بسم الله الرحمن الرحيم

First principles Negative + Positive Feedback.

eg: TSH (pituitary) → stimulates Thyroid hormone T_3, T_4

if T_3 T_4 get increased, they will inhibit TSH, vice versa

↳ Negative feedback

Positive: when hormone stimulates other one, it increases and stimulation won't be inhibited

بالعربي: oxytocin أفرزت pituitary وقالت عشان يصير contraction، هاد الـ result يزيد إفراز الـ oxytocin وهيك ← بالآخر الولادة

Second principles - most hormones bound to certain proteins in Blood

- small fraction is free ⇝ active

eg: Thyroid hormones → Thyroxine binding globulin

T_3 active T_4 not active

Third principle: stimulation + suppression test

eg: Adrenal insufficiency → cortisole ↓ [stimulation test]

بشكل طبيعي، لأنو الهرمون يرتفع، إذا ما ارتفع بكون هناك مشكلة

Deficiency state → stimulation test

↑ → normal

± ↓ → abnormal.

eg: Cushing disease → increse production of cortisole [suppression test]

Dexamethasone suppression test

normally → suppressed ↓

abnormally → not suppressed ↑

excess → suppression test

Fourth principle: Biochemical Dx before imaging studies (localization)

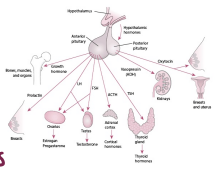
eg: carcinoid syndrome → ↑seretonin 5HA (urine)

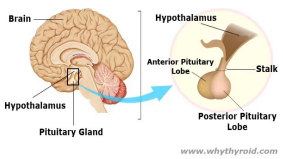
then imaging

Hypothalamus + Pituitary

Anterior
GH, ACTH, TSH
FSH, LH, Prolactin

Posterior
"storage" hypothalamus hormones
ADH,
oxytocin





Prolactin inhibited by Dopamine

stimulated by TRH (thyroid releasing hormone) + TSH

*primary hypothyroidism stimulate TRH → ↑ prolactin

Dopamine has higher effect ↑ TSH

*Hyperprolactinemia is most common cause → physio: preg, breast feeding; pathological: Drugs, adenoma

manifestation → Galactorrhea (milky discharge)

menstrual cycle (amenorrhea ---), How? Prolactin suppressed

infertility, decreased libido GnRH → ↓ LH FSH → ↓ estrogen

osteopenia + osteoporosis

Question: is it possible to have pituitary tumor which doesn't secrete prolactin, and this tumor increase the serum prolactin?

answer: large tumor will press on hypothalamus, so the hormone will be decreased including "Dopamine" → ↑ prolactin. [stalk effect]

Dx → pituitary MRI

Hyperprolactinemia

A. Causes

1. Prolactinoma
   a. Most common cause of hyperprolactinemia
   b. Most common type of pituitary adenoma (up to 40%)
2. Medications (e.g., psychiatric medications, H_2 blockers, metoclopramide, verapamil, estrogen)
3. Pregnancy
4. Renal failure
5. Suprasellar mass lesions (can compress hypothalamus or pituitary stalk)
6. Hypothyroidism
7. Idiopathic

Quick HIT

High levels of prolactin inhibit secretion of GnRH. This leads to decreased secretion of LH and FSH, which in turn leads to decreased production of estrogen and testosterone (see **Clinical Features**).

B. Clinical Features

1. Men
   a. Hypogonadism, decreased libido, infertility, impotence
   b. Galactorrhea or gynecomastia (uncommon)
   c. Parasellar signs and symptoms (visual field defects and headaches)
2. Women
   a. Premenopausal: menstrual irregularities, oligomenorrhea or amenorrhea, anovulation and infertility, decreased libido, dyspareunia, vaginal dryness, risk of osteoporosis, galactorrhea
   b. Postmenopausal: parasellar signs and symptoms (less common than in men)

Quick HIT

Parasellar signs and symptoms (mass effects of the tumor) are more prevalent in men than in women. This is largely because the early symptoms in men (e.g., impotence) are often attributed to psychological causes and medical evaluation is delayed, allowing for larger tumor growth.

C. Diagnosis

1. Elevated serum prolactin level.
2. Order a pregnancy test and TSH level, because both pregnancy and primary hypothyroidism are on the differential diagnosis for hyperprolactinemia.
3. CT scan or MRI to identify any mass lesions.

D. Treatment

1. Treat the underlying cause (e.g., stop medication, treat hypothyroidism).
2. If prolactinoma is the cause and the patient is symptomatic, treat with **bromocriptine,** a dopamine agonist that secondarily diminishes the production and release of prolactin. Continue treatment for approximately 2 years before attempting cessation. **Cabergoline** (another dopamine agonist) may be better tolerated than bromocriptine and is often chosen as first-line therapy.
3. Consider surgical intervention if symptoms progress despite appropriate medical therapy. However, the recurrence rate after surgery is high.

Quick HIT

Microadenomas (<10 mm diameter) tend to either remain the same size or regress with time. Only 10% to 20% continue to grow.

* Growth hormones

- Acromegaly → adult
- Gingaytism → childhood

Types of tests: 1. screening امتحانيّة
2. diagnostic تؤكد، غير تؤكد

* screening test → insulin GF$_1$ (IGF$_1$) الناتب

why not GF? affected by factors

* diagnostic test → suppression test to GH (Glucose)

hyperglycemia decrease GH

* Pituitary MRI

inhibition of GH in hypothalamus → Dopamine.

Acromegaly

A. General Characteristics

1. Acromegaly is broadening of the skeleton, which results from excess secretion of pituitary GH after epiphyseal closure (if before epiphyseal closure, gigantism [excessive height] results).
2. It is almost always caused by a GH-secreting pituitary adenoma (represents 10% of pituitary adenomas).

Quick HIT

Cardiovascular disease (cardiomyopathy) is the most common cause of death in patients with acromegaly.

B. Clinical Features

1. Growth promotion
   a. Soft tissue and skeleton overgrowth
   b. Coarsening of facial features
   c. Abnormally large hand and foot size (ask about increasing glove/ring size)
   d. Organomegaly
   e. Arthralgia due to joint tissue overgrowth
   f. Hypertrophic cardiomyopathy
   g. Enlarged jaw (macrognathia)
2. Metabolic disturbances
   a. Glucose intolerance and DM in 10% to 25% of patients
   b. Hyperhidrosis
3. Parasellar manifestations
   a. Headache
   b. Superior growth leads to compression of the optic chiasm, which results in visual loss (**bitemporal hemianopsia**)
   c. Lateral growth leads to cavernous sinus compression
   d. Inferior growth leads to sphenoid sinus invasion
   e. HTN, sleep apnea

Quick HIT

Other Laboratory Abnormalities in Patients With Acromegaly

- Hyperprolactinemia (tumor secretes prolactin and growth hormone)—30% of patients
- Elevations in serum glucose, triglycerides, and phosphate levels

C. Diagnosis

1. IGF-1, also known as somatomedin C, should be significantly elevated in acromegaly.
2. Oral glucose suppression test—glucose load fails to suppress GH (as it should in healthy individuals). This confirms the diagnosis if the IGF-1 level is equivocal.
3. MRI of the pituitary.
4. A random GH level is not useful because there is wide physiologic fluctuation of GH levels.

D. Treatment

1. Transsphenoidal resection of pituitary adenoma—treatment of choice
2. Radiation therapy if IGF-1 levels stay elevated after surgery.
3. Octreotide or other somatostatin analog to suppress GH secretion

"بركة العمر، حُسن العمل"
- علي بن أبي طالب
نعتذر عن أي خطأ...
نورشهوان

- GH deficiency → short stature

screening → IGF$_1$ D → GH stimulation (Hypoglycemia)