REACTIVE HYPERPLASTIC FIBROUS TISSUE LESIONS

1. Fibroma
2. Giant Cell Fibroma
3. Epulis Fissuratum
4. Inflammatory Papillary Hyperplasia
5. Pyogenic Granuloma
6. Peripheral Giant Cell Granuloma
7. Peripheral Ossifying Fibroma

1) **FIBROMA** (4^{th} – 6^{th})
[IRRITATION FIBROMA | TRAUMATIC FIBROMA | FIBROUS HYPERPLASIA]

- True neoplasm or reactive hyperplasia of fibrous CT in respond to local irritation.

- Site: Buccal mucosa (along the bite line), followed by labial mucosa, tongue & gingiva.

- Size: range from few mm to several cm (average 1.5 cm)

- Clinical Features:
  Smooth-surfaced pink nodule, similar in color to surrounding mucosa.
  Most of them are sessile, some are pedunculated.
  Symptomless unless secondary traumatic ulceration of the surface had occurred.

2) **GIANT CELL FIBROMA** (F++, < Fibroma)

- Site: 50% present in gingiva (mandibular twice as maxillary). Other sites: tongue & palate.

- Size: < 1cm

- Clinical Features:
  Asymptomatic
  Sessile or pedunculated nodules.

- Histopathology:
  Loosely arranged fibrous CT.
  Presence of multiple large **stellate fibroblasts**, with several nuclei, within the superficial CT.
  Covering epithelia is thin & **atrophic** with some **rete ridges** that appear narrow & elongated.

- Treatment: Surgical excision with rare recurrence.

3) **EPULIS FISSURATUM** (F++ 4th and older)
[DENTURE EPULIS | INFLAMMATORY FIBROUS HYPERPLASIA]

- Tumor-like hyperplasia of fibrous CT that develops in association with the flange of an ill-fitting complete or partial denture.

- Site: Facial aspect of the alveolar ridge (anterior portion of the jaw)

- Size: from less than 1cm to a massive lesion that involve most length of vestibule.

- Clinical Features:
  Single or multiple folds of hyperplastic tissue in the alveolar vestibule.
  There are two folds of tissue & the flange of the denture conveniently fits into the fissure between the folds.
  Tissue is firm & fibrous
  Sometimes appears erythematous & ulcerated (similar to pyogenic granuloma)

- Histopathology:
  Hyperplasia of fibrous CT.
  Overlying epithelia is **hyperkeratotic** and demonstrate irregular **hyperplasia of rete ridges**
  Pseudo-epitheliomatous hyperplasia may be seen at base of the grooves between the folds.
  Variable chronic inflammatory cell infiltrate is present
  Rarely, osteoid or chondroid tissues are observed (o & c metaplasia)

- Similar Lesion: **FIBROEPITHELIAL POLYP [LEAF-LIFE DENTURE FIBROMA]**
  Occurs on the hard palate beneath a maxillary denture
  Flattened pink mass that is attached to the palate by a narrow stalk.
  Edge of the lesion is often serrated and resemble a leaf.

- Treatment: surgical removal with relining or remodeling of the ill-fitted denture to prevent recurrence

4) **INFLAMMATORY PAPILLARY HYPERPLASIA**
[DENTURE PAPILLOMATOSIS]

- Reactive tissue growth that sometimes develops beneath a denture. Related to:
  - Ill-fitting denture
  - Poor denture hygiene
  - Wearing the denture 24 hours a day
  - Candida (might have no role)

- Clinical Features:
  Asymptomatic
  Erythematous
  Papillary Surface

- Site: Hard palate (beneath the denture base)

- Histopathology:
  Numerous papillary growths on the surface that are covered by hyperplastic stratified squamous epithelia.
  In advanced cases, pseudoepitheliomatous hyperplasia (mistaken for carcinoma)
  CT vary from loose & edematous to densely collagenized
  Chronic inflammatory cells infiltrate

- Treatment:
  Early Lesion: removal of the denture to let the condition subsite & tissue resume appearance + **Topical & Systemic antifungal therapy.**
  Advanced Lesion: Excision of the hyperplastic tissue before fabricating a new denture

5) PYOGENIC GRANULOMA (F++ due to vascular effects of hormones, 1^{st} – 3^{rd})
includes: **[PREGNANCY TUMOR or GRANULOMA GRAVIDARUM | EPULIS GRANULOMATOSA]**

- Common tumor-like growth of the oral cavity that is non-neoplastic in nature.
- It's not a true granuloma and represents exuberant tissue response to local irritation.

- Site:
  Gingival, lip, tongue & buccal mucosa
  More common in maxillary than in mandibular gingiva
  Anterior areas more than posterior areas
  Facial aspects of gingival is more common than lingual aspects.
  Some lesions extend between teeth to involve both facial & lingual gingival

- Size: Vary from small growths (few mm) to large lesions (several cm in diameter)

- Clinical Features:
  Smooth of lobulated mass that is usually pedunculated, although some lesions are sessile.
  Surface is characteristically **ulcerated**
  Ranges from **pink to red to purple** depending on the age of the lesion.
  Highly vascular in appearance.
  Older lesions tend to become **more collagenized & pink**
  Gingival inflammation is due to poor oral hygiene (precipitating factor in many pts.)
  May exhibit rapid growth (alarms both patient and clinician that the lesion might be malignant)

- Histopathology:
  Highly vascular proliferation (resemble granulation tissue)
  Numerous small & large endothelium-lined channels are formed and are **engorged with RBC**
  Sometimes vessels are organized in lobular aggregates (**lobular capillary hemangioma**)
  Mixed inflammatory cell infiltrate (PMNs) more prevalent near ulcerated surfaces while plasma cells & lymphocytes are more in deeper areas of the specimen.
  Older lesions may have areas with more **fibrous appearance**.

- Treatment:
  Conservative surgical excision
  Occasionally the lesion Is recurred & re-excision is necessary

PREGNANCY TUMOR | GRANULOMA GRAVIDARUM

- Pyogenic granulomas develop in pregnant women (thus the name)
- It develops during the 1st trimester & their incidence increases up through the 7th month of pregnancy.
- The gradual rise of these lesions throughout pregnancy is related to increasing levels of estrogen & progesterone
- After pregnancy & return of normal hormone levels, some of these granulomas resolve without treatment or undergo fibrous maturation & resemble a fibroma.
- Treatment is usually postponed unless significant functional or esthetic problems.
- There is high recurrence rate for pyogenic granuloma that is removed during pregnancy

EPULIS GRANULOMATOSA

- Hyperplastic growth of granulation tissue that sometimes arise in healing sockets.
- Resemble pyogenic granulomas
- Granulation tissue reaction to bony sequestra in the socket.

6) PERIPHERAL GIANT CELL GRANULOMA (F++ 5^{th} – 6^{th}) [GIANT CELL EPULIS]

- Common tumor-like growth of the oral cavity that does not resemble a true neoplasm but rather a reactive lesion caused by local irritation or trauma
- Represents a soft-tissue counterpart of central giant cell granuloma.

- Site: Exclusively in gingival or edentulous alveolar ridge
  Anterior or posterior region of the gingival or alveolar mucosa
  Mandible more than maxilla

- Size: < 2 cm (or larger sometimes)

- Clinical Features:
  Present as a red or reddish-blue nodular mass.
  Resemble pyogenic granuloma but it is more bluish-purple compared with bright red.
  Cupping Resorption of the underlying alveolar bone.

- Histopathology:
  Proliferation of multinucleated giant cells with background of ovoid & spindle shaped mesenchymal cells in a fibrous CT stroma.
  Abundant hemorrhage seen throughout the mass with **hemosiderin deposits** at periphery of lesion.
  Surface ulceration in 50% with acute & chronic inflammatory cell infiltrates.
  Reactive new bone formation & dystrophic calcification may be seen.

- Treatment: Local surgical excision down to underlying bone.
  Adjacent teeth should be carefully scaled to remove any source of irritation & minimize risk of recurrence.

7) PERIPHERAL OSSIFYING FIBROMA (F++ 2nd)
[OSSIFYING FIBROID EPULIS]

- Common gingival growth that is reactive rather than neoplastic.
- Pathogenesis is uncertain but it could develop as pyogenic granuloma that undergo fibrous maturation & subsequent calcification.
- The mineralized product originates from cells of the PDL.
- It does NOT resemble a soft tissue counterpart of the central ossifying fibroma.

- Site: Exclusive on the gingiva
  More than 50% of cases in incisor-cuspid region, teeth are not affected.

- Size: < 2cm

- Clinical Features:
  Nodular mass that is pedunculated/sessile and usually original from interdental papilla
  Red to pink with surface ulceration in some cases.
  Lesion may present for many weeks or months before diagnosis is made

- Histopathology:
  Fibrous proliferation with formation of mineralized products.
  Mineralized components: bone, cementum-like material or dystrophic calcification.
  Bone is usually woven & trabecular.

- Treatment:
  Local surgical excision down to the periosteum because recurrence is more likely if base of lesion is allowed to remain.
  Adjacent teeth should be thoroughly scaled to eliminate any possible irritants.

NEOPLASTIC FIBROUS TISSUE LESIONS

1. Fibrous Histiocytoma
2. Fibromatosis

1) **FIBROUS HISTIOCYTOMA** (4th and older)

- Diverse group of tumors that exhibit both fibroblastic & histiocytic (phagocyte) differentiation

- Site: Anywhere in body, mainly in extremities (dermato-fibromas)
  Uncommon in oral/peri-oral regions, mainly in buccal mucosa & vestibule.

- Size: few mm to several cm.

- Clinical Features:
  Painless nodular mass

- Histopathology:
  Cellular proliferation of spindle-shaped fibroblastic cells with vesicular nuclei.
  Margin of tumor is **not sharply defined**.
  Tumor cells are arranged in short, **intersecting fascicles** known as **storiform pattern.**
  Rounded, lipid-containing histiocyte-like cells **xanthoma cells**
  Multinucleated giant cells can be seen occasionally

- Treatment: Local surgical excision with uncommon recurrence

2) **FIBROMATOSIS** (1st -3rd)

- Broad group of fibrous proliferation that have a biologic behavior and histopathologic pattern that is intermediate between those of benign fibrous lesions and fibrosarcoma.

- Site: **para-mandibular** soft tissue region, resulting in a significant **facial disfigurement.**

- Clinical Features: Soft tissue fibromas of the head & neck is a firm painless mass which may exhibit rapid growth.

- Histopathology: Cellular proliferation of spindle-shaped cells that are arranged in **streaming fascicles** & associated with variable amount of **collagen.**

- Treatment: Wide excision because of its locally aggressive nature. High recurrence rate.

ADIPOSE TISSUE LESIONS

1. Lipoma

1) LIPOMA (4th decade and older)

- Benign tumor of fat. Less frequent in oral & maxillofacial region.
- Uncertain pathogenesis, more common in obese patients.
- Lipoma do not decrease in size although normal body fat may be lost.

- Site: Buccal mucosa & buccal vestibule (50% of cases)
  Some buccal cases are true tumors, but rather herniation (death due to pressure) of the buccal fat pad, which occur subsequent to surgical removal of third molar

- Size: < 3cm

- Histopathology:
  Lobular arrangement of mature fat cells that differ little in microscopic appearance from surrounding normal fat.
  Tumor is well circumscribed & may demonstrate a thin fibrous capsule
  Rarely, cartilaginous or osseous metaplasia may occur within lipoma.

- Microscopic Variants**:**

Fibrolipoma	Fibrous component intermixed with lobules of fat cells
Angiolipoma	Admixture of mature fat & numerous small blood vessels
Spindle Cell Lipoma	Variable amounts of uniform appearing spindle cells with fat.
Myxoid Lipoma	Exhibit a mucoid background
Pleomorphic Lipoma	Spindle cells + bizarre hyperchromatic giant cells.
Intramuscular (Infiltrating) Lipoma	Deeply situated and have infiltrative growth pattern between skeletal muscle bundles.

- Treatment: Conservative local excision. Rare recurrence.

NEURAL TISSUE LESIONS

1. Traumatic Neuroma
2. Neurolemma
3. Neurofibroma
4. Multiple Endocrine Neoplasia Type 2B (Men Syndromes)
5. Melanotic Neuroectodermal Tumor of Infancy

1) **TRAUMATIC NEUROMA** (F++ any age)
[AMUPTATION NEUROMA]

- Reactive proliferation of neural tissue after damage of a nerve bundle.
- After a nerve has been severed, the **proximal portion** attempts to regenerate & reestablish innervations of the distal segment by the growth of axons though tubes of proliferating **Schwann cells.**
- If the regenerating elements encounter scar tissue or can't reestablish innervations, a tumor like mass develop at site of injury.

- Site: Mental foramen, tongue & lower lip.

- Clinical Features:
  Smooth-surfaced, non-ulcerated nodules.
  Neuromas of mental nerve are frequently painful, especially when impinged by denture or palpation.

- Histopathology:
  Haphazard Proliferation of mature myelinated nerve bundles within a fibrous CT stroma.
  Occasional mild inflammatory cell infiltrate.

- Treatment: Surgical excision (including small portion of the involved nerve)

2) **NEUROLEMMA** (2^{nd} – 3^{rd})
[SCHWANNOMA]

- Benign neural neoplasm of Schwann cell origin.

- Site: Tongue

- Size: few mm to several cm.

- Clinical Features: Slowly growing encapsulated tumor associated with nerve trunk. As it grows it push the nerve aside.

- Histopathology: Encapsulated tumor with 2 microscopic patterns:
  - **Antoni A**: streaming fascicles of spindle-shaped Schwann cells arranged in palisaded pattern around central acellular areas known as **Verocay Bodies**
  - **Antoni B**: less cellular & less organized with random arrangement of spindle cells within a loose myxomatous stroma

- Treatment: Surgical Excision.

3) **NEUROFIBROMA** (2^{nd} – 3^{rd})
component of: **[NEUROFIBROMATOSIS]**

- Arises as a solitary tumor or be a component of neurofibromatosis.
- Site: skin, tongue & buccal mucosa
- Size: Variable
- Clinical Features: slowly growing, soft painless lesion
- Histopathology: Interlacing bundles of spindle-shaped cells that often exhibit **wavy nuclei** **Mast cells** tend to be numerous, this a helpful diagnostic feature.
- Treatment: Surgical excision.

4) **MULTIPLE ENDOCRINE NEOPLASIA TYPE 2B (MEN SYNDROMES)**

- Group of rare conditions characterized by tumors or hyperplasia of neuroendocrine tissues.
- Clinical Features:
  Patient have men characteristic facial appearance: narrow face, thick lip with **averted upper eyelid**.
  Oral mucosa neuromas are usually **first sign** of the condition.
  Bilateral neuromas of the commissural mucosa are highly characteristic.
  Phenochromocytoma develop in 50% of cases.
  Development of **medullary carcinoma of the thyroid gland** in 90% of cases
- Histopathology: Marked hyperplasia of nerve bundles in loose CT stroma
- Treatment: Prophylactic removal of thyroid gland.

5) **MELANOTIC NEUROECTODERMAL TUMOR OF INFANCY** (first year of life)

- Neural crest origin

- Site: maxillary anterior region (rapidly expanding mass)
  Skull, mandible, brain, epididymis or testis.

- Clinical Features: blue or black.
  Often destroy the underlying bone & associated with displacement of developing teeth
  May exhibit **sun ray** radiographic appearance (may be mistaken for osteosarcoma)

- Histopathology:
  Biphasic population of cells (cuboidal epithelia & neuroblastic small round cells with hyperchromatic nuclei) that form **nests, tubules or alveolar structures** within a dense collagenous stroma.
  Presence of **dark-brown melanin.**

- Treatment: Surgical removal with removal of 5mm of the margin to prevent recurrence or malignant transformation.

MUSCULAR TISSUE LESIONS

1. Granular Cell Tumor
2. Congenital Epulis
3. Leiomyoma

1) **GRANULAR CELL TUMOR** (F++++ 4th – 6th)

- Benign soft tissue neoplasm (first believed to be of skeletal muscle origin) but recently believed to be derived from Schwann cells or neuroendocrine cells.

- Site: Dorsal tongue (1/3 of cases), followed by buccal mucosa

- Size: <= 2cm

- Clinical Features:
  Asymptomatic sessile nodule
  Pink to yellow in color
  Tumor is usually solitary, but sometimes **multiple especially in black.**

- Histopathology:
  Large polygonal cells with abundant pale eosinophilic, granular cytoplasm & small vesicular nuclei.
  Cells are arranged in sheets with indistinct cell borders.
  Pseudoepitheliomatous hyperplasia of the underlying epithelia in 50% of cases. (Mistaken of SCC)

- Treatment: Conservative local excision with no recurrence.

2) **CONGENITAL EPULIS** (F++++++++ due to hormonal influence, newborn)
[CONGENITAL GRANULAR CELL LESION]

- Site: exclusively on alveolar ridge of newborn
  2-3x more common on maxillary ridge than mandibular ridge
  Lateral to midline in the area of developing lateral & canine.

- Size: <= 2cm

- Histopathology: Large, rounded cell with abundant granular eosinophilic cytoplasm & round to oval, lightly basophilic nuclei.
  The overlying epithelia shows Pseudoepitheliomatous hyperplasia of atrophy of rete ridges.

- Treatment: Surgical excision

3) **LEIOMYOMA**

- Benign tumor of smooth muscle

- Site: rare in oral cavity (Lips, tongue & palate)

- Types:
  - Solid Leiomyoma
  - Vascular Leiomyoma (Angiomyoma)
  - Epithelioid Leiomyoma (Leiomyoblastoma)

- Clinical Features:
  Oral leiomyomas are either solid or vascular in type, angiomyoma accounts for 75% of all oral cases.
  Asymptomatic
  Bluish hue (if angiomyoma)
  Slow-growing firm mucosal nodule

- Treatment: Local surgical excision.

VASCULAR TISSUE LESIONS

1. Hemangioma and Vascular Malformation
2. Sturge-Weber Angiomatosis
3. Lymphangioma

1) HEMANGIOMA & VASCULAR MALFORMATION

- Hemangioma: benign tumor of infancy that is characterized by rapid growth phase with endothelial cell proliferation, followed by gradual involution.
- Vascular Malformation: structural anomalies of blood vessels without endothelial proliferation. It presents at birth & persist throughout life.
- They can be:
    - Capillary
    - Venous
    - Arteriovenous
    - Intrabony Vascular Malformations (F++ 2nd)

HEMANGIOMA

- Site: Head & neck occupy 60% of cases.

- Clinical Features:
  At birth, it appears as pale macule with threadlike telangiectasias may be noted on the skin.
  Few weeks later tumor grows at faster pace & appear as raised & bosselated with bright-red color (**Strawberry Hemangioma**)
  Firm & rubbery to palpation
  Blood can't be evacuated on pressure.

- Complications:
  About half of all hemangiomas will show complete resolution by 5 years of age, normal skill will be restored in 50% of cases. The rest may have permanent changes as atrophy, scarring, wrinkling & telangiectasias.
  Complications occur in 20% of cases like ulceration with or without secondary infection.
  Tumor in the neck & laryngeal area can lead to airway obstruction.

- Histopathology:
    - Early Lesions: numerous plump endothelial cells & often indistinct vascular lumina (Juvenile hemangioendothelioma)
    - Mature Lesion: endothelial cells become flattened with vascular space appearance.
    - Involution stage: vascular spaces are more dilated (cavernous) & widely spaced)

- Treatment:
  Systemic corticosteroids or interferon-alpha may help reduce the size if it does not involute.

VASCULAR MALFORMATION

- **Portwine Stains** are common capillary malformations.

- Site: face on the distribution of the trigeminal nerve.

- Clinical Features:
  Pink or purple macular lesions that grown with the patient till it become nodular.

- Radiographically: Multilocular radiolucency.
  Angiography can be helpful in demonstrating the vascular nature of the lesion

- Histopathology: Do not show endothelial cell proliferation & channels resemble the vessels of origin

- Intrabony vascular malformation may involve jaw bones, mandible twice as common as maxilla. Asymptomatic with occasional teeth mobility.

- Treatment:
  Flashlamp-pulsed dye laser can be effective in portwine stains.
  Sclerotherapy & surgical excision for venous malformation**.**
  Resection for large arteriovenous malformation.

- **Vascular malformation of the jaws is dangerous because of the risk of bleeding.**
  Needle aspiration of any undiagnosed Intrabony lesion before biopsy is a wise precaution to rule out possibility of vascular malformation.

2) **STURGE-WEBER ANGIOMATOSIS**

- Patient born with a dermal capillary malformation of the face (**portwine**) or **nevus flammeus** because of its deep purple color.
- Portwine stain is unilateral along one of more segments of the trigeminal nerve.
- They have meningeal angioma that is usually associated with epilepsy.
- They have ocular involvement: vascular malformation of sclera & conjunctiva.
- They have intraoral involvement: gingival hyperplasia resembling pyogenic granuloma

- Histopathology:
  Excessive number of dilated blood vessels in middle & deep dermis.
  Proliferative gingival lesion resembles pyogenic granuloma

- Treatment: Laser Therapy, neurosurgery.

3) **LYMPHANGIOMA**

- Benign hamartomatous tumors of lymphatic vessels, they are three types:
    - **LYMPHANGIOMA SIMPLEX (CAPILLARY LYMPHANGIOMA)**: consists of small capillary sized vessels
    - **CYSTIC LYMPHANGIOMA (CYSTIC HYGROMA)**: exhibit large macroscopic cystic spaces.
    - **CAVERNOUS LYMPHANGIOMA**: composed of larger dilated lymphatic vessels. This type is more frequent in the mouth, anterior 2/3 of the tongue is the most common site which results in **macroglossia.** The tumor is superficial in location & demonstrates a **pebbly surface** that resemble a cluster of translucent vesicles (**frog eggs appearance**)

- Histopathology: dilated lymphatic vessels beneath the epithelial surface & often replace CT papillae

- Treatment: surgical excision, recurrence is common in oral region because of infiltrative nature.

SOFT TISSUE SARCOMAS

account for less than 1% of the cancer in this area

1. Fibrosarcoma
2. Malignant Fibrous Histiocytoma
3. Liposarcoma
4. Angiosarcoma
5. Kaposi Sarcoma

1) **FIBROSARCOMA**
   - Malignant tumor of fibroblasts (10% in head & neck)
   - Slowly growing masses that reach considerable size before causing pain.
   - Nose and paranasal sinuses are the most common sites.

2) **MALIGNANT FIBROUS HISTEOCYTOMA**
   - Sarcoma with both fibroblastic & histiocytic features
   - Rare in oral region
   - Expanding mass that may or may not be painful or ulcerated.
   - Nose & paranasal involvement produce obstructive symptoms.

3) **LIPOSARCOMA**
   - Malignant neoplasm of fatty origin
   - Rare in oral region
   - Soft, slow-growing, ill-defined mass that may appear normal in color (or yellow)
   - Pain is a **late feature**
   - Cheek is most common oral site.

4) **ANGIOSARCOMA**
   - Rare malignancy of vascular endothelia which may arise either from blood or lymphatic vessels (more than 50% of cases occur in head & neck)
   - Site: Scalp & Forehead. Oral angiosarcomas are most commonly seen in mandible.
   - Clinical Features: Simple bruise which may lead to delay in diagnosis. Lesion continue to enlarge resulting in an elevated, nodular or ulcerated surface.
   - Histopathology: infiltrative proliferation of endothelium-lined blood vessels that form an anastomosing network. Endothelia appear hyperchromatic & atypical with high mitotic activity

5) **KAPOSI'S SARCOMA**
   - Unusual vascular neoplasm.
   - Caused by HHV 8 (Kaposi's sarcoma-associated herpes virus)
   - Clinical Presentation:
     - Classic
       - Disease of adult life, 90% (in men of Slavic, Jewish & Italian ancestry)
       - Appear as multiple bluish-purple macules & plaque on skin of lower extremities
       - Oral lesions, rare and involve palate.
     - Endemic (African)
     - Iatrogenic immunosuppressant-associated
       - Involve recipient of organ transplants, due to loss of cellular immunity
     - AIDS-related

   - Evolves through 3 stages:
     - Patch stage: characterized by a proliferation of **miniature** vessels. This results in an irregular, jagged vascular network that surround the preexisting vessels.
     - Plaque stage: further proliferation of these vascular channels along with development of a significant spindle cell components.
     - Nodular stage: spindle cells increase to form nodular tumor like mass that may resemble fibrosarcoma.

   - Treatment: Depend on clinical subtypes & stage of disease.
     Radiotherapy & surgery.