University of Jordan - Faculty of Medicine
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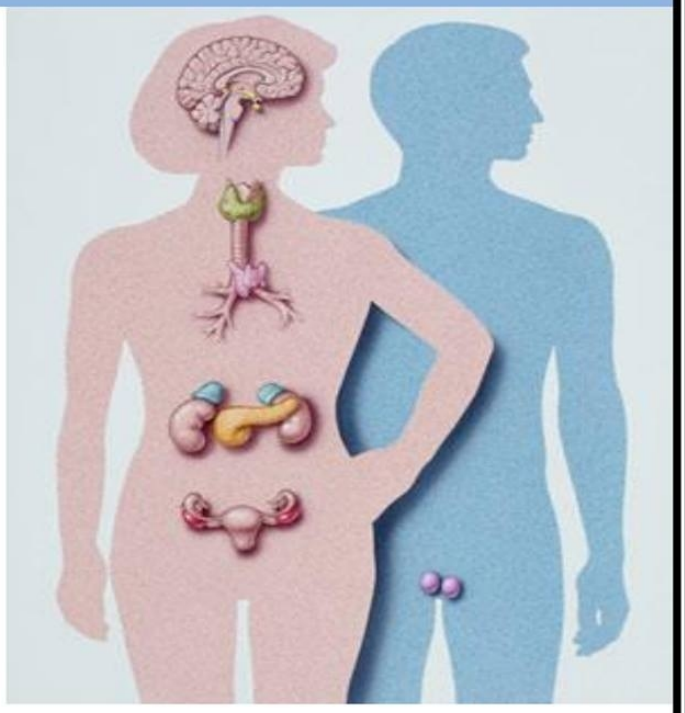
Medical Committee
The University of Jordan

# Endocrine System



- ☐ Anatomy/Embryology/Histology
- ☐ Biochemistry
- ☐ Physiology
- ☐ Pharmacology
- ■ Pathology
- ☐ PBL

☐ Slide ■ Sheet ☐ Handout ☐ Other

Lecture #: **1**

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# DISEASES OF ENDOCRINE SYSTEM

# PITUITARY GLAND

-The sheet was written according to section 1 record.

-The slide's contents are incorporated here so you don't need to refer back to them.

## ♠General Principles:

Before talking about pituitary gland diseases, we'll discuss some basic ideas about diseases of endocrine system.

❖Endocrine diseases can be generally classified as:

1. Diseases of *underproduction* or *overproduction* of hormones, with associated biochemical and clinical consequences. (Disordered hormonal production)
2. Diseases associated with the development of *Mass lesions*, which may be *nonfunctional* or "*functional*" → associated with overproduction or underproduction of hormones.

- **Important note:** there is *No relation between the above two*. I.e. if there is a big mass, that doesn't mean that there will be an overproduction of the hormone. If there is a mass, the hormone could be *normal*, *increased* or *decreased*.

**(No relation between the size of the gland and hormone production status)**

**Example:** if someone has Goiter in the thyroid gland, thyroid hormones can be:

- Normal
- Increased production of thyroid hormones → Hyperthyroidism
- Decreased production of thyroid hormones → Hypothyroidism

❖There are 3 main conditions that affect All Endocrine Glands (any endocrine gland can be affected by one of these conditions) :

## 1. Hyperplasia

- Increased number of cells leading to enlargement of the gland.
- A *physiologic process (non-neoplastic)* starts when we need more hormone production so the gland enlarges as a response. However, to a certain state it is physiologic but after that the Gland becomes ***Autonomous*** which means it doesn't respond to the negative feedback inhibition. The gland keeps enlarging even if you don't need that extra hormonal production and it becomes a pathologic process. *Starts as physiologic then it becomes a pathologic process.*
- Remember that: the increased activity of the target tissue often downregulates the activity of the gland and this is the process of feedback inhibition.
- Furthermore , in hyperplasia, there is "*usually" an overproduction* of the hormone. We said before that the mass effect isn't related to the hormonal status but because we have increased number of cells in hyperplasia which are *usually functional* so we end up with increased hormone production.

## 2. Adenoma

- Benign neoplasm (monoclonal; originating from one cell type)
- Can be functional or non-functional (hormone producing or not )

## 3. Carcinoma

- It refers to a Malignant neoplasm

*Q.: How to differentiate Carcinoma from adenoma in Endocrine system?*

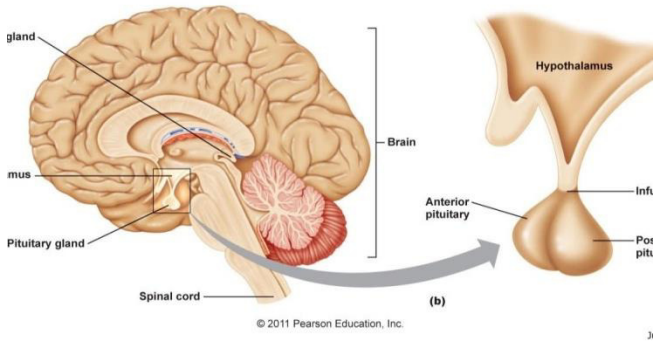
The differentiation between Adenoma and Carcinoma in Endocrine system is not related to cellular features because there is something called *Endocrine atypia* which can be seen in benign neoplasm. So in Adenoma you can see enlarged nuclei, Anaplasia, increased mitotic activity and pleomorphism in addition to other cellular and nuclear changes. These changes are related to malignant neoplasm in general but in endocrine glands you can see these features in adenomas as well so these features cannot differentiate benign from malignant neoplasm in Endocrine system.

(Endocrine atypia: cells of adenoma having atypical features as those of malignant neoplasm.)

If the neoplasm is *infiltrative and potentially metastasizing* then it is carcinoma. So the *differentiation depends on the Behavior more than histological features.*

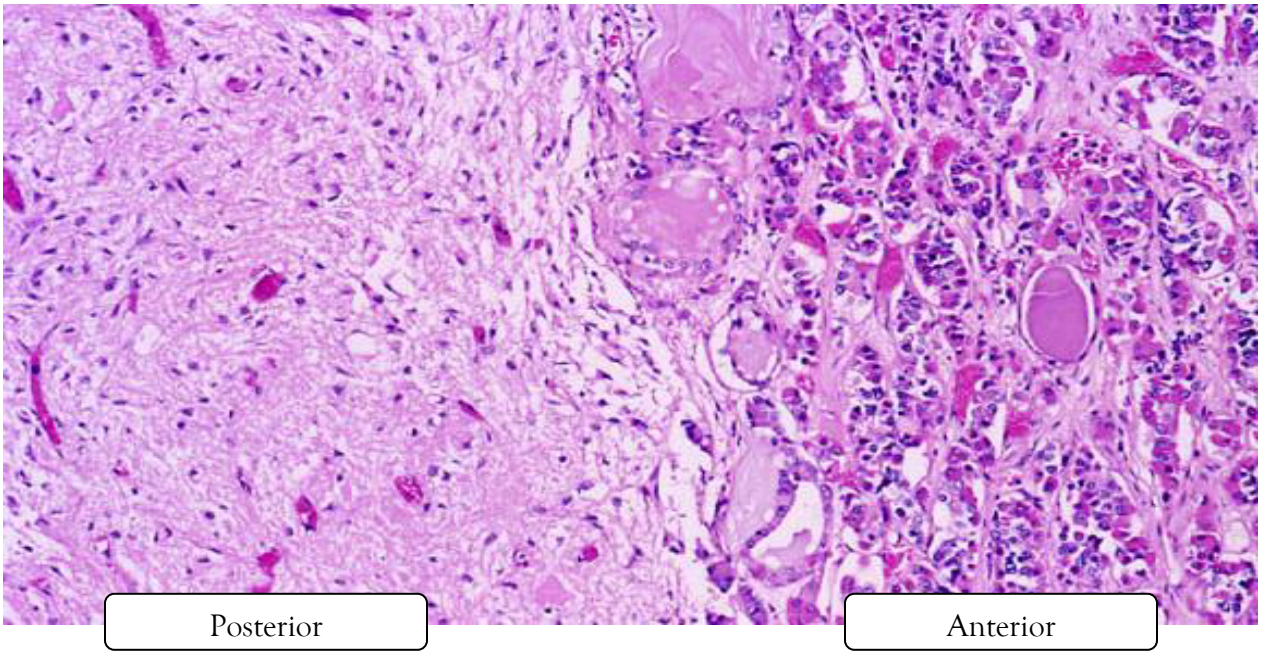
## ♠Pituitary Gland

Pituitary Gland is located at the base of the brain within a protective bony structure, the sella turcica. It is composed



of 2 parts: anterior pituitary and posterior pituitary and both are related to the hypothalamus. Hypothalamus controls the function of pituitary gland and pituitary gland in turn controls the rest endocrine glands EXCEPT *parathyroid glands* and the *islets of Langerhans* (mentioned in section 2). Parathyroid glands effect and function are regulated via calcium levels in the blood.

## ♠Anterior pituitary versus posterior pituitary




### 1. Histological comparison

- The anterior pituitary is also known as Adenohypophysis. The word "adeno" reflects the origin of anterior pituitary being from *epithelial cells.* (adeno means glandular)
- The posterior pituitary is also known as Neurohypophysis originating from neurons. It is composed of modified *glial cells* known as *pituicytes* plus the *axons of neurons* which are derived from hypothalamic nuclei noticing that the body of the neuron is located in the hypothalamus while the axons are located in the posterior pituitary.

- From the figure above you can notice the fibrillar material in the posterior pituitary which are the neural axons and the epithelial cells of the anterior pituitary like the rest of the glands.

## 2. Embryological difference

- Anterior pituitary is derived from *oral mucosa.*
- Posterior pituitary like all other neural tissues from the *neural crest.*

## 3. Hormonal secretion

- Anterior: TSH, Prolactin, ACTH, GH, FSH , LH. Those hormones have a stimulatory effect on the rest of the endocrine glands )
- Posterior: ADH and oxytocin. ( remember that these 2 hormones are synthesized and secreted from hypothalamus and then stored within the posterior pituitary *so the posterior pituitary is a site of storage not secretion* )

# ♠Diseases of the anterior pituitary

Symptoms and signs of pituitary diseases can be grouped into:

## 1. Mass effect (important)

The pituitary gland location is very important. An enlargement of anything in the brain causes a huge problem. If the pituitary enlarges, this will cause several consequences:

- The first things to be seen are Radiographic abnormalities of sella turcica without clinical manifestations : including sellar expansion , bony erosions and disruption of diaphragma sellae . If the gland enlarges this will causes *visual field abnormalities* because of the close proximity between the sella turcica and optic chiasm and the optic nerves, that's why expanding pituitary lesions often compress decussating fibers in the optic chiasm ending with *visual field abnormalities*.
- Elevated intracranial pressure: leading to headache, nausea and vomiting.
- Seizures.

- Cranial nerve palsies
- **Pituitary apoplexy**: it is an acute internal hemorrhage occurring inside a preexisting adenoma . This will lead to Rapid enlargement of the adenoma , decreased consciousness and can cause a sudden death so pituitary apoplexy constitutes a neurosurgical emergency.

## 2. Hyperpituitarism- related effects

Pituitary gland here is giving more and more hormones. When talking about hyperpituitarism we refer to different diseases depending on the hormone which its production is increased. In hyperpituitarism we don't necessarily have all the hormones increased in production. Usually one or two cell types are increased and as a consequence one or two hormones are increased. The effect (signs and symptoms) depends on the hormone which is overproduced.

### ❖Causes of hyperpituitarism:

- MOST COMMON CAUSE: ***functional pituitary adenoma***
- Hyperplasia
- Carcinoma
- Ectopic Secretion of pituitary hormones by nonpituitary tumors
- Hypothalamic disorders

## 3. Hypopituitarism-related effects

Hypopituitarism is caused by deficiency of trophic hormones and results from variety of destructive processes including:

- Ischemic injury
- Surgery or radiation
- Inflammatory reactions

- Non-functional pituitary adenomas may encroach upon and destroy adjacent normal anterior pituitary parenchyma, causing hypopitutarism.

## ♠Pituitary adenomas

- *The most common cause for hyperpituitarism*. They can be *functional* or *nonfunctional*. If they are functional, usually it affects one cell type and one hormone produced or sometimes two. The pituitary adenomas are *classified according to the hormones they overproduce*.
- *There is no relation between histology of the adenoma and the hormone produced.( The functional status of the adenoma cannot be reliably predicted from its histological appearance)* i.e. if you have an adenoma mainly composed of chromophobes that doesn't mean it produces a certain type of hormone so histology has nothing to do with the classification.

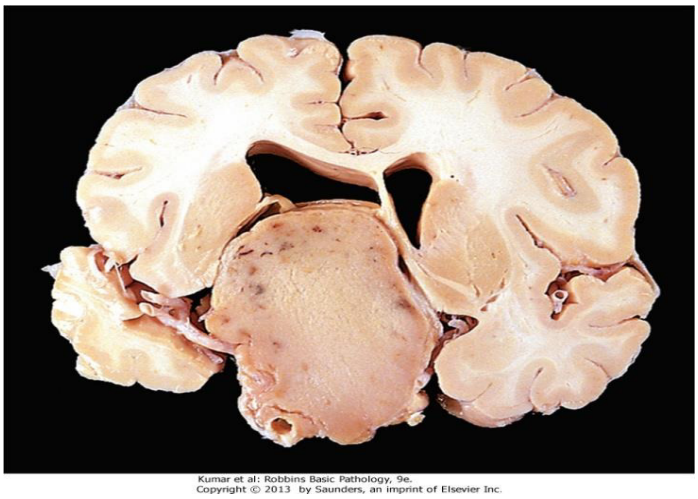
### ❖Types of pituitary adenomas:

* Prolactinomas.. 20-30% (most common)
* Null cell adenoma… 20% (non functional adenoma)
* ACTH cell adenoma.. 10-15%
* Gonadotrophic cell adenoma… 10-15%
* GH cell adenoma… 5%
* Mixed GH/Prolactin adenoma.. 5%
* TSH cell adenoma… 1% (least common)
* Other pleurihormonal… 15%

- Pituitary adenomas constitute 10% of intracranial neoplasms which come to clinical attention. But they are actually more common than that because 25% of autopsies find out that there were pituitary gland

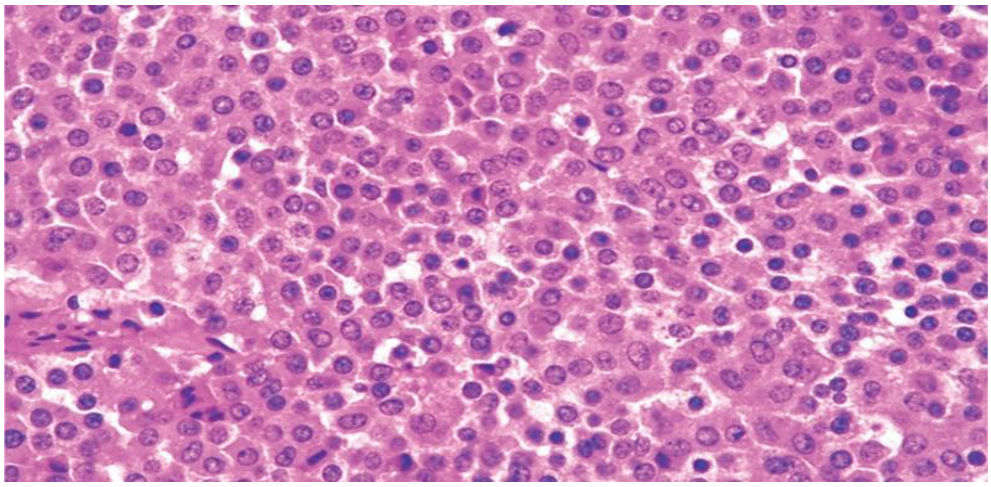
adenomas *(Incidental finding in 25% of autopsies).* This means that 15% of pituitary adenomas where asymptomatic and didn't come to clinical attention.

- *Disease of adults* affecting mainly those between *4th to 6th* decades of life.
- Mostly *single* lesions
- *Micro* and *Macro* adenomas according to size. The *cutoff point = 1 cm* → if less than 1 cm it is micro , larger than 1 cm it is macro.
- Macroscopic appearance: adenomas are benign neoplasms and because of that ,they will be *well circumscribed* , *soft* and *non-infiltrative*. However, 30% of pituitary adenomas are non-encapsulated and infiltrative affecting adjacent structures! (adjacent bone, dura and brain) .




This is a pituitary adenoma ( large one ) . It is well circumscribed and soft.

- Microscopic appearance: *pituitary adenomas are usually composed of one cell type (monotonous)* compared to the normal pituitary which has 3 cell types (chromophopes and chromophils "basophiles and acidophiles" ) and as a result 3 different colors. This cellular monomorphism and the absence (loss) of a significant reticular network distinguish pituitary adenomas from non-neoplastic anterior pituitary parenchyma.



Microscopic appearance of pituitary adenoma

- Adenomas that harbor *TP53* mutations demonstrate high mitotic activity and are designated as atypical adenomas to describe their potentials for aggressive behavior.

## ❶prolactinomas

**The most common pituitary adenoma*

As the name implies, if someone has prolactinoma , prolactin will increase (*Hyperprolactinemia*) causing the following symptoms:

- Amenorrhea and galactorrhea or lactorrhea *(is the spontaneous flow of milk from the breast, unassociated with childbirth or nursing )*
- Loss of libido ( loss of sexual desire ), and infertility

These symptoms are difficult to detect. Unless we were talking about a woman in a productive age , Prolactinomas are usually diagnosed in those women rather than other people as these symptoms are obvious in them. This means prolactinomas are clinically silent most of the time so they can enlarge and become macroadenomas.

### ❖Other causes of hyperprolactinemia:

- Pregnancy, and high-dose estrogen therapy
- Dopamine-inhibiting drugs (e.g., reserpine).
- Any mass in the supra-sellar compartment that may disturb the **normal inhibitory influence of hypothalamic neuropeptides** on prolactin secretion, resulting in hyperprolactinemia ,a mechanism known as the ***stalk effect.***

## ❷Growth Hormone-Producing (Somatotroph) Adenomas

- They are difficult to be detected like in prolactinomas as a result they may be quite large at the time of diagnosis because the clinical manifestations of excessive growth hormone may be subtle.
- Small amounts of immuno-reactive prolactin are often present as well.

### ❖Clinical manifestations:

- If a growth hormone-secreting adenoma occurs *before* the closure of the epiphyses ,where long bones can increase in length we end up with a disease called *gigantism.*

  **Gigantism:** generalized increase in body size, with disproportionately long arms and legs.

- If elevated levels of growth hormone persist, or develop *after* closure of the epiphyses (there will be no increase in length), affected people develop *Acromegaly*, in which:
  a) Growth is most conspicuous in *soft tissues*, skin, and viscera and in the bones of the face, hands, and feet.
  b) Enlargement of the jaw results in its protrusion with spacing between the teeth.
  c) Enlarged hands and feet with broad, sausage-like fingers.

## ❸Corticotroph cell adenomas

- Adenomas that secrete ACTH
- They may be clinically silent or May cause *hypercortisolism*, manifested clinically as *Cushing syndrome* (we will discuss it with adrenal glands pathology).
- Large, clinically aggressive corticotrophic cell adenomas may develop after *surgical removal (ablation) of the adrenal glands* for treatment of Cushing syndrome. When we remove the adrenals ,there will be *no negative feedback* of cortical on the production of ACTH from anterior pituitary. If we lose this negative feedback, ACTH secreting cells enlarge causing corticotrophic adenomas which can be aggressive. This condition is known as *Nelson syndrome*. But this condition is now rare because bilateral adrenalectomy is only used in extreme circumstances .

  **Nelson syndrome:** corticotrophin adenomas caused by loss of negative feedback because we removed the adrenals.
- Because ACTH is synthesized as part of a larger pro-hormone substance that includes melanocyte-stimulating hormone (MSH), hyperpigmentation of the skin may be a feature. → Anything that causes an increase of ACTH will cause hyperpigmentation as a result.

## ❹Gonadotroph LH-producing and FSH adenomas

Can be difficult to recognize (clinically silent), because they secrete hormones inefficiently, and the secretory products usually do not cause a recognizable clinical syndrome.

## ♠Pituitary carcinomas

* Pituitary carcinomas can cause hyperpituitarism but not always, the same in case of pituitary adenoma (not every pituitary adenoma causes hyperpituitarism only functional ones).
* They are exceedingly rare and in addition to local extension beyond the sella turcica, these tumors virtually always demonstrate infiltration and distant metastases.

## ♠Hypopituitarism ( a deeper look) :

- Decreased production of pituitary hormones.
- Symptoms and effects depend on the specific hormone being underproduced.
- To have hypopituitarism you need *loss of at least 75% of anterior pituitary* .

### ❖Causes:

* The most common cause is a *Nonfunctioning pituitary adenomas*. This nonfunctioning adenoma increases to an extent that it becomes large enough to affect and compress the surrounding normal pituitary tissue causing underproduction of a certain hormone.
* Congenital absence(exceedingly rare)
* Hypothalamic tumors, associated with both anterior and posterior pituitary dysfunction. One of the important points to remember here is

that if a person has a *problem in the anterior pituitary and posterior pituitary together, this means in most of the cases it is caused by hypothalamic disorder*.

* Ischemic necrosis of the anterior pituitary, e.g. *Sheehan syndrome.*
* Ablation of the pituitary by surgery or irradiation .
* Inflammatory lesions such as *sarcoidosis* or *tuberculosis*.
* Trauma and Metastatic neoplasms involving the pituitary.

## ❖Sheehan syndrome: (important)

- Sheehan syndrome, or *postpartum necrosis of anterior pituitary*, is the most common form of clinically significant ischemic necrosis of the anterior pituitary.

- It occurs in pregnant women. During the last trimester of pregnancy, the anterior pituitary enlarges considerably, because of an increase in the size and number of prolactin-secreting cells and this physiologic enlargement is not accompanied by an increase in blood supply from the low-pressure portal venous system.

- The enlarged gland is thus vulnerable to ischemic injury, especially in women who experience significant hemorrhage and hypotension during delivery .

## ♠Posterior pituitary syndromes

- Posterior pituitary stores 2 hormones: oxytocin and ADH
- Impairment of oxytocin synthesis and release has not been associated with significant clinical abnormalities (clinically silent).
- The clinically important posterior pituitary syndromes involve ADH.
- *ADH can be overproduced or underproduced:*

1. ADH *underproduction* causes *diabetes insipidus*. As the name of the hormone implies " antidiuretic hormone " , its functions to prevent *diuresis*.

So if there is a deficiency in ADH, urination increases (excessive urination caused by an inability of the kidney to properly reabsorb water from the urine) and we lose more and more water resulting in *polyurea* and *polydipsia (excessive thirst)*. The urine that we are losing is fresh water (doesn't contain electrolytes) which means sodium and other electrolytes will become concentrated in the blood so as a result the patient develops *hypernatremia*.

## ❖Diabetes insipidus can result from other several causes:

* Head trauma and Neoplasms.
* Inflammatory disorders and surgical procedures of the hypothalamus and pituitary (Anything affecting hypothalamus or posterior pituitary will affect ADH secretion).
* The condition may be idiopathic.

**Note:-** Diabetes insipidus from ADH deficiency is designated as *central*, to differentiate it from *nephrogenic DI*.

## ❖The clinical manifestations of DI include: "conclusion""

- The excretion of large volumes of *diluted* urine (no sodium salts contained) with an inappropriately low specific gravity.

- Serum sodium and osmolality are increased as a result of excessive renal loss of free water resulting in thirst and polydipsia.
- Patients who can drink water generally can compensate for urinary loss. However, patients who are obtunded, bedridden, or otherwise limited in their ability to obtain water may develop life *threatening dehydration*.

2. ADH *overproduction* causes SIADH ( *syndrome of inappropriate antidiuretic hormone secretion)*
   - In (SIADH) ADH excess is caused by several *extracranial* and *intracranial* disorders. Extracranial disorders are usually related to the kidney. Intracranial disorders include problems of hypothalamus and pituitary.

❖**The most common causes of SIADH include:**

* The secretion of ectopic ADH by malignant neoplasms e.g. *paraneoplastic syndrome.*
* Non-neoplastic diseases of the lung (the exact mechanism is unknown).
* local injury (trauma and surgery) to the hypothalamus or neurohypophysis

❖**The main clinical manifestation of SIADH is** *hyponatremia*. The increase of ADH leads to reabsorption of excessive amounts of fresh water and the sodium in blood will be diluted leading to hyponatremia.

**Other manifestations include:** Water will concentrate in peripheral tissues due to its excessive amounts of water in the blood and the most dangerous site of edema is the brain so we will have *cerebral edema* ( the water is retained inside the brain ) leading to neurologic dysfunction.

**" نفسك إن لم تشغلها بالحق، شغلتك بالباطل " – ابن تيمية**

خلص الشهر الفضيل، الله يتقبل منّا جميعا و يكتبنا من عتقاء هذا الشهر

ادرسو منيح بس لا تنسو تعيدو كمان

لا تنسونا من صالح دعاكم و كل عام و الجميع بخير