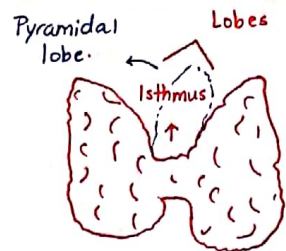


Thyroid Gland



- Isthmus might be absent in 10% & pyramidal lobe is only found in 50%.

- Thyroid Gland is located in the center of the neck, at the Anterior neck triangles.
- It consists of 2 lobes & isthmus (opposite to 2nd & 3rd tracheal rings)
- Pyramidal Lobe (50%) considered an Embryological remnant of Thyroglossal Duct.

Embryology of Thyroid Gland:

- Median thyroid Primordium \Rightarrow Start from the Base of the tongue (Foramen cecum) & descend along the thyroglossal duct to its final location in the neck.
- Lateral thyroid Primordium + Superior parathyroids \Rightarrow From the 4th pharyngeal pouch.
- Thymus + Inferior parathyroid glands \Rightarrow 3rd Pharyngeal Pouch \Rightarrow Higher Risk to be Ectopic

\Rightarrow Search in thyrothymic ligament & thymus substance

Histology:

- 2 Types of Cells
 - \rightarrow Follicular Cells (Thyrocytes) \Rightarrow Synthesis & secrete thyroid Hormones (T_4, T_3)
 - \rightarrow Para follicular cells \Rightarrow Called C-cells because they secrete the hormone calcitonin.
- Colloid is the storage form of Thyroid Hormones.

- C-cells come from neural crest so they are Neuroendocrine cells
- They present in superolateral part of Thyroid Lobes so cannot be found in:
 - 1- Pyramidal Lobes
 - 2- Isthmus
 - 3- Thyroglossal duct cyst.
- \rightarrow That's why Medullary Cell Ca. can't develop in these sites.

(70%) Most common cervical Anomaly
Most common developmental anomaly of thyroid Gland.

Thyroglossal Duct Cyst

- Normally at Birth the Thyroglossal Duct has to involute, if not involuted (Occur in 7% of population), cystic degeneration might occur forming a cyst & in 1/3 of the cases this cyst will contain thyroid tissue.

* Most Common location of the Cyst :-

- 1- Midline at or below hyoid bone
- 2- Suprahyoid (2nd most common)

* Characteristic Physical findings: (Clinical Dx)

- 1- 50% present before Age of 20.
- 2- Midline cystic mass (75%) or near midline (25%)
- 3- Mass move upwards when the Patient Protrudes his tongue. (Because its attached to foramen cecum) or swallowing.

DDx of thyroglossal fistula.

- * What if I didn't see the mass moving up?
 - Repeat with your hands on it because its not only seen but also felt.

* Next step? Confirm Diagnosis:

- ① Ultrasound \Rightarrow Evaluate suspicious features & exclude malignancy as:
 - ① Psammoma Bodies (Microcalcification)
 - ② Mural / solid components.

- The most common cancer in thyroglossal cyst is Papillary thyroid ca. & 2nd most common is SCC.

* Management :-

- In the past they only do cystectomy, with recurrence rate of 60% (Because cystic degeneration can recur in the duct).
- Nowadays we do Sistrunk Procedure: (Recurrence 10%)
 - Emb. remnant -
 - 1- Removal of the cyst
 - 2- The whole tract from Pyramidal lobe to Foramen cecum.
 - 3- Central part of hyoid Bone.

- Aims to \rightarrow Infections
Sinus formation - due to cyst rupture -
Malignancy (< 2%)

- Treatment if malignant:
 - 1- Sistrunk + Thyroidectomy + Radioactive ablation.
 - or 2- Thyroidectomy
- Presence of thyroid tissue at the base of tongue due to failure of descend.
- Here the Goal of ultrasound to make sure that there is normal thyroid tissue in thyroid Gland or this is the only thyroid tissue he has.

lingual Thyroid - Called Strawberry Thyroid -

- Treated only if:
 - 1- Causing obstructive symptoms
 - 2- Bleeding
 - 3- Suspicious of malignancy ①

- Adults (5-15)% while in childrens its (25%).

Nodular Thyroid Disease

Thyroid Nodule: A discrete intra-thyroid lesion that radiologically distinct from its surrounding Parenchyma.

Case: Nodule in the center of the neck at the location of thyroid Gland, move with thyroid upon swallowing, DDx:

- ① Thyroid Nodule (Most Common dx) ⇒ Differentials:
- ② Lymphadenopathy
 - ③ Aneurysm.
 - ④ Tracheal sarcoma
 - ⑤ Parathyroid carcinoma (you can never see parathyroid Adenoma)

- ① Most Common Is Prominent nodule in MNGI.
- ② True Solitary Nodule
 - Has higher chance of malignancy than Dominant nodule in MNGI
 - Most commonly Adenoma. (80%) → Follicular Adenoma
 - Carcinoma (10%)
 - Benign Conditions (10%) - cyst, Colloid nodule, fibrosis.

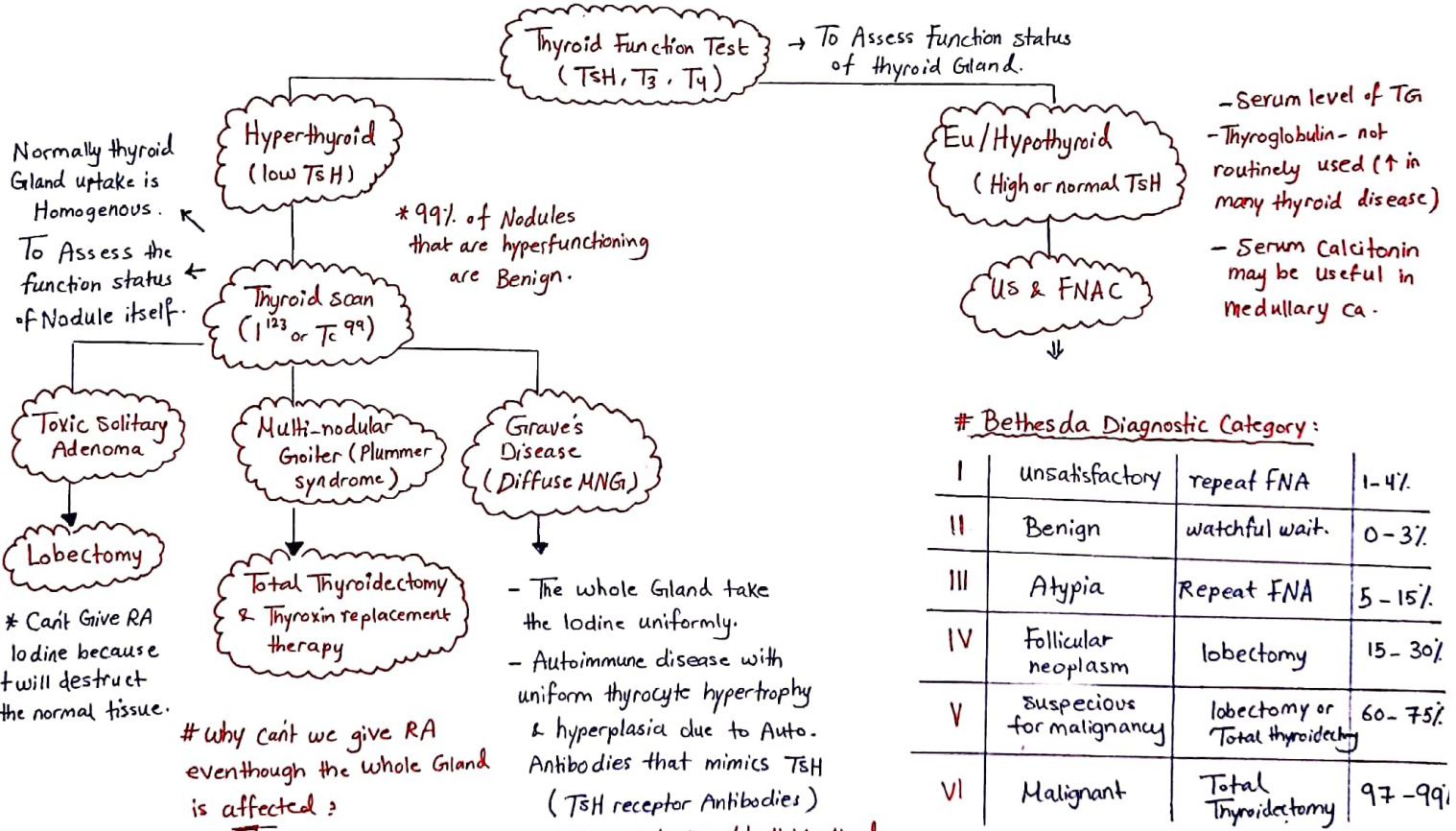
Prevalence of Palpable nodules (5%) < Non-Palpable (76%)

The Risk of malignancy Is the same in palpable & non-palpable.

Factors ↑ likelihood of malignancy in Thyroid Nodule:

1. Male ^{should do Total thyroidectomy}
2. Age <20 >60
3. Family hx
4. Hashimoto thyroiditis
5. Obese
6. Hx of Ionizing RT
7. Cold nodule
8. True solitary nodule
9. Fixation (The only sign that indicate malignancy in physical exam)
10. Hoarsness
11. cervical LN
12. Rapid growing. (↑ in Anaplastic Ca.)

Approach to thyroid Nodule:



Bethesda Diagnostic Category:

I	unsatisfactory	repeat FNA	1-4%
II	Benign	watchful wait.	0-3%
III	Atypia	Repeat FNA	5-15%
IV	Follicular neoplasm	lobectomy	15-30%
V	suspicious for malignancy	lobectomy or Total thyroidectomy	60-75%
VI	Malignant	Total Thyroidectomy	97-99%

Mechanism of Action:

- Inhibit the Enzyme in TH synthesis (thyroid Peroxidase)
- PTU Also Inhibits conversion of T₄ to T₃ peripherally.

- **Total Thyroidectomy** → Best if pregnant.
 - should take thyroxin for life.
- **Radioactive Iodine Ablation** → CI in pregnant or if having Exophthalmus
- **Medical Treatment** (↑ ophthalmic changes)
 - If unfit for surgery / elderly.
 - ① Propylthiouracil (PTU) } liver toxicity
 - ② Carbimazole → Agranulocytosis
 - ③ Methimazole (flu-like → ER) & check CBC

Thyrotoxicosis

- Clinical state results from ↑ circulating T₃/T₄.
- Seen in Hyperfunctioning Gland.
- Also in Thyroiditis (Gland damage result in spen of contents into the Blood)
 - ↳ On thyroid scan show low uptake.

Thyroid Cancer

Classified According to cell Origin:

- Follicular (95%): (Papillary, follicular, Hurthle cell) \rightarrow well differentiated
(Insular, large cell) Anaplastic \rightarrow Undifferentiated.
poorly differentiated
- Parafollicular (5%): Medullary Ca.

(The most common & least aggressive) Papillary Thyroid Ca.

Papillary Thyroid Ca.	Follicular Ca. (2nd most common thyroid ca.)
- Age 30 - 40 yrs	- 50 yrs.
- <u>Assoc with</u> : 1. Radiation Exposure 2. Iodine sufficient Area.	1. Iodine deficient Area 2. Multinodular Goiter 3. rarely with radiation exposure.
- Multicentric in 80% of cases (Don't Adversely effect Prognosis)	- Unifocal (solitary) & non functional (<1% functional)
- <u>Spread</u> : - Mainly Lymphatic - Rarely Hematogenous (Lungs) * Childrens more common to be node +ve than Adults	- Mainly Hematogenous (Bone > Lung) - Lymphatics <10%
# <u>Diagnosis</u> : Based on Nuclear features seen in FNAC (not Histopathology): 1. Optically Clear Nuclei (Orphan Annie) 2. Nuclear Crowding / Overlap. 3. <u>Intranuclear cytoplasmic Inclusions</u> 4. Psammoma bodies. (Seen Also in medullary ca.) 5. Nuclear Envelope / Groove	# <u>Diagnosis</u> : The distinction between follicular adenoma & carcinoma (have Invasion of the capsule is made by Histopathology not cytology.)
# <u>Histological variants of PTC</u> : 1. Papillary growth pattern. 2. Follicular variant (Most common) 3. Oncocytic 4. Diffuse Sclerosing 5. Columnar cell 6. Tall cell (Most Aggressive) - Height of cells three times its width.	# <u>Treatment</u> : - <u>Either</u> : 1- thyroid lobectomy \rightarrow wait for pathology if follicular ca. \rightarrow complete Thyroidectomy within weeks to max. 3 months (after that scarring will occur) 2- Total thyroidectomy from the start.
# <u>Papillary Microcarcinoma</u> : - Its papillary ca. \leq 1cm - Discovered incidentally in US or specimen after lobectomy. - Don't have malignant Behavior (10yrs survival is 100%) - <u>Treatment</u> : - The lobectomy is sufficient if no hx of radiation, single & low Risk. - Observation.	# <u>Minimally Invasive Follicular Ca.</u> - Capsular Invasion without vascular invasion. - Don't Have malignant Behavior (10yrs survival is 85%) - <u>Treatment</u> : - Lobectomy is sufficient & no need for Total thyroidectomy, RA ablation.

Sonographic features Highly suggestive of malignancy

1. Microcalcification (Psammoma Bodies)
2. Irregular margins (Indicates aggressive nature of mass)
3. Taller than wider orientation (Centrifusion pattern of Growth of malignant cells)

If a nodule has these features or > 1cm \rightarrow FNAC

If nodule < 1cm \rightarrow follow up.

Layers of the neck in Thyroidectomy:

1. SKIN
2. Platysma
3. Anterior Jugular vein.
4. Strap. Muscle (thyrohyoid, Omohyoid, sternohyoid, Sternothyroid)

Complications of Thyroidectomy

1. Infection
2. Hematoma \rightarrow can cause Stridor not by compressing the trachea but compressing the lymphatics \rightarrow lymphedema in the Larynx.
3. RLN Injury (2%) - most common injured nerve.
4. Seroma (if drain < 20ml per day remove it.)
5. Hypothyroidism.

\hookrightarrow The most common complication of thyroidectomy is Hypoparathyroidism due to:
1- transient ischemia
2- Mechanical, thermal Trauma (2)

Blood supply of Thyroid Gland: (2)

1. Superior Thyroid A. → Branch from External carotid A.
2. Inferior Thyroid A. → from Thyrocervical Trunk
3. Thyroid Ima A. (Anatomical variant 3%) → Directly from Aorta

Venous Drainage of Thyroid Gland: (3)

1. Superior thyroid vein.
2. Middle thyroid vein > Drain into Internal Jugular
3. Inferior thyroid vein → Drain into Brachiocephalic Trunk.

Lymphatics of Thyroid Gland:

- To prelaryngeal, Pretracheal & Paratracheal LN.
- Laterally → Superior & Inferior deep cervical LN.

* Name of LN group around pyramidal lobe → Delphian LN.

* Before Giving Radioiodine Ablation → starvation of the Gland (cut off iodine) → to ↑ Gland uptake.

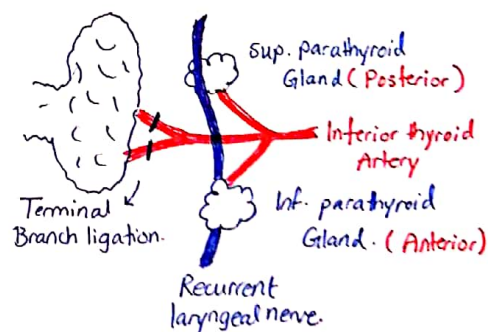
* Amiodarone can cause MNGs.

Parathyroid Glands → PTH secreted from chief cells

Blood supply: Inferior thyroid Artery ⇒ That's why in Thyroidectomy we do Terminal Branch ligation to Avoid Ischemia of parathyroids.

Relation to Recurrent Laryngeal nerve:

- Superior parathyroids lie posterior to it, ⇒ so its called The Posterior Gland.
- Inferior parathyroids lie ventral to it. ⇒ so its called The Anterior Gland.



Hyperparathyroidism:

↳ Hyperfunctioning Parathyroid Gland, which ↑ levels of circulating parathyroid Hormones.

- Etiology

(10%). Parathyroid Hyperplasia (4 Glands Disease seen in MEN syndrome)

↑ Ca
↑ PTH
↳ Primary Hyperparathyroidism: ⇒ [2] Adenoma (90% single Gland disease, 5-10% Two Glands Disease) - 85%
- Surgical treatment.

↓ Ca
↑ PTH
↳ Secondary Hyperparathyroidism:-

1. Most common Cause is Renal failure, due to ↓ 1α hydroxylase.
 2. Vit. D deficiency ⇒
 3. Hyperphosphatemia (Phosphate is Anion & Active form of Ca^{+2} is cation, so phosphate will Bind Ca^{+2} & lead to Hypocalcemia)
- Management is medical, treat underlying cause.

Vitamin "D" Metabolism

- Skin (cholesterol) \xrightarrow{UV} Cholecalciferol
Liver $\xrightarrow{25\alpha$ hydroxylase \rightarrow 25-hydroxycholecalciferol \xrightarrow{Kidney} 1,25 hydroxycholecalciferol (Active form of D)
1,25 hydroxycholecalciferol $\xrightarrow{1\alpha$ hydroxylase \rightarrow 1,25 hydroxycholecalciferol (Active form of D)
↑ Stimulated By PTH
⇒ ↑ Absorption of Calcium from duodenum & Proximal Jejunum.

Indications for surgery:

1. Severe Hypercalcemia
2. Progressive Bone Disease
3. Refractory Hyperparathyroid.
4. Pruritis that don't respond to dialysis or medical Ht.
5. Progressive calciphylaxis & Extra-skeletal calcifications

Nerve supply of Thyroid Gland:

- Branches of vagus nerve
1. Recurrent laryngeal nerve
 2. Superior (External) laryngeal nerve.
- ↳ Run with superior thyroid Artery so in thyroidectomy cut proximal to the Gland to Avoid Injury & if injured ⇒ Deeper Voice.

- Recurrent Laryngeal Nerve Injury - most common injured nerve -

↳ Partial → Unilateral → stridor on exertion
Bilateral → Asphyxia (need Tracheostomy)

↳ Complete → Unilateral → Hoarseness
Bilateral → Aphonia

The Only nodule that we don't do FNA is pure cystic, unless

- Therapeutic: 1- Cosmetic
2- Compression effect.
- Modalities: phenol or ethanol injection then Aspiration.

Symptoms of Hyperparathyroidism:

- ① Painful Bones (1st symptom) ⇒ Due to:
 - ① Osteoporosis
 - ② Osteopenia
 - ③ Bone cysts
 - ④ Osteitis Fibrosa Cystica
 - ⑤ Pathological fractures
 - ⑥ Calciphylaxis (Ca precipitate in small blood vessels)
- ② Renal Stones (The most common type is Ca. Oxalate)
- ③ Abdominal Groans ⇒ DDx of Abd. pain in Hypercalcemia:
 1. Acute Pancreatitis
 2. Peptic Ulcer
 3. Duodenitis
 4. Constipation
 5. Renal colic
- ④ psychic Moans
- ⑤ Fatigue Overtones

↳ Tertiary Hyperparathyroidism

→ Result from persistent HPT after correction of 2ndry HPT, result from Autonomous PTH secretion not responsive to normal -ve feedback due to ↑Ca levels.

Clinical Signs:

- Hypocalcemia need 6-12 hours to manifest:

1. Circumoral numbness (1st sign)
2. Sacral numbness
3. Chvostek sign
4. Trousseau Sign ⇒ ↑ BP cuff above systolic pressure will cause carpopedal spasm.
5. Laryngeal spasm.

Explanation: Na channels are Ca. gated channels → ↓ Ca. from ↓ Blood by cuff → ↑ Na⁺ influx into the cell → Repetitive Action Potentials

Management

- After doing sestamibi scan
- Detect the affected Gland
- Removal of Gland
- ⇒ Parathyroid Hormone Half-life is only 5 mins, so we repeat PTH level after surgery to check if it decreased, if not decreased repeat test up to four times, if not appropriately decreased search for second Adenoma.

Parathyroidectomy Complications:

1. Hypocalcemia
2. RLN injury
3. SLN injury
4. Hematoma

Post-surgical Resp. distress & Stridor:

- ↳ Immediate → RLN injury
- Intubate or Tracheostomy
- ↳ After 6 hours → Hematoma (lymphedema)
- ↳ Next day → Hypocalcemia (laryngeal spasm)

Hypocalcemia

Adrenal Glands

Anatomy:-

- Receives Great Amount of Blood / Gram of tissue among all Endocrine Glands (2nd is Thyroid)
- 2nd most common organ that receive large Blood Supply after Carotid Body.
- Retroperitoneal Organ, covered by a capsule "Gerota's Capsule" 4 Grams.
- Right Adrenal lie between IVC & Right liver lobe, Left Adrenal lie medial to superior Pole of left Kidney & covered with tail of pancreas & spleen.

Embryology:

- Not related to the kidney.
- Cortex → Mesoderm
- Medulla → Ectoderm from Neural crest cells

Blood supply: (3A)

1. Superior suprarenal Artery → Inferior phrenic A.
2. Middle suprarenal Artery → Abdominal Aorta
3. Inferior suprarenal Artery → Renal Artery

Venous Drainage: (1V)

- (3mm) ← 1. Right suprarenal vein → IVC (Posterior Aspect)
 (longer) ← 2. Left suprarenal vein → Left renal vein.

Case :- Patient had flank pain & came to ER & we did CT scan to look for Renal stones, the CT scan showed a suprarenal mass on Right Kidney.

- What's the first thing to do? Exclude Functional Disease

⇒ So we do Biochemical Profile:

1. Hyperaldosteronism "Conn's" → Aldosterone & plasma renin, serum Na, K⁺
2. Hypercortisolism "Cushing's" → Morning Plasma Cortisol, 1mg dexamethasone suppression Test
3. pheochromocytoma → plasma metanephrin & NE
4. Bilateral Hyperplasia

⇒ If the mass is not functioning & Biochemical profile is normal This is an Incidenteloma. (↑ Incidence with Age)

Approach to patients with Incidenteloma:

- Next step is ⇒ Check the size

< 4cm ⇒ Follow up after 6 months then 1 year, then another year By MRI, Hormonal Evaluation.

> 4cm ⇒ There's chance 25% of malignancy so we should remove it.

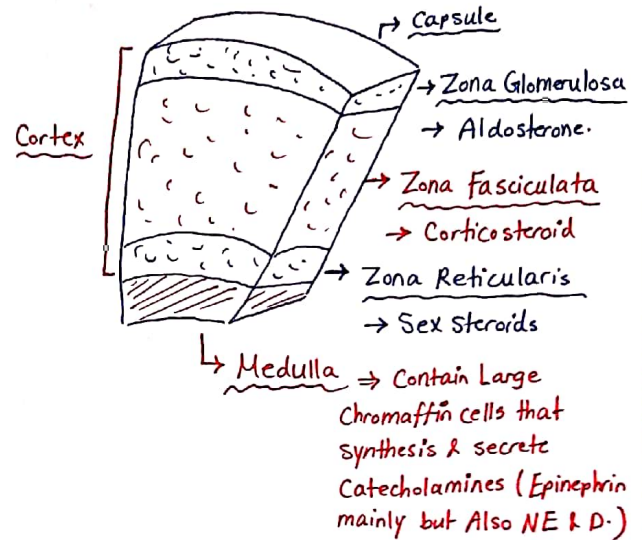
⇒ Observe the rate of Growth if > 1cm in 6 months (Rapid Growth) → Indicate surgery.

② Also Features in CT scan:

- ① Heterogeneity (Indications for surgery)
- ② Areas of Necrosis
- ③ Margin Irregularity
- ④ Venous emboli in proximal veins to the mass.

Other Surgical Indications in Adrenal masses

1. Functional mass
2. Symptomatic Myelolipoma



Adrenal Tumors

1. Incidenteloma (78%)
2. Cushing Adenoma (7%)
3. Adrenocortical Ca (4%)
4. pheochromocytoma (4%)
5. Myelolipoma (fat (2%) Globules)
6. Conn's Adenoma (1%)

Functional Tumors:

Conn's Syndrome

Primary Hyperaldosteronism: Adrenal Hypersecretion of Aldosterone

- Cause of Hypertension (from ↑ Na & water reabsorption in kidney)
- & Hypokalemia (↑ Renal excretion of K⁺ & H⁺) - Adenoma > Hyperplasia > Cancer
- Plasma Renin Activity is suppressed → from -ve feedback inhibition on Renin-Angiotensin-Aldosterone System.

Cases:

1- If no mass is seen on CT with Contrast:

- Differential Dx: 1- Conn's but still small 2- Bilateral Hyperplasia
- How to differentiate? Do Selective Adrenal Venous Sampling
(Intervention Radiology) → from femoral vein to Adrenal vein → sample → Measure Aldosterone difference.
on Both sides → - If High on Both sides → Bilateral Hyperplasia
- If significant difference → Lateralized on one side
- What is the Management? - If Bilateral Hyperplasia 1st line treatment is Medical → Spironolactone (Aldosterone Antagonist) - SE: Gynecomastia, Hyperkalemia
- If Conn's Syndrome → Adrenalectomy.

Secondary Hyperaldosteronism:

- Cause is not the Adrenal it could be: 1) Renovascular HTN 2) Juxtaglomerular Cell Tumor
- Plasma renin Activity is elevated.

2- Mass on left Adrenal:

- Differential: Presence of a mass doesn't mean Conn's:
 - ① Incidentaloma on left side & Conn's on Right side
 - ② Bilateral Hyperplasia→ so we should also do Adrenal venous sampling.

Cushing Syndrome

- # Hypersecretion of Cortisol
 - ACTH dependant ⇒ (2nd most common cause) Pituitary Adenoma (Cushing Disease) or ⇒ Transphenoid Excision
Ectopic ACTH in SCLC & CRH producing Tumors such as medullary thyroid Ca.
 - Non-ACTH dependant ⇒ - Exogenous steroid intake - Most Common Cause.
 - Adenoma (15%) ⇒ Adrenalectomy
 - Carcinoma ⇒ Adrenalectomy.

Pheochromocytoma

Tumor Arise from Chromaffin cells & secretes catecholamines.

Most Common location: Adrenal medulla.

2nd most common location is Organ of Zuckerkandl (where inferior mesenteric Artery leave Abdominal Aorta)

- Clinically: Catecholamines secreted in surges so there's episodic HTN, & palpitations & sweatings.

- Investigations: 1- Most Sensitive is Plasma metanephrin & NE
2- Urinary metanephrin & VMA.

Preparation for surgery:

① ↓ BP By Phenoxybenzamine (Reversible α Blocker)

→ In Surgery if we remove the adrenal → No Catecholamines

(NE action x1 to cause vasodilation → Hypovolemic shock → That's why we use Reversible α Blocker (not phentolamine) → Give Nitroprusside VC)

② Give IV fluids 10 days before surgery & monitor weight Gain.

③ Give Propranolol (β-Blocker) after effect of α Blocker has Achieved. ⇒ After Because of its SE & Tachy-arrhythmias.

- Rule of 10:

1. 10% Bilateral
2. 10% Malignant
3. 10% in childrens
4. 10% Extradrenal
5. 10% Inherited ⇒ NF1, MEN2a
6. 10% Multiple VHL, Para-ganglionoma.

Note: In MEN2a treat HTN (Pheochromocytoma) before anything else Because patients die from malignant HTN In ER.

Salivary Gland

- ↓ Incidence of Tumors
- ↑ Malignancy Rates

Salivary Glands
 - 80% of all Salivary Neoplasms are Benign.
 - < 2% of all head & Neck T.

Major Salivary Glands ⇒ 1. Parotid Gland (80% of neoplasms) 2. Submandibular 3. Sublingual (70% of malignancies)

Minor Salivary Glands ⇒ At the Junction of soft & hard palate. (2nd most common salivary neoplasm)
 ↳ Mucous (palate), serous (Back of tongue) or Mixed (tip of tongue)

Salivary Gland Tumors

Benign

- Pleomorphic Adenoma (Most Common Benign)
- Warthin Tumor (Papillary Cystadenoma lymphomatosum) (2nd most common Benign)

Malignant

- Mucoepidermoid ca. (Most Common Overall)
- Adenocystic ca. (2nd most common in Adults)
- Acinic Cell ca. (2nd most common in peds.)

	Pleomorphic Adenoma	Warthin Tumor
<u>Location</u>	- Mostly Occur in Parotid Gland (In the lower Border of mandible)	- Exclusively occur in Parotid Gland (Mostly in inferior pole of superficial lobe - Parotid tail-)
<u>Epidemiology</u>	- young, middle aged Adults - Male Predominance.	- Age > 50 yrs - ↑ Incidence in females due to smoking.
<u>Grossly</u>	- Asymptomatic, well-circumscribed, slowly Growing, Hard - Rubbery, limited mobility & painless, not fluctuated.	- Soft & fluctuant, Painless - Large cystic spaces. - Could be Multifocal
<u>Bilateral?</u>	-	10% !
<u>Histologically</u>	- Mixture of epithelial cells (Nests / sheets) & myoepithelial cells with stroma (myxoid, chondroid) - No True Capsule. / Have Pseudopods.	- Mixture of epithelial cells & lymphoid tissue. - Surrounded by fibrous Capsule.
<u>Management</u>	- If Tumor In superficial lobe: (superficial to plane of facial n.) → Superficial Parotidectomy (Patey's Procedure) - If Tumor In Deep lobe: → Conservative parotidectomy "Preserve all the Branches of facial nerve" * Avoid Enucleation & Biopsy → ↑ Recurrence rate 80%, Nerve Damage.	- Approach: 1. MRI (Imaging of choice) → Nerve Involvement Bilateral 2. US (operator dependant) 3. FNA (cytology) * True cut Biopsy & wedge Biopsy CI (↑ Recurrence & implantation) - Enucleation Is Accepted (↑ Recurrence) - No Agreement on Treatment → Patey's (if sup. lobe involved) - Tumor Is Radioresistant. → Total conservative Parotidectomy (if Both lobes involved)
<u>Complications</u>	1- Transient facial nerve Palsy (40%) - stretch injury- 2- Nerve injury: 1- Great Auricular n. (MC) 2- Facial nerve. 3- Frey's Syndrome (Auriculotemporal syndrome) → Reinnervation injury → Gustatory sweating & flushing	
<u>Risk of malignancy</u>	< 5%	~3%