# Endocrine surgery 

New- 2016

## Anatomy of head and neck

- Layers of the neck (superficial to deep):
- Skin
- Subcutaneous tissue
- Platysma muscle
- Superficial fascia
- Fat and lymph nodes
- The neck is divided into:
- Anterior compartment (organic compartment): made of two triangles separated by the sternocleidomastoid muscle.
- Anterior triangle
- Posterior triangle
- Posterior compartment (muscular compartment): important in neurosurgery


## - Organic compartment:

- Anterior triangle (borders):
- Superior: inferior border of the mandible
- Medial: midline of the neck
- Lateral: anterior border of sternocleidomastoids
- Anterior triangle (important structures):
- Hyoid bone:
- forms the attachment of many important muscles which lie on the floor of the mouth.
- Divides the muscle into suprahyoid and infrahyoid (strap)muscles.
- Thyroid gland
- Larynx
- Trachea
- Parathyroid glands
- Common carotid artery and its branches
- Internal jugular vein
- Vagus nerve and recurrent laryngeal nerves
- Posterior triangle (borders)
- Anterior: posterior border of sternocleidomastoid
- Posterior: anterior border of trapezius
- Inferior: middle portion of the clavicle

- Apex: occipital bone
- Posterior triangle (contents)
- Levator scapula: a muscle that elevates the scapula
- Scalene muscles: attach to the ribs and originate from the lateral process of the cervical vertebra
- Subclavian vein and artery
- External jugular veins
- Branches of the cervical plexus
- Accessory nerve (innervates the trapezius)
- Posterior triangle (subdivisions):
- Occipital triangle
- Supraclavicular triangle
- Muscular triangle:
- It is part of the anterior triangle
- Thyroid is found in the muscular triangle
- Contents: strap muscles
- Omohyoid
- Sternohyoid
- Sternothyroid
- Thyrohyoid
- Sternohyoid lies superficial to sternothyroid

- Landmarks in the midline:
- Hyoid bone
- Thyroid cartilage
- Cricoid cartilage (the only complete ring of cartilage around the trachea)
- Deep fascia of the neck (deep cervical fascia):
- Pretracheal fascia (holds the following structures together):
- Thyroid gland
- Trachea
- Esophagus
- Larynx
- Prevertebral fascia:
- All the structures located anterior to the vertebra lie within this fascia
- Branches of the cervical plexus run deep to this layer of fascia
- Carotid sheath (contents):
- Common carotid artery
- Internal jugular vein
- Vagus nerve (lies posterior to the artery and the vein)


## - Sensory innervation of the neck:

- Mediated by the anterior cervical nerve which is a branch of the cervical plexus.
- The branches emerge behind the sternocleidomastoid muscle forming a cross
- Greater auricular nerve: upwards
- Innervates the skin of parotid area and ear pinna
- Runs along with external jugular vein
- Anterior cervical nerve:
- Also known as the transverse cervical nerve
- Runs anteriorly
- Posterior cervical nerve:
- Runs posteriorly
- Innervates the posterior aspect of the neck
- Supraclavicular nerve:
- Downwards
- Divides into:
- Anterior division
- Posterior division
- Superior division
- Innervates the shoulder area
- Share exit with the phrenic nerve (C5 root). This is why patients with gallbladder problems have pain referred to the shoulder area


## - Platysma muscle:

- Attached to the clavicle and ribs inferiorly
- Attached to the mandible and mastoid process posteriorly
- It disappears in the midline
- Innervated by the cervical branch of facial nerve
- Muscle of facial expression
- Upon reaching the parotid gland, it will slip to engulf the parotid forming the parotid fascia. This fascia is strong and cannot be stretched; thus, any swelling in the parotid gland will cause severe pain.
- It continues downward to engulf the sternocleidomastoid muscle
- It is not well developed in females; however, in males it is well developed due to the process of shaving.


## Lymphatic drainage of the neck

- It is important to know the primary lymphatic drainage of each area of the neck because most cancers in this area are first transmitted via lymphatic.
- $1 / 3$ of the body's lymph nodes are found in the head and neck
- This area is rich in blood vessels, so wounds heal quickly.
- Lymphatics of the neck are divided into:
- Superficial group (felt under the skin):
- Buccal
- Facial
- Preauricular (parotid): embedded inside the parotid gland
- Auricular
- Occipital
- Deep cervical group (around the internal jugular vein; divided into 6 levels):
- I
- II
- III
- IV
- V
- VI
- If lymph nodes are red and tender think of an inflammation; however, if they are painless, think of a malignancy
- Lymph nodes are found in the fatty tissue or plates around the jugular vein
- Deep lymph nodes:
- Group I:
- Ia: submental nodes; drain midline structures:
- Tip of the nose
- Middle portion of upper and lower lips
- Ib: submandibular nodes
- Nose
- Sides of the tongue
- Group II: upper jugular (Jugulo-digastric)
- Lie behind the posterior belly of digastric muscle
- Group III: middle jugular (jugular omohyoid)
- Lie behind the omohyoid
- Group IV: lower jugular (epithelio-cervical)
- Lie below the omohyoid
- Group V: accessory
- Found in the posterior triangle of the neck
- Related to the accessory nerve
- Group VI: tracheo-esophageal (paratracheal)
- Lie between the trachea and cervical esophagus
- Drain thyroid and subglottic larynx
- Subglottic laryngeal carcinoma will metastasize to this group
- Notes:
- Drainage of the tongue:
- Posterior $1 / 3$ : occipital lymph nodes
- Sides of the tongue: submandibular lymph nodes
- Bulk of the tongue: jugulo-digastric
- Drainage usually starts from the most superficial lymph nodes and moves to the deeper ones in a consequential fashion. Because of this pattern of drainage, it is possible to stop a malignancy from spreading by interrupting the route. This can be done through surgery, radiotherapy, or an enlargement in the neck (compresses lymphatics).


## - Neck dissection:

- Radical dissection (removal of):
- Lymph nodes levels I-V
- Fat plates
- Sternocleidomastoid
- Internal jugular vein
- Accessory nerve
- Indications:
- Extensive cervical involvement or matted lymph nodes with extracapsular spread
- Invasion into sternocleidomastoid, internal jugular vein, or accessory nerve
- Modified radical dissection:
- Exceision of lymph nodes with sparing all or some of the non-lymphatic structures
- Selective dissection:
- Supraomohyoid:
- Removal of groups I-III
- In cases of squamous cell carcinoma (effective in 30-80\% of cases)
- Anterior dissection (extended supraomohyoid):
- Removal of groups I-IV
- Lateral dissection:
- Removal of groups II-IV
- Posterolateral dissection:
- Removal of groups II-V
- Posterior dissection:
- Removal of group V only
- Done in cases of pharyngeal carcinoma
- Central (median) dissection:
- Removal of group VI


## - Complications of neck dissection:

- Removal of both jugulars: edema
- Removal of accessory nerve: shoulder drop, due to a loose trapezius
- Removal of sternocleidomastoid:
- Disfigurement: treated by physiotherapy to activate surrounding muscles
- Its removal will not affect movement of the head
- Sentinel lymph nodes:
- The first lymph node to drain the tumor
- To detect it, the tumor is injected with methyelene blue. The dye is then followed until it reaches the first lymph nodee.
- The lymph node is excised and tested via a probe that detects nuclear activity.
- A positive blue node confirms that the excised node is the sentinel node.
- If positive, neck dissection is performed
- Notes:
- Supraclavicular lymph nodes are found in the supraclavicular fossa. They are involved in malignancies of lung and breast; not those of head and neck
- Virchow's lymph nodes (left supraclavicular lymph nodes) drain stomach and abdominal carcinomas.
- Accessory lymph nodes drain the post-nasal space.
- Papillary thyroid carcinoma will drain to groups III and IV
- Tonstils drain froup II
- Staging LN masses:
- T1: <3 cm
- T2: 3-6 cm
- T3: >6 cm
- T4: bilateral
- Diagnosis:
- CT: $90 \%$ accuracy
- Examination under anesthesia
- MRI: not routine, but better than CT
- Biopsy
- FNA: usually performed on any enlarged lymph node


## Branchial anomalies

## - They are divided into:

- Hereditary/familial: occur due to abnormalities in the genes
- Congenital:
- Occur due to failure of organogenesis
- Usually occur during the $1^{\text {st }}$ trimester
- Influenced by drugs, radiation, infections, and genetic abnormalities
- Down's syndrome is a hereditary disorder, but it is accompanied with some congenital anomalies in the GIT and CVS
- Most of the branchial anomalies are obvious at birth; however, some can be delated for years.
- During embryogenesis, the branchial arches are found in the area of the nech in the pharynx.
- Normally, these arches disappear before birth with the exception of:
- $1^{\text {st }}$ branchial cleft: external auditory meatus
- $1^{\text {st }}$ pouch: auditory (Eustachian tube)
- The area in between the $1^{\text {st }}$ branchial cleft and $1^{\text {st }}$ pouch: tempanic membrane
- $1^{\text {st }}$ arch: bones of the middle ear.
- Branchial apparatus develops from ectoderm and endoderm. The branchial clefts arise from ectoderm, while branchial pouches arise from endoderm.
- Remnants of the branchial apparatus present after birth are called vestigeal parts
- The most common site for problems is the $2^{\text {nd }}$ branchial apparatus
- Branchial cyst:
- Types:
- Dermoid (ectoderm):
- More common
- Lined by skin
- Contains cholesterol (yellow pus-like fluid)
- Mucous (endoderm):
- Lined by a mucous membrane
- Contains mucous secretions
- Differential diagnosis:
- Parotid swelling (superficial to sternocleidomastoid)
- Enlarged lymph nodes (deep to sternocleidomastoid)
- Cold tuberculous abscess (rare)
- Site of presentation:
- In the anterior triangle deep to sternocleidomastoid, so it disappears on muscle contraction
- At the level of the junction between the upper and middle third of the sternocleidomastoid muscle
- Present with a smooth and globular surface (can be aspirated)
- Age of presentation: Mostly in children; however, they can appear at any age
- Clinical presentation:
- They usually lie dormant and unnoticed until they become inflamed. This will lead to enlargement of the lymphatics accompanied by hypersecretion which will cause the cysts to enlarge.
- If the inflammation was strong, supparration and absccess develop
- Treatment:
- If the cyst is infected, give antibiotics until the infection resolves. When it resolves, excise the cyst surgically
- If antibiotics are ineffective, drain the cyst and excise it surgically.
- N.B: if the cyst was treated with incision and drainage without removing the whole cyst, it can recur as a cyst or a fistula.


## - Branchial fistula:

- It is a tract between two epithelial surfaces (ectoderm and endoderm). It forms due to failure of growth of the second branchial arch caudally over the third and fourth arches.
- During development, ectoderm grows and enlarges more than endoderm, so the tract will be oblique.
- Site:
- Anterior triangle of the neck
- It open on the skin at the junction between the middle and lower third of the sternocleidomastoid muscle. Then, it extends as a tract and opens posteriorly $n$ the mouth in the supratonsillar region
- Age: presents direcly after birth. However, sometimes, the opening is too small and cannot be noticed.
- Differential diagnosis:
- Folliculitis
- Pilonidal sinus
- Clinical presentation:
- If patent: The mother brings her child complaining of leakage of milk through the opening in the neck
- If the lumen of the fistula is small, it is liable for infections. Usually presents as a clear discharge (rarely purulent).
- If the opening of the fistula is obstructed the discharge will not come out leading to an infection
- During physical examination, feel the tract of the fistula between your fingers. It feels like a firm, thin rope.
- Treatment:
- Surgical excision. If incomplete, recurrence is likely
- Caution: do not open the fistual using a probe. This might damage the vessels and nerves in that area.


## - Branchial auricle:

- It occurs due to overproduction of mesoderm
- Presents as an osseous or cartilagenous protrusion after birth


## Neck masses

## - History:

- Age:
- <20: congenital > infection > malignancy
- 20-40: benign through swelling/infection/inflammation
- >40: malignancy until proven otherwise
- Gender: males are three times more likely to have a malignancy
- Occupation:
- Gas station: carcinoma of the sinuses
- Crowded areas: tuberculosis
- Outdoor worker: skin carcinoma
- Radiation: thyroid cancer
- Mass:
- Size: if $>2 \mathrm{~cm}$, it must be investigated
- Duration:
- 7 days: infection
- 7 months: carcinoma
- 7 years: congenital
- Number: if multiple masses, think of lymphoma
- Progression: if rapid, think of bleeding into a cyst
- Location: anterior triangle masses are more benign than posterior triangle masses
- Associated symptoms:
- Pain
- Upper respiratory tract infection
- Fever
- Weight loss
- Facial nerve invasion: manifested as bell's palsy. An indicator of malignancy
- 7 cardinal symptoms of malignancy:
- Dysphagia
- Odynophagia
- Voice changes
- Stridor
- Speech disorder
- Globus
- Referred pain to the ear
- Aggravating factors:
- If the size increases with lemon or chewing think of a submandibular obstruction.
- Past medical history: if the patient has a history of carcinoma, it is most probably a recurrence
- Social history:
- Smoking: important in head and neck CA. It increases the risk of recurrence
- Alcohol
- Travel history
- Animal exposure
- Skin contact
- Family history:
- Thyroid cancer
- MEN syndrome


## - Physical examination:

- Inspect all mucosal and cutaneous sites to look for signs of inflammation
- Examination under anesthesia
- Indirect/fibrooptic laryngeoscopy
- Examination of the mass:
- Site/ size / shape
- Skin overlying it: ulceration is malignancy until proven otherwise
- Color
- Edges
- Consistency
- Fluctuation
- Transillumination


## - Investigations:

- CBC: WBC increase, differential count
- FNA: if negative, repeat
- Contrast CT/MRI
- PET scan
- Triple endoscopy with biopsy (avoid excisional biopsy, except in cases of suspected lymphoma):
- Laryngoscopy
- Esophagoscopy
- Bronchoscopy
- In pediatric patients we use ultrasound rather than CT/MRI:
- Less radiation
- Less contrast exposure
- Less sedation
- CT is only indicated if there is a suspected deep neck space infection


## - Differential diagnosis for posterior triangle masses:

- Solid: lymph nodes
- Cystic:
- Cystic hygroma
- Pharyngeal pouch
- Pulsatile: subclavian aneurysm


## - Congenital masses: (usually cystic, swell during URTI)

- Midline masses:
- Sublingual dermoid cyst:
- It is a congenital defect that occurs during embryogenic development due to failure of growth of skin layers.
- Lined by epithelium
- Contents:
- Hair follicles
- Sweat glands
- Sebaceous cysts
- Thyroglossal cyst:
- $1 / 3$ of congenital masses
- Failure of obliteration of the thyroglossal duct after descent of thyroid from foramen cecum to the lower anterior part of the neck
- On physical examination, it moves with swallowing because it is connected to the ligament. Moreover, it moves with tongue protrusion because it is connected to the hyoid bone)
- $50 \%$ present in patients less than 20 years old
- Ultrasound should be done preoperatively to make that this is not the only functioning thyroid tissue in the body
- Rarely transforms into papillary carcinoma
- Treatment: sistrunk procedure (resection of the cyst, tract, and central part of the hyoid bone)
- Subhyoid bursa
- Thymic cyst
- Laryngeocele
- Thyroid nodule
- Pretracheal lymph nodes
- Teratoma
- Lateral masses:
- Branchial cyst:
- $1 / 3$ of congenital masses
- The persistence of the embryological pharyngeobranchial duct
- Can form a cyst, sinus, or a fistula
- Most commonly arises from the $2^{\text {nd }}$ branchial cleft
- Presents as a non-tender fluctuant mass located anterior to sternocleidomastoid. It has a deep tract that travels between the internal and external carotid artery to the tonsillar fossa
- If it arises from the $1^{\text {st }}$ branchial cleft, it presents near the angle on mandible or around the ear. It might be associated with facial nerve or ear canal involvement
- If it arises from the $3^{\text {rd }}$ branchial cleft it presents on the lower aspect of the neck with tracts that end on the thyrohyoid membrane or in the pyriform sinus
- Carotid artery aneurysm
- Carotid body tumor
- Locally invasive
- One physical examination, it moves side to side (not up and down)
- It can transmit the carotid pulse or it can have a pulse on its own
- Diagnosed by a carotid angiogram
- Treated with surgical excision and preoperative embolization
- Laryngeocele
- Thyroid masses
- Masses that can present as midline or lateral masses:
- Cystic hygroma:
- Lymph filled space that arises from the embryogenic remnant of the jugular lymph sac
- Not a true cyst
- Soft, fluctulant, translucent, lobular
- Painless
- Contains clear fluid
- Treated by excision; high recurrence rate
- Hemangioma:
- Reddish-bluish compressible mass
- Bruit on auscultation
- Increase in size with crying/straining
- Associated with subglottic vascular malformation
- Grows rapidly in the first year of life
- Slow involution starts at 18-24 months
- $90 \%$ resolve without treatment
- Indications for treatment:
- Airway compression
- Ulceration
- Eye problems
- Dysphagia
- Thrombocytopenia
- Cardiac failure
- Treated with steroids
- Pharyngeal pouch:
- Diverticulum in the pharyngeal mucosa
- Bulge through a weakness in the pharyngeal constrictor muscle on the left side
- Common in elderly males
- Presents with dysphagia, halitosis, and a swelling in the neck
- Diagnosed by barium swallow
- Lymphatic malformation:
- Presents as a soft, compressible, doughy mass that swells with upper respiratory tract infections.
- Diagnosed using CT/MRI
- Treatment:
- Cosmetic or symptomatic relief
- Complete excision is difficult due to its infiltrative nature
- Treated by debulking or sclerotherapy
- Pharyngeal ranula:
- A ranula is a cystic mucosal extravasation from the sublingual salivary gland
- Plunging ranula: a ranula that extends through the myelohyoid muscle
- Treatment: excision


## - Infective/inflammatory masses:

- Cervical adenitis:
- Due to viral upper respiratory tract infection
- Self-limited
- Generalized lymphadenopathy
- Suppurative bacterial lymphadenitis:
- Due to bacterial infection with Staph aureus or group A streptococcus
- Common in children
- Treatment:
- IV antibiotics
- Incision and draining; if refractory to antibiotics
- Deep neck space infection:
- Caused by a dental infection, tonsillitis, trauma, or suppurative lymph nodes
- Most common organisms are streptococcus, staphylococcus aureus, and oral anaerobic bacteria
- If it was a neck abscess it presents with:
- Fever
- Acute neck swelling
- Induration
- Dysphagia
- Odynophagia
- Stridor
- Redness and tenderness
- Treatment:
- IV antibiotics
- Incision and drainage
- Ludwig's angina:
- Cellulitis of the sublingual and submandibular spaces
- It causes compression of the lymphatics, which leads to edema and airway obstruction
- Treatment:
- Airway control
- IV antibiotics
- Sialedenitis/sialolithiasis
- Other inflammations:
- Sarcoidosis
- Kawasaki's disease
- Lower anterior midline mass (thyroditis)
- Other infections:
- Cat scratch disease
- Atypical mucobacteria
- HIV (diffuse hyperplastic actinopathy)
- Neoplastic masses:
- Benign:
- Paraganglioma:
- Vascular tumor from parapharyngeal cells of the autonomic nervous system
- Treated with surgical excision and preoperative embolization
- Lipoma
- Schwanoma
- Infiltrative fibromatosis
- Neurofibroma
- Salivary gland neoplasm
- Malignant
- Mtaplastic squamous cell carcinoma (most common)
- Lymphoma:
- Hodgkin's:
- $85 \%$ of the cases
- Painless cervical lymph nodes
- Bulky matted
- Non-Hodgkin's:
- Diagnosed by surgical biopsy
- Treated with chemotherapy and radiotherapy
- Thyroid CA
- Adenocarcinoma
- Tonsillar SCC
- Location of the mass is suggestive of the primary site of malignancy
- Oral cavity CA metastasizes to submandibular triangle
- Lateral metastatic SCC metastasizes to level II and III
- Nasopharyngeal or scalp masses metastasize to posterior triangle
- Papillary CA metastasizes to any level of the neck
- Note supraclavicular lymph node enlargement is usually due to an infraclavicular mass. Usually from the GIT (Virchow's and scalene lymph nodes)


## Salivary glands

## - Divided into:

- Major:
- Parotid (the largest)
- Submandibular
- Sublingual (the smallest)
- Minor: distributed all over the oral cavity except for the upper aspect of the tongue
- The minor salivary glands are enough to moisture the mouth; thus, removal of the major glands does not cause dryness of the mouth (xerostomia)
- Causes of xerostomia:
- Sjogren's syndrome (autoimmune)
- Radiotherapy
- Anatomy:
- Parotid gland:
- Location:
- Preauricular area
- Wrapped around the mandibular ramus; superficial to the masseter muscle
- It has a tail that extends to the neck overlying sternocleidomastoid
- To tell whether a mass is superficial or deep to the muscle, put the muscle in action. If it disappears, it is deep. If it remains, it is superficial.
- Shape: upside down pyramid
- Fascia: enclosed within a continuous strong capsule derived from the deep cervical fascia
- Lobes: separated by branches of the facial nerve
- Large superficial (85\% of the gland)
- Small deep: ( $15 \%$ of the gland); in close proximity to the pharynx
- Since the deep lobe is in proximity to the pharynx, tumors lying within the deep lobe are first seen through the mouth as intraoral pharyngeal masses.
- Duct:
- Stenson's duct
- Passes anteriorly and enters the buccinator at a sharp angle
- Opens opposite to the $2^{\text {nd }}$ upper molar
- Secretions: mainly serous
- Other structures:
- The facial nerve passes through the parotid gland without innervating it.
- The nerve divides into five branches:
- Temporal
- Zygomatic
- Buccal
- Mandibular
- Cervical
- Submandibular gland:
- Location:
- Submandibular triangle
- Supported by the myelohyoid muscle. If this muscle is lax, it leads to ptosis of the gland. The gland appears as a mass in the neck
- Secretions: mixed (mucoserous)
- Duct:
- Whartons duct
- Opens at both sides of the frenulum
- On physical examination, examine that area using bimanual palpation.
- If a stone can be felt, it can be operated through the mouth (not through the face)
- Relations;
- Related to the mandibular branch of facial nerve. The mandibular branch of the facial nerve is related to the gland at the point it crosses the facial artery and vein. The nerve is located beneath the skin and platysma. It is prone to injury during surgery
- Related to the lingual nerve (branch of the mandibular branch of the trigeminal nerve).it crosses the lateral surface of the submandibular duct and winds below it. Then, it passes upward and forward on the medial side. Then, both lingual and the duct pass in the floor of the mouth where the lingual nerve passes with the lingual artery and vein.
- Sublingual gland:
- The smallest of the major glands.
- Location: lies deep to the floor of oral mucosa between the mandible and genioglossus muscle
- Duct: Wharton's duct or a separate duct
- Secretions: mucinous
- Relations: related to the lingual nerve
- Any enlargement in this gland appears as a swelling in the floor of the mouth called a ranula
- Drained through 20 ducts; most of them drain to the submandibular duct. Some of them drain directly to the oral cavity
- Serous secretions are light, don't contain proteins or immunoglobulins. On other hand, mucinous secretions are thick, contain proteins, and immunoglobulins.
- Minor salivary glands secrete mixed secretions
- Infections of the salivary glands:
- Acute:
- Viral (mumps)
- More common in children
- Self limited
- Diffuse inflammation
- May be associated with pancreatitis, orchitis, or oophitis
- Bacterial (staph aureus)
- Dryness of mouth is a risk factor
- Ascending infection
- Seen in the elderly
- Post operative
- Common in the parotid
- Chronic:
- Usually autoimmune
- Inflammation causes destruction of the glands
- $90 \%$ in female $35-45$ years of age
- $60 \%$ associated with SLE, RA, or scleroderma
- Parotitis: (parotid sialadinitis)
- Causes:
- Viral: mumps
- Bacterial: staph (most common)
- Autoimmune: Sjogren's syndrome
- Risk factors:
- Dryness of the oral cavity (usually in elderly after a major surgery)
- Lack of immunoglobulins inside the gland'; this makes it more susceptible to infections.
- Clinical presentation:
- Pain: because the gland is surrounded by a dense capsule
- Tenderness, hotness, redness, and swelling at the site of the parotid
- Diagnosis:
- History and physical examination
- Imaging studies (done after treating the infection):
- Plain X-ray: if the stone is radio-opaque
- CT: if the stone is radiolucent
- Sialogram: injection of a radio-opaque substance
- Management:
- Treat the infection with antibiotics (mortality rate is $20 \%$ )
- Aspiration: if it is a complicated abscess
- Submandibular gland infections:
- Causes: mostly secondary to obstruction by a stone
- Clinical presentation:
- Swelling in the gland upon eating.
- When we eat, saliva is secreted, but due to the obstruction in the duct the saliva will accumulate causing a swelling.
- The swelling disappears spontaneously
- Diagnosis:
- History and physical examination
- X-ray of the floor of the mouth for confirmation
- Beaded duct appearance:
- Detected via CT sialgoram (appears as a filling defect)
- Alternating narrowing and dilation of the duct due to chronic inflammation
- Treatment: surgical excision
- If the stone is intra-oral:
- Since the stone is distal to the nerve, the surgery can be done intra-orally (better cosmesis)
- Excision of the stone
- Done under local anesthesia
- Can be complicated with a fistula; however, this is not important because the fistula opens into the floor of the mouth
- If the stone is near the gland (at the hilum)
- Since the stone is proximal to the nerve, there is an increased risk for injuring the nerve. The surgery is done through a cut in the neck
- Excision of the gland
- Done under general anesthesia
- Can be complicated with an injury to the mandibular branch of facial nerve
- Prognosis: poor recovery after infection. Chronicity is common
- Comparison between parotid and submandibular stones:
- Parotid gland stones are rare because:
- Serous secretions
- Duct is sloping down; movement of saliva is with gravity
- Negative suction by oral cavity (produced by cheeks and gums)
- If stones develop, they are usually radiolucent
- Submandibular gland stones are common because:
- Mucinous secretions; form a nidus for calcium deposition and stone formation
- Flow of saliva is against gravity
- Long duct
- Stones are usually radio-opaque
- Sublingual and minor salivary gland disorders:
- Minor mucus retention cysts develop in the floor of the mouth from obstructed minor salivary glands or sublingual gland
- Ranula is a term applied to mucus extravasation cyst arising from the sublingual gland.
- Treatment of ranula: excision of cyst and affected gland


## - Tumors of salivary glands:

- Age group: mostly present in middle age groups (40's)
- Most of these tumors are benign
- The most common tumor of salivary glands is pleomorphic adenoma (70\% of all salivary gland tumors)
- The smaller the gland the higher the risk of malignancy. The risk of malignancy (not the incidence) is as follows:
- Parotid gland $25 \%$
- Submandibular gland: $50 \%$
- Sublingual gland: $50 \%$
- Minor salivary glands: $75 \%$
- $80 \%$ of salivary gland tumors arise from the parotid gland
- Neoplasms of salivary glands:
- Benign:
- Pleomorphic adenoma
- Warthon's tumor (adenolymphoma)
- Tumor due to duct infection
- Malignant:
- Mucoepidermoid
- Lymphoma
- SCC
- Adenoid cystic adenoma
- Acinar cell tumor
- Pleomorphic adenoma:
- Proliferation of epithelial, myoepithelial, and stromal tissue
- Most common tumor of the salivary glands
- Benign
- It doesn't have a complete capsule
- It has protrusions coming out of holes in the incomplete capsule
- Recurs if not managed properly
- Recurrence increases the probability of damaging the facial nerve on a second operation
- Recurrence requires 5 years from the time of operation.
- It can become a malignant tumor if not managed properly (left for more than 10 years).
- It changes into adenocarcinoma: risk of CA increases 1-2\% per annum.
- Causes of recurrene:
- Protrusion
- Multicentric tumor in 5\%
- Gross appearance: irregular, round-ovoid mass with well defined borders.
- Warthin's tumor:
- Papillary cystadenoma
- No malignant potential; $2^{\text {nd }}$ most common tumor of salivary glands
- Usually appears at the tail of parotid gland
- Cystic mass
- Associated with smoking
- More common in males ( $90 \%$ )
- $10 \%$ bilateral
- Malignant tumors:
- Low grade:
- Mucoepidermoid:
- The most common malignant tumor
- 3 grades: high low, intermediate.
- It is specific for the parotid gland
- Acinar cell tumor
- High grade:
- Mucoepidermoid (most common malignant tumor in parotid)
- Adenoid cystic adenoma
- $2^{\text {nd }}$ most common malignant tumor
- It is the most common tumor in the submandibular and minor salivary glands
- Well defined, but not capsulated
- It metastasizes to nerves in 25-30\% of cases
- It has 3 types:
- Tubular: invades nerves in $10 \%$ of cases
- Cribriform
- Solid: the worst type; highest possibility of invading nerves
- SCC (rare and invasive):
- The most common etiology is metastasis from skin (especially in Australia and Iceland)
- In our countries, it is mostly a primary tumor
- Adenocarcinoma (rare and invasive)
- Lymphoma:
- Very common
- 2 forms: localized and generalized
- The most common tumor of parotid gland in children is hemangioma (nonepithelial tumor)
- Treatment:
- Low grade:
- Chemotherapy
- Radiotherapy
- Surgery
- High grade:
- Radical surgery
- Neck dissection
- Post-operative radiotherapy


## - Types of surgery:

- Total parotidectomy: removal of both superficial and deep lobes with preservation of facial nerve
- Superficial parotidectomy: removal of the superficial part of the parotid (as in case of low grade mucoepidermoid tumor)
- Partial parotidectomy: removal of the diseased segment (enucleation)
- Radical parotidectomy: removal of the parotid, facial nerves, muscles, and fascia.
- Neck dissection:
- Indications:
- High grade salivary gland tumor
- Low grade salivary gland tumor with metastasis to lymph nodes
- Ulceration of the overlying skin
- CA with size $>5 \mathrm{~cm}$
- Recurrence
- Postoperative radiotherapy: same indications as neck dissection - Signs and symptoms of parotid malignant CA:
- Facial nerve palsy with a mass (the only significant indication of a tumor)
- Pain with a solitary mass (indicates advanced stage)
- Mass with lymph node involvement at the same side
- Recurrence at the same or conralateral side ( $100 \%$ indication of malignancy)
- Complications of surgery:
- Facial nerve palsy
- Neuropraxia: injury of neural tissue with an intact covering.

Regeneration occurs, and the nerve can become normal again.

- Complete injury
- Cosmetic effects
- Recurrence
- Fistula (discharge especially with eating)
- Frey's syndrome: (Gustatory sweating)
- Flushing, pain, and diaphoresis in the auricotemporal nerve distribution. It is initiated by chewing
- Cause: cutting the auricotemporal nerve.


## Thyroid gland

## - Embryology:

- The thyroid gland appears as an epithelial proliferation in the floor of the pharynx at the base of the tongue at foramen cecum
- It descends inferiorly to reach a position anterior to the hyoid bone and laryngeal cartilage (during its migration, it stays connected to the tongue through a narrow canal; the thyroglossal duct)
- Parafollicular cells are derived from the neural crest
- Thyroxin's production starts at the $20^{\text {th }}$ week of gestation
- Anatomy:
- Structures:
- 2 lobes
- Isthmus
- Pyramidal lobe (in $50 \%$ of the population
- Blood supply:
- Superior thyroid artery: $1^{\text {st }}$ branch of external carotid
- Inferior thyroid artery: ranch of the thyrocervical trunk
- Thyroid ima artery (innominate artery) - rare
- Venous drainage:
- Superior thyroid vein
- Middle thyroid vein
- Inferior thyroid vein
- The lymph nodes around the pyramidal lobe are called Delphian lymph nodes
- The ligament that connects the thyroid to the trachea is the ligament of Berry
- The most posterior extension of the lateral thyroid lobes is called the tubercle of Zuckerkandle


## - Be careful during surgery:

- Recurrent laryngeal nerve:
- Found between the trachea and esophagus
- Found behind the cricothyroid muscle
- 1 cm anterior or posterior to the inferior thyroid artery
- If injured unilaterally $\rightarrow$ hoarseness
- If injured bilaterally $\rightarrow$ airway obstruction
- Superior laryngeal nerve:
- If damaged, the patient will have a deeper, quieter voice


## - Physiology:

- The thyroid gland secretes two hormones; T3 and T4
- T3 is the active form
- The most common site of conversion of T4 to T3 is the liver
- T4 is only secreted from the thyroid
- The hypothalamus releases TRH, a hormone that release TSH from the pituitary gland. TSH stimulates the thyroid gland to produce T3 and T4. T3 and T4 exert a negative feedback action on the hypothalamus and pituitary.
- Parafollicular cells (C-cells) secrete calcitonin
- Levothyroxine is T4; its $\mathrm{t} 1 / 2$ is 7 days.
- Investigations:
- TFT
- Ultrasound
- Uptake
- Scan
- FNA and biopsy
- Uptake measures the function of the gland' while a scan assesses the anatomy of the gland.


## - Thyroid nodule:

- Can be found in $5 \%$ of the population
- Differential diagnosis:
- Adenoma/hyperfunctioning adenoma
- Multinodular goiter
- Cyst
- Thyroditis
- Carcinoma
- Parathyroid CA
- Studies done to evaluate a nodule:
- Ultrasound $\rightarrow$ solid or cystic nodule
- FNA $\rightarrow$ cytology
- $\mathrm{I}^{123}$ scinti-scan $\rightarrow$ hot or cold nodule
- Types of non-thyroid masses:
- Inflammatory lesions (lymphadenitis/abscess)
- Congenital lesions (thyroglossal duct. Branchial cleft)
- Malignant lesions (lymphoma/SCC)
- FNA is the diagnostic test of choice for a thyroid nodule; has a false negative in up to $5 \%$ of cases.
- Approach:
- History and physical examination
- Ultrasound:
- Suspicious features: FNA (regardless of shape, size, TSH)
- Non-suspicious:
- Consider TSH
- If high/normal $\rightarrow$ FNA
- If low: scan:
- Hot nodule $\rightarrow$ do nothing
- Cold nodule $\rightarrow$ FNA
- A hot nodule is a nodule with an increased iodine uptake. A cold nodule is a nodule with a decreased iodine uptake
- Hot nodules are never malignant; thus, they are never biopsied
- The majority of nodules are cold nodules, and the majority of cold nodules are benign. However, you should always biopsy a cold nodule to rule out a malignancy
- Multinodular goiter: a cold nodule in a multinodular goiter has the same risk of malignancy of a solitary nodule. Always biopsy any cold nodules
- Toxic: (Plummer's disease)
- Functioning; associated with thyrotoxicosis, decreased TSH, increased T3 and T4
- Scan shows more than one nodule
- Treatment:
- Antithyroid medications (temporarily)
- Radioactive iodine ablation
- Surgery: indicated if there are compression symptoms or in case of a nodule refractory to Iodine treatment
- Non-toxic: (simple multinodular goiter)
- More common in females
- Asymptomatic; the patient is euthyroid with normal levels of TSH
- Presents as a goiter with or without pressure symptoms
- Indications for treatment:
- Symptomatic compression
- Cosmetic
- If you cannot rule out CA
- Treatment:
- Radioactive iodine ablation
- Bilateral subtotal thyroidectomy


## Thyroid cancer:

- Evaluation:
- History:
- Neck radiation
- Family history (thyroid cancer, MEN)
- Extremes of age
- More common in males
- Signs:
- Single nodule
- Cold nodule
- Increased calcitonin levels
- Lymphadenopathy
- Hard, immobile nodule
- Symptoms:
- Voice change (vocal cord paralysis)
- Dysphagia
- Discomfort
- Rapid enlargement
- If a patient presented with a thyroid nodule with a history of radiation, but a negative FNA $\rightarrow$ remove the gland surgically
- Most thyroid cancers are euthyroid
- Most thyroid cancers are associated with mutations in the RAS and RET protooncogenes families.
- If a patient has medullary hyperplasia, the risk of malignancy is $100 \%$
- Work-up
- FNA
- Ultrasound
- TSH
- Chest X-ray
- $\mathrm{I}^{123}$ scan
- $\mathrm{Ca}^{2+}$ levels
- Types of cancers:
- Well differentiated:
- Papillary - 80\%
- Follicular - $10 \%$
- Murthle cell-5\%
- Medullary - 5\%
- Poorly differentiated
- Anaplastic - 1-2\%
- Lymphoma
- Thyroid cancer is more common in females, but if a nodule is found in a male there is a higher chance that it is malignant.


## - Papillary CA:

- The most common thyroid cancer
- Average age: <40 (most common between 30-40)
- Gender: female > male (2:1)
- Histology: Psammoma bodies
- Route of spread: lymphatics
- Rate of spread: slow

Papillary CA: (7 P’s)

1) Popular: $80 \%$
2) Psammoma bodies
3) Palpable lymph nodes
4) Positive $I^{123}$ uptake
5) Positive prognosis
6) Post-op I ${ }^{131}$ scan ( $\mathrm{Dx} / \mathrm{Tx}$ )
7) Pulmonary metastasis

- Tumor marker: thyroglobulin
- $I^{123}$ uptake: good uptake, because it is differentiated
- Prognosis: good; 10 years survival rate $95 \%$
- Treatment:
- If $<1.5 \mathrm{~cm}$, without history of radiation exposure:
- Thyroid lobectomy + isthmectomy
- Near total thyroidectomy
- Total thyroidectomy
- If $>1.5 \mathrm{~cm}$ or bilateral or positive lymph nodes or history of radiation exposure:
- Total thyroidectomy
- In papillary carcinoma, positive lymph nodes do not affect the prognosis
- Neck dissection:
- Only if positive lymph nodes
- If lateral palpable cervical lymph nodes $\rightarrow$ perform modified neck dissection
- If central palpable lymph nodes $\rightarrow$ perform central neck dissection (selective)
- Post-operatively (after total thyroidectomy):
- Thyroxine replacement is not given directly; we wait for 4-8 weeks, then we measure TSH levels. If TSH $>30$, we start iodine ablative therapy, then we start thyroxine therapy
- Post-operative iodine scan can lovate residual tumor and distant metastasis that can be treated with radioactive ablative iodine therapy. If, postoperatively, TSH was not high enough this means that there is remnant thyroid tissue.
- Prophylactic neck dissection is not recommended in cases of papillary CA


## - Follicular CA:

- $10 \%$ of all thyroid CA
- Age: rare before that age of 30
- Sex: female > male
- Route of transmission: hematogenous; mostly to bone, lung, and liver. It is more aggressive than papillary CA
- Iodine uptake: good uptake
- Histological findings: capsular or blood vessel invasion
- Prognosis: worse than papillary; 10 years survival rate $85 \%$
- FNA is not diagnostic; tissue structure is needed.
- Treatment:
- Total thyroidectomy

Follicular CA: 5 F's:

1) Far away metastasis
2) Female : male (3:1)
3) FNA is NOT diagnostic
4) Favorable prognosis
5) Favorable uptake

- Postoperative: $\mathrm{I}^{131}$ scan for diagnosis and treatment of remnant tissue


## - Hurthle cell CA:

- Cancer of the Hurthle cells (oxyphilic cells)
- $5 \%$ of thyroid CA
- Cell origin: follicular cells
- Iodine uptake: no uptake
- Diagnosis: FNA can identify cells, but definitive diagnosis is only determined through histology
- Route of metastasis: lymphatics > hematogenous
- Prognosis: 10 years survival $80 \%$
- Treatment: total thyroidectomy


## - Medullary CA:

- The only of a parafollicular origin
- $5 \%$ of thyroid CA
- Iodine uptake: poor, because it originates from parafollicular cells
- Diagnosis: FNA; amyloid bodies
- Sex: Female > Male (1.5:1)
- Route of metastasis: lymphatics to liver, lung and bone
- Associated with MENII:
- MENII: pheochromocytoma, medullary CA, hyperparathyroidism
- Treat pheochromocytoma before treating medullary carcinoma
- Associated with RET proto-oncogene mutations
- Prognosis:
- Negative lymph nodes: $80 \%$
- Positive lymph nodes: $45 \%$
- Treatment:
- Total thyroidectomy
- Median lymph node dissection, if positive.
- Detection test: pentagastrin stimulation test
- Tumor marker: calcitonin


## - Anaplastic CA:

Medullary CA: 4 M's

1) MEN II
2) aMyloid bodies
3) Median lymph node dissection
4) Modified neck dissection (if +ve lateral lymph nodes)

- Poorly differentiated tumor; 75\% of the cases arise from a previously differentiated thyroid CA (most commonly follicular CA)
- $1 \%$ of thyroid CA
- Sex: female > male
- Histology: giant cells, spindle cells
- Iodine uptake: very poor uptake
- Diagnosis: FNA
- Differential diagnosis: lymphoma; it has a better prognosis
- Treatment: (palliative)
- If small tumor: total thyroidectomy + radiotherapy + chemotherapy
- If airway compromise: debulking surgery + tracheostomy + radiotherapy or chemotherapy
- Prognosis:
- Most patients present at stage IV.
- $3 \%$ are alive after 5 years
- Median survival rate: 6 months


## - Complications of thyroid surgery:

- Hemorrhage:
- 6 hours postoperatively
- Presents as postoperative shortness of breath
- Postoperative shortness of breath can be due bilateral recurrent laryngeal nerve injury or due to a hematoma
- Management: ABC , then hematoma evacuation
- Hypocalcemia:
- Usually transient, due to parathyroid blood supply compromise
- During surgery, the parathyroid gland along with its blood supply should be preserved
- As a prophylactic measurement, parts of the parathyroid gland are taken and are autografted into the sternocleidomastoid or in the forearm
- Recurrent laryngeal nerve injury: $1 \%$


## - Benign thyroid disease:

- Hyperthyroidism:
- Signs and symptoms:
- Increased appetite with weight loss
- Tremor/anxiety/restlessness/palpitations
- Heat intolerance
- Diarrhea
- Thrill over superior thyroid artery
- Grave's disease:
- Most common cause of hyperthyroidism
- Characteristics: diffuse goiter with hyperthyroidism, exophthamlus, and peritibial myxedema (the last two are characteristic of Grave's)
- Cause: circulating antibodies that activate TSH receptors on follicular cells. This leads to deregulated production of thyroid hormone
- More common in females (6:1)
- Diagnosis:
- Increased T3 and T4
- Positive anti-TSH receptor antibodies
- Decreased TSH
- Global uptake of iodine radiation
- Diffuse goiter on scan
- Physical examination:
- Eye disease (diplopia, corneal ulcers, proptosis, chemosis, periorbital edema)
- Clubbing (thyroid acropachy)
- Peritibial myxedema
- Treatment:
- Medical treatment:
- Iodide (for short term use; usually given before surgery to decrease hormone synthesis)
- Propranolol (symptomatic treatment)
- Propylthiouracil (PTU)
- Works through decreased incorporation of iodine into T3/T4 through blocking the action of peroxidase enzyme
- Decreased peripheral deiodination of T4
- Metimazole/carbimazole
- Steroids to decrease peripheral conversion of T4 to T3

Indications for surgery:

1) If you cannot rule out CA
2) Non-compliant patient
3) If patient refuses radiation
4) Failure of medical treatment
5) Pregnancy or young age

- Radio-iodine ablation:
- Treatment of choice
- Absolute contraindications: pregnancy, newborn, patient's refusal, decreased uptake
- Relative contraindications: children and young adults due to long term oncogenic effects
- The major complication is post-treatment hypothyroidism
- Surgical treatment: bilateral subtotal thyroidectomy.
- Plummer's disease: Toxic adenoma/ toxic multinodular goiter
- Risk factor: amiodarone intake
- Iodine scan is diagnostic; one hot spot with surrounding suppressed tissue
- Treatment: radiation or surgery
- Factitious hyperthyroidism: decreased thyroglobulin
- Iodine induced
- Pituitary TSH secreting adenoma
- Trophoblastic tumor (molar)
- Stroma ovarii
- Non-toxic goiter $\rightarrow$ usually benign, solitary
- Hypothyroidism:
- Signs and symptoms:
- Weight gain, edema
- Cold intolerance
- Menorrhagea
- Weakness
- Dry skin
- Thinning of hair
- Constipation
- Causes:
- Iatrogenic (surgery or radioactive therapy)
- Iodine insufficiency (most common cause)
- Hashimoto's thyroditis:
- Chronic autoimmune destructive lymphocytic infiltration of the thyroid
- Antithyroglobulin antibodies, antiperoxidase antibodies (anti-TPO), microsomal antibodies:
- Females > males ( $95 \%$ of cases are females)
- Indications for surgery: cosmetic, congestive symptoms, suspicion of malignancy
- Reidel's thyroditis:
- Chronic like Hashimoto's
- Benign progressive inflammatory thyroid enlargement with fibrosis
- Presents as a large painless thyroid gland
- Fibrosis may involve surrounding tissue
- Associated with sclerosing cholangitis and mediastinal fibrosis
- Treatment: surgical tracheal decompression
- Acute supparative thyroditis: step or staph infection. Treated with antibiotics or incision and drainage.
- Subacute thyroditis (de Quavian):
- Rare
- Young females after upper respiratory tract infection
- Increased ESR
- Full recovery (treatment is only supportive)
- FNA: giant cells


## - Uptake:

- Differential diagnosis for increased uptake:
- Grave's disease
- Hot nodule
- TSH secreting pituitary tumor
- hCG secreting tumor
- iodine deficiency
- Differential diagnosis for decreased uptake:
- Thyroditis
- Iodine excess
- Excess exogenous T3/T4
- Factitious hyperthyroidism
- Scan:
- Diffuse uptake: Grave's
- Patchy uptake: Plummer's
- Localized uptake: toxic adenoma


## Parathyroid gland

## - Embryology:

- Endodermal origin
- Superior parathyroid glands are derived from the $4^{\text {th }}$ pharyngeal pouch
- Inferior parathyroid glands are derived from the $3^{\text {rd }}$ pharyngeal pouch
- Long descent pathway; thus there is an increased incidence of an ectopic gland:
- If undescended: cranial to the super lobe of thyroid
- Excessive descent: mediastinum ( $1 \%$ of population)
- Other sites: thymus is the most common ectopic site
- Anatomy:
- Number of glands:
- $85 \%$ of the population has 4 glands
- $5 \%$ of the population has 5 glands
- $10 \%$ of the population has 3 glands
- Site: postero-lateral aspect of the thyroid gland
- Superior glands:
- \% found on the junction between the upper third and lower two thirds at the posterior aspect of the thyroid lobe
- Superior to the inferior thyroid artery ( 1 cm above it)
- Posterior to the recurrent laryngeal nerve: the upper parathyroids are used as a landmark for the recurrent laryngeal nerve
- The superior glands are the most functional; during surgery, do not remove them until you find the other glands.
- Inferior glands:
- Found inferio-lateral or posterior to the inferior pole of the thyroid gland
- Anterior to the recurrent laryngeal nerve
- Blood supply: in $80 \%$ of the population, it comes from the inferior thyroid artery
- Types of cells:
- Fat cells
- Chief cells: secrete PTH
- Oxyphil cells: secrete PTH only when there is hyperparathyroidism or hyperplasia


## - Physiology:

- Normal calcium levels: 8.4-10.4
- Calcium levels are controlled by:
- PTH:
- Acts on bone to increase resoprtion of bone which leands to increased $\mathrm{Ca}^{2+}$ and $\mathrm{PO}_{4}{ }^{2-}$
- Acts on kidneys to increase $\mathrm{Ca}^{2+}$ absorption and increase $\mathrm{PO}_{4}{ }^{2-}$ excretion
- Acts on intestines via the kidney by increasing the activity of alpha-1-hydroxylase, which is responsible for the production of vitamin D.
- It also increases $\mathrm{HCO}^{3-}$ excretion and $\mathrm{Cl}^{-}$re-absorption leading to hyperchloremic acidosis
- Vitamin D:
- Absorbed from small intestines
- $25(\mathrm{OH}) \mathrm{D}_{3}$ in liver and is transformed to $1,25(\mathrm{OH}) \mathrm{D}_{2}$ in the kidneys
- Calcitonin:
- PTH antagonist
- Decreases bone and kidney re-absorption of $\mathrm{Ca}^{2+}$ so it decreases its serum concentration
- Notes:
- PTH is made of 84 amino acids
- PTH levels are controlled by calcium serum levels and number of chief cells
- Calcium is absorbed in the duodenum and proximal jejunum
- Functions of calcium:
- Contraction and secretion of most glands and muscles
- Neuromuscular junction conduction
- Secondary messenger
- Coenzyme for many metabolic pathways
- Blood coagulation
- Mental activity
- Bone is the largest calcium reservoir in the body
- Calcium in serum:
- $40 \%$ bound to albumin
- $50 \%$ free
- $10 \%$ is bound to phosphate and citrate
- DiGeorge's syndrome is the congenital absence of the parathyroid and thymus
- Normal PTH value is about 80 ; in primary hyperparathyroidsim it ranges between 100-140; in secondary hyperparathyroidism it ranges between 400-500; in tertiary hyperparathyroidism it is above 1000.


## - Hyperparathyroidism:

- Primary: increased secretion of PTH by the parathyroid gland manifested as an increase in calcium and decrease in phosphate
- Secondary: increased serum PTH secondary to calcium wasting
- Tertiary: persistent hyperparathyroidism after correction of secondary hyperparathyroidism resulting in autonomous PTH secretion not responsive to the negative feedback


## - Primary hyperparathyroidism:

- Causes:
- Adenoma (most common): 1 gland; $85 \%$
- Hyperplasia: 4 glands; $10 \%$
- Carcinoma: 1 gland; $1 \%$
- Risk factors:
- Family history
- MENI, MENIIa (chromosome 11)
- Radiation
- Common in postmenopausal women
- Mostly sporadic
- Clinical presentation: "Stones, Bones, Groans, and psychiatric moans"
- Stones: kidney stones; nephrolithiasis
- Bones: Bone pain, pathological fractures, osteoporosis, subperiosteal bone resorption
- Groans: abdominal pain, weakness, pancreatitis, constipation, gout
- Psychiatric moans: depression, anorexia, weight loss, anxiety, emotional disturbances.
- Hypertension, polyurea/polydypsia, lethargy
- X-ray findings: subperiosteal bone resorption usually in the hands
- In adenoma, only $5 \%$ of patients have more than 1 gland involved.
- In patients with primary hyperparathyroidism due to hyperplasia, always rule out MEN syndromes.
- Parathyroid carcinoma:
- $50 \%$ have a palpable neck mass
- Serum $\mathrm{Ca}^{2+}>15$
- Increased PTH
- Paralysis of recurrent laryngeal nerve leading to a change in voice
- Hypercalcemic crisis
- Tumor marker: hCG
- Investigations:
- Phosphate
- Creatinine
- Alkaline phosphatase
- 24-hour urine collection to rule out Fanconi's syndrome
- $\mathrm{Cl}^{-}: \mathrm{PO}_{4}{ }^{2-}$ ration $>33: 1$
- PTH-level radioimmunoassay
- Systamibi scan (99mTc)
- Treatment:
- Initial medical treatment for hypercalcemia consists of IV fluids and bisphosphanates. Do not use furosemide, unless the patient is overloaded.
- Adenoma: surgically remove the adenoma (send for a frozen section) and biopsy all abnormally enlarged glands
- Hyperplasia: neck exploration removing all parathyroid glands and leaving at least 30 mg of parathyroid tissue placed in the forearm muscles. We leave 30 mg in order to retain the parathyroid function. Moreover, if hyperparathyroidism re-occurs, we can remove some tissue from the forearm (easier access)
- If carcinoma: remove the carcinoma, the ipsilateral thyroid lobe, and all enlarged lymph nodes. Modified neck dissection is indicated if lymph nodes are positive.
- Complications of surgery:
- Postoperative hypocalcemia:
- Transient: if severe (<7.5) you should treat
- Persistent: if hypocalcemia persists for more than 6-8 weeks; treat with calcium carbonate.
- Signs and symptoms:
- Perioral numbmess
- Parasthesia and tetany
- Chovstek's sign
- Toutesser's sign
- Recurrent laryngeal nerve injury
- Unilateral: voice change
- Bilateral: airway obstruction
- Neck hematoma
- Superior laryngeal nerve injury


## - Familial hypocalciuric hypercalcemia: (FHH)

- Mild increase in calcium, increased to normal PTH $\rightarrow$ asymptomatic
- Decrease urine calcium
- Autosomal dominant mutation in calcium sensing receptors leading to loss of feedback inhibition
- Labs: 24-hours urine collection, renal $\mathrm{Ca}: \mathrm{Cr}$ clearance ratio (if $<0.01$ it is diagnostic of FHH)
- Surgery is not indicated for these cases
- Hungry bone syndrome: severe hypocalcemia seen after surgical correction of hyperparathyroidism as chronically calcium deprived bone absorbs calcium aggressively post-surgically
- Secondary hyperparathyroidism:
- Causes:
- Renal failure
- Vitamin D deficiency (Ricket's, osteomalacia)
- Decrease GI absorption of calcium
- Labs:
- Decreased calcium
- Increased PTH
- Treatment:
- Correct calcium and phosphate
- Correct the underlying cause
- No role for parathyroid surgery


## - Tertiary hyperparathyroidism

DDx of hypercalcemia: CHIMPANZEES

1) Calcium overdose
2) hyperparathyroidism
3) Immobility/iatrogenic
4) Metastasis/milk alkali syndrome
5) Paget's disease
6) Addison's/acromegaly
7) Neoplasm
8) Zollinger Ellison syndrome
9) Excessive vitamin A
10) Excessive vitamin $D$
11) Sarcoidosis

- Persistent hyperparathyroidism after correction of secondary hyperparathyroidism.
- Results from autonomous PTH secretion not responsive to negative feedback
- Treatment:
- Correct calcium and phosphate
- Surgical removal of the parathyroids wand implanting some tissue in the forearm, if refractory to medical treatment
- Bone disorders seen in hyperparathyroidism:
- Renal osteodystrophy
- Osteporosis
- Osteomalacia
- Ostitis fibrosa cystica
- Brown tumors
- Indications of surgery in asmptomatic hyperparathyroidism:
- Age < 50
- Patients who cannot get appropriate follow up
- Serum $\mathrm{Ca}>1 \mathrm{mg}$ above normal range
- Urine $\mathrm{Ca}>400 \mathrm{mg}$ (obsolete criterion)
- $30 \%$ decrease in creatinine clearance
- Complications of hyperparahyroidism including nephrocalcinosis and osteofibrosis
- Notes:
- Parathyromatosis:
- Multiple, small, hyperfunctioning masses found in the neck and mediastinum due to spillage of otherwise benign parathyroid tissue during surgery.
- One of the most important differential diagnoses is recurrent hyperparathyroidism after parathyroidectomy.
- Surgically remove excess masses.
- The most common cause of hypercalcemia in hospitalized patients is cancer
- Most common cause of hypercalcemia is outpatients is hyperparathyroidism


## Pancreas

## - Embryology:

- Originates from the diverticula in the foregut endoderm
- Forms during the $5^{\text {th }}-6^{\text {th }}$ week of gestation


## - Anatomy:

- Structures:
- Uncinnate process
- Head
- Neck: lies in front of the superior mesenteric vein
- Body
- Tail: touches the spleen
- Ducts:
- Wirsung duct
- Santorini duct (small duct)
- Blood supply:
- Celiac trunk gives rise to the gastroduodenal artery which divided into the anterior and posterior superior pancreaticoduodenal arteries
- Superior mesenteric artery which gives rise to anterior and posterior inferior pancreaticoduodenal arteries
- Splenic artery which gives rise to dorsal pancreatic artery
- Types of pancreatic cells:
- Endocrine cells (islets of Langerhans_
- Alpha cells: secrete glucacon, which promotes the conversion of hepatic glycogen and increases systemic gluocse levels
- Beta cells: secrete insulin which promotes glucose transport into the cells and decreases systemic glucose levels. They also secrete C-peptide
- D-cells: secrete somatostatin which decreases the release of GI hormones, gastric acid, and small bowel electrolytes
- PP cells: secrete polypeptides/vasoactive intestinal polypeptide (VIP)
- Exocrine cells:
- Secrete digestive enzymes
- Pancreatic islet cell tumors:
- Rare
- All malignant except for insulinoma


## - Insulinoma:

- Insulin secreting beta cell tumor of the pancreas
- Most common type of islet cell tumor
- Rule of $90 \%$ :
- $90 \%$ benign
- $90 \%<1.5 \mathrm{~cm}$
- $90 \%$ solitary
- $90 \%$ intrapancreatic
- Can be part of MENI or von Hippel Lindau disease
- Clinical presentation:
- Profound hypoglycemia during fasting and after exercise
- Neuroglycopenia: (anxiety, tremor, confusion, obtundation)
- Symptomatic response to hypoglycemia: (hunger, sweating, tachycardia)
- Whipple's triad for diagnosis:
- Hypoglycemic symptoms
- Blood glucose <50 during the attack
- Symptoms relieved after administration of IV glucose
- Before making the diagnosis, you should exclude facticious and postprandial reactive hypoglycemia
- The diagnostic test of choice is 72 hours fasting test with the following results:
- Inappropriate increase of plasma insulin (>500)
- Hypoglycemia (<50)
- Increased C-peptide
- Increased pro-insulin (>20\%)
- Investigations:
- Dynamic CT scan at 5 mm intervals with contrast
- Endoscopic ultrasound

90\% of all insulinomas cannot be detected through CT or MRI.

- Selective arteriography to detect excessive blood supply at the site of tumor
- Mamora test (no longer done): injection of calcium will increase he activity of all endocrine cells, so you see the hyperfunctioning areas of an insulinoma.
- Treatment:
- Surgical removal of the tumor
- Preoperatively give: diazoide, casopamil, octreotid
- Debulking surgery: removing part of the tumor because the rest of the tumor passes through important structures.
- Medical treatment is indicated in patients who are not candidates for surgery. Moreover, it is done preoperatively to decrease the size of tumor as not to remove a lot of pancreatic tissue, which might lead to DM.


## - Gastrinoma:

- Second most common islet tumor; however, it is the most common tumor in patients with MEN (more common than insulinomas in these patients)
- G-cell tumor
- Premalignant
- Usually, there are no G-cells in the pancreas
- G-cells secrete gastrin which increases gastric acid and pepsinogen secretion
- Zollinger Ellison syndrome is associated with severe ulcers that regractory to medical treatment. These ulcers develop due to gastrin related gastric acid secretion.
- Clinical presentation:
- Epigastric pain
- Diarrhea
- Weight loss
- Common sites:
- The most common site is at the duodenum
- $80 \%$ of the tumors are found in the gastrinoma triangle, which is made of:
- Cystic duct/common bile duct junction
- Head and neck of the pancreas
- Junction of the second and third part of duodenum
- Gastrinomas occur in MENI:
- The most common tumor in MENI
- Gastrinomas associated with MENI follow a more benign course than sporadic cases
- Treatment of parathyroid (which is usually part of MENI) can relieve gastrinoma
- Usually multiple
- When to suspect Zollinger Ellison syndrome?
- Recurrent multiple ulcers typically located distal to the jejunum
- Peptic ulcer disease refractory to medical treatment
- Peptic ulcer disease with significant diarrhea
- Complicated peptic ulcer disease
- Peptic ulcer disease as part of MENI syndrome
- Diagnosis of Zollinger Ellison:
- Fasting serum gastrin >100 (>500 is diagnostic)
- Basal gastric acid output >15 mg/hour (normal level: <10)
- Differential diagnosis:
- Gastric outlet obstruction
- G-cell hyperplasia
- Renal failure
- Atrophic gastritis
- Patients taking $\mathrm{H}_{2}$-blockers or PPI's
- Secretin stimulation test is used to distinguish gastrinoma from the other differentials
- Localization of gastrinoma:
- $80 \%$ within gastrinoma triangle
- Done by MRI/CT, endoscopic ultrasound, scintigraphy
- Treatment:
- Surgery
- Medical by PPI if the patient is not fit for surgery


## - VIPoma:

- VIP secreting tumor
- $2 / 3$ is pancreatic and $1 / 2$ are malignant
- Clinical presentation:
- Secretory watery diarrhea
- Hypocalcemia
- Achlorohydria/hypochlorohydria
- Diagnosis: increased VIP (>190), decreased K ${ }^{+}$
- Treatment:
- Resection; since it usually occurs in the distal pancreas, distal pancreatectomy is performed
- Medical using somatostatin analogues


## - Glucagonoma:

- Glucagon secreting tumor
- Presents with type II DM $\rightarrow$ persistent hyperglycemia
- Anemia/weight loss
- Hypoaminoacidemia
- Characteristic skin rash
- Diagnosis: plasma glucagon >1000
- Treatment: resection


## - Somatostatinoma:

- Rare
- D-cell tumor; secreting somatostatin
- Usually in the head of pancreas
- Clinical presentation (3D's):
- Diarrhea
- Diabetes
- Dilated gallbladder with stones


## Diabetic foot

- $25 \%$ of all diabetic patients develop foot problems
- Diabetic foot is the most common cause of admission for diabetics
- $50 \%$ of all causes of amputations
- Most commonly caused by undetected or untreated trauma to the neuropathic foot
- Most commonly found on the heels and the plantar surface of the metatarsal heads
- Pathophysiology (multifactorial)
- Peripheral neuropathy:
- Sensory:
- Loss of light touch, vibration, and pressure sensations
- Causes harmful distribution of pressure forces
- Starts distally and migrates proximally in a gloves/stockings distribution
- Increases at night
- Motor:
- Atrophy of the intrinsic muscles of foot
- Collapse and loss of stability
- Abnormal pressure points (shifts weight more on metatarsal heads)
- This causes deformities:
- Hallux valgus
- Hammer toes (claw toes): weakness of both extensors and flexors, but, usually, flexors are stronger than extensors.
- Flat foot due to collapse of medial arch
- Overriding ingrowing nails
- Management: off-loading to decrease inflammation and accelerate repair
- Autonomic:
- Failure of sweating
- Inadequate lubrication
- Dry skin
- Mechanical breakdown and fissuring making an entry site for bacteria.
- Peripheral vascular disease (vascular insufficiency)
- Occlusion of vessels due to atherosclerosis "lead pipe arteries"
- Failure of autoregulation of microcirculation, so arterial blood will be shunted past the capillaries into the venous circulation, which decreases blood flow and impedes the process of healing.
- Diagnosis:
- Measuring ABPI
- Micro and macro angiography
- On physical examination:
- AV shunt: weak pulses, warm, pink
- Ischemia: weak pulses, cold, blue
- Metabolic hyperglycemia:
- Increased sorbitol: damage of Schwann cells, which causes nerve ischemia and impaired transmission
- Intraneural accumulation of advanced glycosylation products
- Decreased insulin which causes delayed healing (insulin is anabolic)
- Immune deficiency: both cellular and humoral immunity
- Decreased growth factors: TGF-1, IGF
- Impaired phagocytosis
- Increased metalloproteases


## - Charcot foot

- Cartilaginous fibrillation and destruction along with subcondral/endocondral bone formation
- Fragmentation of periarticular areas (midtarsal joints) and sublaxation which leads to painless collapse of ligaments of the joints and foot arches.
- Most common sites:
- Subtalar joint
- Ankle joint
- Interdigital joints
- Clinical presentation:
- Acute: swelling/hotness/pain $\rightarrow$ managed by bisphosphonates
- Subacute: dislocation/sublaxation/calcification on X-ray
- Chronic: rocker-bottom deformity managed by immobilization or amputation
- Manifestations:
- Skin disease:
- Dermopathy: most common on the shin of tibia
- Brownish scar produced by red or blistering spots
- Self-limiting
- Bullea/blebs/chilblain/blisters
- Nail abnormalities
- Thickening
- Onchogryphosis
- Oncchomycosis
- Macerated webs (tinea pedis)
- Cellulitis (increased ESR)
- Soft tissue lesions:
- Ulcers
- Necrotizing fascitis
- Serious/life-threatening
- Swollen cyanotic foot
- Blisters on the skin with a foul smelling discharge
- Gangrene
- Abscess
- Bone: the navicular bone is the most medial bone in the foot and is the most affected by Charcot changes. The most important complication is amputation.
- Osteomyleitis
- Charcot neuropathy
- Deformities
- Physical examination:
- Examine the following:
- Lower $1 / 3$ of the leg
- Forefoot
- Midfoot
- Hindfoot
- Skin (comment on):
- Color (dusky skin indicates soft tissue necrosis that led to venous congestion)
- Texture
- Blisters, blebs, bullae
- Hyperkeratosis (skin response to increased pressure is to increase number of cells)
- Scaliness
- Dryness
- Dermopathy, gangrene
- Thick callus
- Heel: fissures, ulcers, hyperkeratosis
- Nails: healthy/ trophic/ thickened (if ischemic)/ onchogryphosis/ onchomycosis/ in-growing nails
- Web spaces: fissuring of the skin
- Bone and joint deformities
- Ulcers
- Distal pulses
- Neurological exam
- Lymph nodes


## - Levels of amputation:

- Above knee amputation
- Below knee amputation
- Syme's amputation
- Transmetatarsal amputation
- Toe amputation
- Ray's amputation: removal of the toe and the head of the metatarsal
- Signs of infection (in an ulcer): for definitive diagnosis, take a tissue biopsy
- Redness, hotness, swelling and loss of function
- Foul smelling discharge

- Purulent secretions
- Presence of friable tissue
- Undermined edge
- Ulcer classification (Wegner's classification):
- $0 \rightarrow$ intact skin
- $1 \rightarrow$ superficial
- $2 \rightarrow$ deep (to tendon/bone/ligament)
- $3 \rightarrow$ osteomylitis
- $4 \rightarrow$ gangrene of toe or forefoot
- $5 \rightarrow$ gangrene of the whole foot
- Investigations:
- Blood sugar
- CBC
- ESR, CRP
- Urea, electrolytes
- Tissue specimen
- X-ray $\rightarrow$ to detect ostemylitis or gas in soft tissue


## - Treatment

- Control blood sugar
- Decrease pain (analgesia) $24 \%$ heal in 12 weeks/ $30 \%$ heal in 20 weeks
- Vitamin B complex $\qquad$
- The best management is prevention
- Daily inspection for signs of trauma
- Attention to hygiene
- Off-loading orthotic devices
- Debridement: "piece meal debridement"
- Debride all necrotic tissue
- All surface should be bleeding
- Wound edges should be healthy
- Manage according to the grade:
- Low grade ulcer: superficial, no hyperemia or swelling, no ischemia
- Give antibiotics orally for 1 week
- $100 \%$ complete recovery in 2-4 weeks
- Moderate grade ulcer: pale, necrotic tissue, pus formation, hyperemia, but NO ischemia:
- Admit the patient, IV antibiotics for 2-4 weeks
- $80 \%$ full recovery in 3 months
- High grade ulcer: gangrene, ischemia, infected deep tendon and bone, necrotizing infection
- Admit the patient, IV antibiotics 4-6 weeks, vascular reconstruction or amputation
- $20 \%$ will heal in 12 months; $80 \%$ will need amputation
- Notes:
- Antibiotics should cover: staph aureus, staph epidermedis, and streptococcus
- $2^{\text {nd }}$ generation cephalosporins
- Wet-dry dressing
- Aliginate dressing:
- Minimizes contact of the wound
- Used four wounds that have a large amount of exudate
- If IV $\rightarrow$ give cephalosporins and flagyl
- Grafts and flaps should not be put over weight bearing areas


## Adrenal gland

## - Anatomy:

- Cortex:
- Zona Gromelulosa: aldosterone
- Zona Fasciculata: glucocorticoids
- Zona Reticularis: androgens
- Medulla:
- Epinephrine and norepinephrine
- Controlled by the autonomic nervous system


## - Physiology:

- CRH is secreted in response to stress, decreased serum cortisol, and in a circadian rhythm. It increases ACTH secretion
- ACTH follows a circadian rhythm, level are highest in the morning
- ACTH increases the secretion of all cortex hormones, but it has no effect on the adrenal medulla


## - Cushing's syndrome:

- This term is a general description for any increase in cortisol levels. If the problem is in the pituitary, it is called Cushing's disease
- Symptoms:
- Emotional lability
- Facial plethora
- Moon face
- Buffalo hump
- Hirsutism
- Hypertension
- Truncal obesity
- Striae (pink-purple)
- Easy bruising
- Osteporosis
- Muscle wasting
- Edema
- DM type II

- Pseudocushing's syndrome is a clinical syndrome that resembles Cushing's in its presentation; however, the adrenals are normal. The most common causes include obesity, alcoholism, and depression.
- Since ACTH increases the secretion of cortison, aldosterone, and androgens, many patients with cushing's disease have increased DHEA levels (presents as virilization in females).
- In cases of adrenal adenoma, there are increased levels of cortisol. However, ACTH and DHEA are low
- Low-dose dexamethasone suppression test is the screening test.
- Algorithm for detection of Cushing's syndrome:
- Clinical suspicion: (if the following tests are normal, Cushing's syndrome is highly unlikely)
- Urine free cortisol
- Low dose dexamethasone suppression test
- Night time salivary cortisol
- If the aforementioned tests are abnormal, take plasma ACTH levels:
- Low:
- ACTH independent; most likely caused by an adrenal tumor.
- Adrenal CT/MRI
- Treat by adrenalectomy with or without chemotherapy or radiotherapy
- If high:
- ACTH dependant, this can be due to a pituitary tumor or an ectopic ACTH secreting tumor. In the past, they used to differentiate between these two conditions using the high dose dexamethasone suppression test. However, this test is no longer used.
- Once you detect high ACTH levels, order a CT/MRI for the pituitary. If you find no tumor, order a pan-CT or MRI to detect an ectopic tumor.
- If results are still negative, perform petrosal venous sinus sampling. This process is complicated, and requires taking blood samples from the venous circulation in the pituitary. This is used to detect microadenomas. A positive test will show increased local ACTH levels.
- Extra tests: DHEA
- Adrenal adenoma will result in decreased ACTH ad increased DHEA
- Adrenal carcinoma will result in decreased ACTH, severely increased DHEA, and urine 17-ketosteroids.


## Pheochromocytoma

- Rare, usually benign tumor that arises from chromaffin cells of the sympathetic nervous system. Symptoms are due to secretion of catecholamines: epinephrine, norepinephrine, and dopamine.
- The rule of 10:
- $10 \%$ are extra-adrenal (most common site is the organ of Zuckerandl, which is found at the bifurcation of the aorta)
- $10 \%$ malignant
- $10 \%$ in children
- $10 \%$ bilateral or multiple


## - Differential diagnosis:

- Labile essential hypertension
- Anxiety
- Hyperthyroidism
- Hypoglycemia
- Menopausal flushing
- Carcinoid (rare)


## - Symptoms:

- Excessive sweating
- Headache
- Hypertension
- Palpitations and tachycardia


## - Risk factors:

- Family history of pheochromocytoma
- Hamily history of: MENII, neurofibromatosis, or von Hippel-Lindau disease
- Controlled HTN + DM
- Regractory HTN
- HTN in a young person without a family history
- Adrena incidenteloma
- Idiopathic dilated cardiomyopathy
- History of hypertension during procedures


## - Diagnosis:

- Low risk patients: 24 hours fractionated metanephrines and catecholamines. Note, TCAs tamper with the test's results; thus, all patients taking TCA's should discontinue them.
- High risk patients (patients with any of the aforementioned risk factors): plasma fractionated metanephrnie. The test has high sensitivity, but low specificity
- If the above mentioned tests gave negative results, and the clinical suspicion is high do the following:
- Clonidine (alpha agonist) suppression test: after the suppressive dose has been administered, patients with pheochromocytoma, will have high levels.
- CT/MRI to locate the tumor
- Radioactive metaiodobenzaguanidine scan
- PET scan
- Total body MRI
- Genetic testing


## - Treatment:

- Preoperatively, give patients antihypertensive drugs (first alpha blockers, then beta blockers). Phenoxybenzamine is the most commonly used drug; give it for 2 weeks prior to the procedure. Add a beta blocker 3 days before the procedure. Never give beta blockers alone, as this might lead to a hypertensive crisis.
- Surgery: if patients are not treated surgically, their prognosis is poor. However, with surgical treatment, the prognosis is excellent with 5 year survival rate of about $95 \%$.
- Notes:
- $1 / 3$ of pheochromoxytomas cause death prior to their diagnosis
- Death is usually due cardiac arrhythmias and strokes


## - Adrenal incidentelomas:

- Any mass $>1 \mathrm{~cm}$, discovered by accident on an imaging study
- Most of them are non-functioning masses
- Up to $15 \%$ are bilateral masses
- If found to be malignant, there is a $50 \%$ chance that they are a metastasis
- Without a history of carcinoma, you have to exclude a functioning tumor or adrenal hyperfunction. Moreover, you have to determine whether the mass is primary or a metastatisi mass. Metastatic masses tend to be larger, bilateral, irregular, and inhomogenous.
- All patients with incidentelomas should have the following tests:
- Blood pressure and serum potassium (Zona glomerulosa)
- 24 hour urine cortisol (Zona fasciculata)
- Plasma fractionated metanephrine (to exclude pheochromocytoma)
- Females with virilization or males with feminization should have their androgens tested
- If results are normal and mass $<4 \mathrm{~cm}$; observe and repeat image in3-6 months.
- Indications for adrenalectomy:
- Functioning tumor
- Mass >4-6 cm
- Imaging suspicious of CA


## Multiple endocrine neoplasia (MEN)

- All endocrine glands originate from endoderm
- All MEN are hereditary endocrine tumor syndromes and are autosomal dominant
- MENI: Wermer's syndrome (chromosome 11q13)
- Pituitary ( $40 \%$ present in MENI)
- Types:
- Benign prolactin producing adenoma (most common)
- Growth hormone secreting adenoma
- ACTH secreting adenoma
- Nonfunctioning adenoma
- Clinical presentation:
- Headaches
- Diplopia
- Amenorrhea
- Acromegaly
- Galactorrhea
- Treatment:
- Medical: bromocreptine (decreases tumor bulk)
- Surgical: trans-sphenoidal hypophysectomy (definitive)
- Parathyroid ( $100 \%$ present in MENI)
- The first one is usually detectable
- Generalized 4 gland hypertrophy
- Treatment options:
- 3.5 gland removal
- Removal of all the gland and auto-transplant of some tissue in the forearm
- Recurrence is $50 \%$
- Pancreatic islet cells ( $50 \%$ present with MENI)
- Types:
- Gastrinoma (ZES) most common $50 \%$
- $25 \%$ of ZES patients have MENI
- Gastrinoma occurs in proximal duodenum and the gastrinoma triangle
- Multiple
- Always malignant
- Insulinoma 20\%
- VIPoma
- Glucagonoma
- Somatostatinoma
- Patients with MENI can present with adrenal cortex tumors, so they must be investigated. Moreover, all family members of these patients should be screened for MEN syndromes.
- MENII: Sipple's syndrome
- Caused by a gain of function mutation in the RET proto-oncogene which encodes a transmembrane tyrosine kinase receptor
- MEN IIa:
- Medullary thyroid carcinoma ( $100 \%$ )
- Early presentation
- Increased calcitonin
- Pheochoromocytoma: 30\%
- Hyperparathyroidism: 50\%
- MEN IIb:
- Medullary thyroid carcinoma: 85\%
- Bilateral and very aggressive
- Presents early at the age of 1-2
- Mucosal neuromas (ganglioneuromatosis) in 100\%
- Neurofibromatosis
- Multiple
- Marfanoid body features:
- Characteristic physical appearance
- Hypergigantism
- Pes cavus/planum (large arch of foot)
- Pheochromocytoma in 30\%
- Prophylactic thyroidectomy is indicated for all RET mutation carriers:
- MEN IIa: at age 5
- MEN IIb: at age 1

