Soft Tissue Tumors

Basic objectives for individual lesions identification and characteristics

1. Identify the cause (etiology; pathogenesis), cell or tissue of origin, and frequency (prevalence rate)
2. List the predilection GAL
   - **G**ender predilection
   - **A**ge predilection
   - **L**ocation predilection
3. Describe the typical clinical appearance
   - Unusual clinical variants
   - Look-alike lesions (differential diagnosis)
   - Systemic or genetic associations
   - Drug, foreign material, etc. associations
4. Describe the basic microscopic features
5. Describe the usual biologic behavior (pathophysiology)
   - Rate and pattern of growth
   - Prognosis without treatment
6. State the typical treatment(s) and the prognosis for such treatment(s)
7. Describe unique variants or features (microscopic, physiologic, clinical, etc.)

Irritation fibroma (fibroma, traumatic fibroma, reactive fibrous hyperplasia):

1. From acute or repeated trauma (poor healing; exuberant scar tissue)
   - May develop from pyogenic granuloma
   - Most common soft tissue mass; 3rd most common mucosal lesion in adults
   - Prevalence: 12 lesions/1,000 adults
2. GAL:
   - None (but 2x females for biopsied cases)
   - 4th-6th decades
   - Buccal, lip, tongue, gingiva
3. Smooth-surfaced, pink (normal color), painless nodule
   - May be pigmented (racial pigment of surface epithelium)
   - May have surface frictional keratosis or traumatic ulcer
   - Usually sessile, may be pedunculated
4. Micro: dense, avascular fibrous stroma
   - No capsule
   - Epithelium often atrophic
   - Small numbers of lymphocytes in fibrous stroma
5. Usually grows to <1 cm. within 6 months; minimal increase after that
   - May become 3-4 cm.
     - Does not go away
   - No malignant transformation
6. Treat: Conservative surgical excision
7. Unique lesion: **Leaf-shaped fibroma** is flat fibroma growing under a denture base

– Often with small papules along the "leaf"s" edges
– 6th most common mucosal lesion; prevalence = 7/1,000, with strong female predilection
– Treat same as for regular irritation fibroma

Giant cell fibroma (reactive fibrous hyperplasia):

1. Etiology: unknown, presumed to be not related to trauma
   – 2-5% of fibrous oral masses biopsied
2. GAL:
   – Slight female (biopsied cases only)
   – Younger persons
   – 50% on gingiva
3. Small, often lobulated, smooth-surfaced or pebble-surfaced, painless nodule
4. Micro: like irritation fibroma, but has very large, stellate, subepithelial fibroblasts
   – Sometimes with multiple nuclei
5. Remains less than 5 mm in size; remains indefinitely
6. Treat: conservative surgical excision
7. Unique lesion: **retrocuspid papilla**:
   – Small fibrous gingival nodule behind mandibular cuspid; often bilateral
   – More frequent in children (at least 25%) than in adults (at least 6%)
   – Same giant fibroblasts as giant cell fibroma

Epulis fissuratum (reactive fibrous hyperplasia; inflammatory fibrous hyperplasia; denture injury tumor; denture epulis):

1. Etiology: repeating trauma from denture flange
   – 11th most common mucosal mass; prevalence = 4/1,000 adults
2. GAL:
   – None (but strong female in biopsied cases)
   – Middle-aged and older
   – Anterior vestibule, posterior vestibule, anterior oral floor
3. Linear, often lobulated, painless fibrous mass with a base along the vestibular depth or facial alveolus
   – May have traumatic ulcer in depth of a fissure
   – May have multiple parallel masses ("**redundant tissue**")
   – May have areas of papillary hyperplasia along edges
4. Micro: like irritation fibroma but has many more chronic inflammatory cells in stroma, may have very hyperplastic surface epithelium; may have surface ulcer
   – Problem: **pseudoepitheliomatous hyperplasia** can look like **squamous cell carcinoma** islands if cut tangentially or in cross section
5. Continues to elongate over time (and continued trauma)
   – New parallel masses develop, may ulcerated
   – No malignant transformation (although it was once thought to be premalignant)
6. Treat: dual treatment: conservative surgical excision and replace/repair denture

Inflammatory papillary hyperplasia (papillary hyperplasia of the palate; denture papillomatosis):

1. Etiology: repeating trauma from denture base, especially in persons who sleep with denture in place
   – Candidiasis often accompanies lesion (cause? result?)
   – 15th most common mucosal lesion; prevalence = 3/1,000 adults
   – May be seen in non-denture patients with high arched palate or immune deficiency (e.g. AIDS)
2. GAL:
   – 2x female
   – Middle-age and older
   – Hard palate (under denture)
3. Multiple painless fibrous papules scattered across hard palate, concentrated in the midline
   – Early lesions are edematous and erythematous
   – May have burning sensation if secondary candidiasis occurs
4. Micro: Each papule is like a small irritation fibroma; early lesions are comprised of edematous granulation tissue with chronic inflammatory cells
   – Problem: **pseudoepitheliomatous hyperplasia** can look like **squamous cell carcinoma**
5. Continues indefinitely, even after new denture is made (early, edematous lesions may disappear)
   – No malignant potential
6. Treat: dual treatment: conservative surgical excision or laser/electrosurgical removal
   – And replace or repair denture
   – Early (edematous) lesions may disappear with cessation of denture use for several weeks

Fibromatosis (juvenile aggressive fibromatosis; extraabdominal desmoid):
1. Etiology: unknown (neoplasm?); rare in mouth
2. GAL:
   – None
   – Children and young adults
   – Mandibular gingiva
3. Painless, firm, often lobulated mass
   – May destroy underlying bone
4. Micro: Fibrous stroma with many spindle cells in streaming fascicles
   – Not encapsulated
   – Cells are mature
5. Can grow to considerable size
   – May destroy underlying bone
   – No metastasis
6. Treat: wide excision, including affected bone
   – 1/4 recur with this treatment
   – May cause considerable local disfigurement

Fibrosarcoma:
1. Etiology: malignant neoplasm of fibroblasts
   – Etiology = unknown
   – 10% of all are in head & neck region
2. GAL:
   – None

– Children, teenagers and young adults
– Palate, tongue, buccal
3. Painless, firm, sometimes lobulated mass
– May have surface ulceration
– Slow-growing in beginning
4. Micro: Mature spindle cells with more or less collagen in background
– Spindle cells may be dysplastic (Grades I - IV)
– Not encapsulated
– Mitotic figures
– Herring bone pattern
5. Can grow rapidly toward end
– Destroys underlying bone (also, there is an intraosseous version of fibrosarcoma, so it could be perforating out of bone)
6. Treatment: radical surgical removal, including affected bone
– 5-year survival = 50%

Fibrous histiocytoma (fibroxanthoma, dermatofibroma):
1. Etiology: neoplasm of histiocytes, with fibrous differentiation; rare in mouth
2. GAL:
– None
– Middle-age and older (but skin lesions: young adults)
– Buccal, vestibule
3. Painless, firm nodular mass; no capsule
4. Micro: Very cellular proliferation of spindle cells with open nuclei (like histiocytes)
– Storiform pattern
– May see rounded histiocyte-like cells
– Malignant variants may look very benign microscopically
5. Can grow to considerable size
6. Treat: Moderately conservative surgical excision
– Recurrence = uncommon
7. Malignant variant: **malignant fibrous histiocytoma**
– Most common soft tissue malignancy in adults
– 40% recur
– 5-year survival = 30%

Pyogenic granuloma:
1. Etiology: Lack of reduction of granulation tissue during normal healing process; not an infection
– 50th most common mucosal lesion; prevalence = 1/10,000 adults
2. GAL:
– None (although strong female predilection in biopsied cases)
– Children & young adults
– Gingiva (75%), lips, tongue, buccal
– **Pregnancy tumor**: pyogenic granuloma of gingival papilla in pregnant woman (may be multiple)
– **Epulis granulomatosum**: pyogenic granuloma in poorly healed extraction socket
3. Painless erythematous mass (may be hemorrhagic) with lobulated surface

– Often ulcerated
4. Micro: Edematous granulation tissue with chronic and acute inflammatory cells
5. Generally remains less than 2 cm.
–May shrink over time
– May become **irritation fibroma**
– Pregnancy tumor may disappear after birth of baby
6. Treat: Conservative surgical excision
– For pregnancy tumor, wait until after birth, if possible
– May recur if original cause (infection, trauma) is not removed

Peripheral ossifying fibroma (peripheral cementifying/ossifying fibroma):
1. Etiology: Inflammatory proliferation of fibrous tissue with potential to make bone or cementum
2. GAL:
– 2/3 females
– Teenagers and young adults
–Gingival papilla (must be in this location)
3. Painless, red or pink firm mass
– May be lobulated
– May be ulcerated
– Often shows calcification on radiograph
4. Micro: Primitive spindle cells in fibrous stroma, with immature bone formation, often with osteoblasts
5. Usually remain less than 2 cm., occasionally up to 3 cm.
6. Treat: Conservative surgical excision with curettage of base
– And cleaning/scaling of adjacent teeth
– 15% recur

Peripheral giant cell granuloma (peripheral giant cell lesion; giant cell epulis):
1. Etiology: Inflammatory proliferation of phagocytic cells
– Secondary to local irritation or trauma or infection
2. GAL:
– 60% in females
– Fifth-sixth decades
– Gingiva (must be in this location)
3. Painless, perhaps hemorrhagic, red or bluish nodular mass
– Somewhat soft to palpation
– May cup out underlying bony cortex (**saucerization**)
– May show calcifications on radiograph;
– Often ulcerated
4.Micro: immature fibrous stroma with multinucleated giant cells,
– Extravasated erythrocytes
– Spindled mesenchymal cells
5. Generally remain less than 2 cm., may become more than 4 cm.
– No malignant transformation
6. Treat: Conservative surgical excision with curettage of base
– And cleaning/scaling of adjacent teeth

– 10% recur
– Caution: large or multiple or recurring lesions might be **brown tumor of hyperparathyroidism**

Lipoma:
1. Etiology: benign neoplasm of fat cells; some are developmental
   – Most common soft tissue tumor in the body, but not so common in the mouth
   – 38th most common mucosal lesion in adults
   – Prevalence = 3/10,000
2. GAL:
   –None
   – Middle-aged
   – Buccal, vestibule
3. Painless, sessile, yellowish, soft mass
4. Micro: mature adipocytes with collagen trabeculae
   – May or may not be encapsulated
   – May "infiltrate" great distances into surrounding stroma
5. Slowly enlarge, usually remain less than 3 cm.
   – No malignant transformation
6. Treat: conservative surgical excision
   – Usually do not recur
   – Except the infiltrating types

Liposarcoma:
1. Etiology: malignant neoplasm of adipocytes
   – Second most common soft tissue sarcoma of adults (after malignant fibrous histiocytoma)
2. GAL:
   – None
   – 40-60 years of age
   – Neck (most common H&N site), buccal (50% of oral lesions), tongue
3. Soft, slowly enlarging, ill-defined submucosal mass
   – Yellow color, if superficially located, otherwise pink in color
   – Pain or tenderness are uncommon except in late stages

5-year survival = 60-70%

Traumatic neuroma:
1. Etiology: reactive proliferation of neural tissue after nerve injury
2. GAL: none; middle-aged; mental foramen
3. Smooth-surfaced soft, nonulcerated nodule; less than half are tender or painful, may be burning
4. Micro: Intertwining, tortuous nerve fibers in a fibrous stroma
5. Usually remain less than 1 cm.; no malignant transformation
6. Treat: conservative surgical excision with small part of affected nerve
   – May lead to paresthesia and pain may recur

Neurofibroma:
1. Etiology: benign neoplasm of Schwann cells and perineural fibroblasts

– The most common peripheral nerve tumor

2. GAL:
   – None
   – Young adults
   – Tongue, buccal
3. Smooth-surfaced soft, nonulcerated nodule
   – Painless
   – May be huge and pendulous
4. Micro: Well circumscribed interlacing bundles of spindle-shaped cells with wavy nuclei, in a fibrous stroma
5. Usually remain less than 2 cm., may become huge
   – Oral lesions seldom become malignant, less likely than skin lesions
6. Treat: conservative surgical excision
   – Recurrence is rare
7. Unique disease: **Neurofibromatosis type I** (**von Recklinghausen disease**):
   – Multiple neurofibromas (some **schwannomas**) throughout body (maybe hundreds)
   – Autosomal dominant inheritance (gene is on chromosome 17)
   – 5-10% chance of malignant development
   – **Café au lait spots** (brown skin patches)
   – Oral lesions in 1/4 of cases
   – Abnormal bone development
   – **Lisch nodules** (brown spots on iris)

Neurilemoma (Schwannoma):

1. Etiology: benign neoplasm of Schwann cells
   – Up to half occur in head and neck area
2. GAL:
   – None
   – Young adults and middle-aged;
   – Tongue, hard palate
3. Smooth-surfaced, nonulcerated soft nodule
   – Painless
4. Micro: Encapsulated with two tissue types:
   – **Antoni A** (streaming fascicles of spindled Schwann cells forming **Verocay bodies**)
   – **Antoni B** (disorganized neurites in loose fibrous stroma)
5. Usually remain less than 2 cm
   – Oral lesions seldom become malignant, skin lesions can but it is uncommon
6. Treat: conservative surgical excision
   – Recurrence is rare

Malignant peripheral nerve sheath tumor (neurofibrosarcoma; malignant schwannoma)

– Dysplastic spindle cells
– Few recognizable nerves
– Treat: radical surgery
– 5-year survival = 40-50%

Multiple mucosal neuromas syndrome (multiple endocrine neoplasia syndrome III; MEN III; MEN IIB):

1. Etiology: Autosomal dominant inherited disease with multiple tumors or hypeplasias of neuroendocrine tissues
   - – Mutation of RET protooncogene on chromosome 10
   - – Rare, but oral signs are often the first evidence of disease
2. GAL:
   - – None
   - – Teenagers and young adults
   - – Tongue, lips
3. Sessile, smooth-surfaced, painless yellowish white, soft nodules
   - – Narrow face
   - – Long extremities
   - – Abraham Lincoln appearance
   - – Weak muscles
   - – **Pheochromocytomas** (50%)
   - – **Medullary thyroid carcinomas** (90%)
   - – Elevated serum and urinary calcitonin (from thyroid tumor)
   - – Elevated urinary vanillylmandelic acid (VMA)
   - – Increased epinephrine-to-norepinephrine ratio (from adrenal tumor)
4. Micro: intertwining, tortuous nerve fibers with thick perineurium and with spaces (artifactual) around them
5. Oral neuromas remain small (less than 5 mm)
   - – Oral neuromas do not become malignant
6. Treat: no treatment needed for oral lesions, except for esthetic purposes
   - – Treat systemic problems and tumors

Melanotic neuroectodermal tumor of infancy (progonoma; retinal anlage tumor):

1. Etiology: neoplasm of neural crest cells
   - – Very rare
2. GAL:
   - – None
   - – Infancy; newborns
   - – Anterior maxillary alveolus
3. Rapidly expanding blue/black painless mass
   - – Usually destroys underlying bone
   - – Elevated urinary vanillylmandelic acid (VMA), from oral tumor
4. Micro: two cell types:
   - – Small dark round neuroblastic cells
   - – Large epithelioid cells with melanin deposits
5. May reach alarming size and destroy much of the anterior alveolar bone
   - – Malignant variants have been reported (very rare)
6. Treat: Moderately severe surgical excision
   - – 15% recurrence

Granular cell tumor (granular cell myoblastoma):

1. Etiology: benign neoplasm of Schwann cells
    – Originally thought to be from striated muscle cells
2. GAL:
    – 2x females
    – Fourth-sixth decades
    – Tongue (50% of all body cases)
3. Sessile, painless, pale firm mass
4. Micro: large, polygonal cells (like histiocytes) with granular cytoplasm and small nuclei, in sheets and globules
    – May be spindled and infiltrate between muscle fibers
  – Problem: **pseudoepitheliomatous hyperplasia** may look like **squamous cell carcinoma**
5. Usually remain 1-2 cm., seldom enlarge after initial notice
    – No malignant transformation risk
6. Treat: conservative surgical excision
    – Recurrence is very rare

Granular cell epulis (congenital epulis):
1. Etiology: developmental tumor of unknown histogenesis
2. GAL:
    – Strong female predilection (90%)
    – Newborn
    – Anterior maxillary alveolus
3. Pedunculated, soft, smooth-surfaced pink or pale nodule
4. Micro: large, polygonal cells with granular cytoplasm
    – Like cells in granular cell tumor, but with different immunohistochemistry
5. Usually remains less than 2 cm but may become up to 9 cm
6. Treat: conservative surgical excision as soon as baby can tolerate surgery
    – Does not recur
    – If left untreated, small lesions shrink and often disappear (they do not interfere with eruption)

Hemangioma:
1. Etiology: benign developmental growths or benign neoplasms
  – 6th most common oral mucosal lesion
    – Prevalence = 6/1,000 adults
  – Head and neck is the most common location in the body
2. GAL:
    – 3x females
    – Children and teenagers
  – Seldom congenital, but develop shortly after birth
    – Tongue, buccal, lips
3. Sessile, often lobulated soft red, painless and smooth-surfaced mass
    – Fluctuates and blanches
    – Blue color if venous blood; red if arterial
    – On skin: **port wine stain**, **berry angioma**

4. Micro: many dilated (**cavernous hemangioma**) or collapsed (**capillary hemangioma**) endothelium-lined channels without encapsulation, endothelial nuclei are enlarged in growing lesions
5. Infancy lesions may spontaneously regress, later lesions do not
    – Some lesions continue to enlarge throughout growth of the patient, perhaps even after
    – No cancer development
  – Problem: hemorrhage
6. Treat: often left alone
    – Childhood lesions might respond to corticosteroids or interferon-"-2a
    – Laser therapy can be effective
    – Injection of sclerosing solutions, such as 95% ethanol

Angiosarcoma:
    – Similar clinical appearance to hemangioma but rapid growth
    – Poor prognosis (10-year survival = 21%)
  – **Hemangioendothelioma** = a vascular neoplasm with features intermediate between **hemangioma** and angiosarcoma

Sturge-Weber angiomatosis (Sturge-Weber syndrome, encephalotrigeminal angiomatosis):
1. Etiology: vascular plexus forms around cephalic part of neural tube at six weeks but does not regress after the ninth week (as is usual)
    – Rare
    – Not inherited
2. GAL:
    – None
    – Congenital
    – Face, buccal, maxilla
3. Purple/red macule(s) of trigeminal nerve distribution of face (**port wine stain**, **nevus flammeus**)
    – Often with involvement of oral mucosa
    – Angiomas of ipsilateral leptomeninges may cause seizures or mental retardation
    – Calcifications of gyri
4. Micro: same as cavernous hemangioma above
5. Vascular macule remains constant throughout life, oral lesions may cause hemorrhage
6. Treat: laser therapy might reduce color of port wine stain; intraoral lesions are treated with sclerosing solutions

Kaposi sarcoma (Kaposi's sarcoma):
1. Etiology: vascular proliferation (neoplasm?) in **AIDS**
    – Stimulated by herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus)
2. GAL:
    – Strong male predilection
    – Young adults and middle-aged
    – Tongue, lips, gingiva

3. Soft-to-firm red or purple macules or nodular mass
    – Painless
    – Nonhemorrhagic
4. Micro: Combination of proliferating spindled cells and endothelial cells
    – Extravasated erythrocytes
    – **Staghorn clefts**
5. Multiple purple, brown or red soft masses
    – May be macule
    – Granular or lobular surface
    – Slowly enlarge, with new lesions developing over time
6. Treat: lesions disappear with successful AIDS treatment (protease inhibitors, etc.)

Traumatic angiomatous lesion (venous pool, venous lake, venous aneurysm):
1. Etiology: acute trauma to subepithelial vein, with focal dilation or "aneurysm"
2. GAL:
    – None; middle-aged and older; lips, buccal
3. Small, painless red bleb
    – Blanches
4. Micro: single dilated venous structure
    – Perhaps with **thrombus** in the lumen (may calcify)
5. Remains indefinitely the same after first few weeks
    – Usually remains less than 4 mm
    – No malignant development
6. Treat: conservative surgical removal
    – OK to leave alone, except for esthetics

Lymphangioma:
1. Etiology: benign neoplasm or hamartoma of lymph vessels
2. GAL:
    – None
    – Children and teenagers
    – Tongue (produces **macroglossia**)
3. Soft painless cluster of clear blebs
    – Often with outlying or satellite blebs several mm from main mass
    – May be only scattered vesicle-like blebs
4. Micro: same appearance as **hemangioma**, but without the blood cells in the lumina
5. Slowly enlarges with body growth
    – No spontaneous regression, as with **hemangioma**
    – No cancer development
6. Treat: conservative surgical removal
    – Usully deliberately leave some tumor behind (debulking)
    – Repeat surgery is not uncommon
7. Unique lesion: **cystic hygroma**: congenital cavernous lymphangioma of lateral neck

Lymphangiosarcoma
    – Malignancy of lymph vessels

– Similar clinical appearance to lymphangioma but more rapid and larger growth
– Dysplastic endothelial lining cells around lumina without erythrocytes
– Poor prognosis

Leiomyoma:

1. Etiology: benign neoplasms of smooth muscle
   – Very rare
2. GAL:
   – None
   – Infancy or childhood
   – Tongue, lips
3. Usually sessile, firm, painless mass
   – Normal surface color and smooth surface
4. Micro: cellular proliferations of smooth muscle cells
   – Usually encapsulated
5. Usually remain less than 2 cm.
   – No cancer transformation
6. Treat: conservative surgical removal
   – Few recurrences

Rhabdomyoma:

1. Etiology: benign neoplasms of striated muscle
   – Very rare
2. GAL:
   – None
   – Infancy or childhood
   – Tongue, lips
3. Usually sessile, firm, painless mass
   – Normal surface color and smooth surface
4. Micro: cellular proliferations of striated muscle cells
   – Usually encapsulated
5. Usually remain less than 2 cm.
   – No cancer transformation
6. Treat: conservative surgical removal
   – Few recurrences

Leiomyosarcoma

– Lobulated, relatively firm mass
– May have surface ulceration
– Treat: radical surgery
– Poor prognosis

Rhabdomyosarcoma

– Lobulated, relatively firm mass
– May have surface ulceration
– Treat: radical surgery

– 70% 5-year survival

Cartilaginous choristoma (soft tissue chondroma; chondroid hamartoma):
1. Etiology: tumor-like proliferation of normal tissue (cartilage) in the wrong place
2. GAL:
   – None
   – Teens and young adults (probably started much earlier)
   – Tongue
3. Sessile, firm, painless mass with normal surface color or pallor
4. Micro: Normal cartilage (hyaline or fibrous) in a fibrous stroma
5. Usually remain 1-2 cm
   – No cancer transformation
6. Treat: conservative surgical removal
– No recurrence
7. Special variant: **Cutright tumor**:
   – Presumably secondary to continuing, low-level trauma
   – Older persons
   – Anterior maxillary alveolar midline
   – Firm, sessile nodule under denture
   – Treat: conservative surgical removal and fix denture (seldom recurs)

Osseous choristoma (soft tissue osteoma):
1. Etiology: tumor-like proliferation of normal tissue (bone) in the wrong place
2. GAL:
   – None
   – Teens and young adults (probably started much earlier)
   – Tongue
3. Sessile, firm, painless mass with normal surface color or pallor
   – Painless
4. Micro: Normal but immature bone (perhaps with marrow) in fibrous stroma
5. Usually remain 1-2 cm
   – No cancer transformation
6. Treat: conservative surgical removal
   – No recurrence

Metastasis to the oral cavity:
1. Etiology: metastatic spread from an extraoral source, usually carcinoma
   – Usually from lung, breast and gastrointestinal cancers
   – 1-2% of all oral cancers
2. GAL:
   – Moderate male predilection
   – Middle-aged and older
   – Gingiva, tongue
3. Firm, smooth-surface nodule with normal color
   – May have surface ulceration

– May be painful

4. Micro: same appearance as the primary cancer
5. Enlarge rapidly
   – Eventually with surface ulceration
6. Treat: radical surgical excision, radiotherapy or chemotherapy
   – Depending on the condition of the primary tumor and other metastases