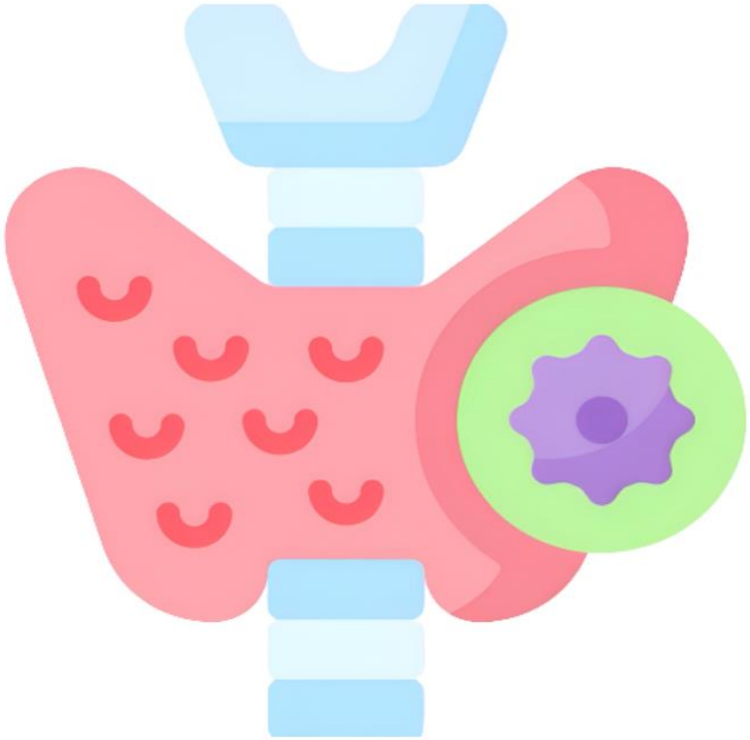
Endocrine system 1

physiology



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Organ systems of the human body:

The doctor started the lecture by talking about the different organ systems that unite to form the human body and the most important functions of each one.

System	Main function(s)
Nervous	**Controls the activities of all other systems**
Skeletal	**Support**, mineral storage , **hematopoiesis**(production of blood cells)
Cardiovascular	Transport of nutrients, gases, metabolic end products and hormones between organ systems
Respiratory	Oxygen take up and carbon dioxide release
Digestive	Digestion, food storage and absorption of nutrients
Urinary	Homeostasis of ECF (extracellular fluid) volume, **consequently regulating blood pressure**
Endocrine	**Regulates reproduction, growth , metabolism , energy balance and ECF composition**
Reproductive	Reproduction and sexual gratification
Lymphatic	Fluid balance, transport of digested fat (through lacteals) , houses lymphocytes
Immune	Resists infection, parasitization and cancer

Harmony between these systems (homeostasis) is controlled and regulated by the **nervous system and the endocrine system**, we call them the **control systems of the body**. The main difference between them is that the action of the nervous system is immediate while the action of the endocrine system is somewhat delayed (generally).

Here's is a comparison between these two systems:

Characteristic	Nervous system	Endocrine system
Mechanism of control	Neurotransmitters a-neuron to neuron (production of action potential) b-neuron to muscle c-neuron to gland	Hormones which are **usually** released into the blood to reach their targets.
Cells affected	Neurons, muscle cells, and glands	Virtually all body cells
Type of action	**In neurons:** action potential **In muscle cells:** contraction **In gland cells:** secretion	Changes in metabolic activities, whether anabolic or catabolic
Time to onset of action	Immediate	Delayed (seconds to hours or days) Sometimes fast e.g. Adrenalin
Duration of action	Generally briefer	Generally longer

Types of glands:

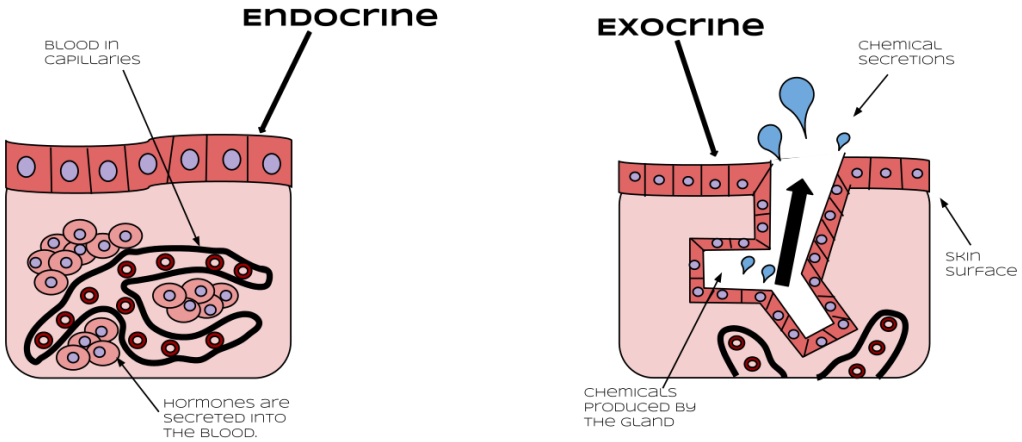
we have 2 types of glands exocrine glands and endocrine glands.

1- Exocrine glands: They secrete their secretions into ducts that lead either to lumens as in the GIT (liver, stomach, testis, ..) or to body surfaces as in sweat glands.

-Its secretion is usually enzymes or solution containing other elements.

2- Endocrine glands: Are groups of cells that produce and secrete hormones, endocrine glands are also called ductless glands as they do not contain ducts and release their hormones into the blood (circulation) or body fluids which transport them into their target tissues.

-Its secretion is usually hormones which are chemicals.



- Endocrine glands that secrete their hormones into the blood are called classic endocrine glands and the hormones are called classic hormones. And usually, theglands are classic endocrine glands.

There are other modes of hormone delivery to the target cells.

(The doctor considered the following as different subtypes of endocrine glands but in his slides they are considered different modes of delivery, keep that in mind).

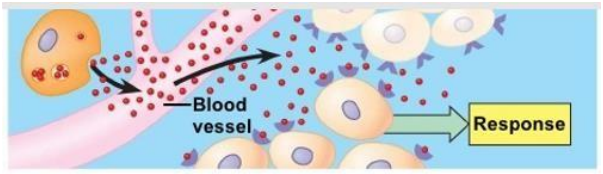
Modes of delivery of hormones to their target cells:

1- Classic endocrine delivery: As was mentioned briefly the hormones (classic hormones) are secreted into the blood then reach their targets.

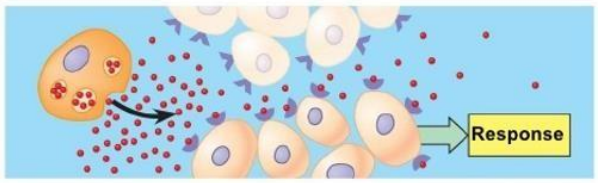
2-Autocrine delivery: Here the secreted hormones affect the secretory cells themselves.

3- Paracrine delivery: Here the hormones are secreted into the interstitial space and affect neighboring cells.

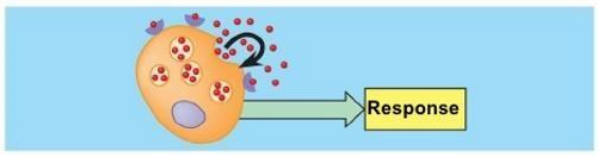
4- Neuroendocrine delivery (e.g. hypothalamus): Here neurons produce hormones which are called neurohormones.



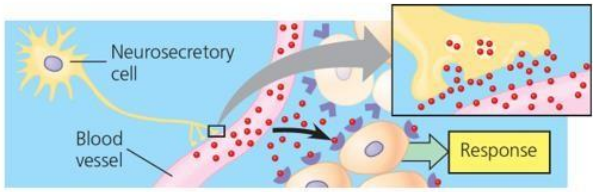
(a) Endocrine signaling



(b) Paracrine signaling



(c) Autocrine signaling



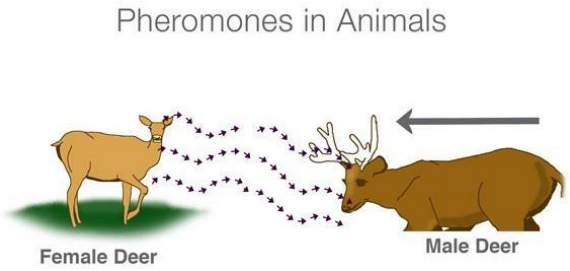
(e) In **neuroendocrine signaling**, neurohormones diffuse into the bloodstream and trigger responses in target cells anywhere in the body.

- Neuroendocrine delivery is divided into 2 subtypes depending on whereneurohormones are being secreted, so it can be secreted either:

a- Into the blood and transported to their targets.

b- Into the synaptic cleft between two neurons affecting the postsynaptic cells.

> **Note (from slides):**
>
> -Neuroendocrine**:** hormones synthesized in neurons and released into extracellular space; interacts with receptors of cells at different site.
>
> -Neurocrine: hormones synthesized in neurons and released into extracellular space; binds to receptor in nearby cell and affects its



5-Pheromonal delivery: Pheromones are volatile hormones that are released by animals into the environment acting at a distance on olfactory cells of other animals producing hormonal, physiological or behavioural changes (e.i. chemistry between animals or people).

In humans they exert behavioural changes that are not necessarily sexual.

*The doctor mentioned 2 examples on animal pheromones:

a-Musk, which is produced by male musk deer, specially the Siberian ones where the glands are larger and the smell is severe because the area is cold so they need too much severe smell to attract the other animal for reproduction.

-These glands are just in the males because they're the ones that need to attract females.

b- **Ambergris** is a solid, waxy, flammable substance of a dull grey or blackishcolor produced in the digestive system (biliary secretion) of sperm whales.

c- **The sex attractants** of certain insects are particularly well-known examples.

The following points are very important points that add to the complexity of the endocrine system:

1-**A single endocrine gland may produce multiple hormones**; each is under different control mechanisms and has different functions. **The anterior pituitary**, for example, secretes six different hormones: some being tropic and others showing nontropic effects.

Tropic hormone: A hormone that has other endocrine glands as its targets.

2-**Most hormones have multiple actions in their target tissues and are said to have a pleiotropic effect**. This phenomenon occurs when a single hormone regulates several functions in the same target tissue. For example, in skeletal muscles, **insulin** stimulates glucose uptake, stimulates glycolysis, stimulates glycogenesis, inhibits glycogenolysis, stimulates amino acid uptake, stimulates protein synthesis and inhibits protein degradation. So normal blood sugar predicts the functions of insulin. (Pleiotropic effect =>A single hormone having many functions in the same target tissue).

3- **Some hormones are known to have different effects in several different target tissues**. For example, **testosterone**, promotes normal sperm formation in the testes, stimulates growth of the accessory sex glands, such as the prostate and the seminal vesicles, and promotes the development of several secondary sex characteristics, such as beard growth and deepening of the voice. **Vasopressin** is another example as it promotes reabsorption of water in the kidney as well as vasoconstriction of arterioles throughout the body.

4- **The same hormone (functionally and chemically) may be secreted by 2 or more endocrine glands**, **Somatostatin** for example is secreted by both the pancreas as ahormone and the hypothalamus as a neurotransmitter.

5- **The same chemical messenger may be either a hormone or a neurotransmitter,depending on its source and mode of delivery to the target cells**. The prime example is **norepinephrine** which is released as a neurotransmitter from sympathetic postganglionic nerve fibers, and as a hormone from the adrenal medulla.

6- Multiplicity of regulation is also common in the endocrine system. The input information from several sources allows highly integrated response to many stimuli, which is of ultimate benefit to the organism. For example, **several different hormones**, including insulin, glucagon, epinephrine, thyroid hormone and adrenal glucocorticoids regulate liver glycogen metabolism. **(1 metabolic pathway, many hormones)**

Many hormones have the same function, e.g., on the growth, growth hormone isthe most important effector but there are other hormones that function on the growth and even growth hormone doesn't function properly if the insulin isn't present.

7- **A single target cell may be influenced by more than one hormone**; these cells contain on their membranes an array of different receptors for different hormones allowing different responses.

For example, liver cells are affected by insulin and glucagon. Insulin promotes the conversion of glucose into glycogen in hepatocytes, by stimulating one enzyme, whereas glucagon promotes the degradation of glycogen into glucose in hepatocytes by activating yet another enzyme.

8-**Some organs of the endocrine system are exclusively endocrine in function**, (they only secrete hormones e.g. **Anterior pituitary gland and thyroid gland**), **whereas other organs perform nonendocrine functions in addition to secreting hormones, these organs are called mixed organs**. **The testes** for example secrete testosterone (endocrine function) and produce sperms (nonendocrine).

function). Other examples include the ovaries, the intestines, the kidneys, the pancreas, the stomach and the heart and the brain.

(In each case except for the brain, nonendocrine function occurs because the organ houses nonendocrine tissue plus isolated clusters of endocrine cells that has migrated to the organ during embryonic development, as for the brain it derives its endocrine function by having neurosecretory cells) '' this part was not mentioned by the doctor ''.

9- In addition to **changing receptor number (down regulation), many target cells regulate receptor function. Chronic exposure of cells to a hormone may cause thecells to become less responsive** to subsequent exposure to the hormone by a process called **desensitization**.

- Remember that for hormones to function properly it must find its specific receptor and the number and function of the receptors must be efficient.

Desensitization

There are 2 types of desensitization:

a- Homologous desensitization: Exposure of cells to a hormone for long duration decreases the response of receptors to subsequent exposure to the same hormone. This decreases the receptor's function sharply and may delete it completely.

b- Heterologous desensitization: Exposure of cells to a hormone decreases the response of receptors even to different hormones.

Hopefully this will make it clearer:

A person steals from a supermarket => the supermarket bans this person. (Homologous desensitization)

In another incident a person steals from a supermarket => the supermarket bans his father. (Heterologous desensitization)

Person=hormone 1, his father=hormone 2, supermarket=receptor

*** In desensitization, the number and/or the function changes. ***

Physiological effects of hormones on body functions:

1- Metabolism: Regulate different metabolic processes (Both anabolic and catabolic).

-Changes in metabolism doesn't occur at all if there are no hormones, so the role of hormones in metabolism is essential.

2- Reproduction: Development of the sex organs, secondary sexual characteristics, gametogenesis and the menstrual cycle.

This means that castrated males won't have sperms and females who undergo ovariectomy won't have follicles/ova.

3-Digestion: Regulate gut motility and secretions.

4-Blood circulation: regulate blood pressure by altering cardiac output, vascular constriction, and blood volume via the control of water excretion by the kidneys.

5- Transport of substrates to tissues (blood composition): Regulate plasma concentrations of glucose, minerals, gases, water, blood cells and hydrogen ions(pH regulation).

6-Defense against pathogens: regulate Immune system responses, including leukocyte activation, inflammation, antibody production and fever.

7- Growth: control cell division and differentiation. (Growth hormone among other hormones)

8- Stress response: regulate the body's response to stress. e.g. the release of adrenaline and cortisol.

9- Behavior: control sexual and social behavior.

Note: Estrogen is called the blessing hormone because it's against everything (blood pressure, lipids, cholesterol, osteoporosis, tension, etc..).

Chemical classification of hormones:

1- Proteins (which include glycoproteins and polypeptides). This category constitutes most of the hormones, so we can say that hormones are mainly proteins.

-Proteins are usually large water-soluble molecules that can't penetrate the cellmembrane or nuclear membrane.

Note: Peptide hormones are made of <20 amino acids, while protein hormones are made of >20 amino acids.

2- Amino acid derivatives (Tyrosine derivatives): A small group that contains **catecholamines** (**Epinephrine and norepinephrine and dopamine**) and **thyroid hormones** (**T4 aka thyroxine and T3**).

-Amino acid derivatives are small and thus can penetrate the cell membrane and nuclear membrane except for catecholamines. Although the structure of catecholamines is composed of 1 amino acid and thyroid hormones is composed of 2 amino acids, **thyroid hormones can penetrate while catecholamines can't**. This is because thyroid hormones are lipid soluble while catecholamines are water soluble and therefore **Catecholamines are transported via ATP-dependent carrier transport.**

3- Steroids: Synthesized from cholesterol precursors. This group contains **adrenalcortex hormones** (**Aldosterone, cortisol**), **male and female sex hormones** (**testosterone, estrogen, progesterone**) and **vitamin D.**

-Steroids are lipid soluble so it can penetrate the cell membrane and nuclear membrane.

(Just memorize 2 + 3 and all other hormones are proteins).

Regulation of Hormone Secretion

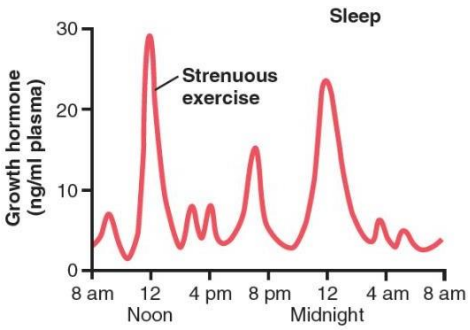
Hormones are needed within certain levels in the body requiring constant regulation:

1- **Neural control:** Pain, emotion, sexual excitement, fright, injury, and stress can all modulate hormone secretion through neural mechanisms. These neural mechanisms include Adrenergic, Cholinergic, Dopaminergic, Serotonergic, endorphinergic and enkephalinergic mechanisms *(one or more can be activated).* Here usually there's an increase in hormone production. In stress, adrenalin and Ach are mainly increased.

2- **Chronotropic control:** This control mechanism is related to **time**. So being at a specific time whether during different times of the day or different seasons of the year can affect the level of hormones. Chronotropic control has many rhythms, such as:

a- **Diurnal rhythm:** the rhythm of secretion of hormones during day and night, **growth hormone** secretion is controlled by this mechanism.

Looking at the figure to the right, you can see that the level of hormone secretion variations at different times throughout the day (Strenuous exercise increases GH lvls)



b- **Sleep-wake cycle:** the level of secretion of some hormones changes during **sleep and wake**.

c- **Menstrual rhythm:** the level of some hormones changes during the **menstrual cycle**.

d- **Seasonal rhythm:** one example is the increase of **sex hormones** levels in mammals duringbreeding seasons.

e- **Developmental rhythm:** Different levels of the hormone during different **developmental stages**. An example is the **growth hormone** level.

> ***Note:*** *Hormones are released either in a **regular manner**, increasing and decreasing (**Oscillating**) or in **pulses** (**Pulsatile**).*

3- **Feedback control:** Almost all hormones are regulated by this mechanism. The relationship between the response and the stimulus is called feedback control.

When the response decreases the stimulus thereby decreasing the release of the hormone, this is called **negative feedback control**. When the response increases the stimulus, increasing therelease of the hormone, this is called **positive feedback control.**

> ***Note:*** *Regulation may occur in **gene transcription** and **translation** of the **hormone**, or in the **processing** and **release** of the hormone.*

Feedback control may occur on a:

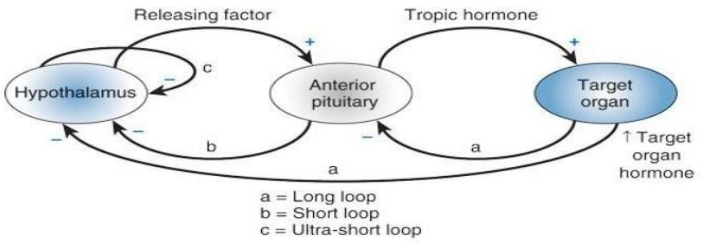
a- **Hormone-hormone level:** One hormone causing the release or the inhibition of the release of another hormone, e.g., increase in **thyroxin level** inhibits the release of **thyroxin-releasing hormone** from the hypothalamus *(negative feedback control).*

b- **Substrate-hormone level: Hyperglycemia** causes the release of **insulin**, while **hypoglycemia** causes **glucagon** release.

c- **Mineral-hormone level: Hypocalcaemia** causes the release of **parathyroid hormone** as a response and transversely, **Hypercalcemia** causes the release of **Calcitonin**.

Negative Feedback Loops:

Negative feedback usually occurs in loops, an important example of these loops is the **hypothalamus-pituitary-peripheral gland axis**.



1- **Ultra-short loop 'c': Regulation in an autocrine manner**, e.g. the hypothalamus produces a hormone, this hormone affects the hypothalamus **itself** altering the secretion of this hormone.

2- **Short loop 'b': Regulation by an intermediate product**, e.g. the hypothalamus produces a hormone (releasing factor), which affects the pituitary gland causing the release of another hormone, this is an example of **Hormone-Hormone** feedback mechanism. Consequently, the hormone released by the pituitary affects the hypothalamus altering its hormone levels.

3- **Long loop 'a': Regulation by the hormone produced by the end product**, e.g. the hypothalamus produces a hormone, which affects the pituitary gland causing the release of another hormone. This pituitary hormone affects the thyroid gland for example, and the thyroid gland responds by releasing another hormone affecting either the pituitary gland or the hypothalamus in a long loop.

Positive Feedback Loops:

As for positive feedback loops, there are 2 main examples:

1- **Neural-hormonal positive feedback loop**: The act of breastfeeding by an infant stimulates certain receptors in the mammary gland (Present in the breast), and thus neural signals travel to the hypothalamus stimulating the release of **oxytocin** from the neurohypophysis (posterior pituitary), i.e. **more sucking = more oxytocin release** until the baby is fully-grown.

2- **Uterine contractions** push the fetus against the cervix, this causes **oxytocin** release through neuroendocrine reflexes. Oxytocin increases uterine contraction either directly or indirectly by increasing the production of prostaglandins, this continues until the baby is delivered.

Regulation of Receptor Number

Hormones determine the sensitivity of the target tissue by regulating the number or activity of receptors.

1- **Down-regulation of receptors**: A hormone decreases the number or affinity of receptors for itself or for another hormone. Down-regulation may occur when exposing cells to an **excess** of hormone for a **sustained** period of time (chronically) causing a decreased number of receptors for this hormone on the cell, as well as decreasing the affinity.

> ***Note:*** *Down-regulation of receptors found on the cell membrane is done by* ***endocytosis*** *of these receptors to the inside of the cell followed by their* ***destruction by lysosomes****.*

2- **Up-regulation of receptors**: A hormone increases the number or affinity of receptors for itself or for another hormone.

Hormones can not only change the number of receptors but can also affect their function. For example, in many old, obese individuals, the insulin level is normal or high, but the insulin **doesn't function properly** because of the **decreased** number and **activity** of its receptors. Glucose level, therefore, remains **higher than normal** resulting in **diabetes mellitus type II**. This could also happen in young, obese or **inactive** persons of normal weight. These individuals are advised to exercise and stick to a healthy diet. If that is applied, their weight may return to normal (if they were obese), thereby insulin returns to its **normal** function.This is due to an increase in the **number** and **affinity** of insulin receptors, in a process called upregulation.

Interactions Between Hormones

Most hormones do not function separately, rather, they function together. This is called hormonal interaction.

1- **Permissive effect (Permissiveness):** In this type of hormonal interaction the effect of one hormone on a target cell requires **previous** or simultaneous **exposure** to **another** hormone(s). Such previous exposure **enhances** the response of a target cell or **increases** the activity of another hormone. (0+1=2) (That is the first hormone **Permits** the second hormone to function efficiently)

Example:

- **Fat cells and fatty acid release**

- Fat cells affected by thyroid hormone alone result in no fatty acid release.
- Fat cells affected by adrenalin (epinephrine) alone result in a small amount of fatty acid release.
- Fat cells affected by thyroxine first then adrenaline result in increased fatty acid release (optimal effect).

⇨ In the third case, adrenalin functions properly only when the cells are previously exposed to thyroxine first.

i.e. Thyroxine alone =0, adrenalin alone =1 , both together =2

- **Another example is the exposure of the uterus first to estrogens and then progesterone for implantation.**

2- **Synergistic effect (Synergism):** The effects of two or more hormones complement each other in such a way that the target cell responds effectively to the **sum of the hormones** involved. (1+1>2)

Example:

The production and secretion of milk by the mammary glands requires, among others, the **synergistic effects** of estrogen, progesterone, prolactin (PRL), and oxytocin (OT). **Mammogenic hormones** (promote cell proliferation) function together. **Lactogenic hormones** (promote milk production) function together. **Galactokinetic hormones** (promote milk ejection) function together.

In these cases, each hormone functions in **different degrees** compared to other hormones, but when more than one of them function simultaneously a **better response** can be achieved.

3- **Antagonistic effect (Antagonism):** The effect of **one hormone** on a target cell is **opposed** by **another** hormone. **Example**: calcitonin (CT), lowers blood calcium level, and parathyroid hormone (PTH), raises blood calcium level. Insulin reduces blood glucose level, and Glucagon increases blood glucose.

The End