone.

Table 41–2. Determinants of the Target Cell Response

The number, relative activity, and state of occupancy of the specific receptors on the plasma membrane or in the cytoplasm or nucleus.

The metabolism (activation or inactivation) of the hormone in the target cell.

The presence of other factors within the cell that are necessary for the hormone response.

Up- or down-regulation of the receptor consequent to the interaction with the ligand.

Postreceptor desensitzation of the cell, including down-regulation of the receptor.

Regarding to the previous slide:

- Point1: occupancy of the receptors means do the receptors are available for hormones or the occupied by inhibitors for example…
- relative activity means do they have high or low activity and this depends on the pleomorphic structure of the receptor(three dimensional structure).

- Point3:factors that are necessary for activation of the hormone.

- Point4: relating to the number of receptors

- After attachment of the hormone and the cells were stimulated and no more effect is needed the cell does mechanisms to end up this action (by down regulation of the stimulated receptor)

HORMONE RECEPTORS ARE OF CENTRAL IMPORTANCE

- Type of the receptor plays the major rule in the response of the target cells to the hormone because of their:
  - specificity
  - they can transduce the signals(signal transduction)

- Signal transduction: transferring the signals from outside to inside the cell

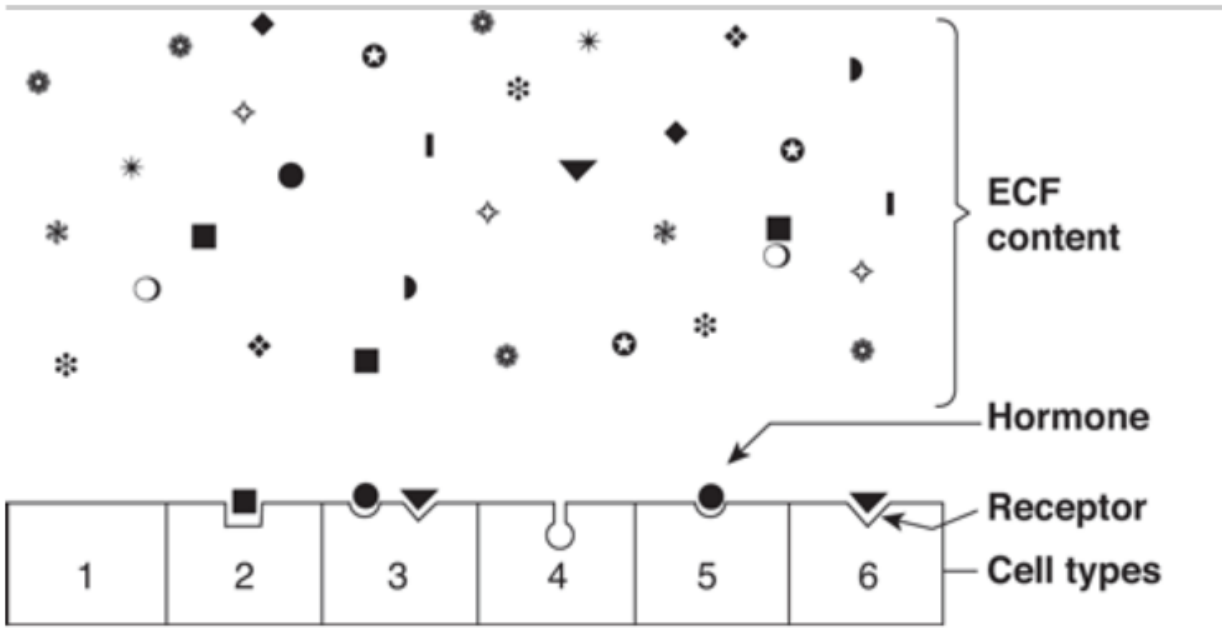
Receptors Discriminate Precisely

Hormones are present at very low concentrations in the extracellular fluid, generally in the atto- to nanomolar range (10^{-15} to 10^{-9} mol/L).

This high degree of discrimination is provided by cell-associated recognition molecules called receptors.

hormone-induced actions generally but not always terminate when the effector dissociates from the receptor

Note that there is several types of receptors on the cell depending on which hormones does it response to



Source: Murray RK, Bender DA, Botham KM, Kennelly PJ, Rodwell VW, Weil PA: *Harper's Illustrated Biochemistry, 28th Edition:* http://www.accessmedicine.com

Both Recognition & Coupling Domains Occur on Receptors

All receptors have at least two functional domains (but we could have more).
The firs domain is for attachment and the other one for signal transduction

Coupling (signal transduction) occurs in two general ways:

1. Polypeptide and protein hormones and the catecholamines bind to receptors located in the plasma membrane.(hydrophilic hormones)

2. Steroid, retinoid, and thyroid hormones interact with intracellular receptors.(hydrophobic hormones)

Receptors Are Proteins

Because they are expressed by certain genes, and when we say they have domain that means they are only proteins

- Insulin receptor is a heterotetramer composed of two copies of two different protein subunits.

- Insulin-like growth factor I (IGF-I) receptor and epidermal growth factor (EGF) receptor are generally similar in structure to the insulin receptor.

- Receptors of the steroid or thyroid type are members of a large superfamily of nuclear receptors.

- Orphan receptors: No ligand was identified (they were considered receptors because they have specific structure and action)

Regarding to the previous slide:

- Insulin receptor :

heterotetramer : hetero means it's made up of two different types of proteins (alpha and beta) tetra means 4 sub units ,so insulin receptors has the structure

Alpha-beta + alpha-beta

- (IGF-I) and (EGF) don't bind to insulin receptors even if their receptors are similar to insulin ones.

- Nuclear receptors : the target of hormones are nuclear site and these receptors act on the genes by regulating it's action.

HORMONES CAN BE CLASSIFIED IN SEVERAL WAYS

1. Chemical composition,
2. Solubility properties,
3. location of receptors,
4. Nature of the signal used to mediate hormonal action within the cell. (signal transduction)

Table 41–3. Classification of Hormones by Mechanism of Action

I. Hormones that bind to intracellular receptors

Androgens

Calcitriol ($1,25[OH]_2$ -D3)

Estrogens

Glucocorticoids

Mineralocorticoids

Progestins

Retinoic acid

Thyroid hormones (T_3 and T4)

You don't have to memorize the name of the hormones

It's not a steroidal hormone

II. Hormones that bind to cell surface receptors

A. The second messenger is cAMP

α_2 -Adrenergic catecholamines

β-Adrenergic catecholamines

Adrenocorticotropic hormone (ACTH)

Antidiuretic hormone

Calcitonin

Chorionic gonadotropin, human (CG)

Corticotropin-releasing hormone

Follicle-stimulating hormone (FSH)

Glucagon

Lipotropin (LPH)

Luteinizing hormone (LH)

Melanocyte-stimulating hormone (MSH)

Parathyroid hormone (PTH)

Somatostatin

Thyroid-stimulating hormone (TSH)

You have just to know the types of the second messengers, the mechanism will be discussed later on

B. The second messenger is cGMP

Atrial natriuretic factor

Nitric oxide

C. The second messenger is calcium or phosphatidylinositols (or both)

Acetylcholine (muscarinic)

⇩

IP

α1-Adrenergic catecholamines

Angiotensin II

Antidiuretic hormone (vasopressin)

Cholecystokinin

Gastrin

Gonadotropin-releasing hormone

Oxytocin

Platelet-derived growth factor (PDGF)

Substance P

Thyrotropin-releasing hormone (TRH)

D. The second messenger is a kinase or phosphatase cascade

Adiponectin

Chorionic somatomammotropin

Epidermal growth factor

Erythropoietin

Fibroblast growth factor (FGF)

Growth hormone (GH)

Insulin

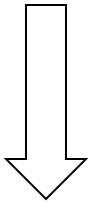
Insulin-like growth factors I and II

Leptin

Nerve growth factor (NGF)

Platelet-derived growth factor

Prolactin



Protein kinase C

Table 41–4. General Features of Hormone Classes

Types		
Steroids, iodothyronines, calcitriol, retinoids		
Polypeptides, proteins, glycoproteins, catecholamines		
Solubility	Receptor	
Lipophilic	Intracellular	
Hydrophilic	Plasma membrane	
Transport proteins(carrier)	Mediator	
Yes	Receptor-hormone complex	
No	cAMP, cGMP, Ca2+, metabolites of complex phosphinositols, kinase cascades	
Plasma half-life		
Long (hours to days)		
Short (minutes) Most of them		

DIVERSITY OF THE ENDOCRINE SYSTEM

Hormones Are Synthesized in a Variety of Cellular Arrangements

Hormones are synthesized in discrete organs designed solely for this specific purpose, such as the thyroid (triiodothyronine), adrenal (glucocorticoids and mineralocorticoids), and the pituitary (TSH, FSH, LH, growth hormone, prolactin, ACTH).

The same hormone could activate different types of tissues and could have different types of actions.

Example: sex hormones in males and females, they are similar but in the same time they do different actions and have different types of target cells.

From the recording

Hormones Are Chemically Diverse

- Due to ability to modify them by:

1- adding or removing certain groups

2-chosmatic effect (iodination)

3-cleavage

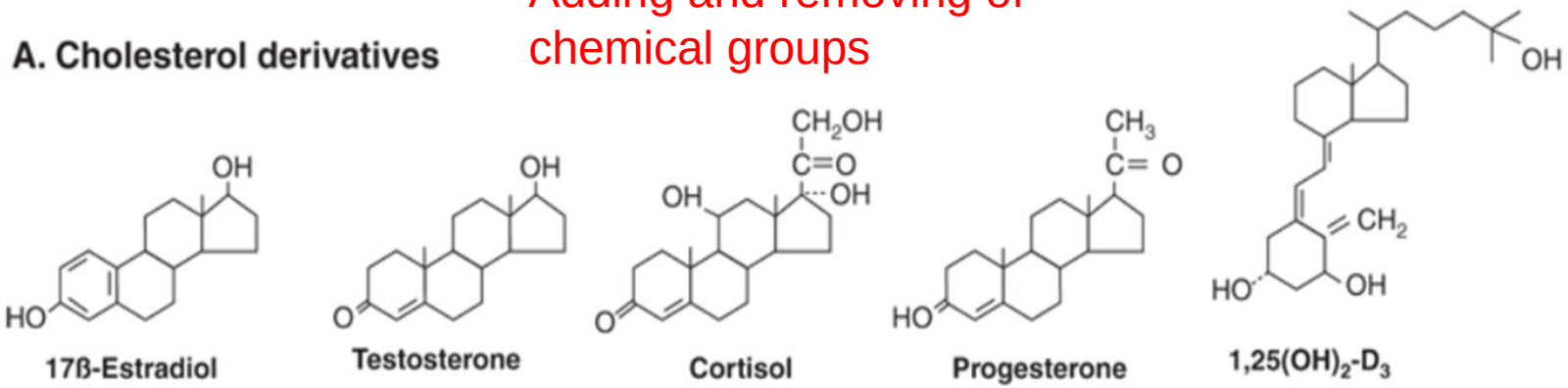
4-forming small polypeptide structures

5-glycocylation

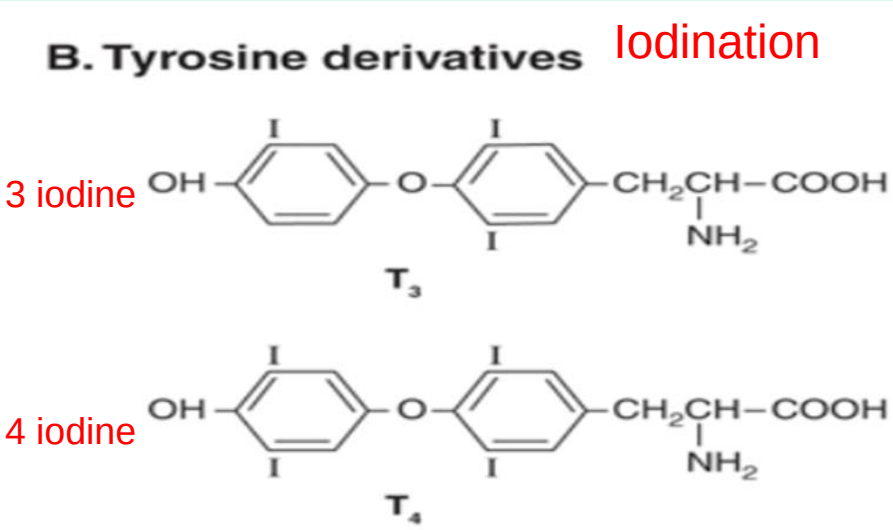
- All is done by enzymes located in the target cells

Hormones Are Chemically Diverse

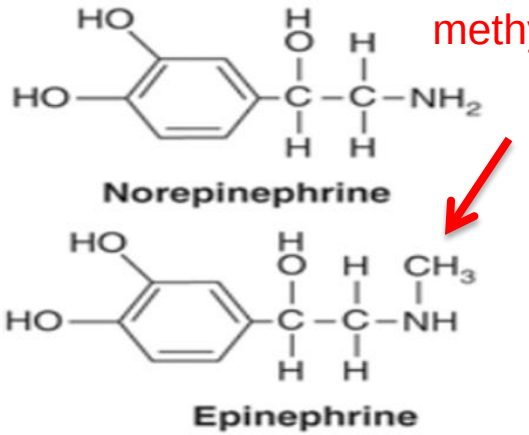
Adding and removing of chemical groups



Iodination

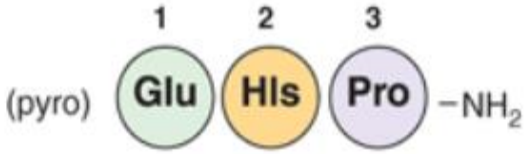


methylation

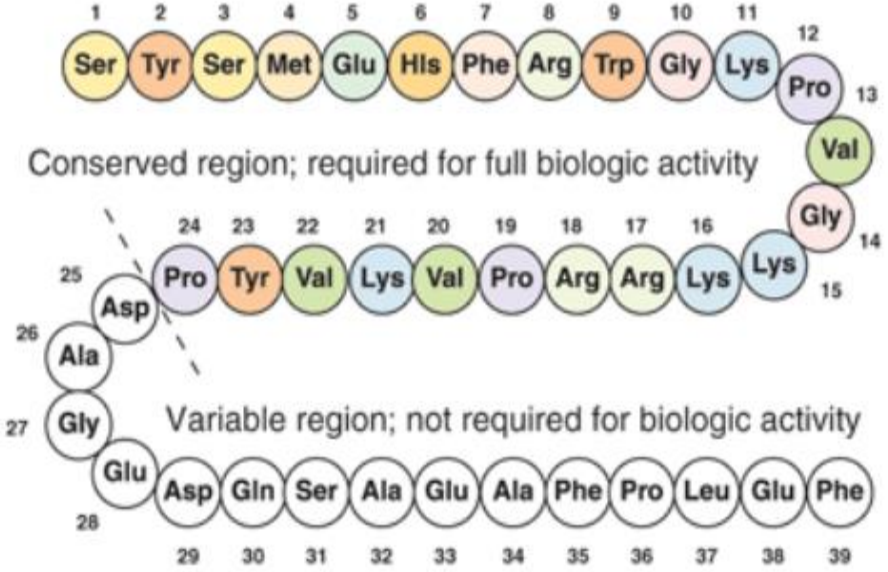


C. Peptides of various sizes

forming small polypeptide structures



TRH



D. Glycoproteins (TSH, FSH, LH) glycosylation

common α subunits

unique β subunits

ACTH

↓

cleavage

Synthesis & Secretion of Peptide Hormones

1- transcription

2- translation

3- producing the hormone

4- Storage in vesicles

5- stimulation to secretion

6- secretion

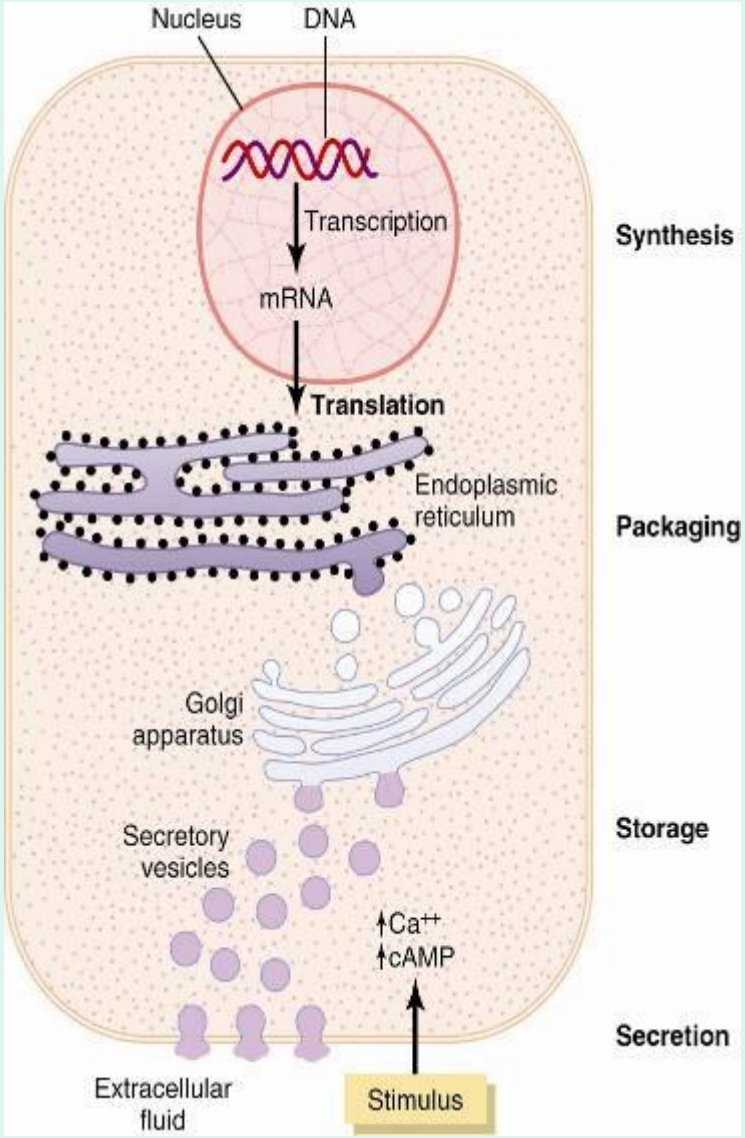


Figure 75-2