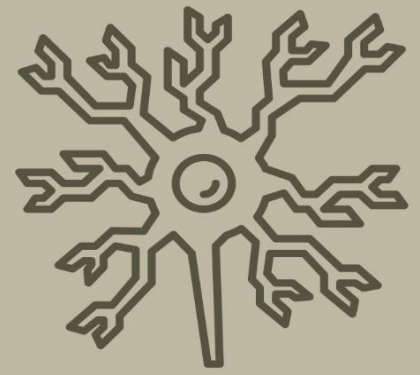
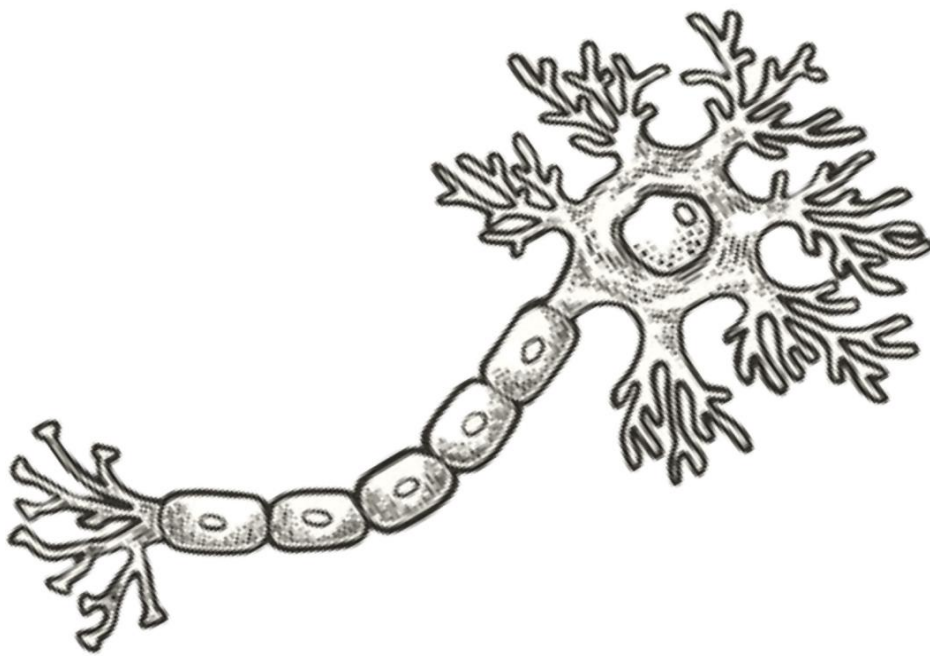


PHYSIOLOGY



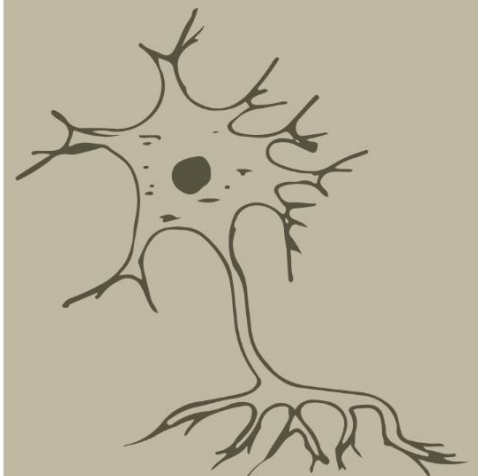
SHEET NO.

17

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Signal transduction

Before talking about synthesis of hormones you should know that some hormones are not synthesis into the final form directly.

❖ There is different form of hormones other than the active (final) form:

1. **Prohormone:** Precursor is a longer chained polypeptide that is cut and spliced together to make the hormone. (ex, Proinsulin which is larger than insulin – gives insulin)
2. **Preprohormone:** Prohormone derived from larger precursor molecule (ex, Preproinsulin)

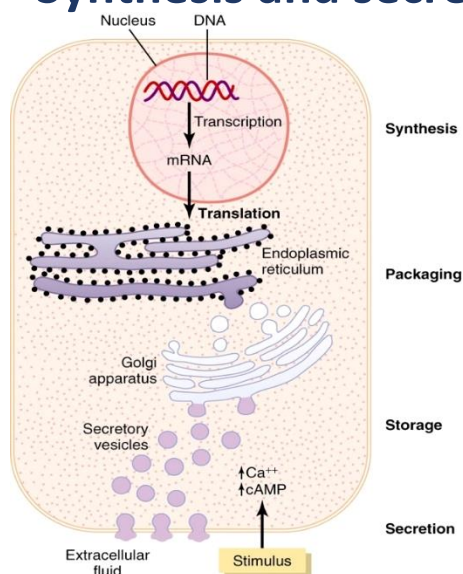
- Stages of insulin production:

Preprohormone (Preproinsulin) → prohormone (proinsulin) → hormone (insulin)
→ Cutting, splicing, modification.

3. **Prehormone:** Molecules secreted by endocrine glands that are **inactive** until changed into hormones by target cells. (ex ,T₄ (tetra-iodothyronin) converted to T₃ (tri-iodothyronin)

- بمعنى يكون الهرمون موجود بحالة ال inactive وحتى يؤدي وظيفته لازم ينعمله activation عن طريق conformational change أو طرق أخرى مثل حذف ذرة معينة، ومثال على ذلك هو ال T₄ المتواجد بالغالبية العظمة للدم ولكن لإحداث التأثير المطلوب لازم يتحول ل T₃ عن طريق انزيم موجود بالغشاء البلازمي وبالتالي ال T₄ هو ال **prehormone**.

■ Synthesis and secretion of peptide hormones:



Note: Most Common hormone,
Majority of hormone: family of
peptide and protein

- Transcription
- Translation in ER
- Packaging to golgi
- Storage
- Secretion after stimuli

Note: Releasing of hormone need signaling

■ Chemical classification of hormones:

Endocrine hormones: hormones that are transported from secreting cell to target cell through blood

Table 10-4 Chemical Classification and Function of Hormones

Chemical Classification	Examples	Regulated Function
Endocrine Hormones		
Amino acid derivatives	Epinephrine (adrenaline) and norepinephrine (both derived from tyrosine)	Stress responses: regulation of heart rate and blood pressure; release of glucose and fatty acids from storage sites
Peptides	Thyroxine (derived from tyrosine) Antidiuretic hormone (vasopressin) Hypothalamic hormones (releasing factors)	Regulation of metabolic rate Regulation of body water and blood pressure Regulation of tropic hormone release from pituitary gland
Proteins	Anterior pituitary hormones	Regulation of other endocrine systems
Steroids	Sex hormones (androgens and estrogens) Corticosteroids	Development and control of reproductive capacity Stress responses; control of blood electrolytes
Paracrine Hormones		
Amino acid derivative	Histamine	Local responses to stress and injury
Arachidonic acid derivatives	Prostaglandins	Local responses to stress and injury

(glycoproteins ممكن يكون)

Local hormone:
paracrine/autocrine

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Note: The doctor didn't mention the regulated function in the lecture.

❖ Depending on this classification, now we will discuss each hormone from which glands or tissue secreted:

● Steroid Hormones:

intracellular receptors يرتبطوا ب
cell surface receptors وممكن يرتبطوا ب

Gland/Tissue	Hormone
Adrenal Cortex	Cortisol, Aldosterone, Androgens
Testes	Testosterone
Ovaries	Estrogens, Progesterone
Corpus Luteum	Estrogens, Progesterone
Placenta	Estrogens, Progesterone
Kidney	1,25 Dihydroxycholecalciferol (calcitriol)

ملاحظات على الجدول السابق:

ليس بالضرورة أن تكون الخلية endocrine وحتى يكون عنا endocrine hormone ممكن يكون خلية أو عضو ليس ضمنهم مثل الكلية والكبد ومثال على ذلك ال active form of vitamin D الذي يفرز من الكلية ويعتبر من ال steroid hormones

معلومة على السريع :

Cortisol: stress hormone

Aldosterone: يشغل على الكلية والضغط وامتصاص الأملاح

Androgen: sex hormone

● Peptide & Protein Hormones:

*بحتاجوا cell surface

Gland/Tissue	Hormone
Hypothalamus	TRH, GnRH, CRH GHRH, Somatostatin
Anterior pituitary	ACTH, TSH, FSH, LH, PRL, GH
Posterior pituitary	Oxytocin, ADH
Thyroid	Calcitonin
Pancreas	Insulin, Glucagon, Somatostatin
Liver	Somatomedin C (IGF-1)
Parathyroid	PTH
Placenta	HCG, HCS or HPL
Kidney	Renin (Enzyme)
Heart	ANP

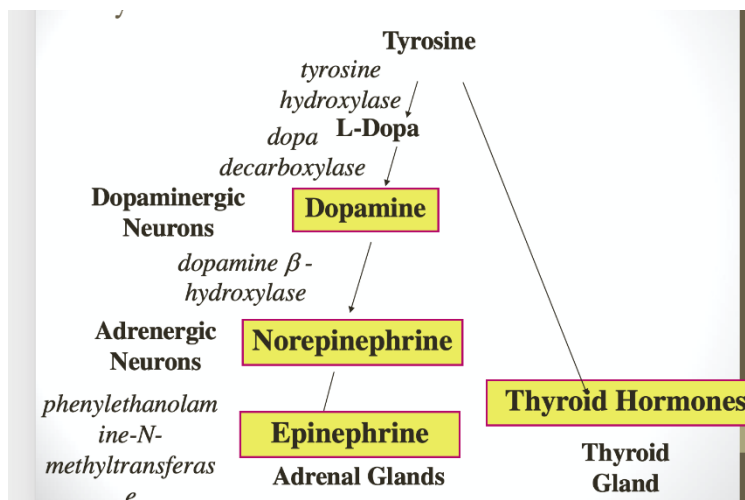
G.I. tract	Gastrin, CCK, Secretin, GIP, Somatostatin
Adipocyte	Leptin

*ملاحظة: لن يتم السؤال من وين تم الافراز ولكن السؤال يكون كيف يشتغل الهرمون ونوع المستقبل وشو ال signaling وال messenger الي رح يعمله

• Amine Hormones:

Gland/Tissue	Hormone
Hypothalamus	Dopamine
Thyroid	T ₃ , T ₄ <div style="border: 1px solid black; padding: 5px; display: inline-block; margin-left: 20px;">Note: T₃ is lipophilic</div>
Adrenal medulla	Epinephrine and Norepinephrine (NE, EPI)

❖ Synthesis of Amine Hormones:



*ملاحظة: غير مطلوب حفظ الانزيمات

■ Hormone Activity:

- Hormone response depends not only on present of hormone itself but also a receptor for the hormone should be existing to have a response and hormones affect only specific target tissues with specific receptors.

- الاستجابة للهرمون تعتمد على وجود المستقبلات وتركيز الهرمون.

- **Receptors:** considered as proteins, it is part of the cell, dynamic and constantly synthesized and broken down.

dynamic: بمعنى انها بتتحرك وبخلاف عددهم ومكانهم ووجودهم في كل مرحلة عمرية ، يعني ممكن بنفس الخلية يكونوا موجودين بال membrane ويحدث لهم internalization ويدخلوا بداخل vesicles* يتخبّوا

❖ There are two conditions for receptors:

1. Down-regulation- when there is decreasing in receptor number or response.
2. Up-regulation- when there is increasing in receptor number or activity.

■ Effects of [Hormone] on Tissue Response:

1. Priming effect (upregulation): Increase number of receptors formed on target cells in response to particular hormone and greater response by the target cell.

يعني بتكون الخلية غير معرضة لهذا الهرمون بس مجرد ما زاد تركيزه بتعمل

activatin/upregulation of its receptors to have a better response.

2. Desensitization (downregulation): Prolonged exposure to high concentration of polypeptide hormone, Subsequent exposure to the same [hormone] produces less response then decrease in number of receptors on target cells. **Ex, Insulin in adipose cells.**

بمعنى التعرض لوقت طويل للهرمون ببخلي الخلية exhausted وبالتالي بتعمل signaling to cause downregulation

Example

High glucose level → continues stimulation of insulin → high insulin level → downregulation → type 2 diabetes.

***Downregulation
cause low response**

-How does the body avoid or prevent downregulation?

- via Pulsatile pattern for the secretion of glands

من خلال انه الهرمون يفرز بوقت معين ثم يوقف افرازه لوقت اخر ثم يفرز مرة أخرى

■ Effects of hormone concentration on Tissue Response:

- **Kd:** If we have a large Kd we need a high concentration of the hormone meaning we have a low affinity
- **Half-life:** time that is needed to have 50% of hormone present in plasma and it is different from one hormone to another it takes minutes to days
- Normal tissue responses are produced only when hormones are present within physiological range.
- Sometimes different concentrations of hormones can give different responses such as neurotransmitters.

- **Kd:** Is a constant that give how much we need concentration of hormone to bind to their receptor.

- بمعنى كل ما كانت قيمة ال Kd أعلى فبحتاج تركيز أعلى ليرتبط الهرمون بالمستقبل تبعه ولو كان Kd أقل ف ما بحتاج تركيز كثير عالي ليرتبط الهرمون بالمستقبل يعني ال affinity للهرمون تكون اكبر بهاي الحالة

- أحيانا اذا كان تركيز الهرمون عالي ممكن يرتبط بمستقبل مش كثير بحب

يرتبط فيه بالعادة يعني مش هو ال most favorable

*Affinity -concentration : العلاقة بينهم عكسية

استجابة الخلية تعتمد على :

1-تركيز الهرمون

2-half life of hormone

❖ These pictures showing the different locations of classes of hormone receptors expressed by a target cell:

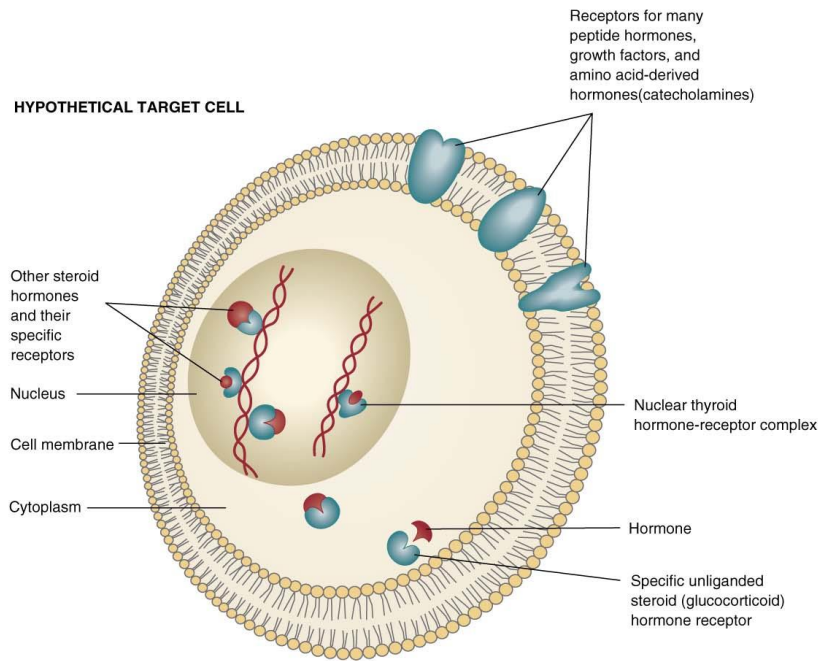
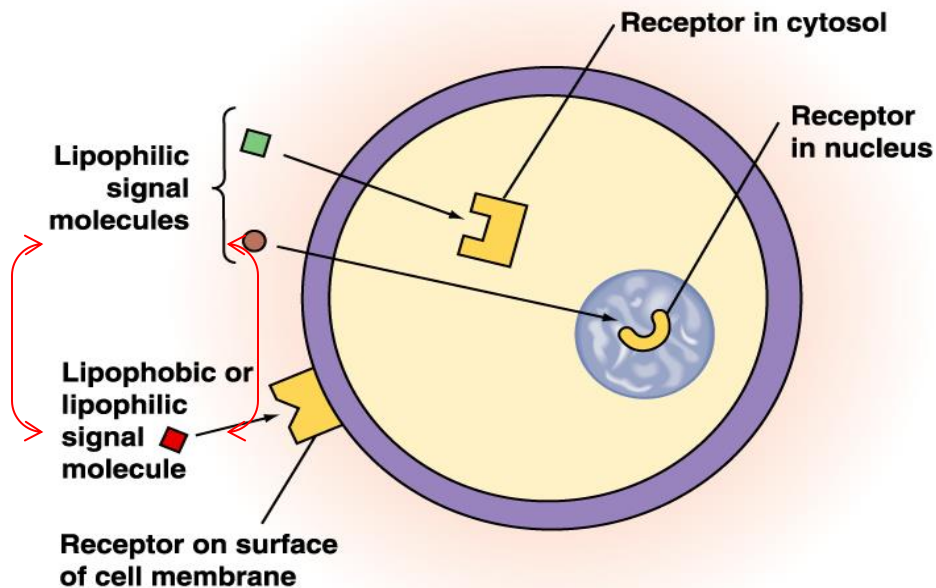


Figure 23.1. Diagram showing the different locations of classes of hormone receptors expressed by a target cell.

Textbook of Biochemistry With Clinical Correlations, Sixth Edition, Edited by Thomas M. Devlin. Copyright © 2006 John Wiley & Sons, Inc.

***Cell surface receptors: lipophilic, lipophobic**

***Receptors in cytosol/ nucleus: lipophilic**



THE END OF SHEET #17

هانت !: