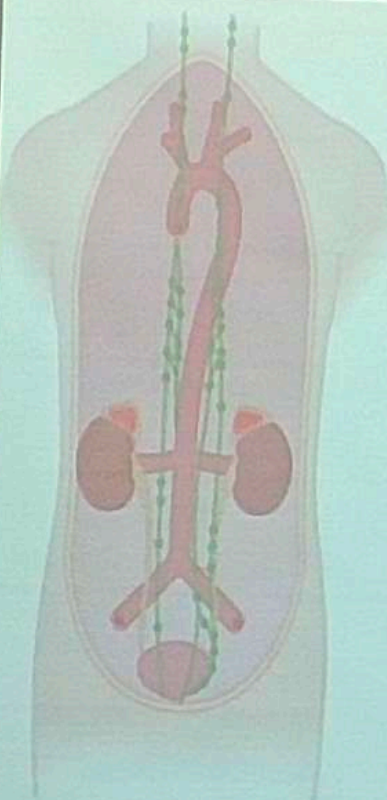


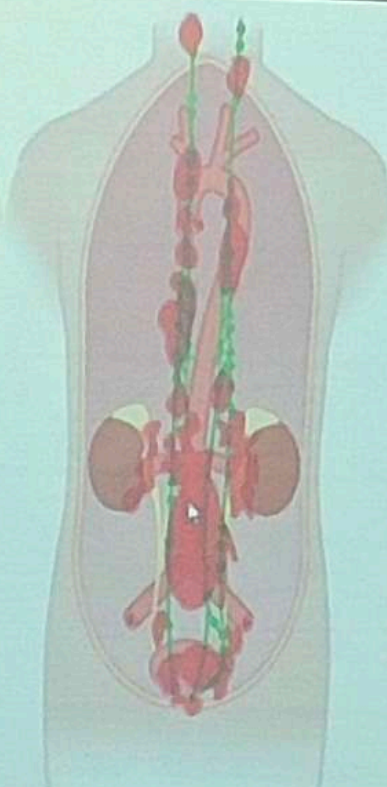
Pheochromocytoma

Introduction

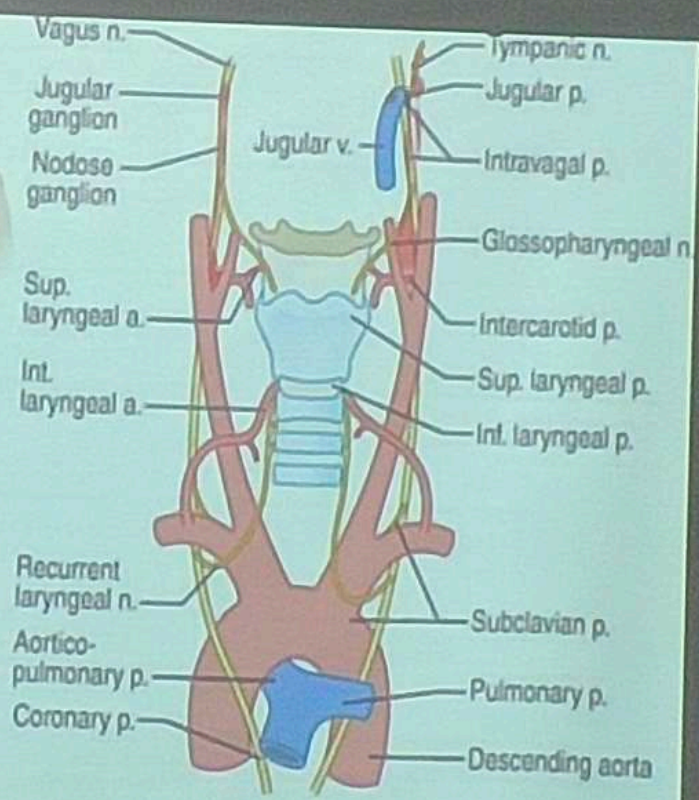
Pheochromocytomas are vascularised **catecholamine-producing tumors** derived from the sympathetic or parasympathetic nervous system.



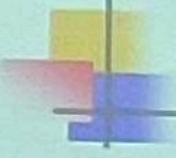
A Adrenal pheochromocytoma



B Extra-adrenal pheochromocytoma



C Head and neck paraganglioma



Pheochromocytoma

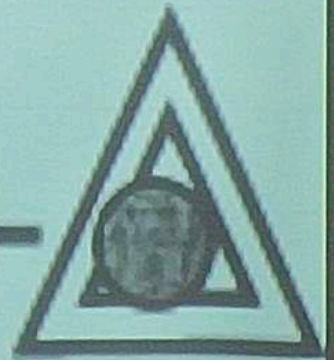
- 10% extraadrenal
- 10% bilateral
- 10% familial
- 10% children
- 10% malignant
- 10% assoc with MEN
- 10% present with a stroke

FIGHT AND FRIGHT

Hypertension

Headaches

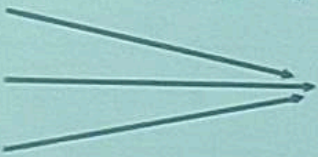
Catecholamines



Palpitations

Sweating

Signs and Symptoms of Pheochromocytoma

- resistant hypertension (95%)
 - headache
 - sweating
 - palpitations
 - chest pain
 - anxiety
 - glucose intolerance
 - increased metabolic rate
- classic triad
- 

- General features: **Sweating, Flushing**, heat intolerance, pallor, Weakness, pyrexia.
- Neurological: Headache, **Tremors**, visual disturbances, Anxiety, panic attacks, seizures.
- Cardiovascular: **Hypertension, Palpitations**, chest tightness, dyspnea, faints.

- Gastrointestinal: Abdominal pain, **hunger**, Nausea, Weight loss, constipation.
- Asymptomatic.

Investigations

1. Demonstrate excess catecholamines
2. Tumor localization

Biochemical Testing:

- Pheochromocytomas and paragangliomas synthesize and store catecholamines, which include norepinephrine (noradrenaline), epinephrine (adrenaline), and dopamine.
- **Elevated plasma and urinary levels of catecholamines and the methylated metabolites, metanephrines.**

Investigations Cont'd

- **MRI** (Preferred study): to localise the tumor
- **I-MIBG** (Meta-iodobenzylguanidine) Single Photon Emission Computerized Tomography
 - Identify 90% of primary tumors
 - Detects multiple extra-adrenal tumors & metastases

Management

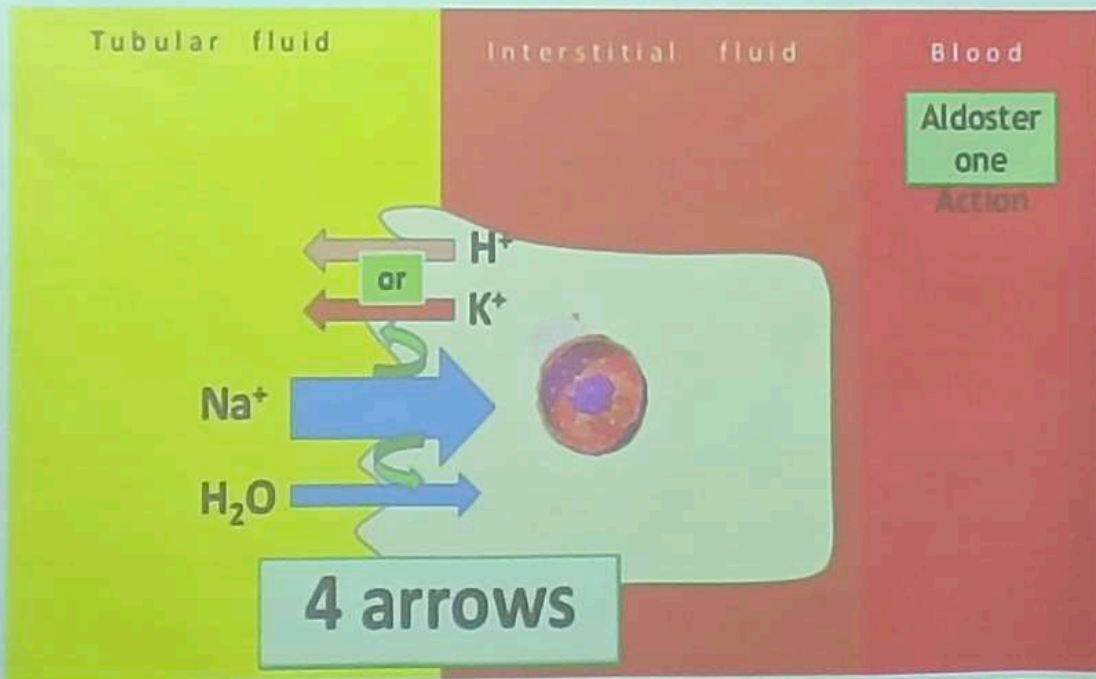
- **Surgical** resection of the mass is the treatment of choice
- **Medical treatment:** Pre-operatively, for management of hypertensive crises.
- Alpha blockers (Phenoxybenzamine)
- Beta blockers: Propranolol. If arrhythmia or tachycardia occur.

Treatment

- ⌘ Alpha-blockers or Calcium channel blockers are used, either alone or in combination for treatment of hypertension.
- ⌘ Blood pressure is controlled before cardioselective beta-blockers are added for control of tachyarrhythmias

Hyperaldosteronism

Action of Aldosterone



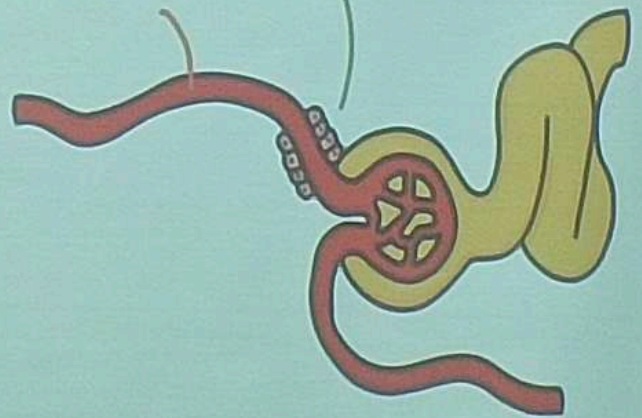
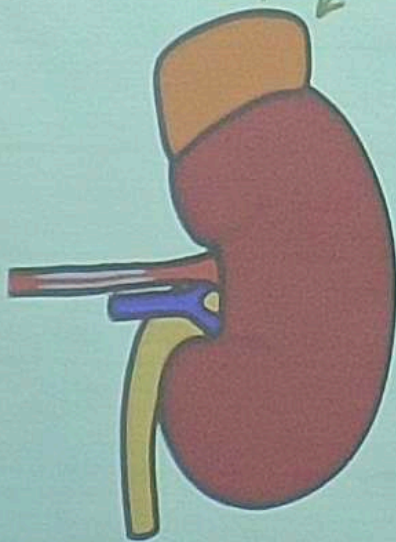
Hyperaldosteronism is a disease caused by excess production of the normal adrenal hormone, aldosterone, by the adrenal glands.

SECONDARY HYPERALDOSTERONISM

ALDOSTERONE

RENIN

↓ BP



Causes of Secondary Hyperaldosteronism

- Increased renin production.
- Conditions like congestive heart failure, liver failure, kidney disease, cirrhosis, and dehydration
- Certain medicines like diuretics and fludrocortisone.
- Anything that decreases blood flow to the kidneys, lowers blood pressure, or lowers sodium levels.

*Renin - An enzyme secreted by and stored in the kidney area that stimulates aldosterone and therefore, raises blood pressure

Clinical presentation

- Features of Uncontrolled hypertension
- Features of Unexplained hypokalemia

Headache

Fatigue

Anxiety, depression

Memory loss

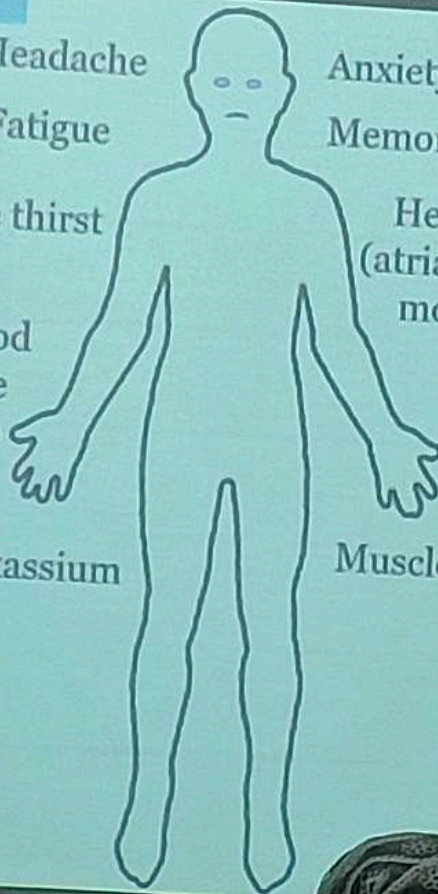
Excessive thirst

Heart arrhythmia
(atrial fibrillation is
most common)

High blood
pressure
(Mild to
severe)

Low potassium

Muscle cramps



Diagnosis of Hyperaldosteronism

- Elevated **aldosterone** measured in the blood or urine.
- **PRA (Plasma renin activity)**, is used to distinguish between primary (low PRA) and secondary Hyperaldosteronism (high PRA).
- **Abdominal CT scans** = adrenal masses
- **Electrocardiograms (ECGs)** = show abnormalities in heart rhythm that are often associated with low potassium level.

Adrenal vein sampling

- Measurement of aldosterone sample in adrenal venous blood.
- Unilateral four fold increase of aldosterone diagnostic

Plasma aldosterone conc/Plasma renin activity ratio

- PAC > 15 ng/dl
 - Ratio of PAC/PRC > 20
- } Diagnostic of
Conn's
- Test to be performed in the morning 8:00 AM
 - Paired random sample to be collected
 - Certain drugs contraindicated prior to test

Treatment

- ⌘ Medical treatment include a potassium-sparing diuretic, **spironolactone, eplerenone, or amiloride.**
- ⌘ **Spironolactone** is the most effective drug, has antiandrogen activity and men frequently experience breast tenderness, gynecomastia, or reduced libido.
- ⌘ **Eplerenone** is favored during pregnancy and for men, since it does not have antiandrogen effects.

Treatment

- ⌘ Blood pressure must be monitored daily when beginning these anti-mineralocorticoid medications;
- ⌘ Other antihypertensive drugs may be required, particularly amlodipine, and ACE inhibitors or ARBs.

Hypertension with
Low Plasma Renin ?

consider

Conn's Syndrome
(1° hyperaldosteronism)

- Hypokalemia ← *may present with hypokalemia, diabetes & parosmia*
K ↓
- Metabolic Alkalosis
Bicarbonate ↑

@jatmedicine

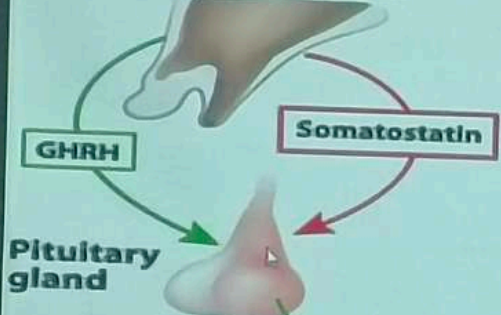
Acromegaly

- ⌘ Acromegaly - Rare (3 per million per year)
- ⌘ Disfiguring
- ⌘ Shorten life span (average 10 Years)
- ⌘ Equally prevalent in both ♂ and ♀
- ⌘ Average age 44 years at diagnosis
- ⌘ Delay in diagnosis (8 to 10 years)

Growth Hormone

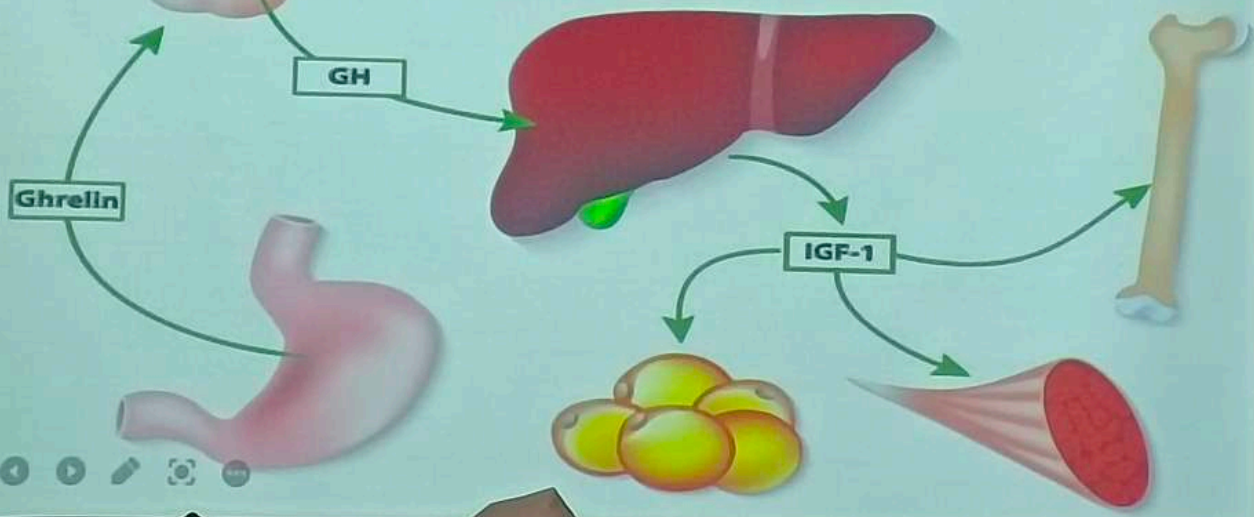
- ⌘ More than **95%** of patients with acromegaly harbor a GH-secreting **pituitary adenoma**
- ⌘ GH release is **intermittent and mainly nocturnal**, especially during REM sleep.
- ⌘ The frequency and size of GH pulses increase during the growth spurt of adolescence and decline thereafter.
- ⌘ Acute stress and exercise both stimulate GH release.
- ⌘ Normal subject, **hyperglycaemia suppresses it**.

Hypothalamus



GHRH - Growth Hormone Releasing Hormone
GH - Growth Hormone
IGF-1 - Insulin-like Growth Factor

Pituitary gland



Clinical Features

Clinical features

Depends on the age of onset of the GH excess

- In **child hood or adolescence** prior to epiphyseal fusion gigantism results(extreme tall stature)
- In **adult hood** or after fusion of the epiphysis **enlargement of acral parts** or tips of body (nose;lips;hands and feet) in addition soft tissues & internal parts of the body enlarge except brain

Clinical Manifestations

Mass effects of tumor

- Headache
- Visual field defects
- Hyperprolactinemia
- Pituitary stalk section

Hypopituitarism

Hypothyroidism

hypogonadism

hypocortisolism

Systemic effects of GH/IGF-I

- Visceromegaly
- Soft tissue and skin changes
- Thickening of acral parts
- Increased skin thickness and soft tissue hypertrophy
- Hyperhidrosis/Oily texture
- Skin tags and acanthosis nigricans

Cardiovascular features

- Hypertrophy (biventricular or asymmetric septal)
- Congestive Heart Failure (systolic and/or diastolic)
- Coronary disease
- Arrhythmias
- Hypertension
- Cardiomyopathy

Respiratory manifestations

- Macroglossia
- Jaw malocclusion
- Upper airway obstruction
- Sleep disturbances
- Sleep apnea (central and obstructive)
- Ventilatory dysfunction

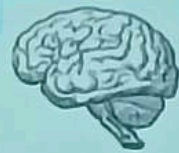
Clinical Manifestations

- Impaired glucose tolerance
- Diabetes mellitus
- Insulin resistance

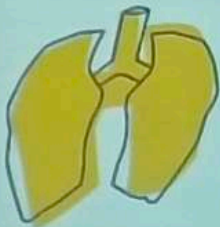
Bone and joint manifestations

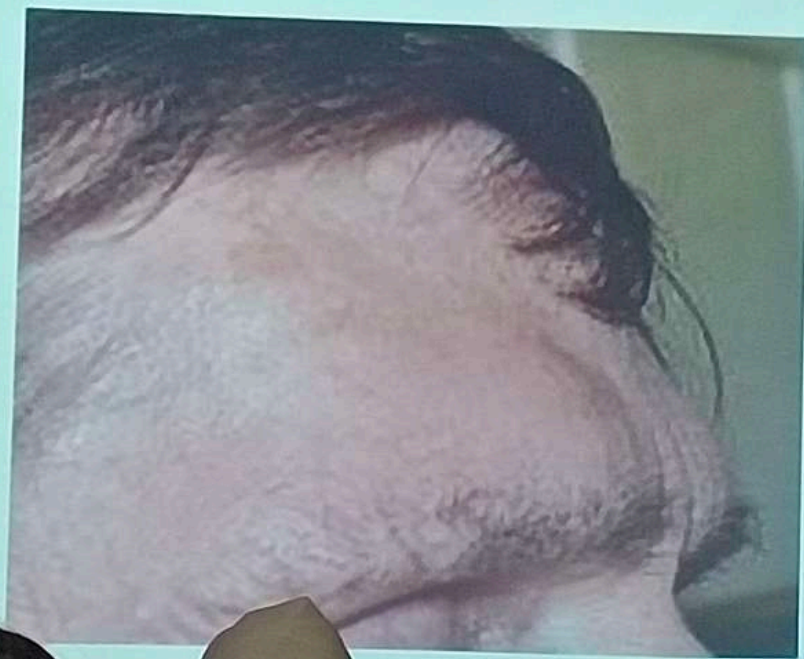
- Increased articular cartilage thickness
- Arthralgias and arthritis
- Carpal tunnel syndrome
- Osteopenia

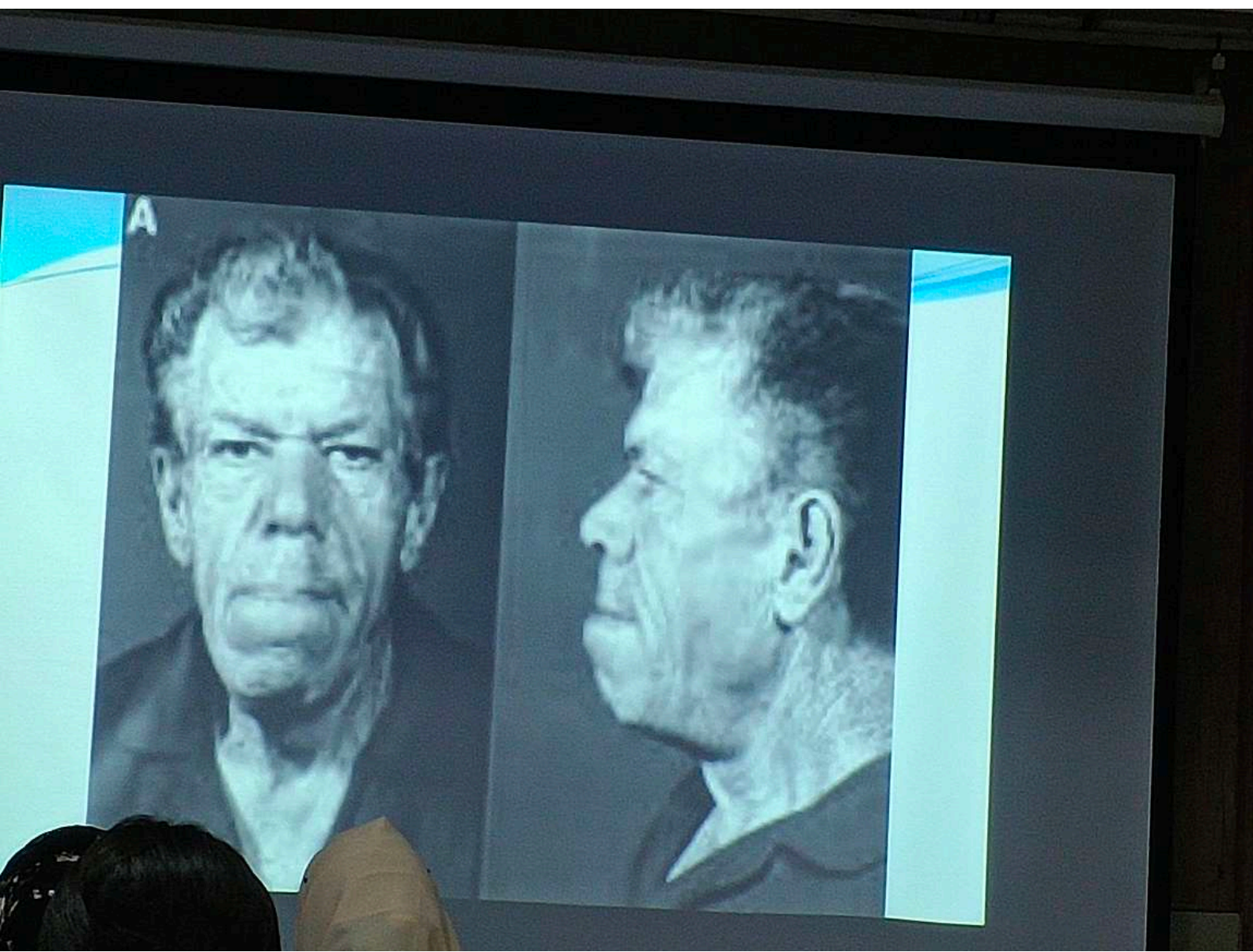
Complications



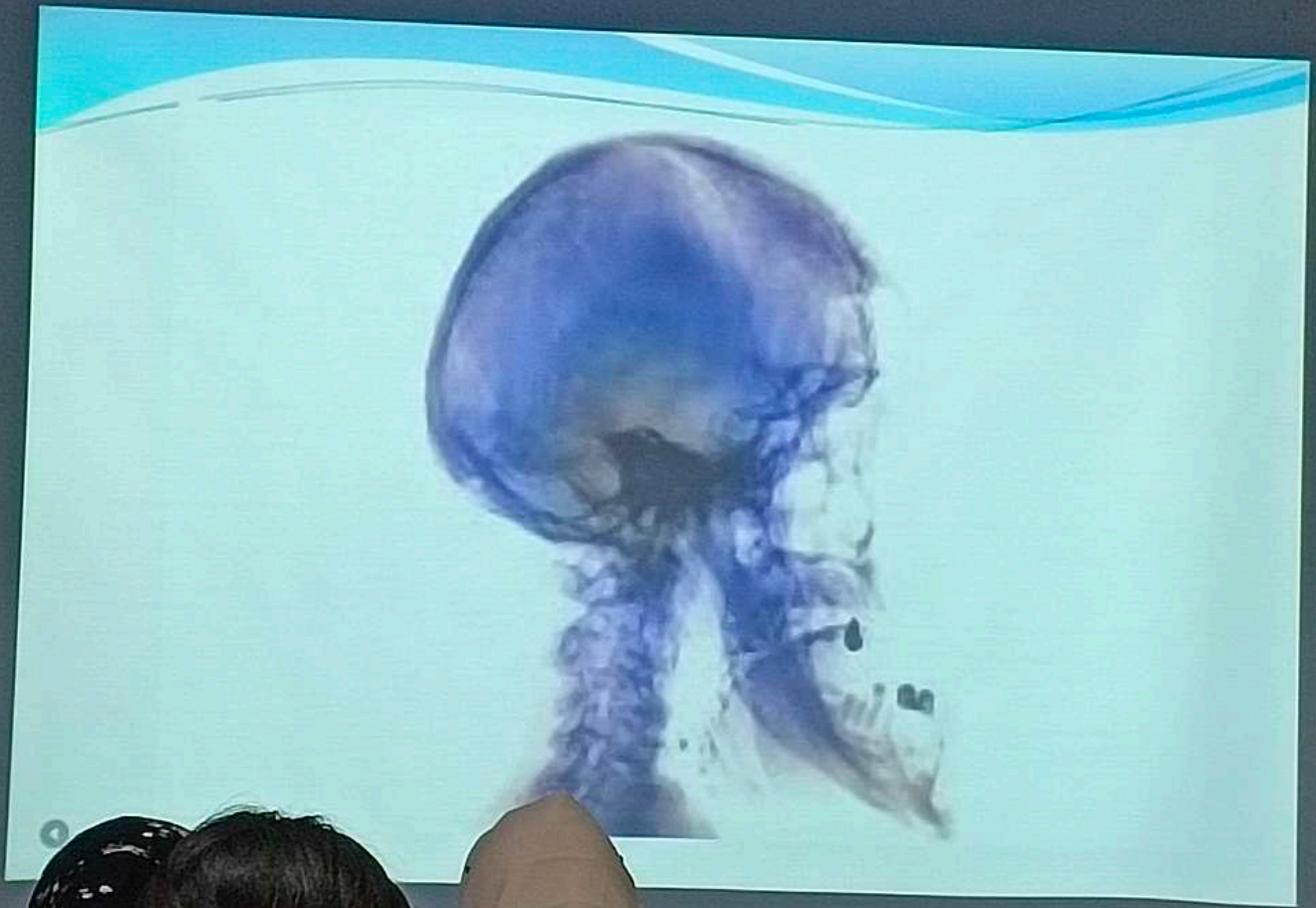
Acromegaly
Co-morbidities

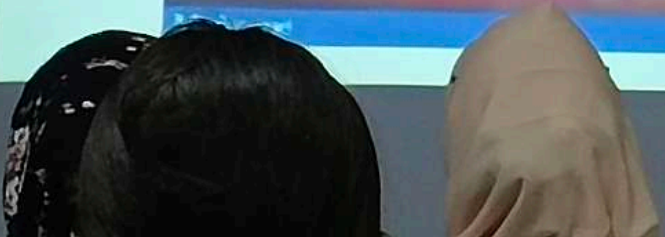


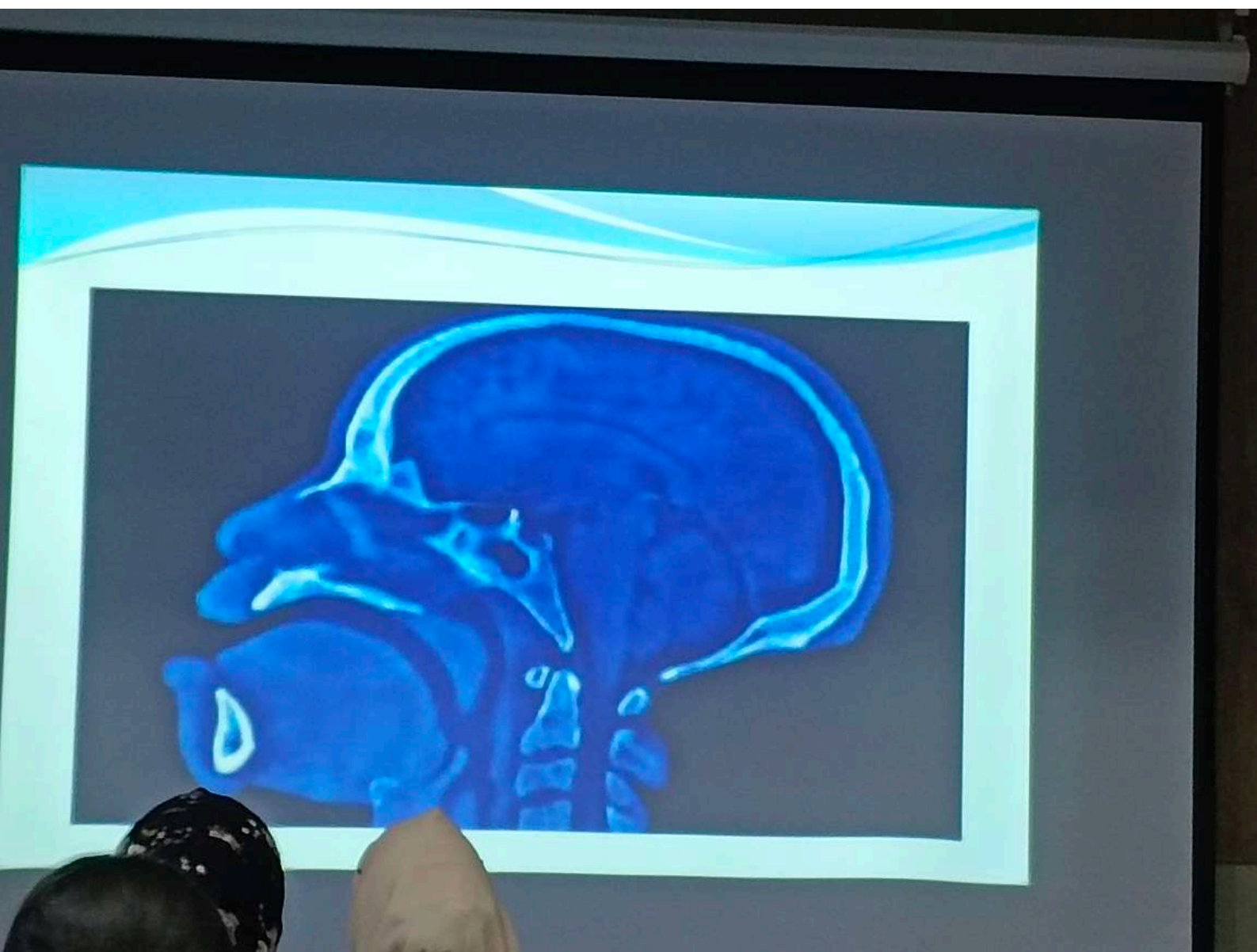












Acromegaly

“spade-like” hands



>23 mm



< 23 mm

- The **cancers** in acromegaly are colon, breast, and prostate carcinomas

Investigations

- Increase in shoe and/or ring size
- Using old photographs for comparison



4



Investigations

- ⌘ GH levels
- ⌘ IGF levels
- ⌘ Failure to suppress GH after OGTT (glucose suppresses GH secretion)
- ⌘ Prolactin levels
- ⌘ Visual field examination
- ⌘ MRI brain with contrast
- ⌘ ECG
- ⌘ ECHO
- ⌘ Glucose levels

Surgical Management

- Well-circumscribed adenomas resected by transsphenoidal surgery.
- Transsphenoidal surgery is the appropriate **first-line therapy**.
- Successful resection alleviates compression effects and preservation of anterior pituitary function.
- Very high preoperative GH and IGF-1 levels are poor prognostic markers of surgical cure.

Medical Management

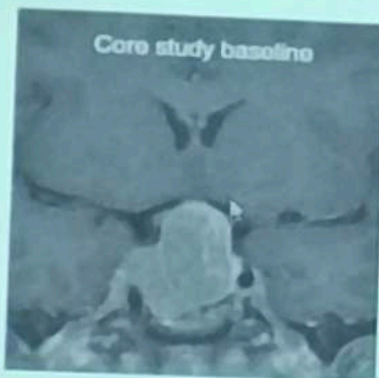
- Dopamine Agonists
- Somatostatin analogues.
- Growth Hormone Receptor Antagonist.

Dopamine Agonists

- Bromocriptine and cabergoline
- The drug causes **minimal tumor shrinkage**.
- These side effects include gastrointestinal upset, transient nausea and vomiting, headache, transient postural hypotension with dizziness, nasal stuffiness rarely, cold-induced peripheral vasospasm

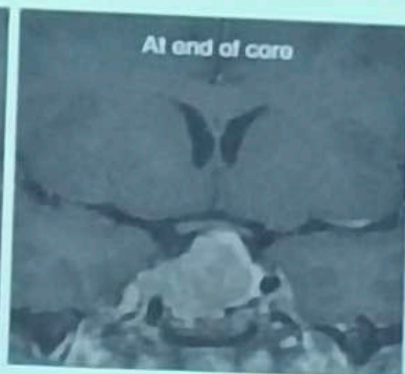
Somatostatin analogues

- The two analogues of somatostatin **octreotide** and **lanreotide**
- Given as monthly injections
- Reduce the levels of GH and IGF



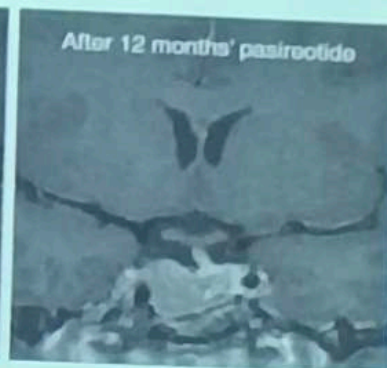
Core study baseline

Tumor volume
11,193 mm³



At end of core

Tumor volume
7350 mm³
Reduction = 34%



After 12 months' pasireotide

Tumor volume
5364 mm³
Reduction = 52%

2 Coronal T1 MR images of a patient, illustrating significant tumor volume reduction during treatment with pasireotide

GH receptor antagonist

- Pegvismont
- Injectable treatment
- It does not lower GH levels or reduce tumour size but has been shown to **normalize IGF-1** levels in 90% of patients.
- In patients who have persistently elevated IGF-I levels despite maximal therapy with other treatment modalities SR.

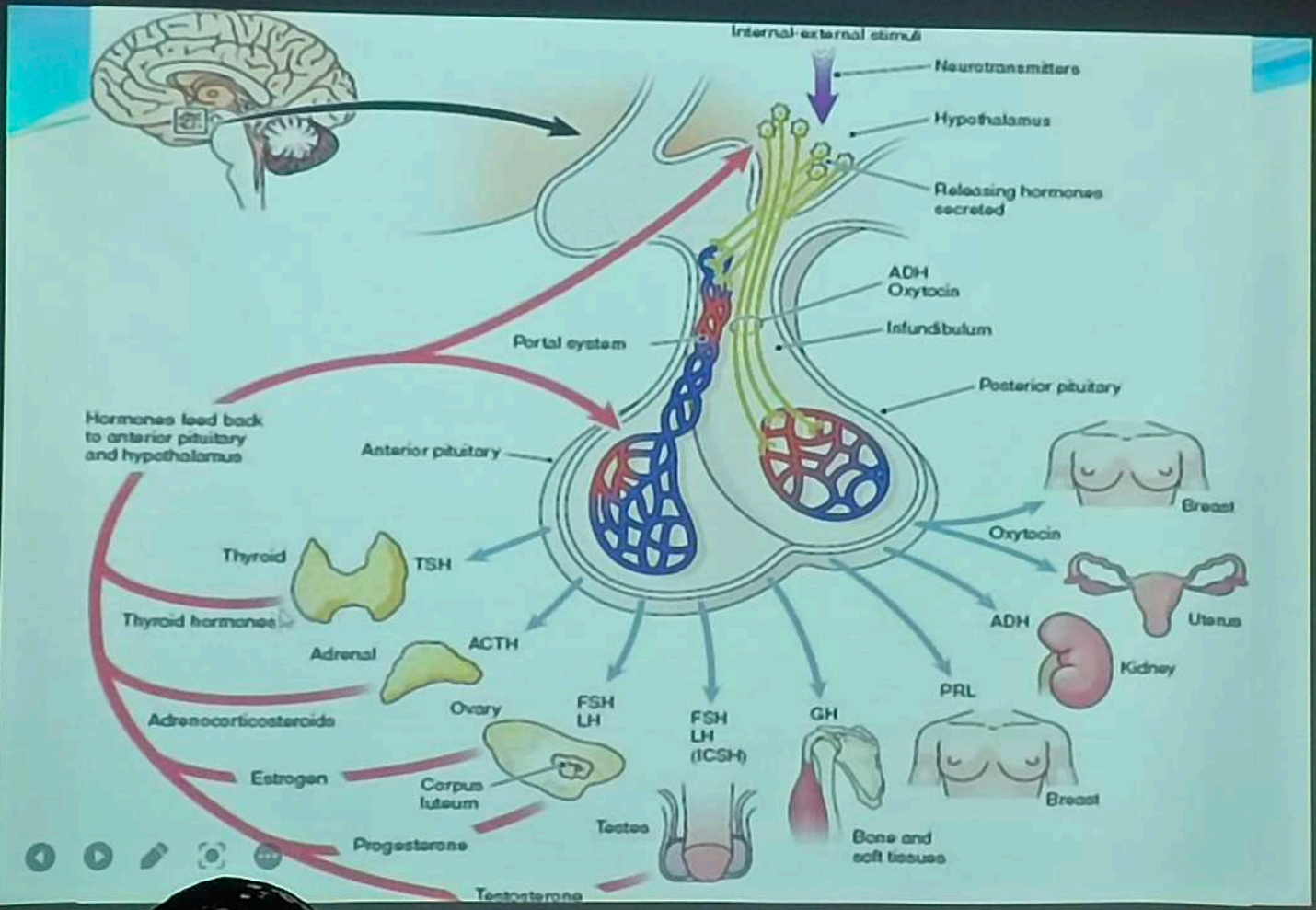
Radiation Therapy

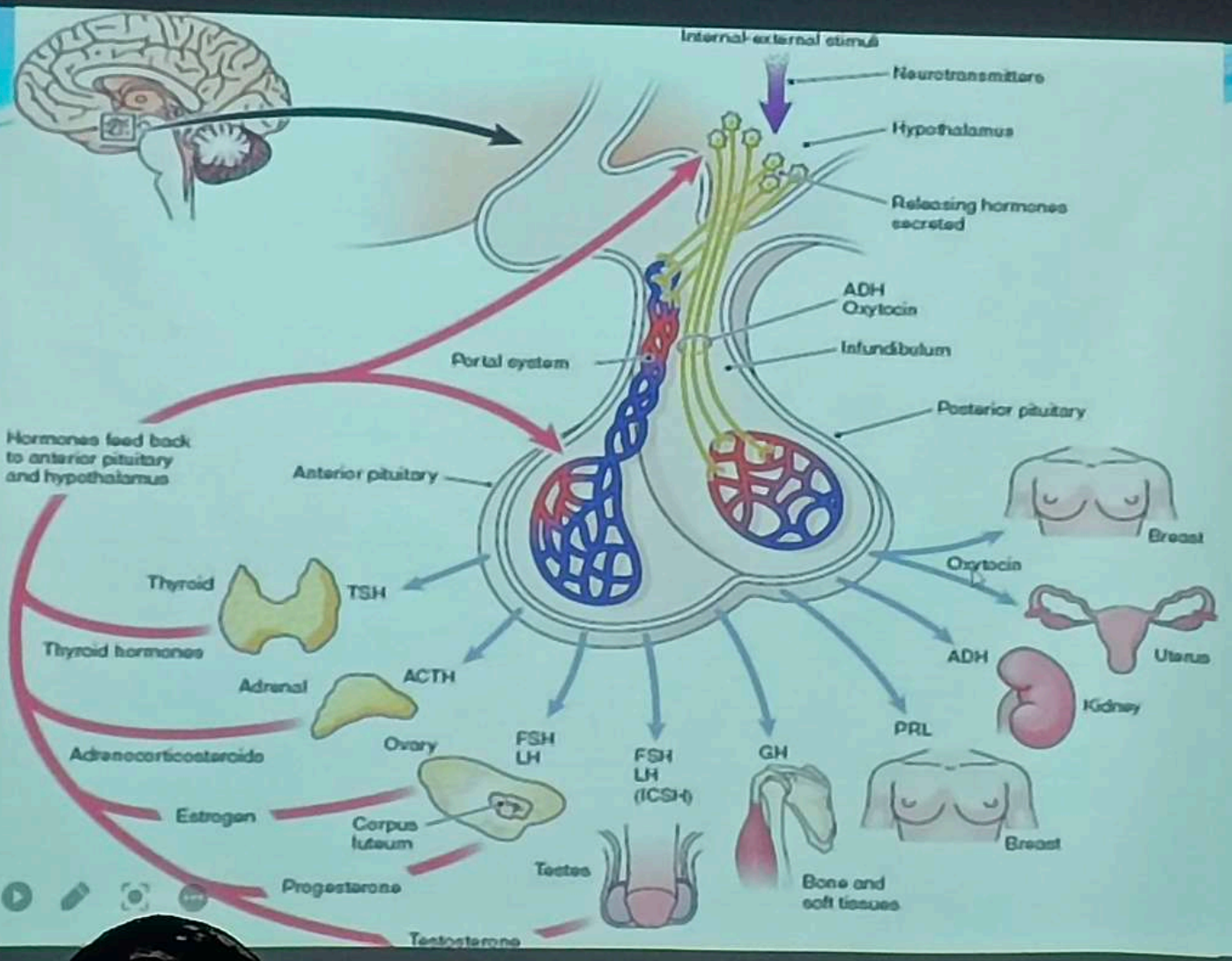
- Radiation therapy reserved for **third-line treatment**.
- Patients who do not have tumor growth control or normalization of hormone levels with surgery (for example, after debulking of a nonresectable tumor) and/or medical therapy are possible candidates for radiation therapy
- Stereotactic(gamma-knife) radiotherapy is used in some as it delivers a more concentrated field of radiation.

Treatment modalities

1. Surgery
2. Medical therapy
 - Dopamine Agonists (Bromocriptine, Cabergoline) shrink tumor size
 - Somatostatin Analogue (Octreotide LAR, Lanreotide Autogel) Dec GH and IGF level
 - GH receptor Antagonist (Pegvisomant) Dec IGF level
3. Radiotherapy (not widely used) Stereotactic Gamma Knife

Panhypopituitarism





Clinical features of hypopituitarism

Fatigue, lethargy, generalised weakness

Low mood, poor motivation, difficulty with concentration

Reduced appetite, unexplained weight loss or gain

Dizziness (with hypotension, especially postural)

Male: sexual dysfunction, reduced shaving frequency

Female: Oligo-/amenorrhoea, reduced axillary or pubic hair