The Endocrine System

PATHOLOGY

☑ Sheet ☐ Slide ☐ Handout

Number:	1
Subject:	**Pathology of Pituitary gland and introduction of thyroid gland**
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Endocrine system pathology

We have multiple glands and each gland has its own diseases but we have a common feature of diseases.

Endocrine pathology usually it results from either functional or tumor (development of mass lesions).

*The function may be increased or decreased (diseases of overproduction or underproduction of hormones) which will cause a systemic symptoms

Pituitary gland

The anterior part is the most important part it secretes trophic hormones

Tropic hormones are hormones that have other endocrine glands as their target which cause another hormone to be released

Histologically-

There are two types of cells

-The pink one it is called **acidophil**:

- Somatotrophs : they are the most abundant cells in the anterior lobe, their main function is to secrete growth hormone GH.
- Prolactin

-**the basophil**, which is blue in color:

- Corticotrops: they secrete ACTH (adrenocorticotrophic hormone)
- Gonadotrophs: they secrete FSH and LH
- Thyrotrops: secretes TSH

Regulation of the pituitary

-The release of trophic hormones is under the control of factors produced in the hypothalamus – most are stimulatory

-regulation from the systemic glands by negative feedback

(Causes negative feedback inhibition of the pituitary gland)

Most of the diseases they arise from the pituitary gland itself, sometimes-in rare cases the hypothalamus causes the disease.

We said that diseases result from abnormality in the function, which can be increased or decreased

When it is increased, we call it **hyperpituitarism –** pituitary can secrete a large amount of hormones. Mostly one hormone is increased. **The most common cause of hyperpituitarism is adenoma** there are other causes: hyperplasia, carcinoma and sometimes exogenous source but they are very rare.

- The difference between adenoma and hyperplasia

Adenoma is a tumor; it means that we have mutations.

It is benign neoplasm (monoclonal; originating from one cell type, the cells have same genetic features)

While the hyperplasia there are other sources affect its proliferation, they do not have mutations

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

* Few adenomas are bilineage – secrete two different hormones, GH and prolactin (acidophilic cells)being the most common combination.

In contrast, hypopituitarism is caused by deficiency of one or more of trophic hormones, to have hypopituitarism you need loss of at least 75% of anterior pituitary

Causes:

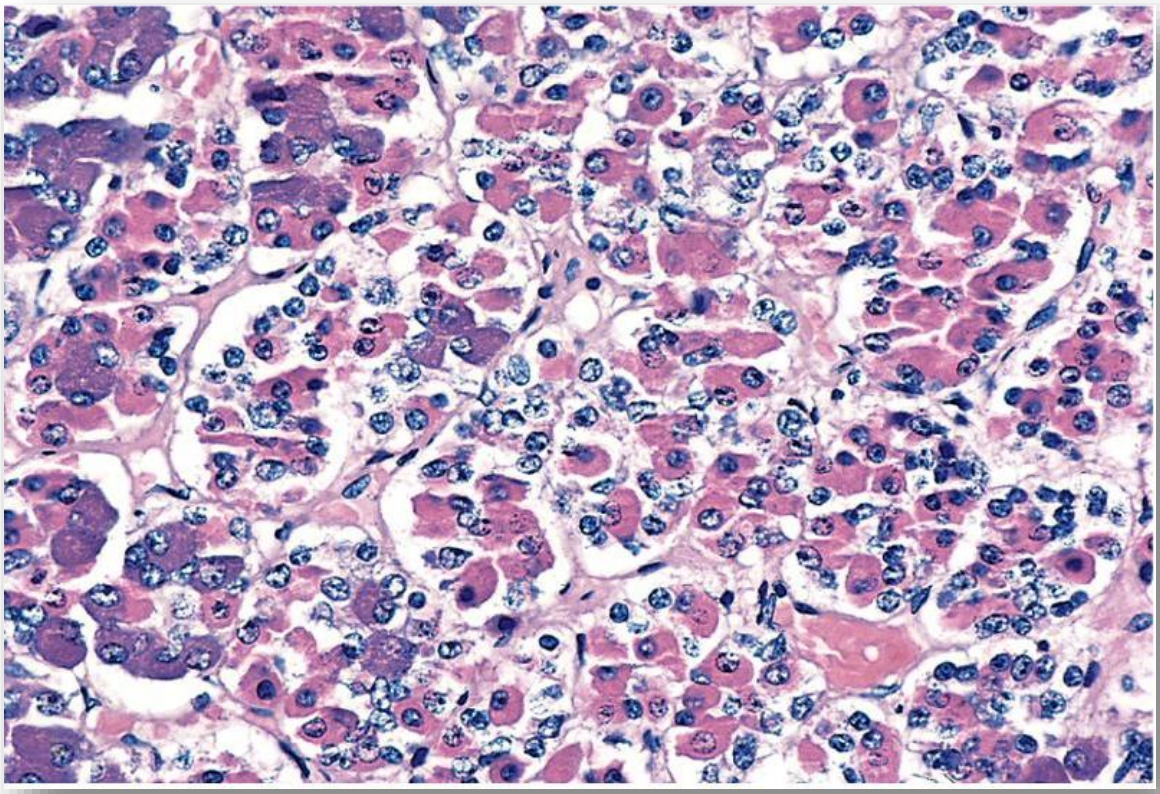
- **Most common is *nonfunctional* adenoma** may be encroach upon and destroy adjacent normal anterior pituitary parenchyma causing hypopituitarism.

> In both hypopituitarism and hyperpituitarism the most common cause is adenoma in hyperpituitarism it is functional and in hypopituitarism it is non-functional.

- Congenital hypoplasia
- Ischemia – (Sheehan syndrome, post-partum)

  Most obvious condition occurs in women –post-partum- because of the increased demand of hormones consequently the pituitary gland enlarges during pregnancy 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
- surgery
- radiation
- inflammatory diseases (infections, sarcoidosis)
- bone diseases (osteopetrosis) – proliferation of the bone so the bone that surround the pituitary gland can destroy the gland and results in hypopituitarism

Normal histology of pituitary gland



- We see pockets of cells; group of cells together within a limited space and the cells are mixture of basophil and acidophil cells, the border of the pockets contain reticulin fibers.

> Normal architecture of the anterior pituitary. Several distinct cell types containing a variety of stimulating (trophic) hormones populate the gland. Each of the hormones has different staining characteristics resulting in a mixture of cell types in routine histologic preparation. Note the presence of a fine reticulin network.
>
> *Robbins Basic Pathology*

Pituitary adenoma

- The most common disease of the pituitary gland.
- It is classified according to the cell of origin
- The most common pituitary adenoma is prolactinoma
- Can be functional, silent (non secretory) (25%) or hormone negative (non synthesizing) (rare)

Most cases are functional so it results in **hyperpituitarism** .

Nonfunctional adenoma according to the histology it is two types

- Silent/ non secretory – the cells contain the hormone but they don't secrete it to the blood , under the microscope we see either acidophilic or basophilic cytoplasm
- Hormone negative / non synthesizing – the cells in this case even don't synthesize the hormone, under the microscope we don't see the normal acidophilic or basophilic

- Most cases of pituitary adenoma are sporadic (individual case and individual tumor in the body)
- 3% are syndromic "multiple endocrine neoplasia" (means that we have other tumers in the endocrine system)
- According to size :
  <1cm microadenoma
  >1cm macroadenoma
  Up to 20% of healthy adults have silent micro-PA (3 mm), discovered accidently because the patient shows no symptoms it is not pathologic disease.

macroadenoma – may cause disease related to the tumor itself, causes damage to the surrounding structures

So sometimes pituitary adenomas when they are large they cause symptoms:

- because of the close proximity of the optic nerves and chiasm to the Sella, expanding pituitary lesions often lead to optic nerve damage leading to blindness (bitemporal hemianopsia/ Bitemporal hemianopic visual field impairment)
- Elevated intracranial pressure: leading to headache, nausea and vomiting.

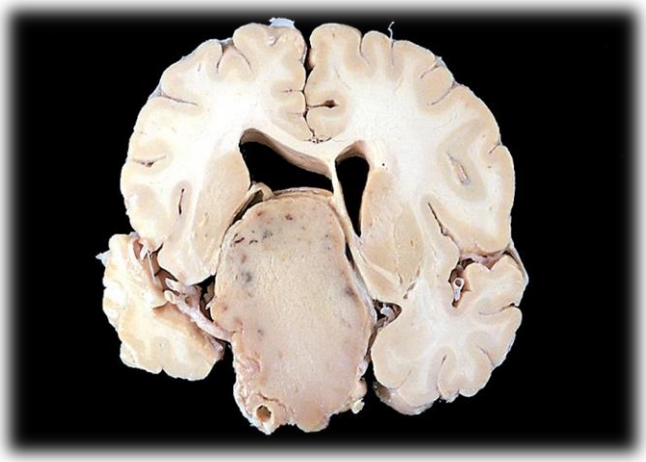
Pituitary adenoma is a disease of middle age 30-50 years Disease of adults

Pathogenesis –

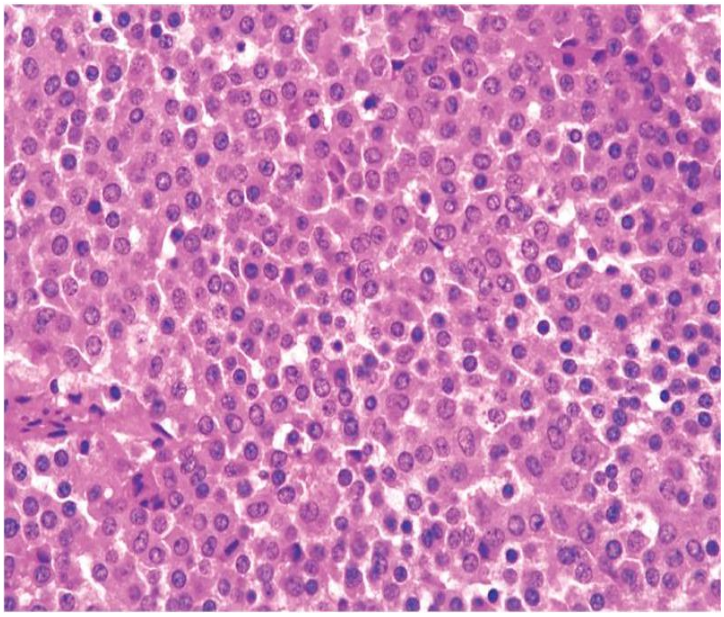
G protein mutations are the best- characterized molecular abnormalities in these neoplasms.

G protein transmits signals from cell surface receptors to intracellular effectors (adenylate cyclase) which generate second messengers (cAMP). A mutation in G protein causes persistent generation of cAMP and unchecked cellular proliferation.

Grossly this is how pituitary adenoma looks like



We see a tumor that causes shifting in the brain



Under the microscope

-We don’t see the pockets which are found in normal tissue, now we see sheets of cells and

-the cells are uniform we don’t see the mixture

-We don’t see the the reticulin fibers (H&E).

Types of pituitary adenoma

Classified according to the cell of origin, with corresponding hormonal synthesis

1- The most common type is ***prolactin adenoma– prolactinoma***

Prolactin interferes with the sex hormones and it is important for milk production

prolactin will increase (Hyperprolactinemia) causing the following symptoms:

- Amenorrhea – loss of menstrual cycle
- 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.
  Symptoms most obvious in menstruating women

Symptoms appear earlier in premenopausal women than in men and postmenopausal women. This means prolactinomas are clinically silent most of the time so they can enlarge and become macroadenomas.

- Sometimes prolactin increases without adenoma

Most of the diseases arise from the pituitary itself but sometimes it arises from the hypothalamus or from the other glands in the body. Normally the hypothalamus suppresses the production of prolactin, in case there is damage in the stalk that connects the hypothalamus to the pituitary, this means that prolactin will increased without adenoma this is called Stalk effect it occurs secondary to a trauma. Therefore, in both situations there is will be increase in prolactin secretion.

2- Second most common type is ***Growth Hormone-Producing Adenomas***

This adenoma is functional but the secretion of GH is slow and in small amount, it causes increase in GH and it causes symptoms in the body but it takes a long time so at the time of discovery we will have large adenoma.

GH stimulates secretion of insulin-like growth factor-1 from liver, insulin-like growth factor-1 stimulates body growth.

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: Growth is most conspicuous in soft tissues, skin, and viscera and in the bones of the face, hands,

and feet. Enlargement of the jaw results in its protrusion with spacing between the teeth. Enlarged hands and feet with broad, sausage-like fingers.
In both acromegaly and gigantism, the patients would have hypertension, it is a systemic disease not only in the bone, the hypertension causes heart failure and they will have diabetes because of the direct effect of GH on beta cells, which will ultimately get over stimulated and exhausted (GH antagonize the insulin)

3- Corticotroph Cell Adenomas

Adenomas that secrete ACTH
Most are small at the time of diagnosis , because in contrast to GH producing adenomas , corticotroph cell adenomas have high secretion rate .

They Causes Cuching disease- characterized by increased secretion of adrenocorticotropic hormone (ACTH) from the anterior pituitary (secondary hypercortisolism). This is most often as a result of a pituitary adenoma and in this case there will be bilateral enlargement of the adrenals.

*** there's a difference between cuching disease and cuching syndrome

Cuching ***syndrome***
– the origin of the disease is from the adrenal gland. It will be discussed in more detail with diseases of adrenal gland

-characterized by unilateral enlargement of adrenal glands

Cuching ***disease***
– the origin of the disease is the pituitary

-characterized by bilateral enlargement of adrenal gland

In both situations cortisol level in the blood will be elevated

**** Nilson syndrome**

if both adrenal gland are absent (removed by surgery or destructive disease) 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– aggressive enlargement of pituitary gland causing physical symptoms.

In addition because ACTH is synthesized as part of a larger prohormone substance that include MSH (melanocyte stimulating hormone), hyperpigmentation may be a feature.

So patients with corticotroph cell adenoma have cuching disease and hyperpigmentation

If the cortisol increases as a result of adrenal disease we don't have MSH and there's no hyperpigmentation .

So,

Cuching disease- high cortisol level, pituitary adenoma, bilateral adrenal enlargement and hyperpigmentation.

Cuching syndrome- adrenal secretes high amount of cortisol but we don't have pituitary adenoma we only have unilateral enlargement of adrenal and we don't have skin pigmentation

4- Gonadotroph & thyrotroph adenoma

These are very rare and not important because they produce very little amount of hormones. They are usually asymptomatic but the problem is caused by the tumor effect of the gland (physical damage caused by the tumor mass)

Posterior pituitary gland

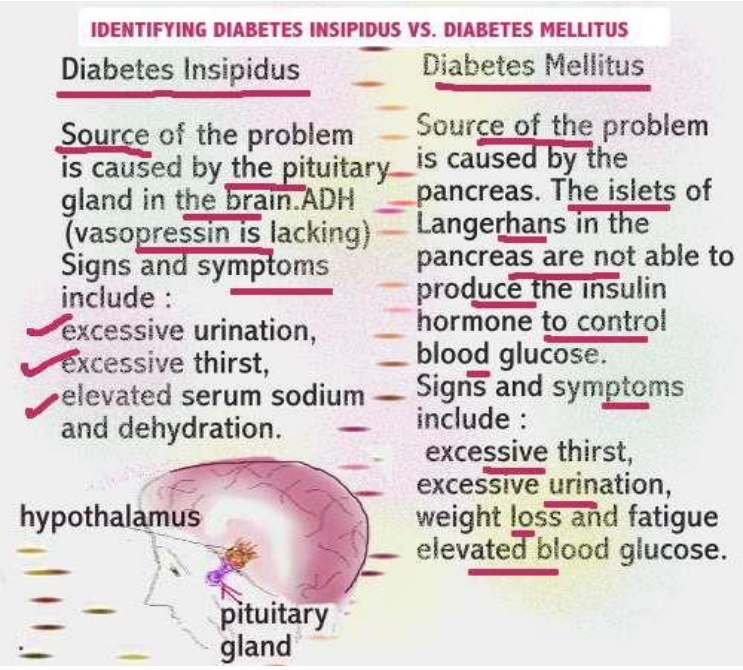
It secretes 2 main hormones: oxytocin and ADH

ADH – this act as an antidiuretic hormone, which helps in water absorption from renal tubules.

When it lost so we don't have reabsorption of water so patients will have diuresis – they urinate a lot as a consequence patients will have diluted urine and concentrated blood and hypernatremiathis situation is called diabetes insipidus.

What causes deficiency of ADH?

Head trauma, tumors, surgery.



If we have, excessive amount of ADH → causes Syndrome of inappropriate ADH (SIADH)

The clinical manifestations of SIADH are

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.

Cerebral edema and death

*The most common causes of SIADH include the secretion of ectopic ADH by malignant neoplasm (particularly small cell carcinoma of the lung)- paraneoplastic syndrome.

Thyroid gland

Again, the disease can be related to the function: increased decreased or related to the tumors and we have many tumors in the thyroid

Thyrotoxicosis–hypermetabolism in the body due to elevated circulating levels of free T3 and T4

- Normally most of the thyroid hormone is bound and only small concentration is free and can perform the function
  Therefore, if this free part increased it will cause disease → thyrotoxicosis

Causes of thyrotoxicosis:

- Most commonly, it is related to hyperthyroidism (the increased function of thyroid hormone)

- Exogenous source – thyroid gland is normal but serum T3 and T4 increases because of long-term use thyroxine as a treatment for hypothyroidism

- Thyroiditis- we have physical damage to the thyroid which causes the release of the hormone in the blood

Thyrotoxicosis often is referred to as hyperthyroidism because it is caused most commonly by hyper function of the thyroid gland. In certain conditions, however the oversupply either is related to excessive release of pre-formed thyroid hormones (e.g. in thyroiditis) or comes from an extra thyroidal source, rather than hyper functioning gland. Thus, strictly speaking, hyperthyroidism is only one category of thyrotoxicosis. Despite this clear distinction, clinicians use the two terms interchangeably.

Symptoms:

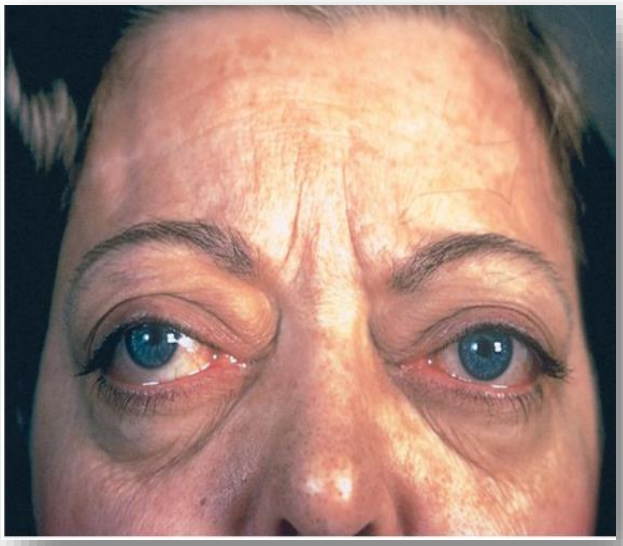
Thyroxin is essential for metabolism so when it increase it will cause increased metabolism in the entire body. Every organ in the body will has its own symptoms.

The symptoms in general

- Heat intolerance – because of the increased production of energy and heat.
- Excessive sweating
- Skin: soft, flushed, warm – because of increased circulation of the blood
- Increased CNS function, Nervousness, increased sympathetic stimulation ,tremor, irritability
- GI: diarrhea, malabsorption , Change how fast food moves through your digestive tract
- Tachycardia – increase in heart rate, and Arrhythmia
- Muscles: proximal muscle weakness – the proximal parts of the muscles are weaker than the distal parts, these patients have difficulty to stand up when they are on the floor
- Ocular: lid lag– the failure of the normal downward following movement of the upper lids on looking downward
  Lid lag causes a strange staring appearance also their eyes are bulging ,staring, wider than normal and exophthalmos

Thyroid storm: Sudden increase of thyroid hormones
It is a rare but severe and potentially life-threatening complication of hyperthyroidism. It is characterized by a high fever, fast and often-irregular heart beat.

Apathetic hyperthyroidism: refers to thyrotoxicosis occurring in old age, old age already have lower metabolism than young people so sometimes the hyperthyroidism it doesn't manifest, they are discovered accidently



Normally, the white part of the eye around the iris is not obvious, but in case hyperthyroidism, they will develop exophthalmos abnormal protrusion of the eyeball

So, you can easily see the white part below the iris.

In Graves' disease, one of the most important causes of hyperthyroidism, this feature (eye bulging) is obvious (will be discussed later).

Hypothyroidism

The thyroid gland does not produce enough thyroid hormone

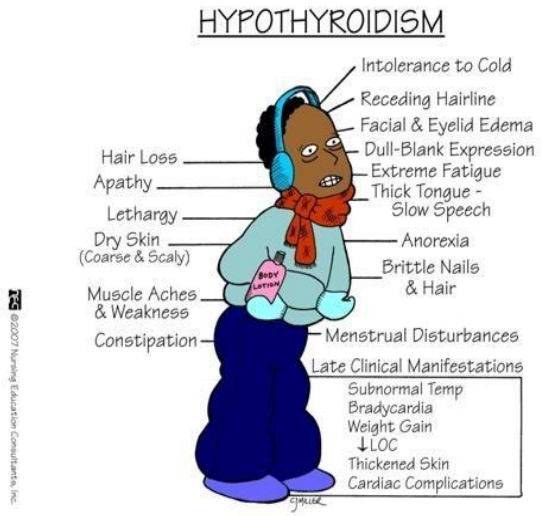
- Can affect any age
- **Cretinism –** refers to hypothyroidism developing n infancy or early childhood

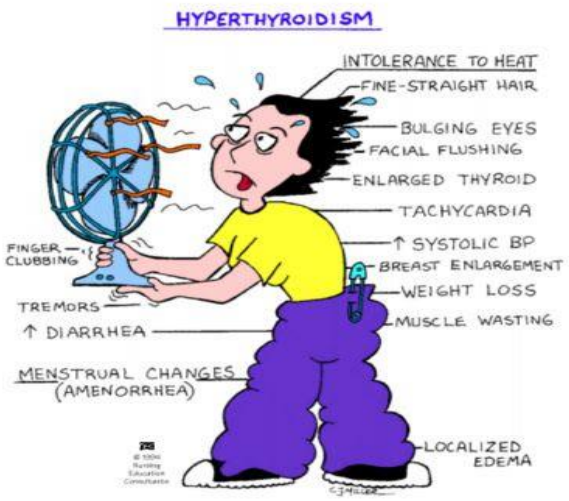
Clinical features of cretinism include impaired development of the skeletal system and central nervous system if not treated patients will end up with mental retardation so it is very critical.

Other symptoms:

Short stature, coarse face features and a protruding tongue

- **Myxedema-** hypothyroidism in adults
  Symptoms
  Very thick skin, slow mental process, apathy, cold





intolerance, constipation, anemia, bradycardia, heart failure, confusion.

Good luck☺😍☺

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References

Robbins basic pathology

Dr. Tareq's record (section2)