Salivary gland pathology

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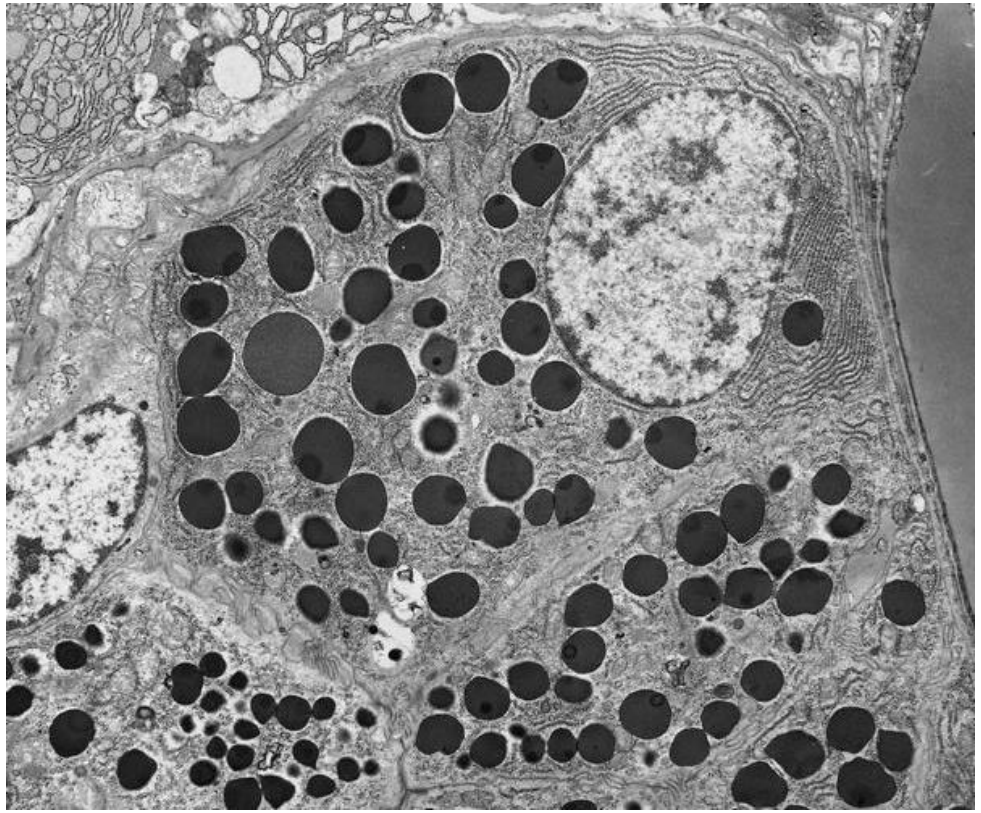
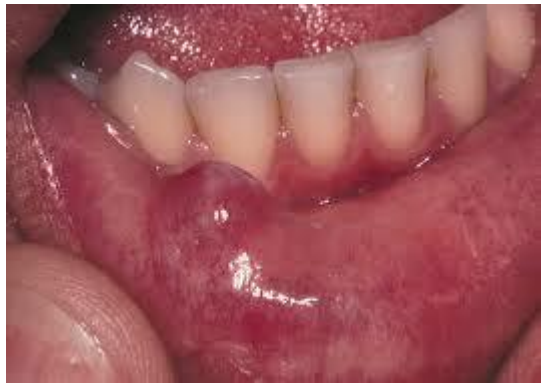
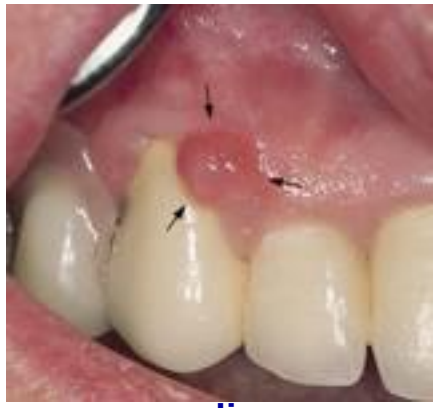
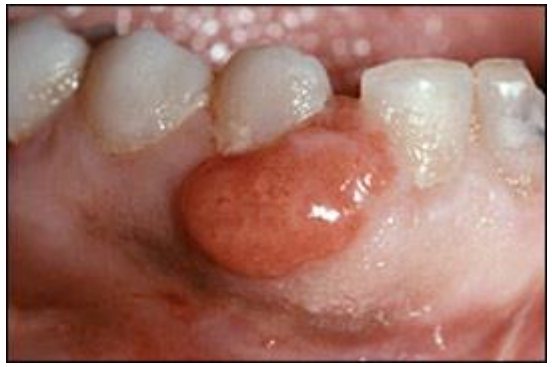




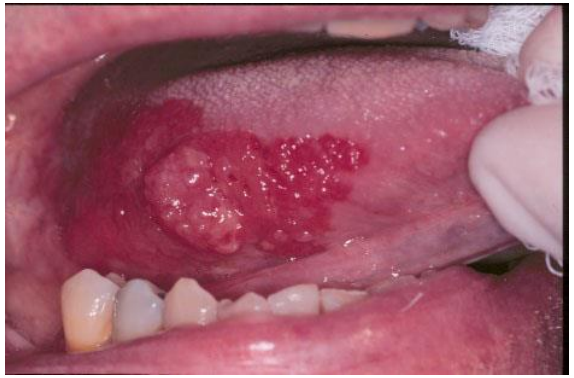
mucocele



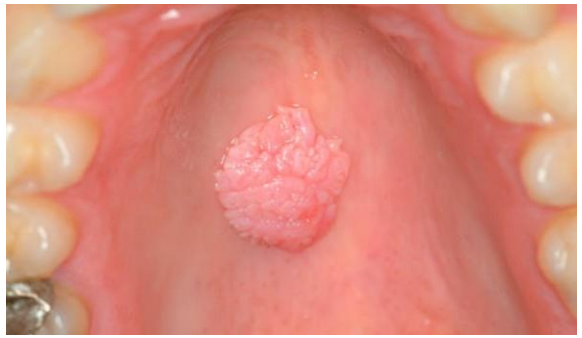
epulis



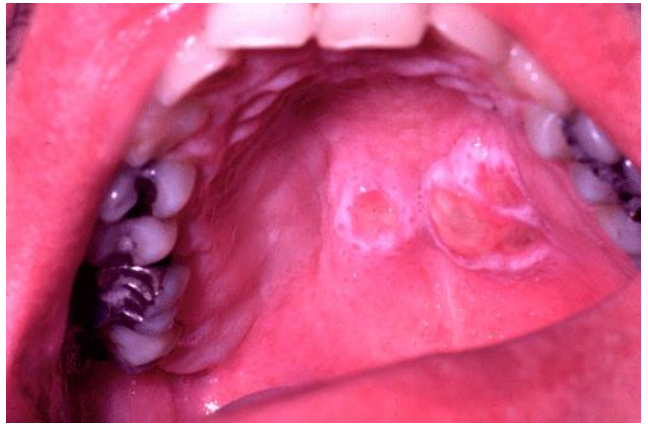
pyogenic granuloma



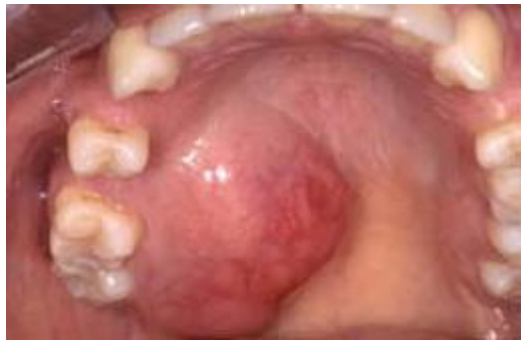
squamous cell cc.



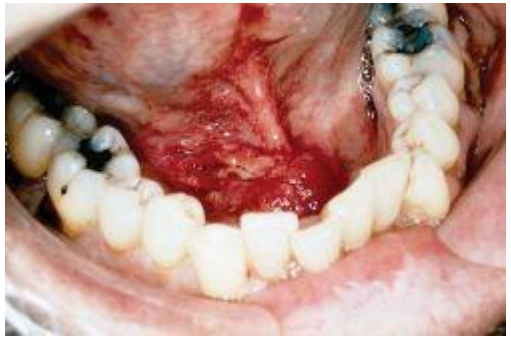
papilloma



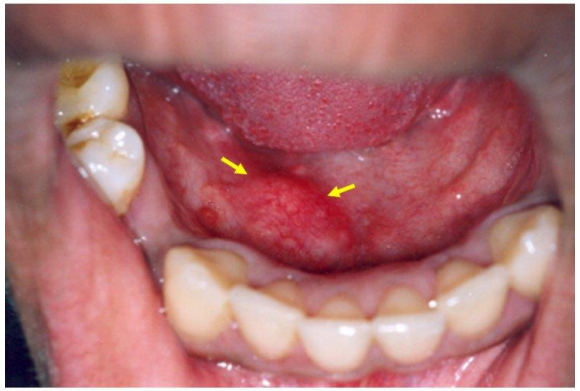
necrotising sialometaplasia



pleomorphic adenoma

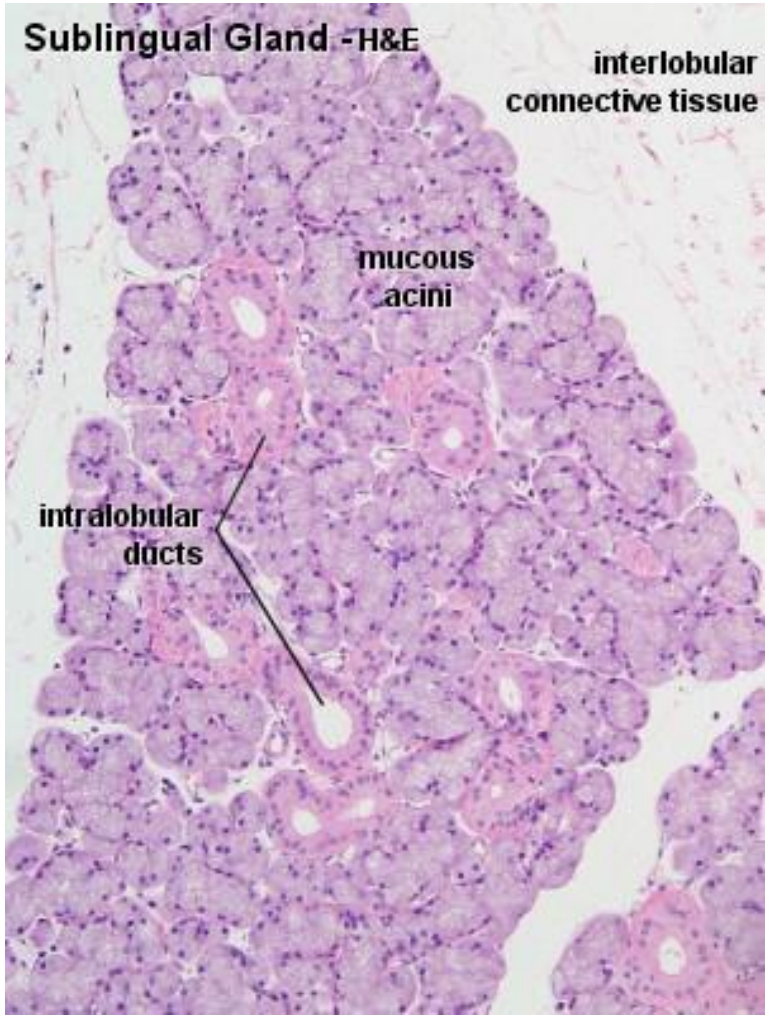


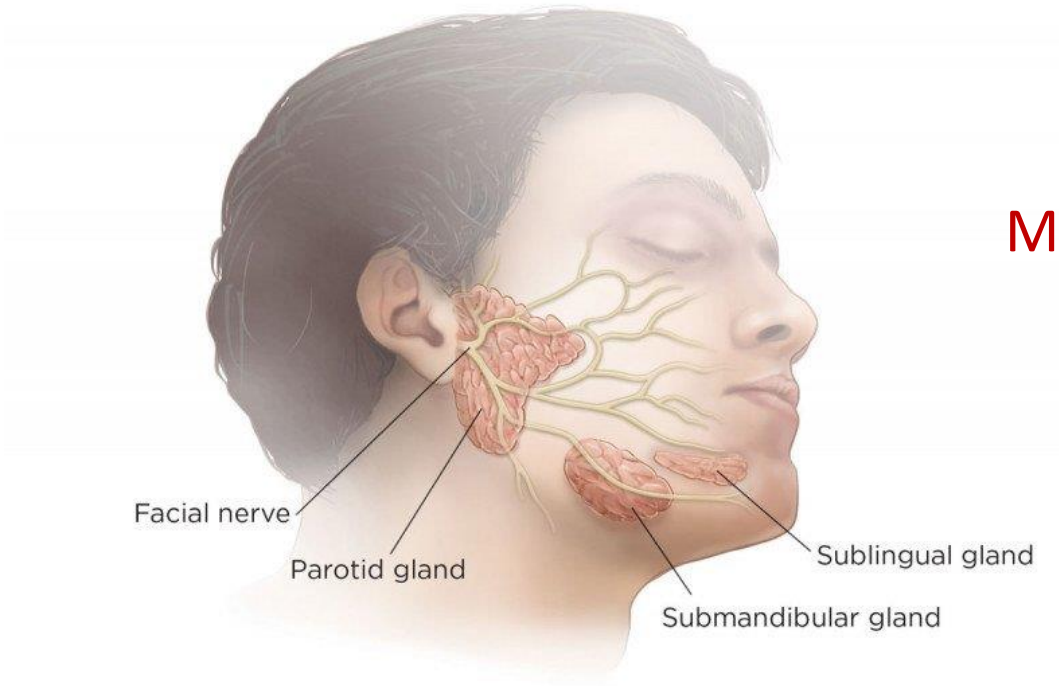
adenoid cystic cc.

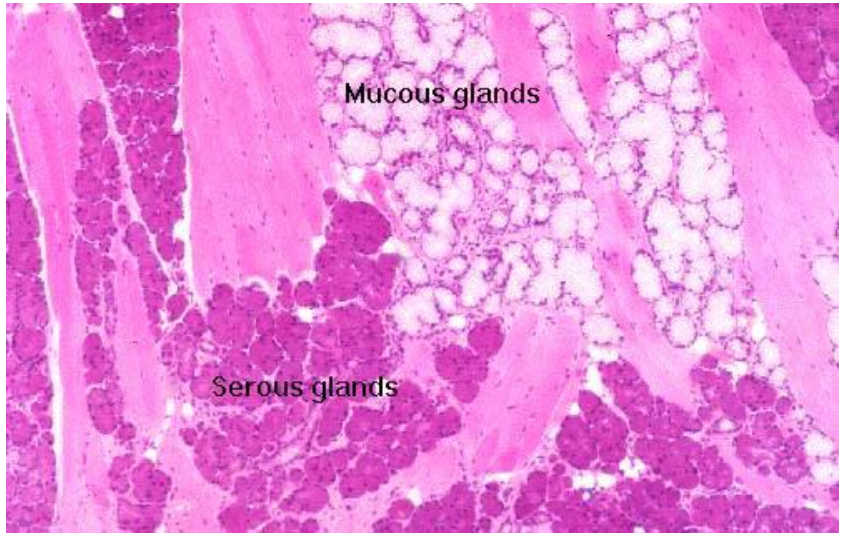


mucoepidermoid cc.

Major salivary glands





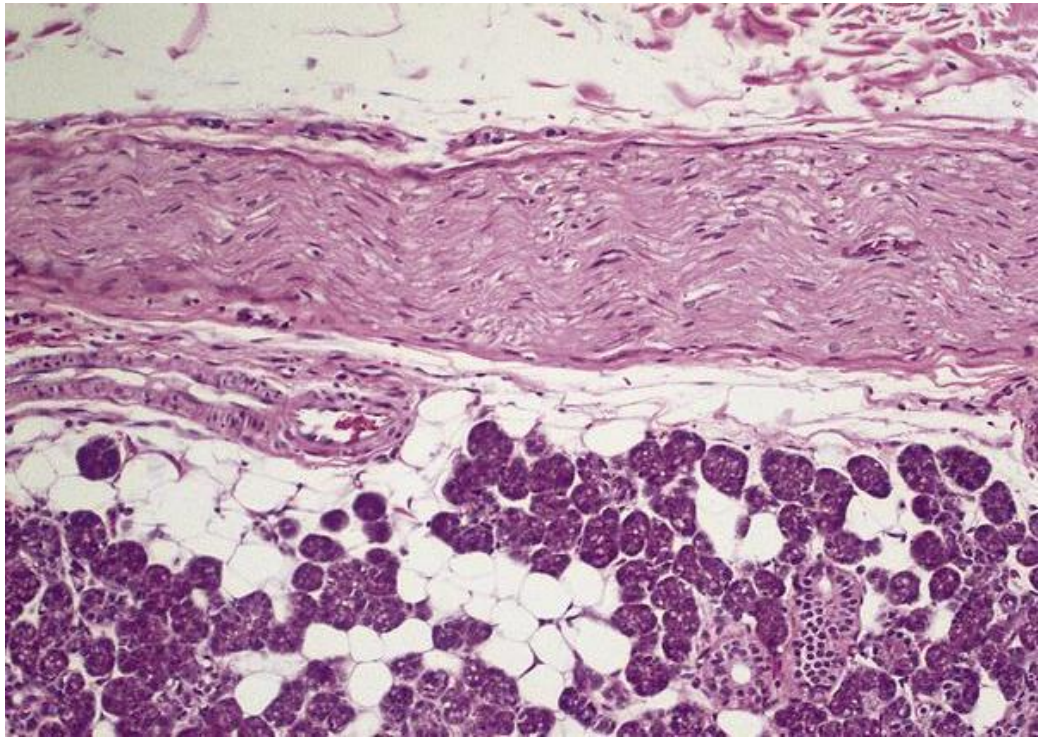


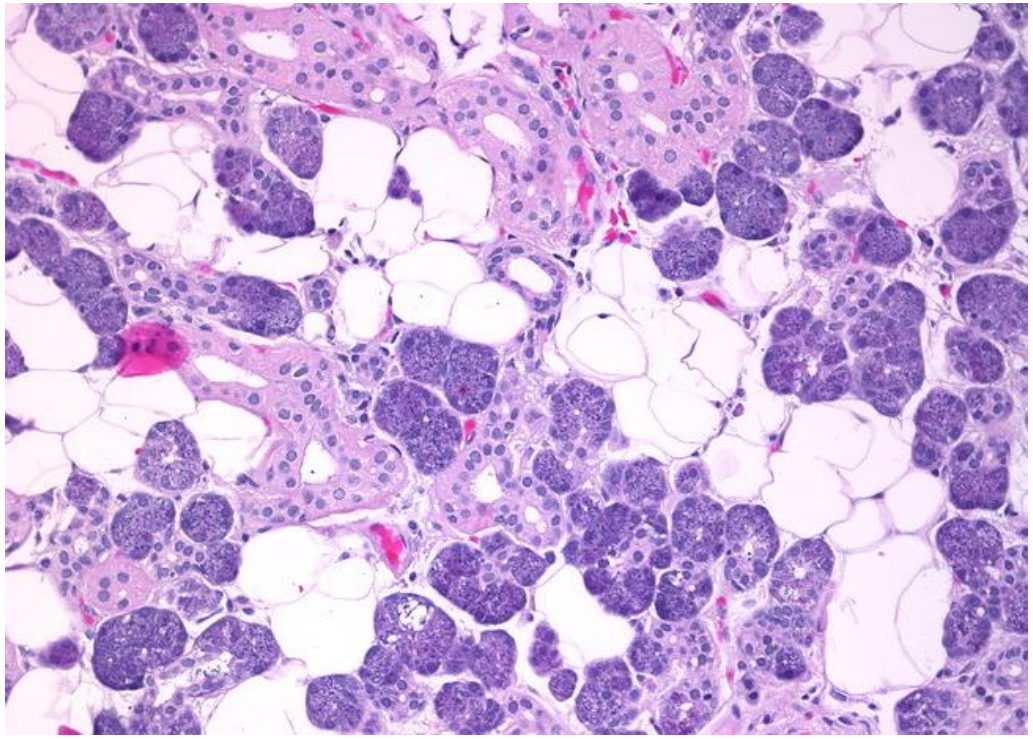
Serous glands produce thin watery fluid containing alpha amylase, which digest starches

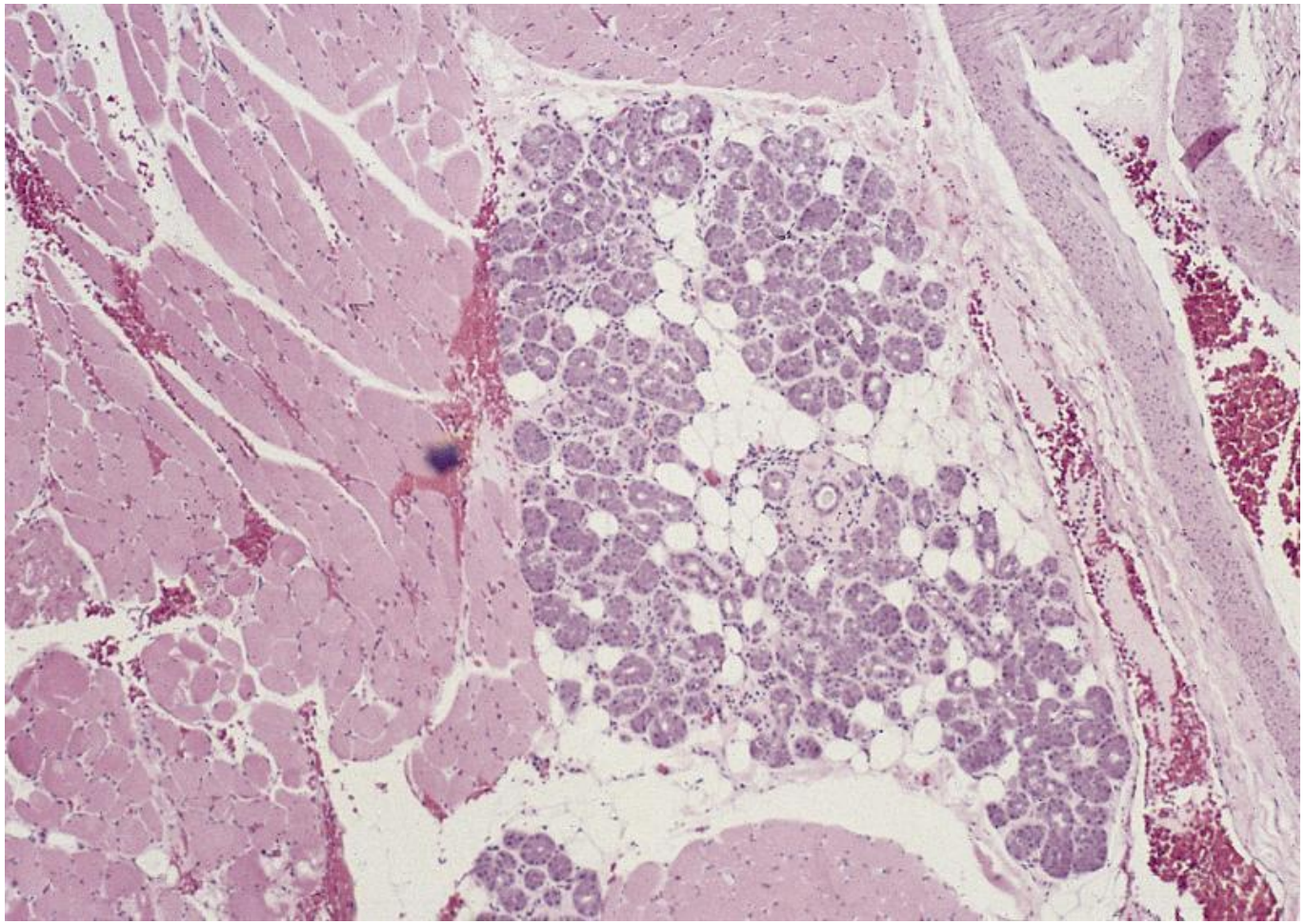
Mucinous glands produce viscous mucinous fluid higher in glycoproteins, which provides a lubricating film on oral mucosa

Minor salivary glands

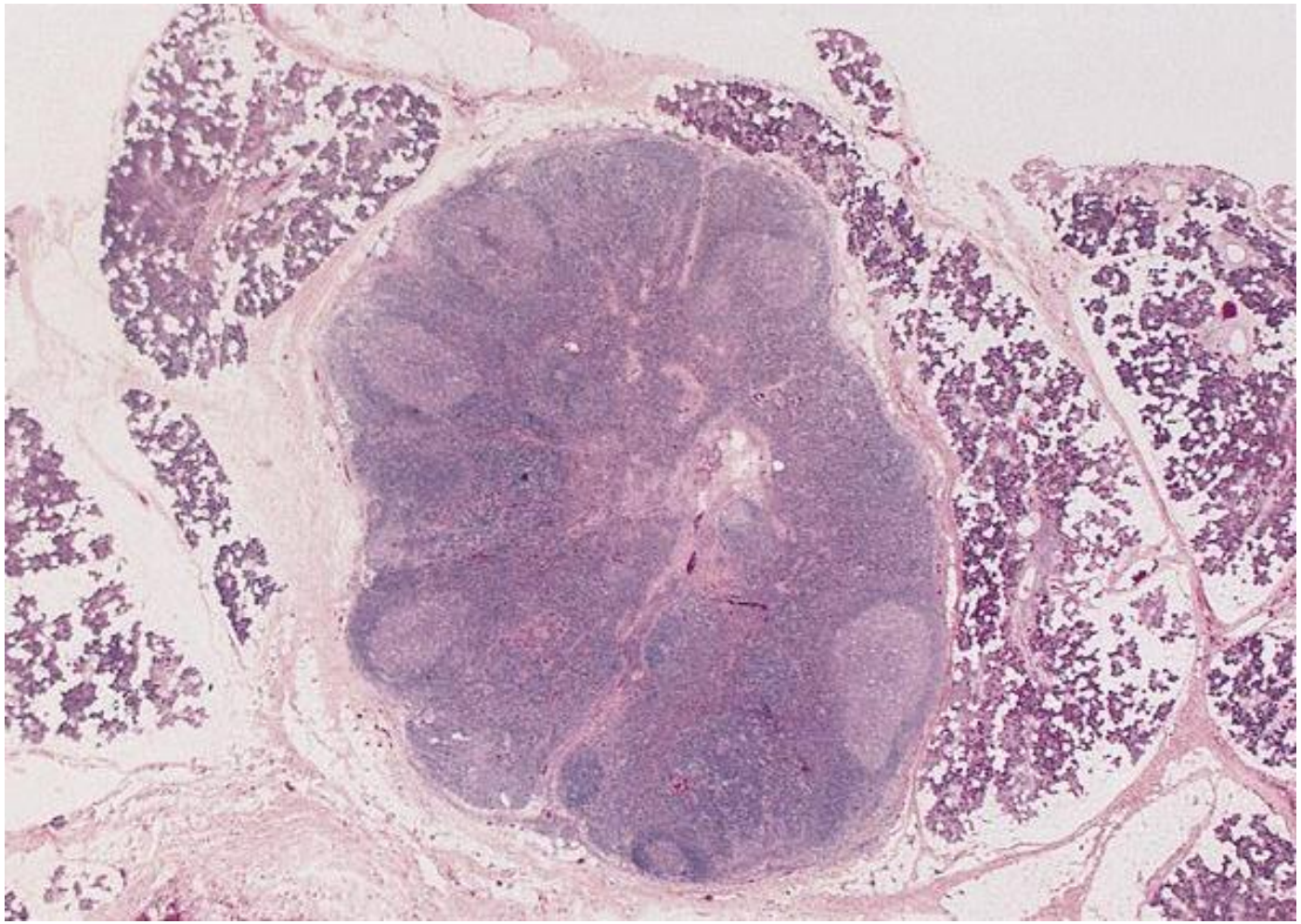
- Except for the gingiva and anterior hard palate, minor salivary glands (500-1000, 1-5 mm each) are located throughout the submucosa of the oral cavity
- More numerous in posterior hard palate
- Each salivary unit has its own simple duct
- Mainly the minor salivary glands are mucinous



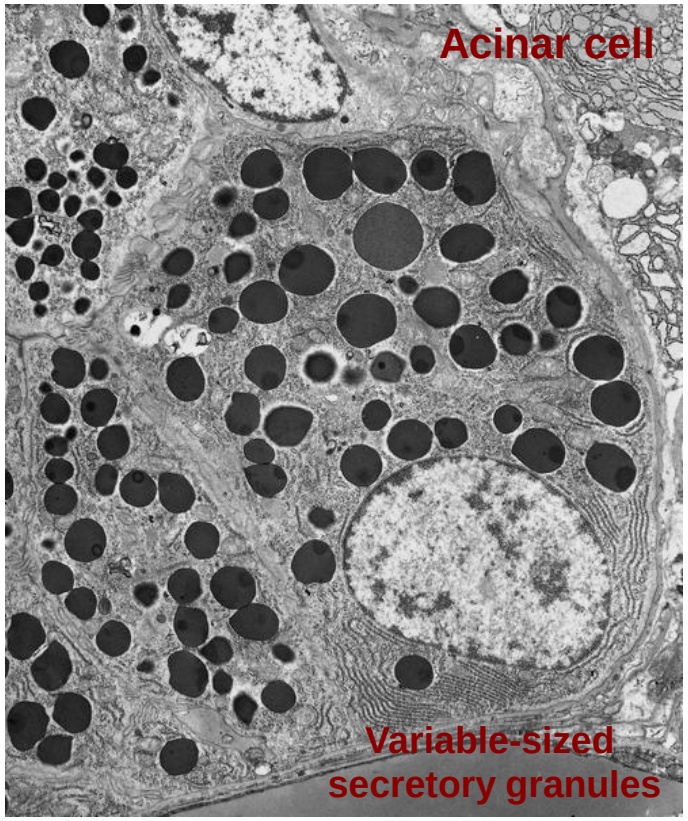


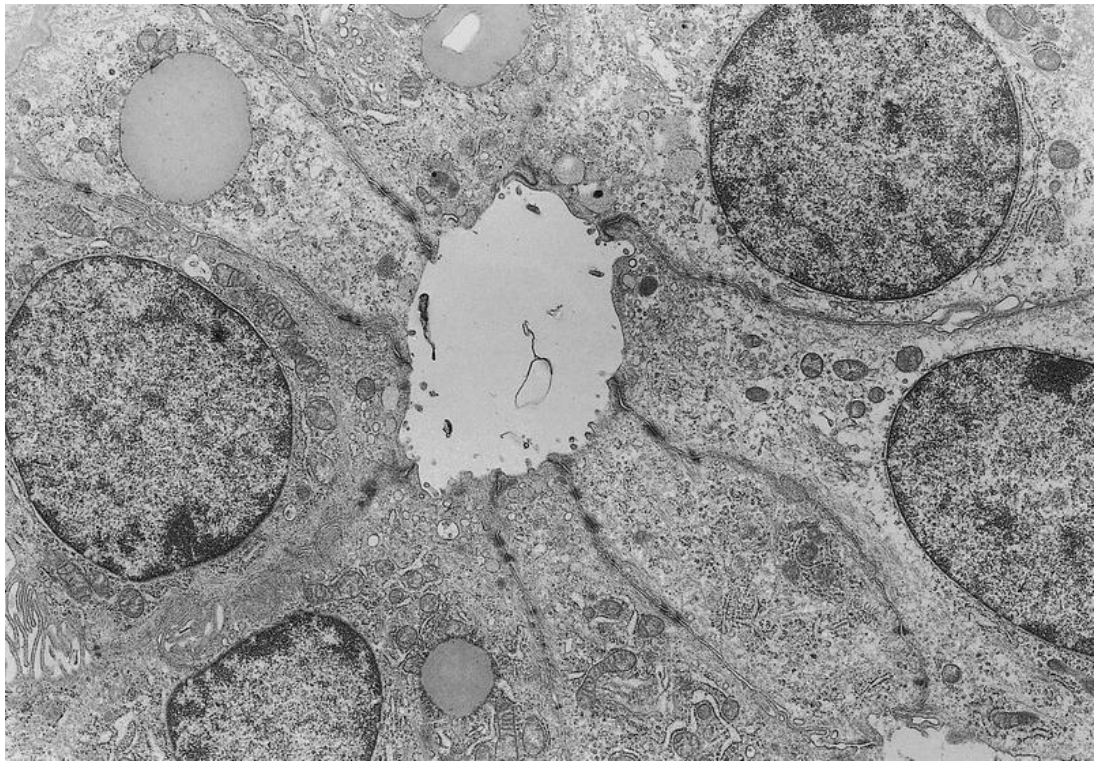


The minor salivary glands are small aggregates of unencapsulated mucous or serous glands.
In the tongue they are in intimate contact with the striated muscle tissue.

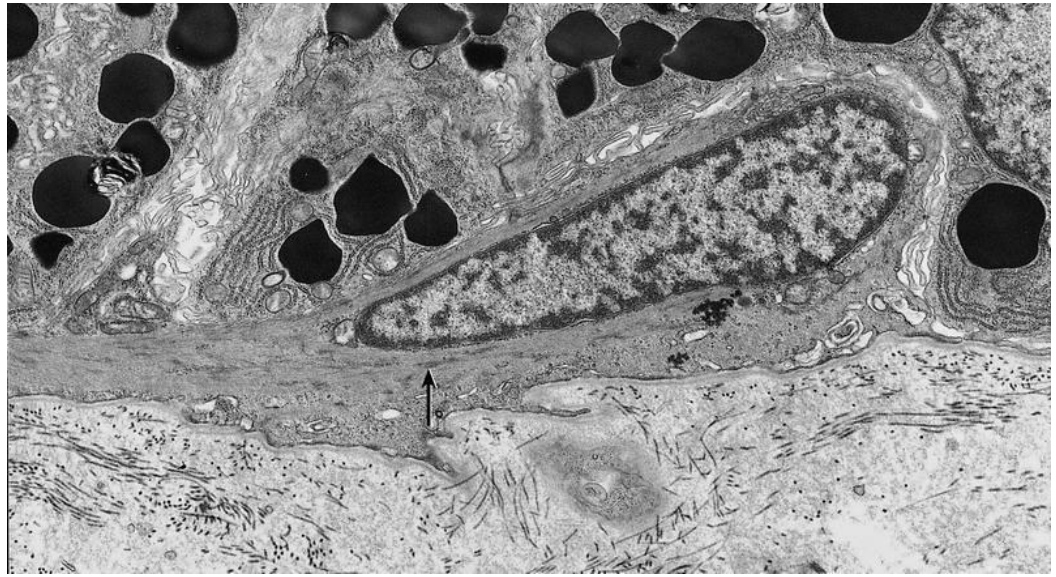


Intraparotid lymph nodes are encapsulated
and have subcapsular sinuses and germinal centers.

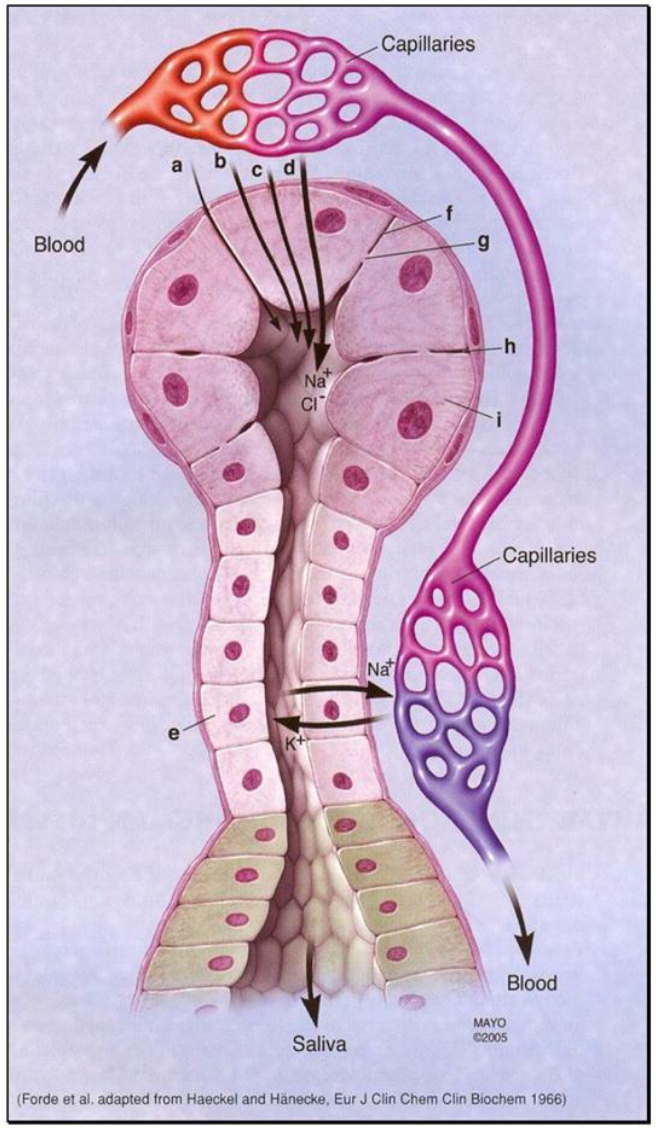




Intercalated duct cells: few special ultrastructural features



The myoepithelial cell lies between the basal lamina and the basal plasma membranes of the acinar cells.



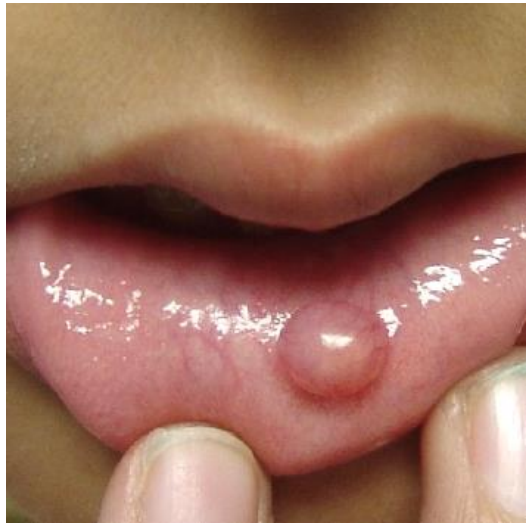
Mechanism of molecular transport from serum into salivary gland ducts

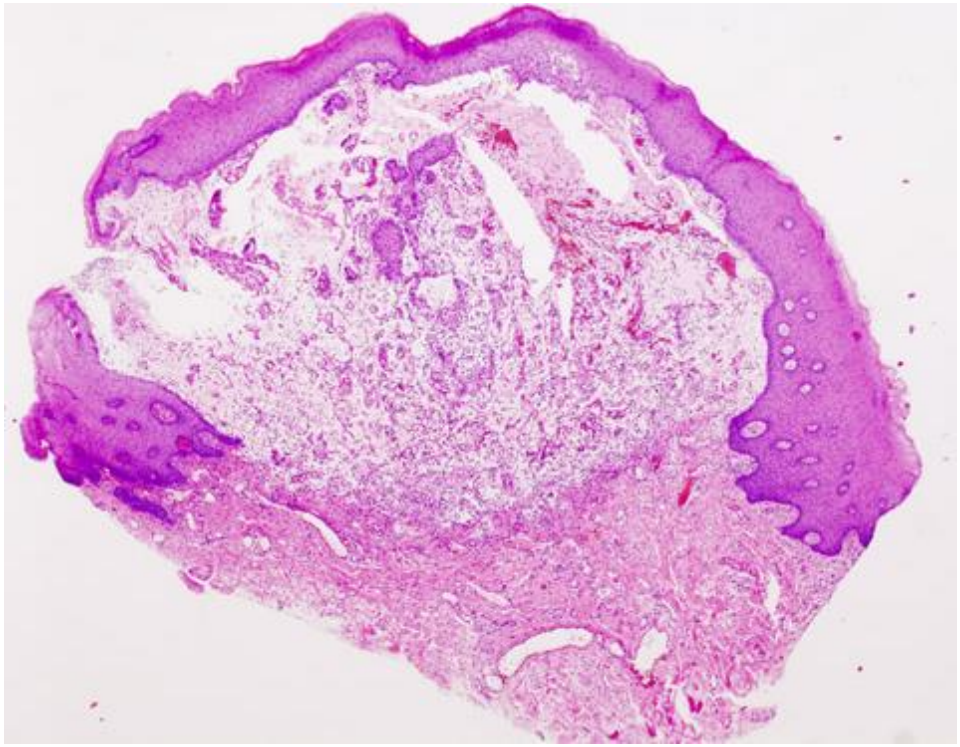
Saliva

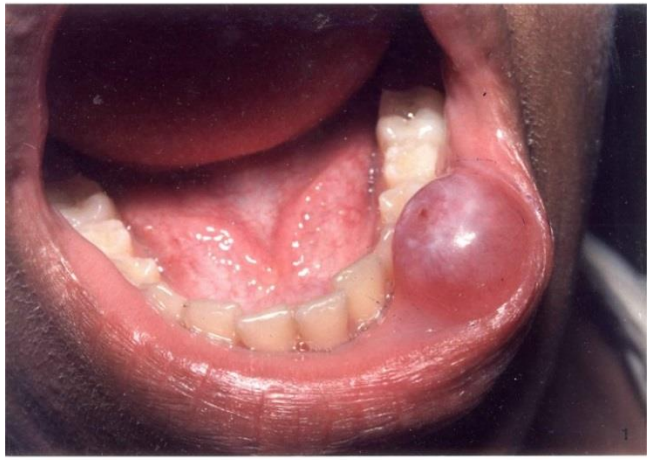
- Formed by acinar cells
- High in amylase if secreted by serous glands
- High in sialomucin (neutral and acid) if secreted by mucous glands
- Saliva may be used for diagnostic testing, because it is composed of various molecules that are filtered, processed and secreted from the vasculature that nourish the salivary glands.

Mucocele

- A "mucous cyst of the oral mucosa" is a clinical term that refers to two related phenomena: mucus extravasation phenomenon, and mucus retention cyst.
- Swelling of connective tissue consisting of collected mucin due to a ruptured salivary gland duct usually caused by local trauma
- Most common location: the surface of the lower lip
- Bluish translucent color, and is more commonly found in children and young adults

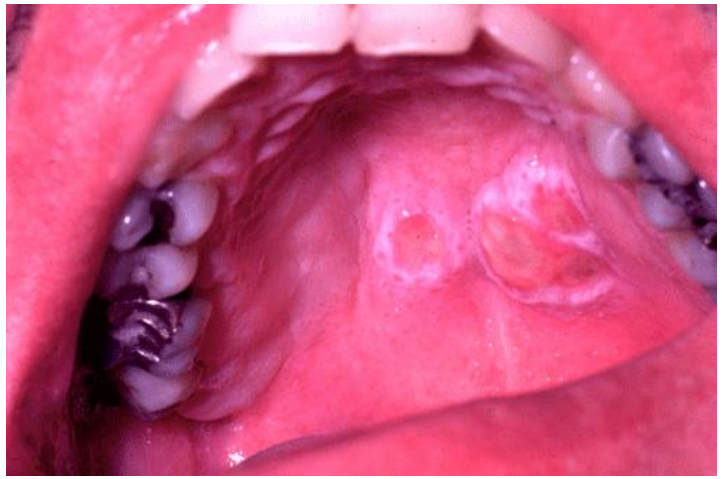




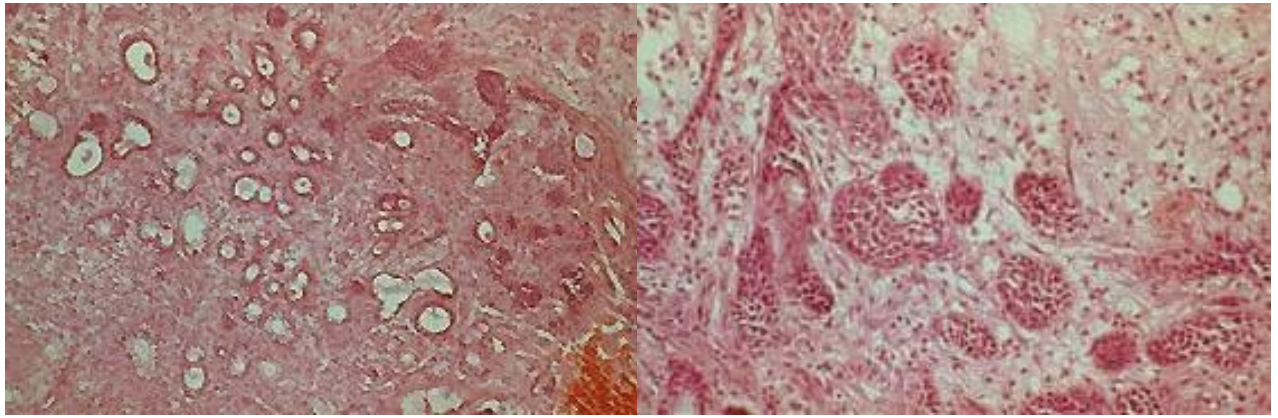


Necrotizing sialometaplasia

Reactive, self resolving condition of minor or occasionally major salivary glands, often hard or soft palate, probably due to ischemia or vasculitis



Crater-like ulcerated lesion of hard palate



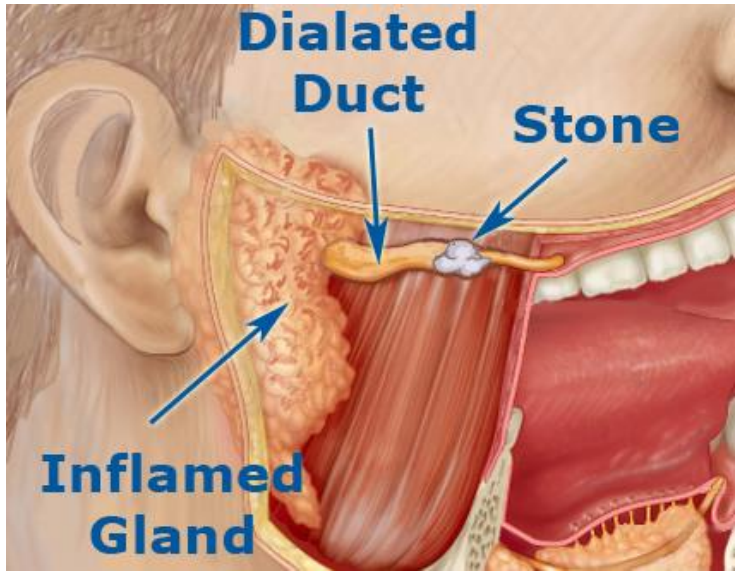
- **Ulcerated surface mucosa**
- **Intraductal proliferation of metaplastic squamous epithelium containing trapped mucous cells in lobular but noninfiltrative pattern**

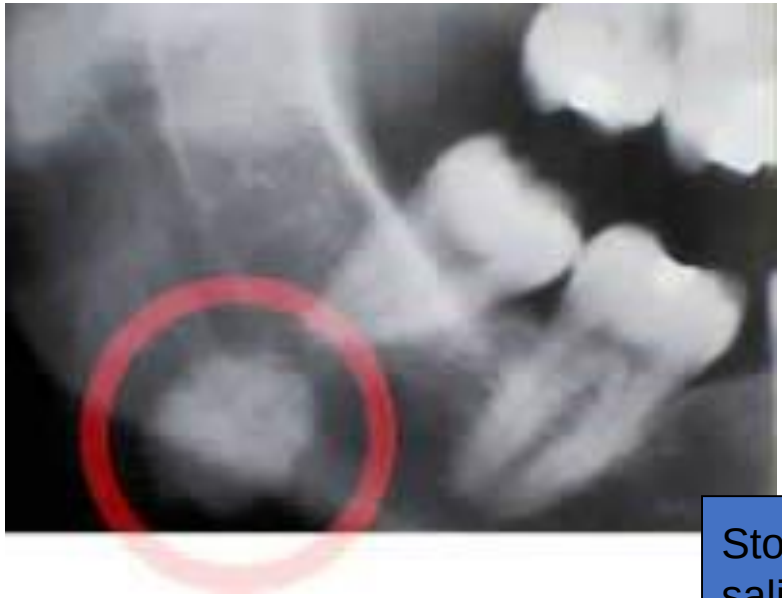
Differential diagnosis: Squamous cell carcinoma, mucoepidermoid carcinoma, post-radiation changes

Sialadenitis

Bacterial, acute sialadenitis

- Rare, usually due to ascending infection of ductal system by Staph aureus, Staph viridans or gram negative bacteria
- Predisposing factors include obstructive lesions such as sialolithiasis, dehydration, malnutrition or immunosuppression
- Usually presents with unilateral painful enlargement of salivary gland
- May cause abscess requiring surgical drainage

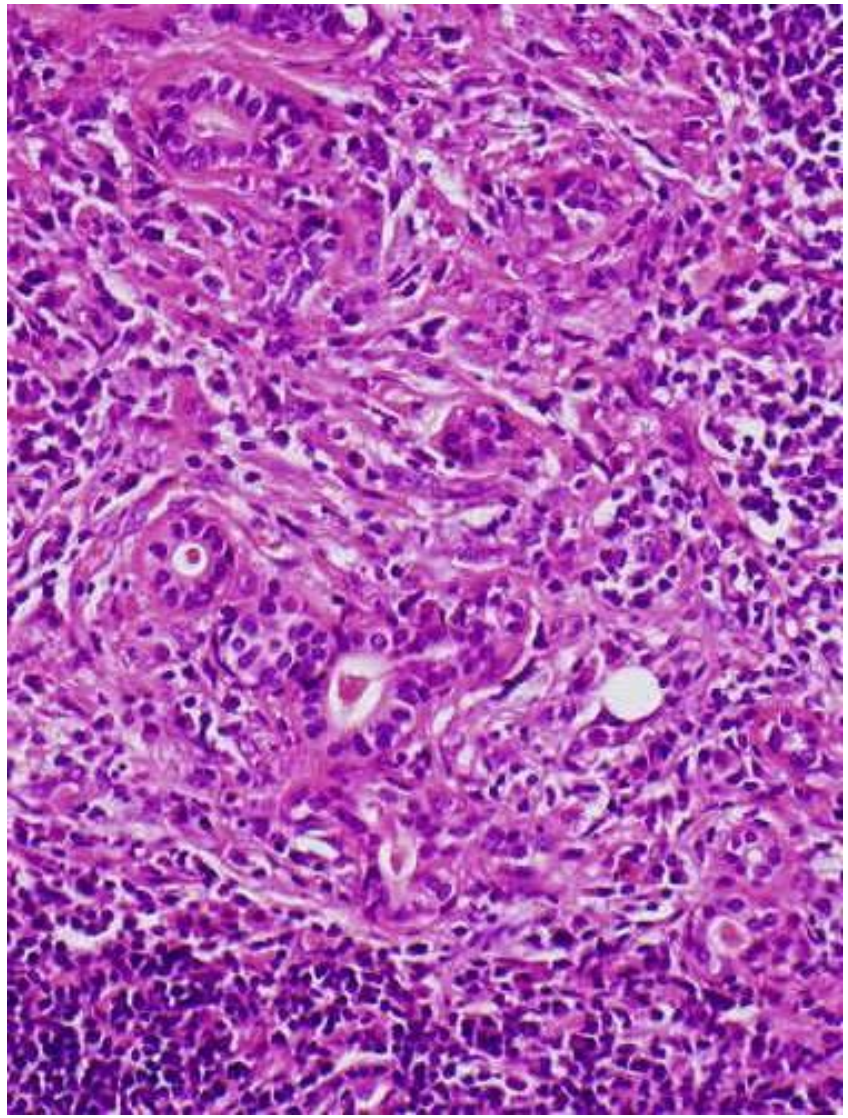




Stones (calculi) within salivary ducts
Most common within submandibular gland
Stones may have foreign body or bacterial core

Chronic sialadenitis

- Also called lymphoepithelial sialadenitis
- Relatively common
- Chronic lymphocytic inflammation, often without symptoms
- Associated with obstruction (with atrophy and fibrosis), rheumatoid arthritis (older women), Sjogren's syndrome, sialolithiasis, mumps
- 50% are monoclonal by PCR, but MALT lymphoma has ducts surrounded by broad coronas of monocytoid cells,
- Micro description: markedly hyperplastic lymphoid infiltrates with loss of salivary gland acini; ducts are surrounded by and infiltrated by lymphoid cells

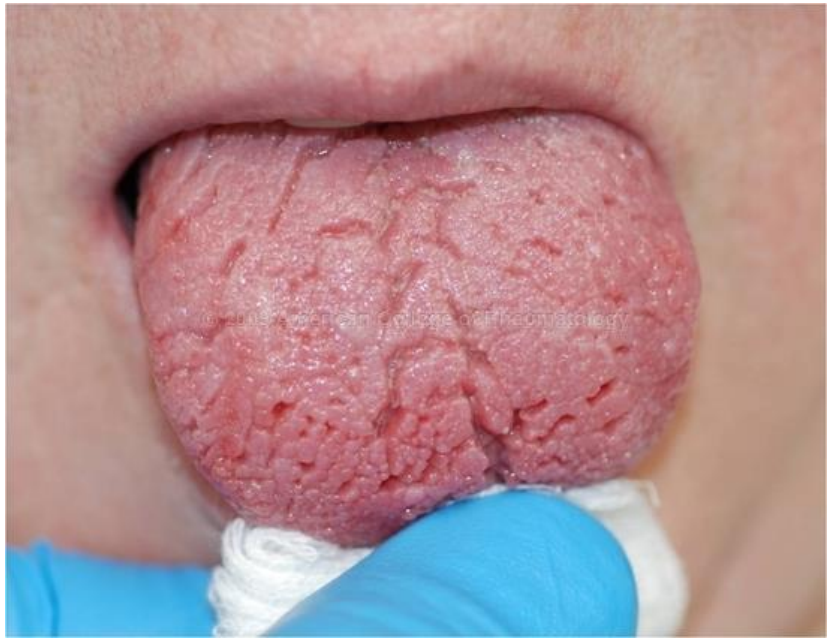


Chronic sclerosing sialadenitis

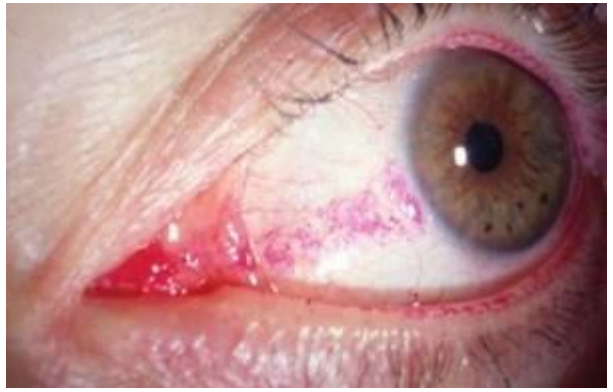
- Presents as stony hard Kuttner's tumor if involves the submandibular gland

Sjogren's syndrome
(sicca syndrome)

- Systemic autoimmune disease presenting typically with xerostomia (dry mouth), keratoconjunctivitis sicca (dry eyes), rheumatoid arthritis, hypergammaglobulinemia
- Occasionally involving lymph nodes, lung, kidney, bone marrow, skeletal muscle, skin, liver
- Associated with autoimmune thyroiditis, systemic vasculitis, MALT lymphomas
- Variable amyloid deposition outside the salivary glands

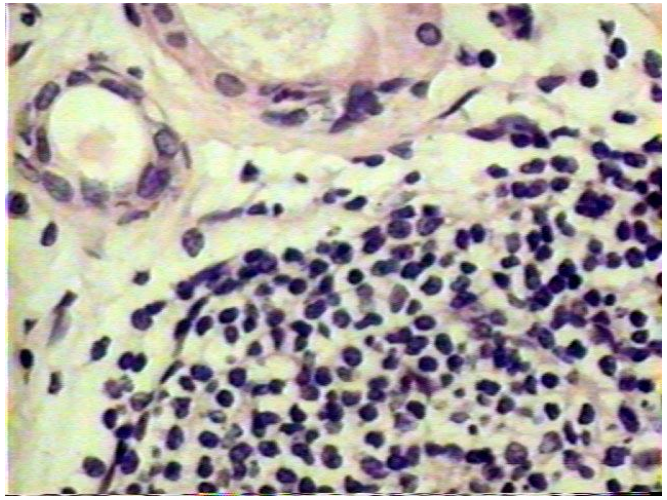


Note the extensive fissuring and loss of filiform papillae. The velvety fungiform papillae are preserved.



Keratoconjunctivitis

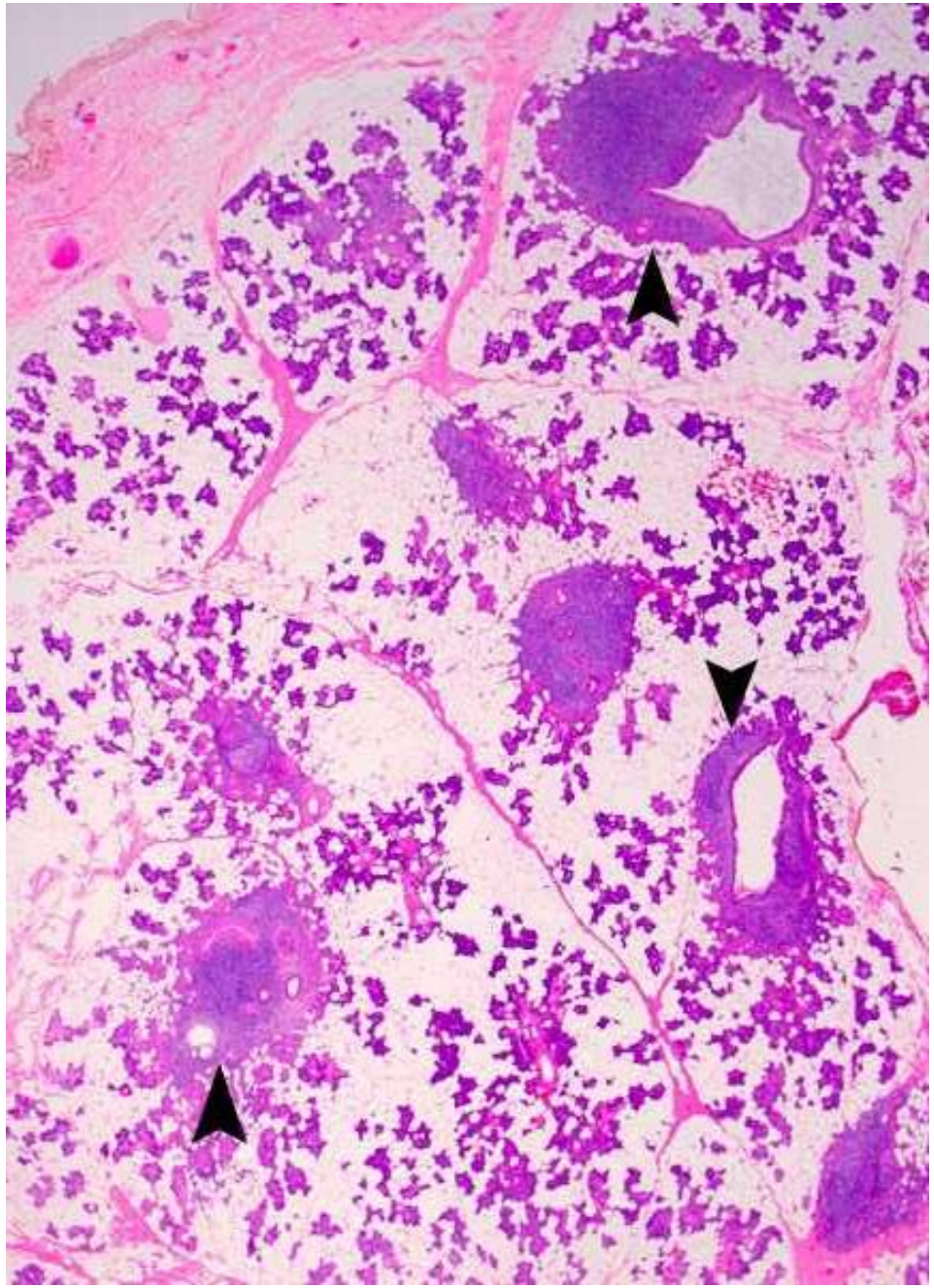
- The histological hallmark is a focal lymphocytic infiltration of the exocrine glands, determined by a biopsy of the minor labial salivary glands.
- The spectrum of the disease extends from sicca syndrome to systemic involvement.
- When sicca symptoms appear in a previously healthy person, the syndrome is classified as primary SS.
- When sicca features are found in association with another systemic autoimmune disease, most commonly rheumatoid arthritis (RA), systemic sclerosis, or systemic lupus erythematosus (SLE), it is classified as associated SS.



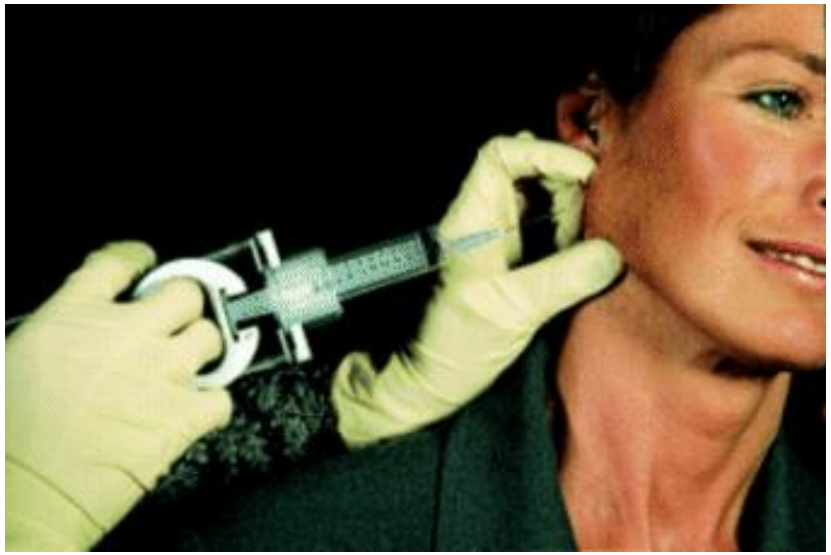
Adequate biopsy of minor salivary glands (5 or more glands) with a focus score of more than 1 focus/4mm2 has been proposed as the diagnostic criteria

MALT lymphoma

- 3% of tumors of major salivary glands
- Indolent, excellent prognosis
- Most common lymphoma of salivary glands
- Often associated with Sjogren's syndrome or benign lymphoepithelial lesion, perhaps due to chronic antigenic stimulation
- May arise post-transplantation
- Diagnosis: monoclonality by immunohistochemistry or flow cytometry or monocytoid infiltrates in regional lymph nodes; monoclonality in lymphoid infiltrates PCR is insufficient for diagnosis alone
- Micro: monocytoid cells surround ducts

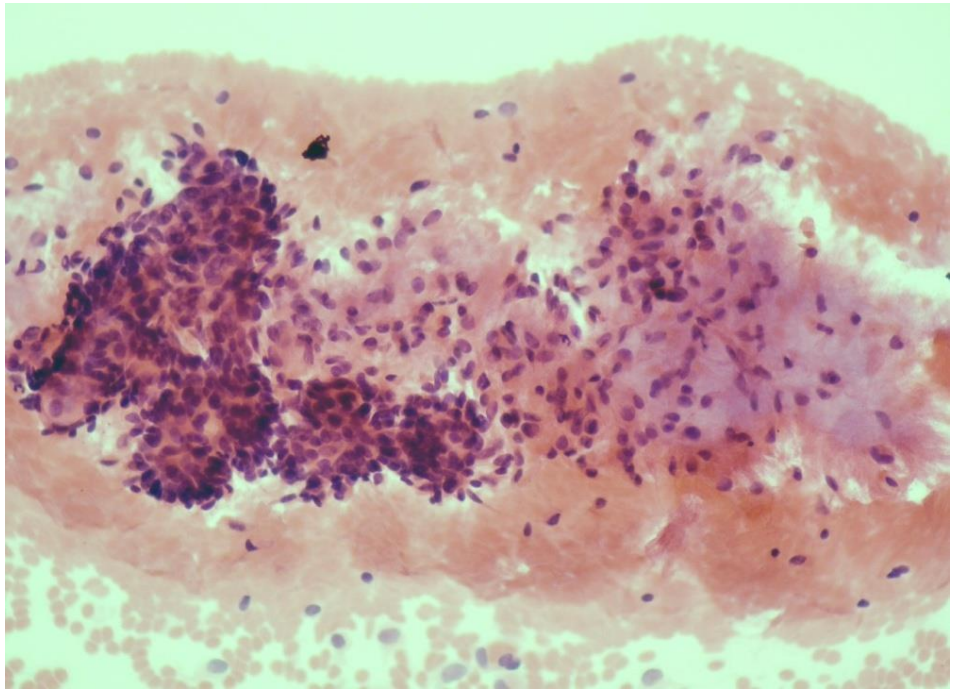


lymphoid clusters around ducts and glands in the parotid parenchyma

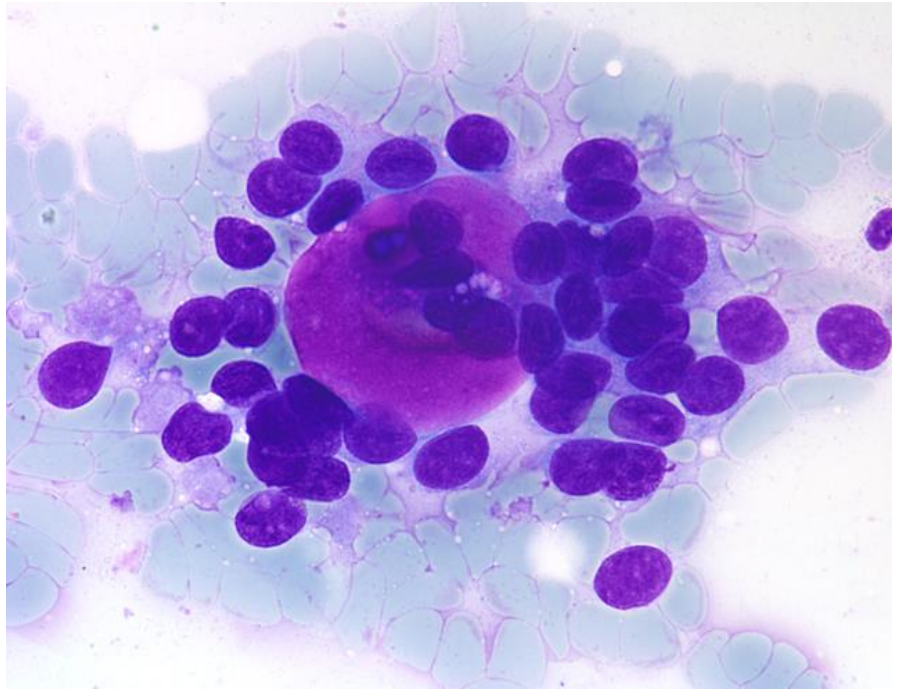


Fine needle aspiration cytology

- **Rapid, reliable, safe**
- **FNA > 90% sensitive, but may induce necrotic and reparative changes in tumor,**
- **Core biopsy not recommended as tumor may implant along needle tract**
- **Recommended to initially classify as normal tissue/inflammation, benign or malignant tumors**



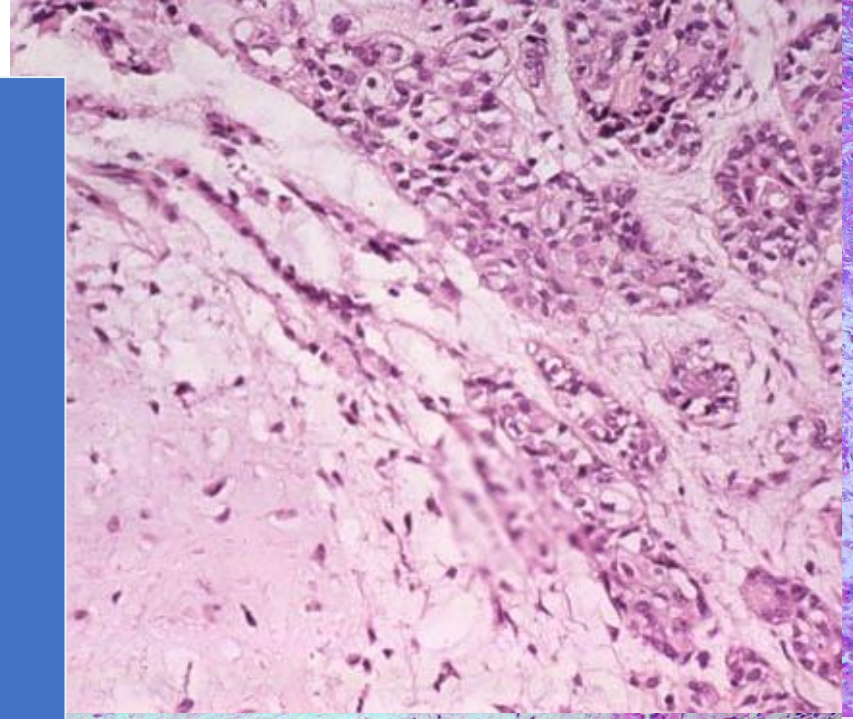
Pleomorphic adenoma

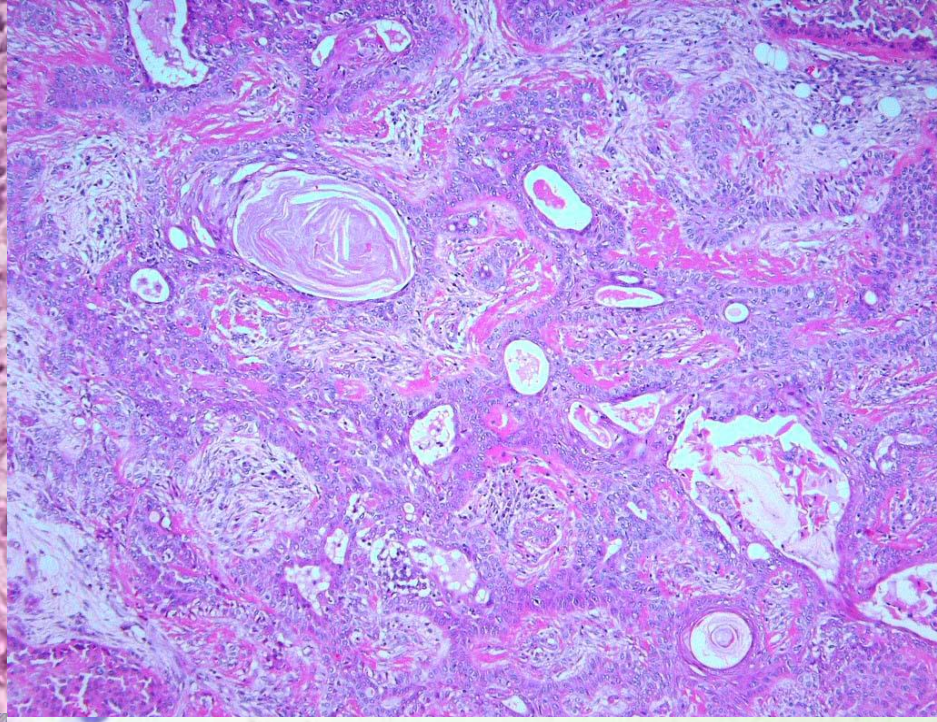


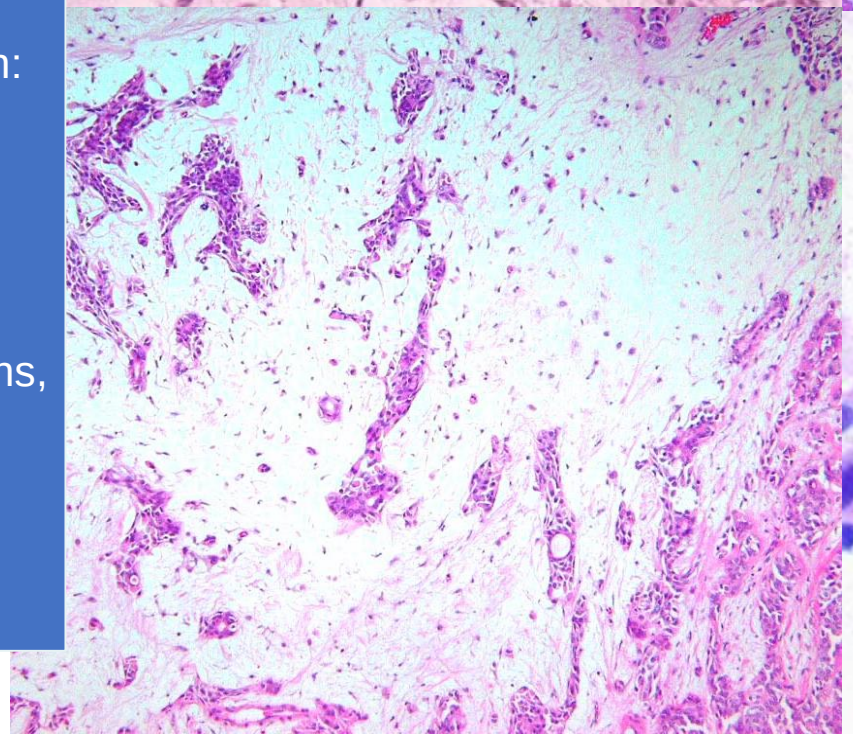
Adenoid cystic carcinoma

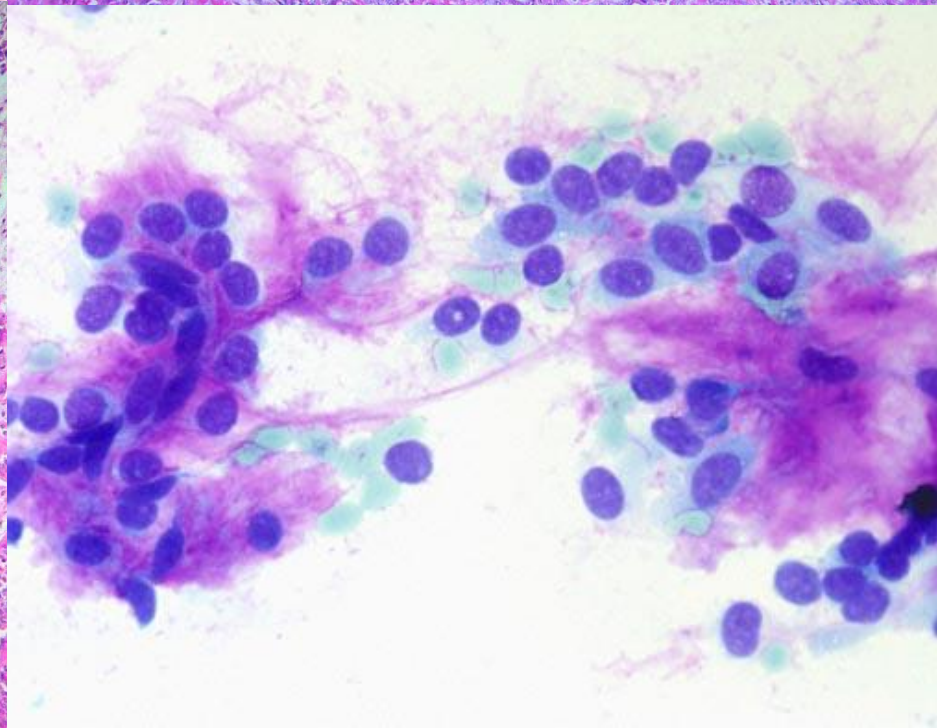
Pleomorphic adenoma

- Also called benign mixed tumor
- Most common tumor of salivary glands
- Often women in 30's, but any age
- Painless, slow growing tumor
- 90% occur in parotid gland
- Epithelial and mesenchymal (myxoid, hyaline, chondroid, osseous) cells often arise from same cell clone, which may be a myoepithelial or ductal reserve cell
- No difference in behavior based on proportion of various elements
- Risk factors for malignant transformation: prominent hyalinization, increased mitotic rate
- Treatment: wide local excision (25% recur with enucleation, 4% with adequate parotidectomy)
- Recurrences are usually within 18 months, but also up to 50 years later;
- Gross: well-demarcated, partially encapsulated, gray-white myxoid, rubbery mass with solid cut surface.



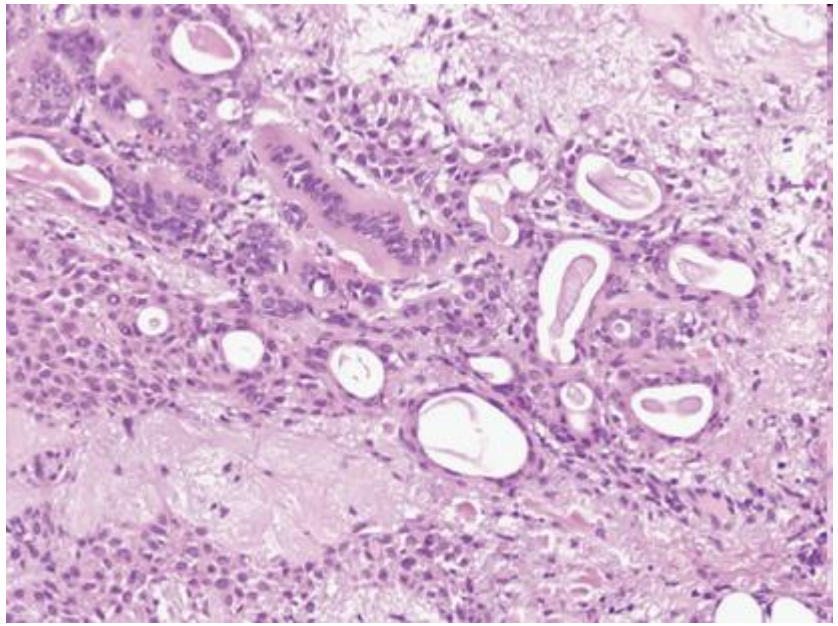


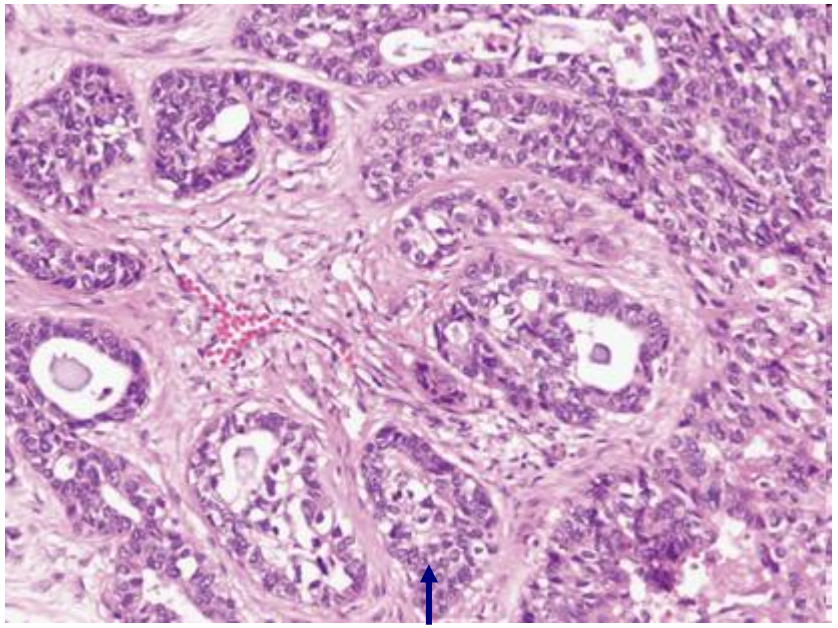




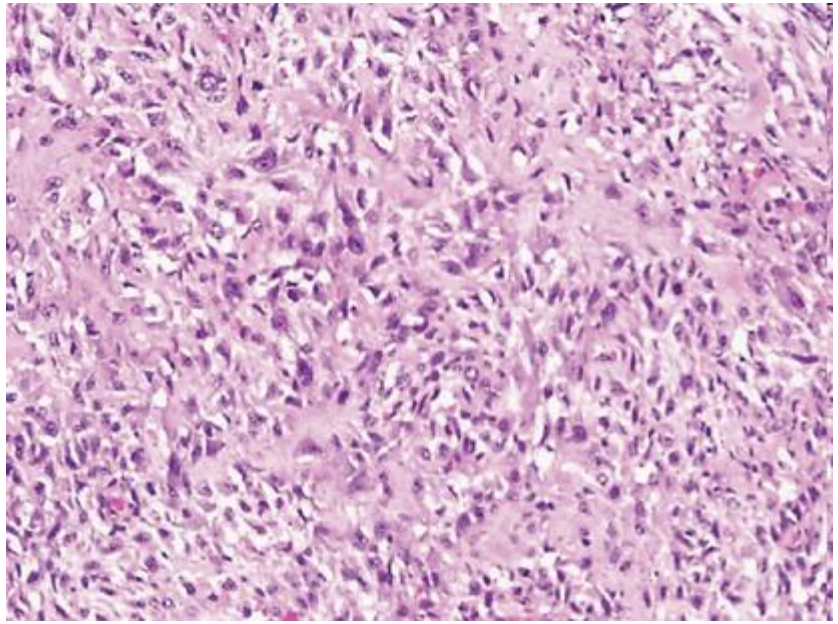
Malignant mixed tumor

- Also called carcinoma ex pleomorphic adenoma,
- carcinosarcoma if malignant epithelial/myoepithelial and mesenchymal components
- Rare
- Usually malignant transformation of benign pleomorphic adenomas; 2% risk if present < 5 years, 10% risk if 15 years duration for pleomorphic adenoma
- Clinically, have sudden increase in growth, pain or facial paralysis
- Associated with surgery or radiation therapy
  Note: must rule out malignant mixed tumor if a high grade carcinoma of salivary glands is difficult to classify, by vigorous searching for a benign mixed tumor (may be 5 mm or less)
- 50% survival at 5 years
- Metastases to regional lymph nodes, lungs, bone (vertebral column), abdominal organs
- Micro: malignant epithelium, often salivary duct carcinoma, undifferentiated carcinoma or adenocarcinoma usually with benign stroma; Note: clinical malignant behavior is associated only with cytologically malignant foci beyond the capsule of original tumor; Less commonly the stromal component is chondrosarcoma or other malignancy

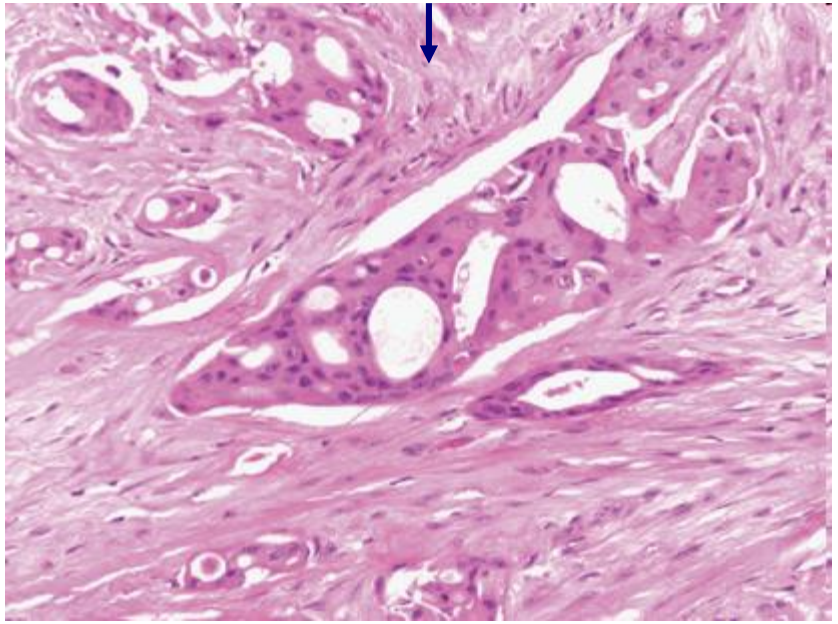


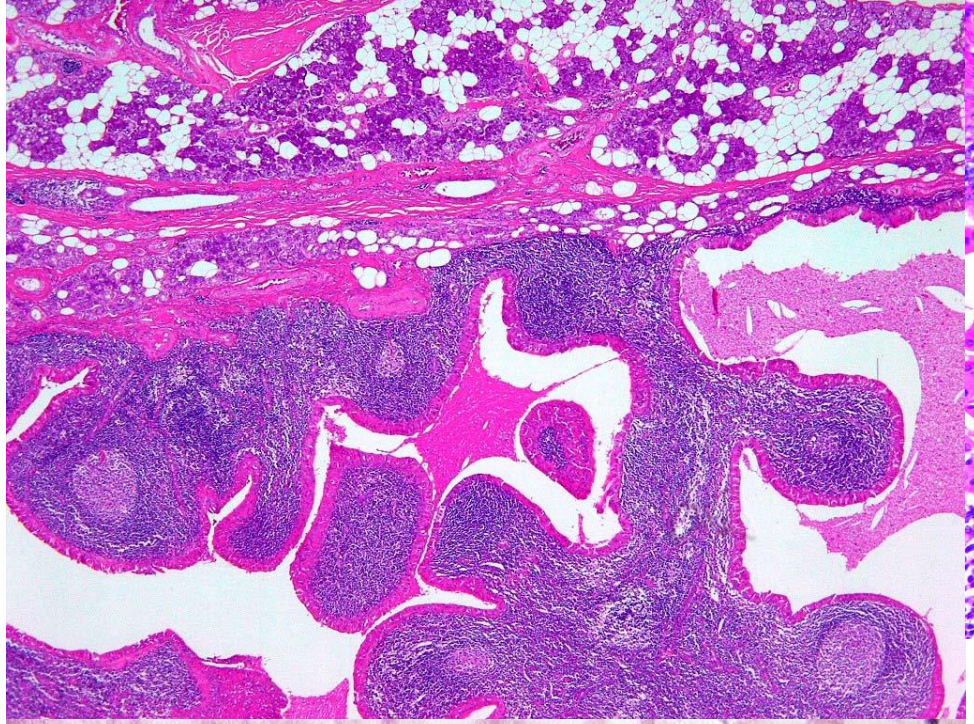


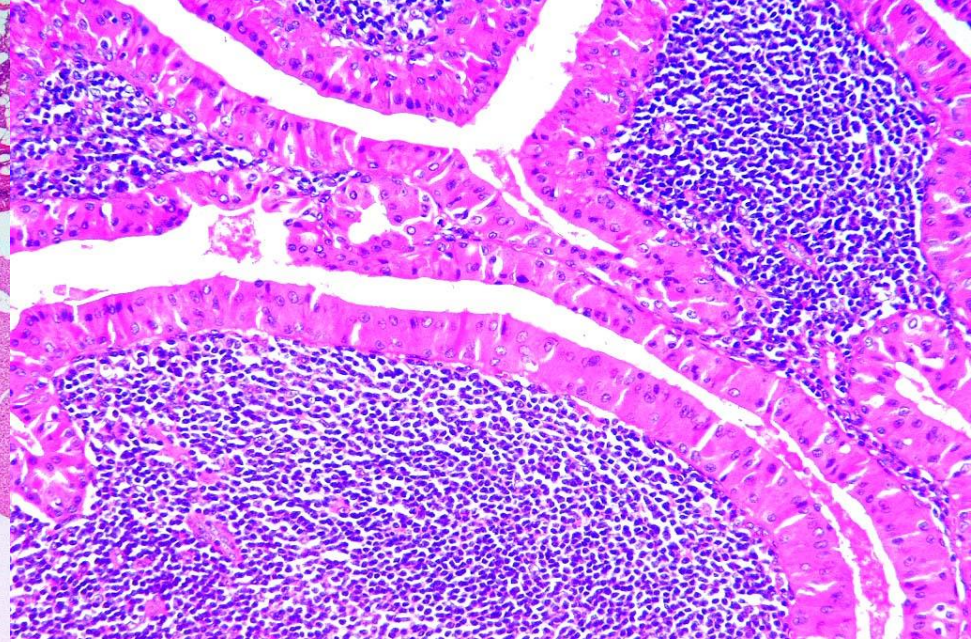
adenocarcinoma

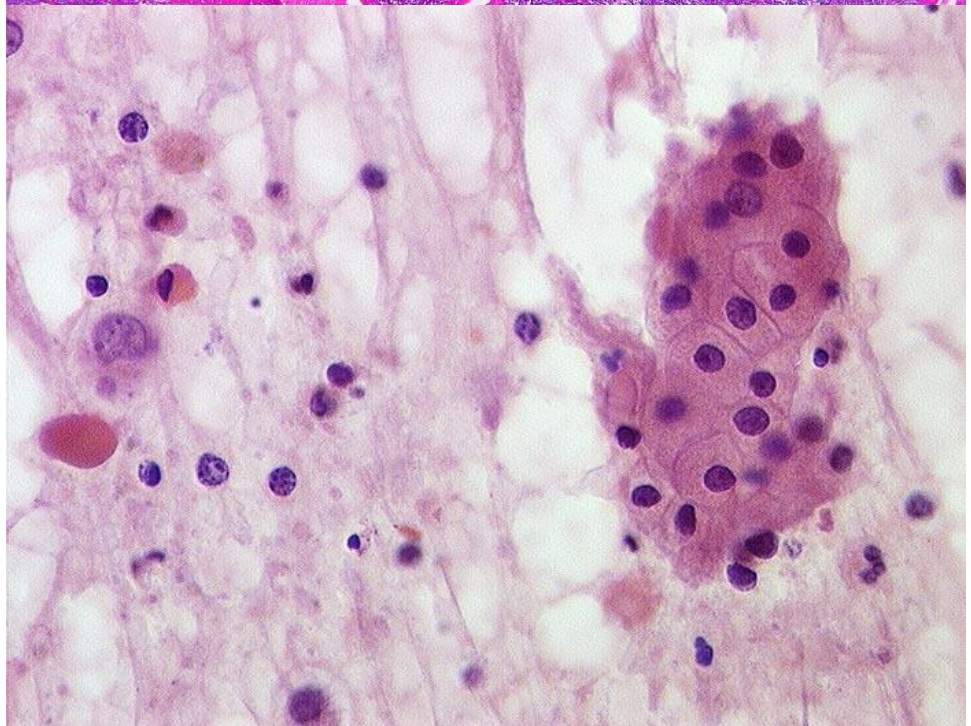


sarcoma









Warthin's tumor

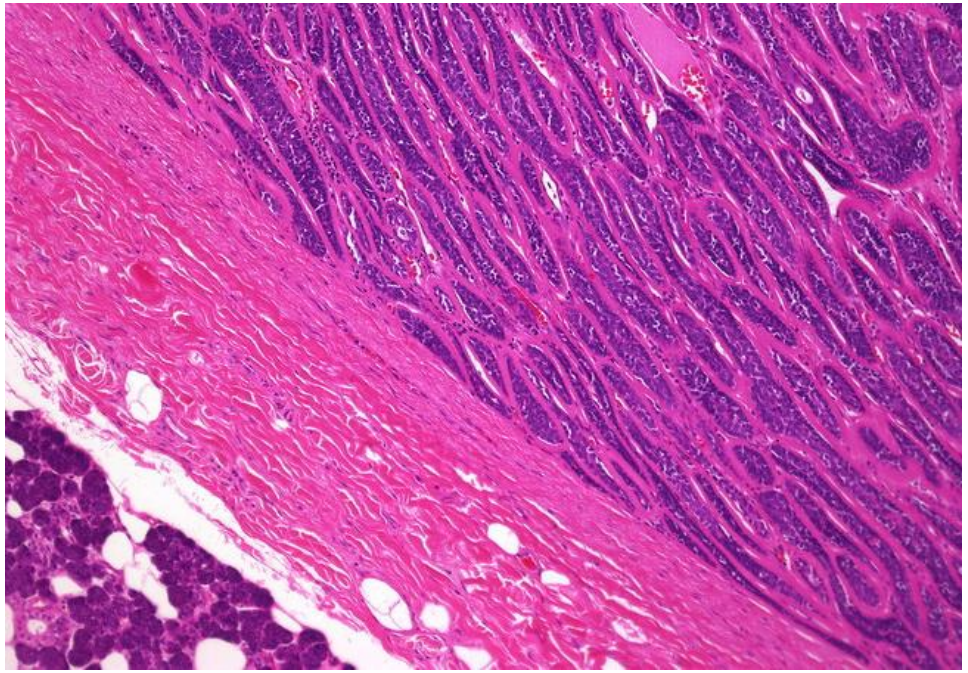
- Also called cystadenoma lymphomatosum papilliferum, adenolymphoma
- Almost always in parotid gland
- Usually male smokers age 40+ years
- Arise from incorporation of lymphoid tissue in parotids or induction of cystic and oncocytic changes by inflammatory infiltrate
- 70% of bilateral salivary gland tumors are Warthin's tumors
- Rarely transforms to lymphoma, adenocarcinoma

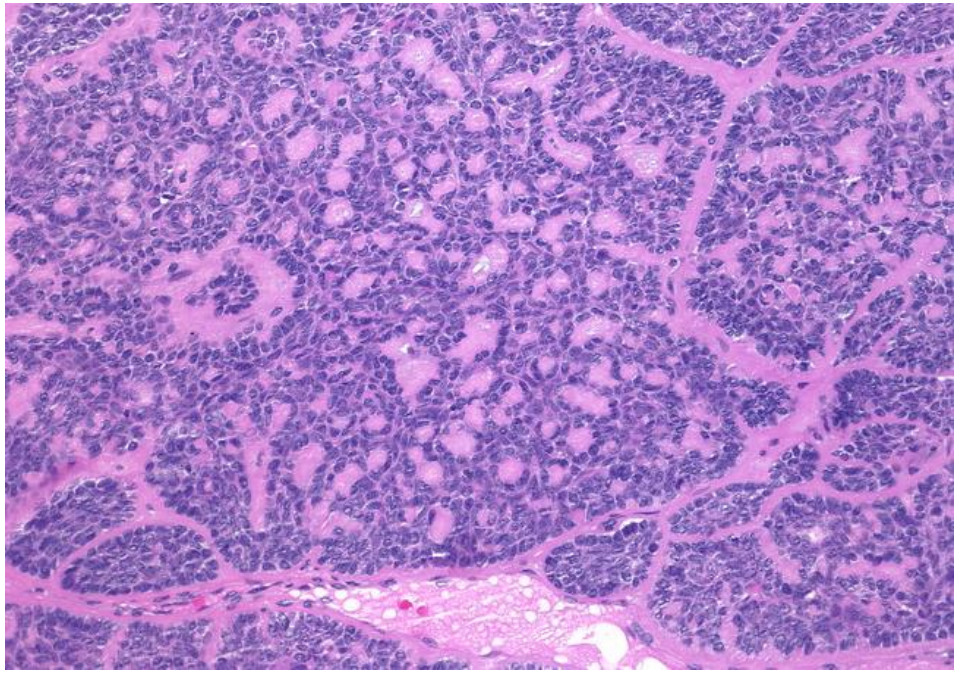
Treatment: surgical excision; 2% recur after resection

Micro: double layer of epithelial cells resting on dense lymphoid stroma, cystic spaces narrowed by polypoid projections of lymphoepithelial elements

Basal cell adenoma

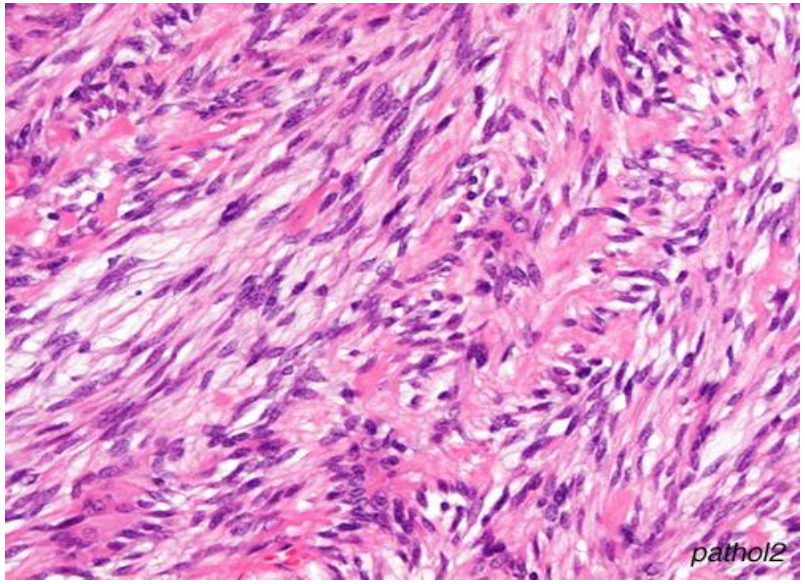
- Also called monomorphic adenoma
- 2% of benign salivary gland tumors
- Usually adults, 2/3 female, mean age 58 years; rarely is congenital and resembles embryoma
- Parotid gland or periparotid lymph nodes
- Benign; rarely transforms, more likely if dermal analogue variant
- Usually some myoepithelial differentiation using immunostains
- Treatment: excision
- Gross: encapsulated, often cystic, relatively small
- Micro: solid, trabecular or tubular growth of epithelial cells resembling pleomorphic adenoma but with peripheral palisading; no histologic evidence of myoepithelial differentiation; fibrous stroma present; no invasion, no mesenchymal component, no perineurial invasion, no myxoid matrix

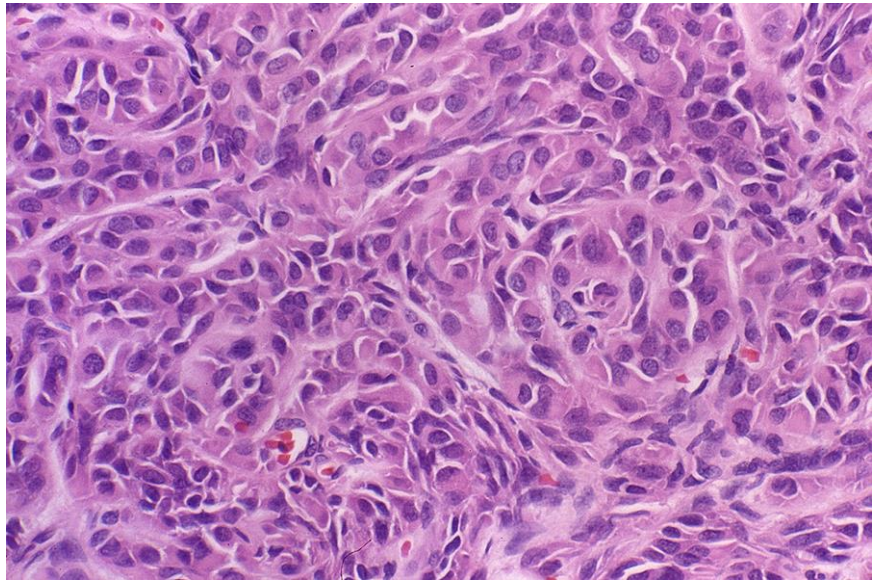


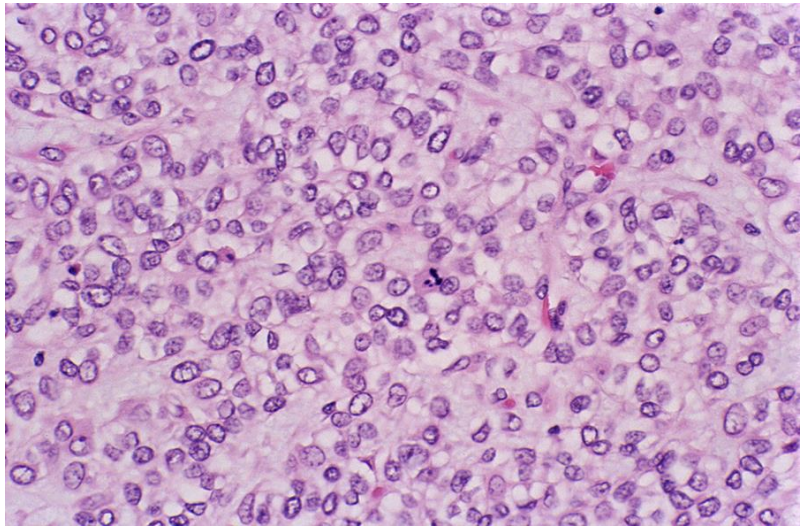


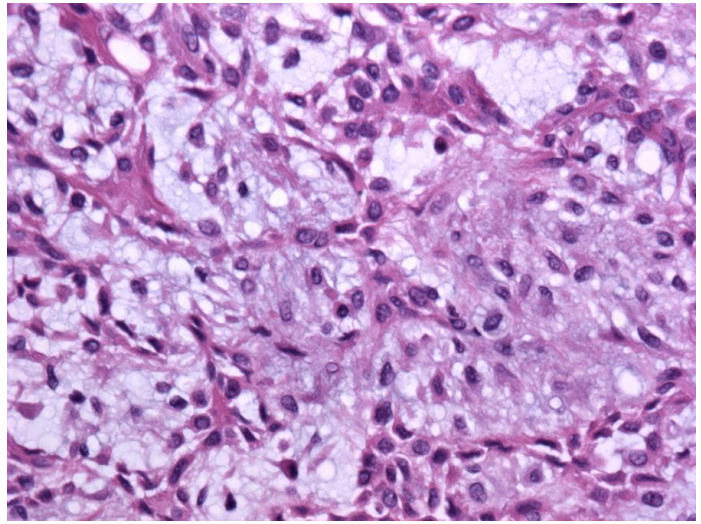
Myoepithelioma

Defined as benign tumor composed only of myoepithelial cells
May have hyalinization and myxoid matrix production

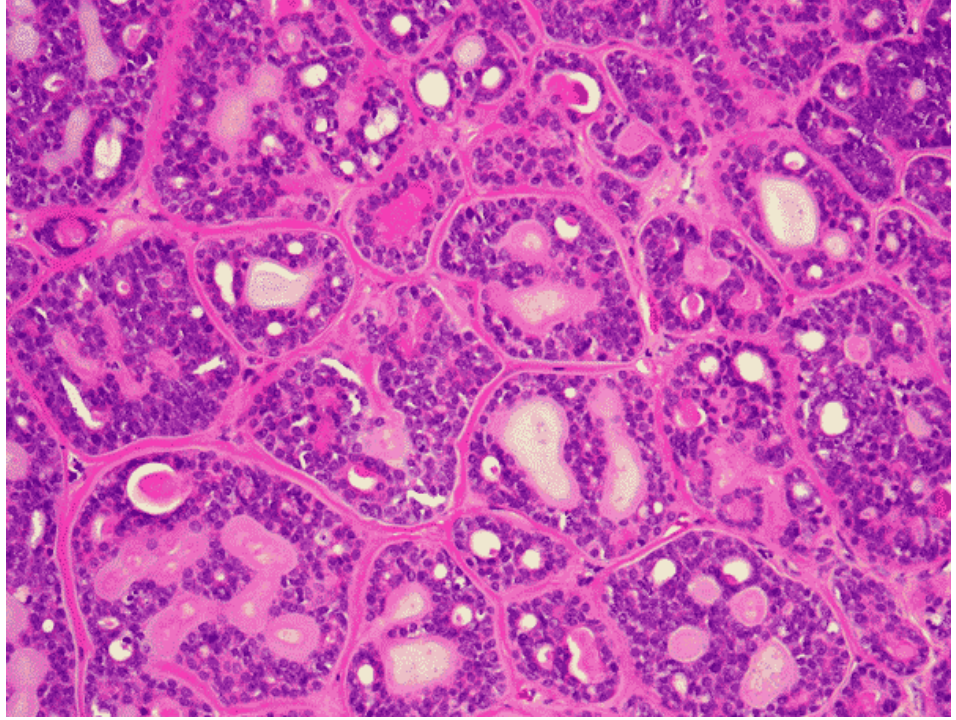


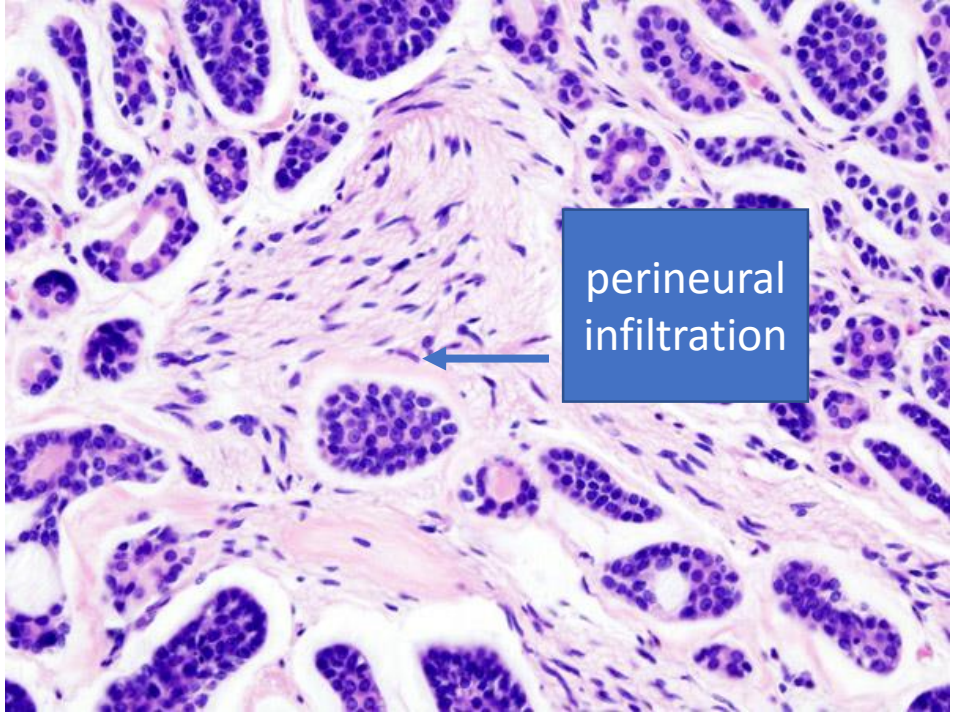


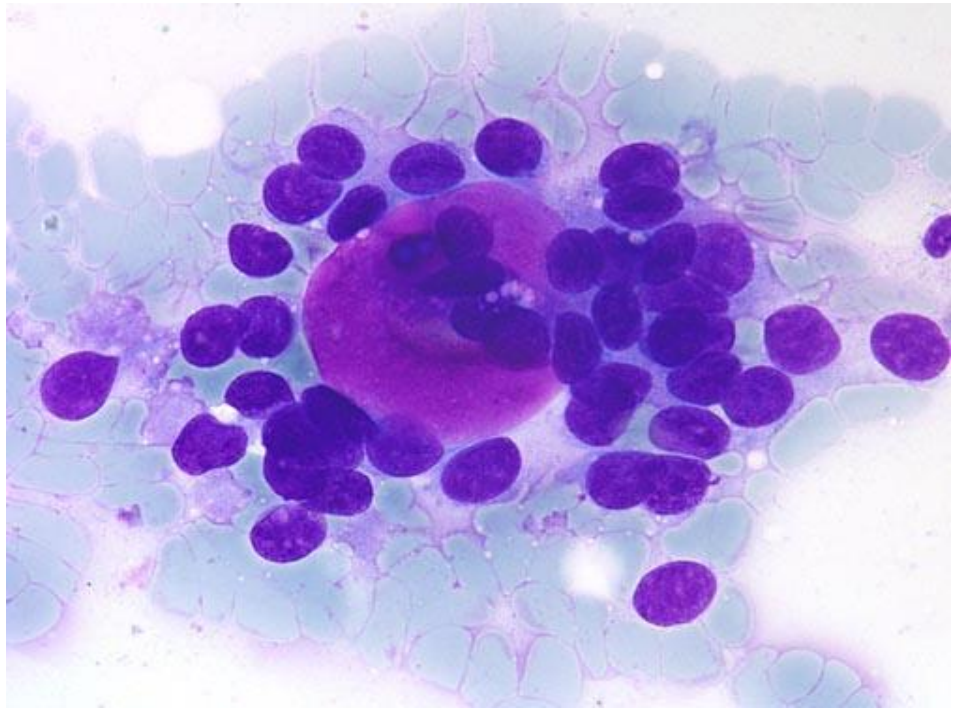




nests of tumor cells, interrupted by sharply punched-out spaces filled with basophilic matrix

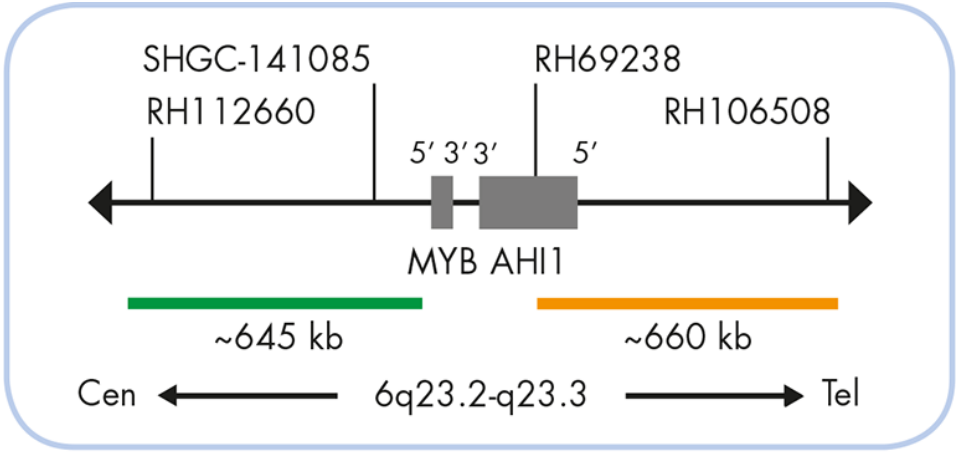






Adenoid cystic carcinoma

- Formerly called cylindroma
- Most common in submandibular, sublingual or minor salivary glands; ~ 10% of all mal. salyvary gland tumours
- Slow growing but aggressive; 50% metastasize, often silently to lung or bone; recurrences are frequent and often late
- 5 year survival is 60%, 10 year is 30%, 15 year is 15%
- Higher recurrence rates for solid (100%) vs. cribriform (89%) vs. tubular (59%) patterns
- Small bland (myoe)pithelial cells with scant cytoplasm pseudoglandular spaces with PAS+ excess basement membrane material and mucin, perineurial invasion and small true glandular lumina



SPEC MYB Probe map (not to scale).

t(6;9) (q22–23; p23–24)

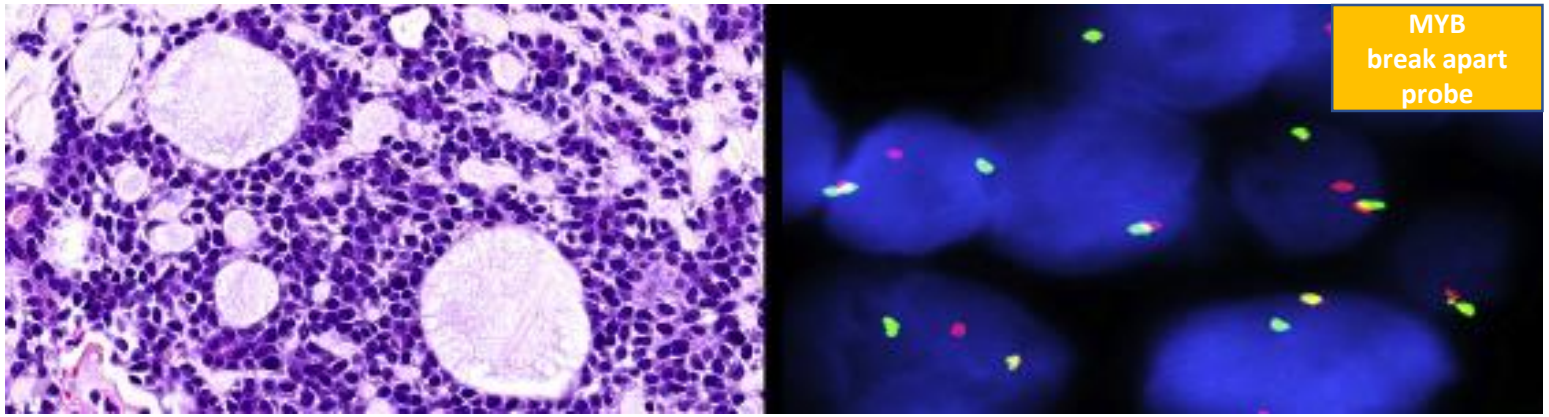
↓

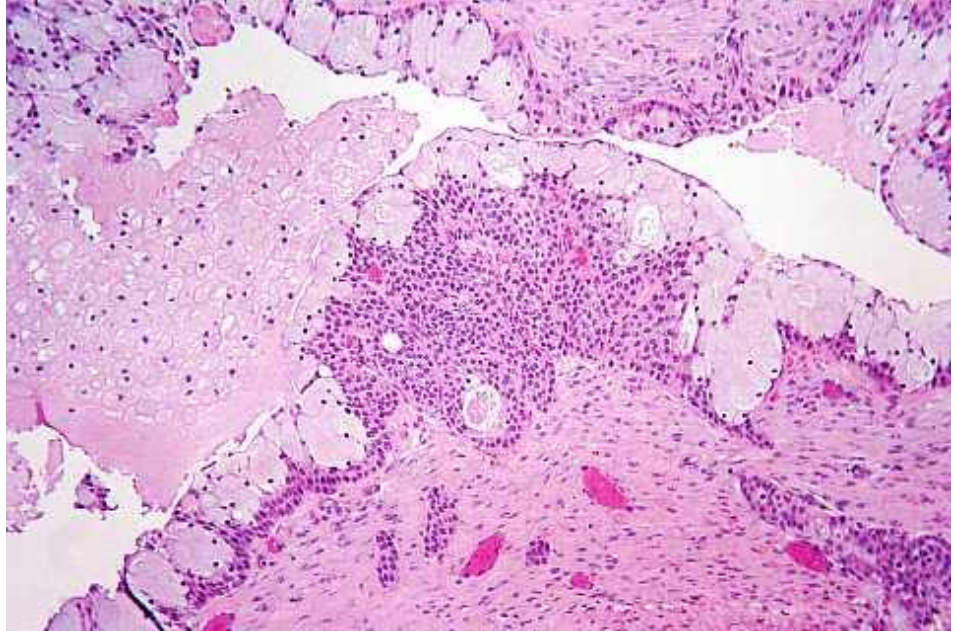
MYB-NFIB gene fusion

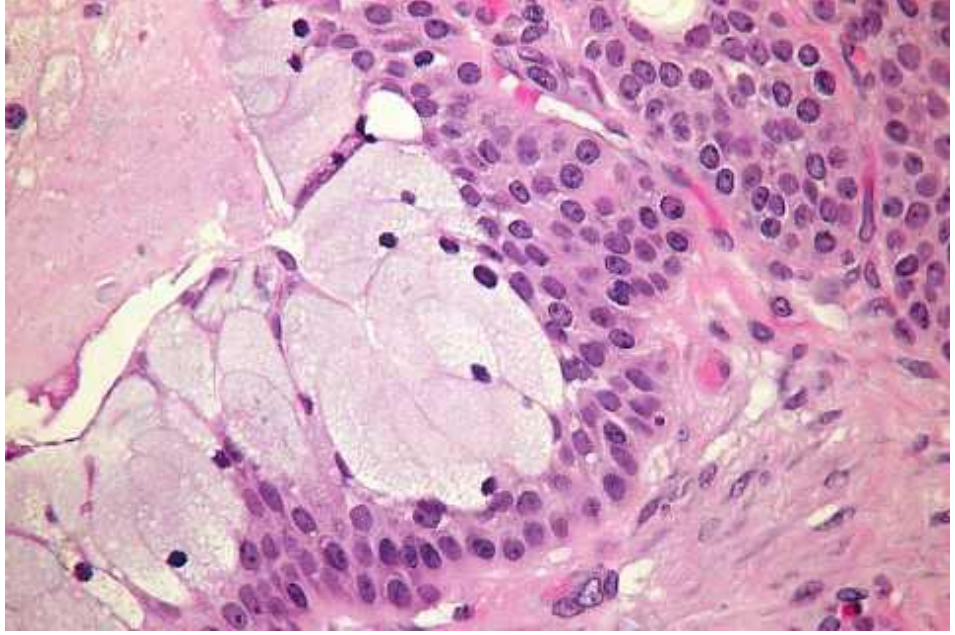
ACC displays the t(6;9) translocation resulting in the MYB-NFIB gene fusion and immunopositivity for MYB by immunohistochemistry.

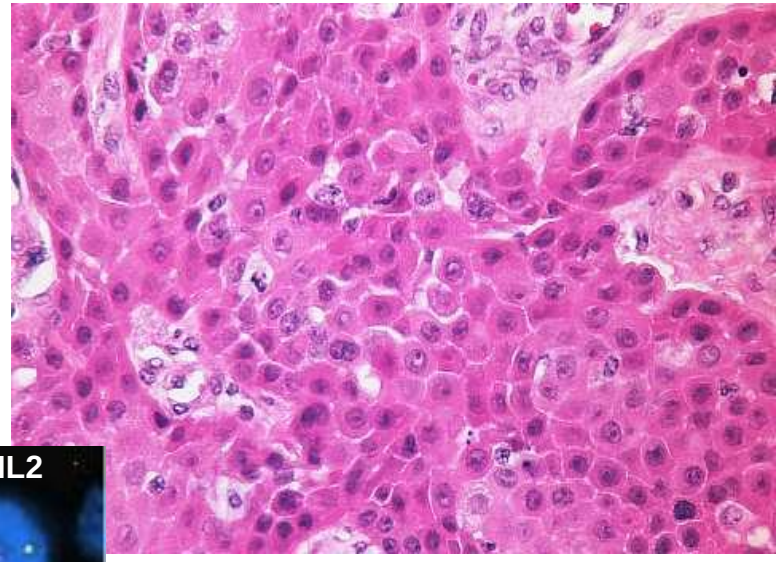
A balanced translocation between MYB and NFIB is present in 50-86% of adenoid cystic carcinomas but is not identified in other salivary gland tumors.

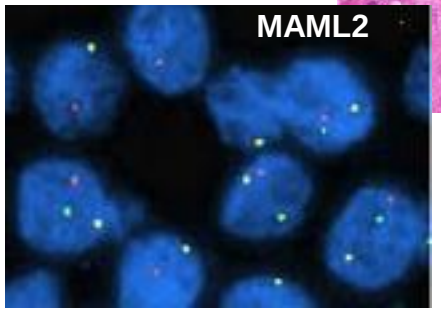
Small intraoral biopsies!









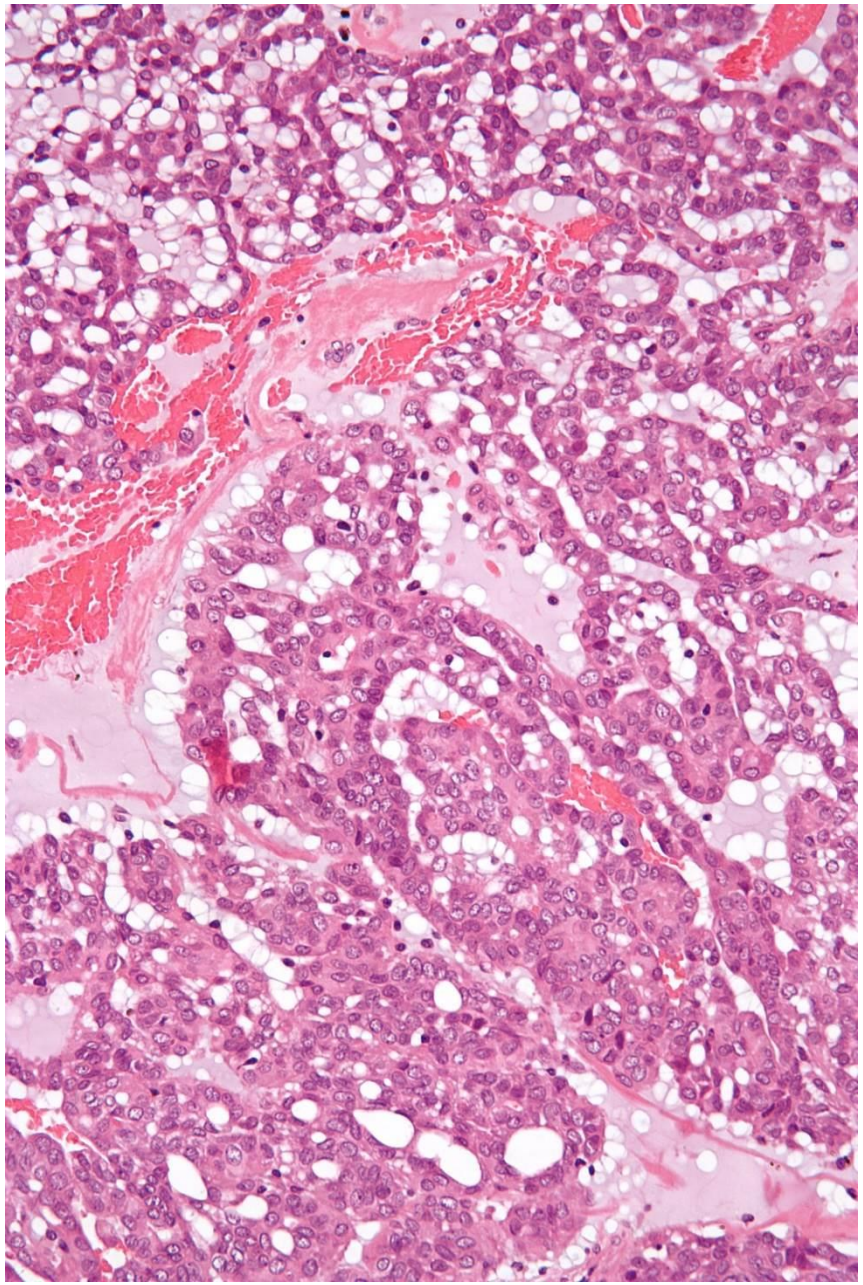


Mucoepidermoid carcinoma

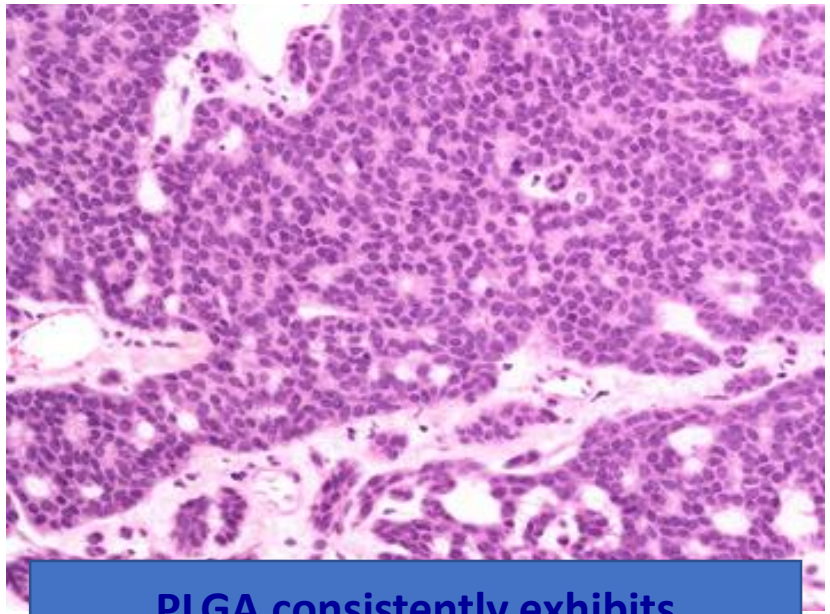
Most common malignant tumor in salivary glands;
2/3 occur in parotid gland;
Wide age range, mean 49 years,
Low grade: 15% recur, 5 year survival 90-98%;
High grade: 25% recur, 5 year survival 50-56%;
deaths usually within first 5 years
Treatment: complete excision, possible radiation therapy
Micro: cords, sheets, clusters of mucous, squamous/intermediate and clear cells
MECT1/MAML2 translocatio (MAML2 FISH!)
Small intraoral biopsies!

(Polymorphus) low-grade adenocarcinoma (PLGA)

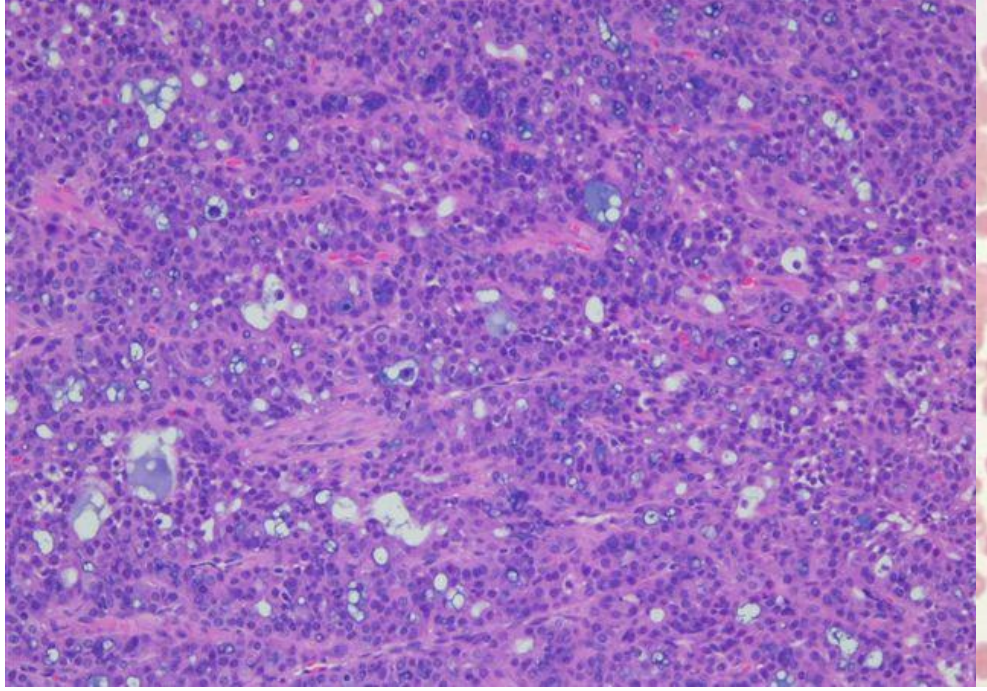
- Second most common intraoral malignancy
- Range: 16-94 years, mean: 59
- Mainly in palate
- Usually long duration; can be as much as 40 years
- Circumscribed, but not encapsulated
- Cytologicaly uniform!, but histologic diversity with komplex structures: lobular, papillary, cribriforme, trabecular or small duct like structures
- Infiltrative, neurotrophism

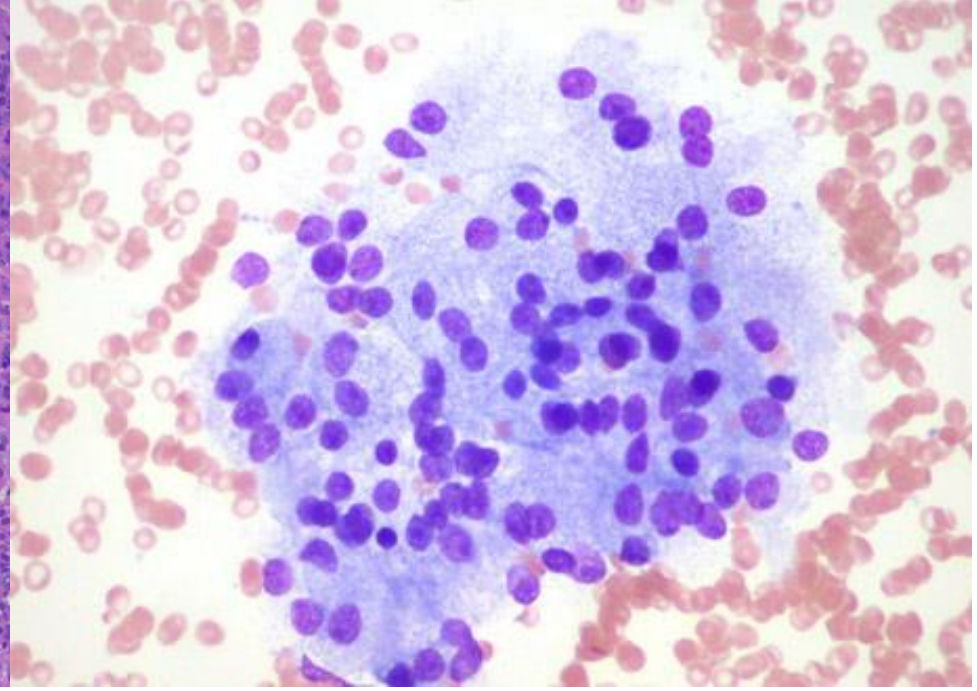


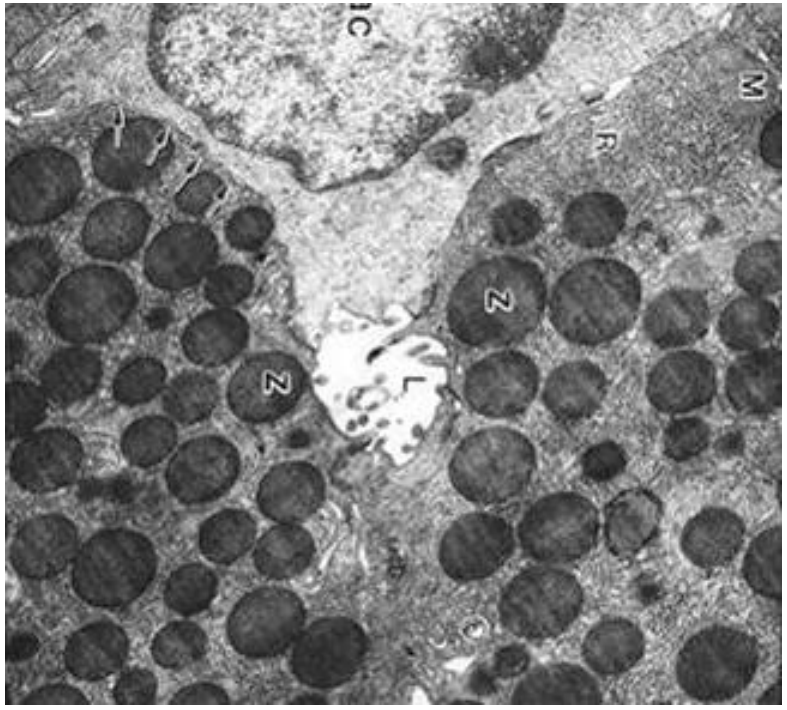
Small intraoral biopsies!



PLGA consistently exhibits a p63+/p40– immunophenotype







Acinic cell carcinoma

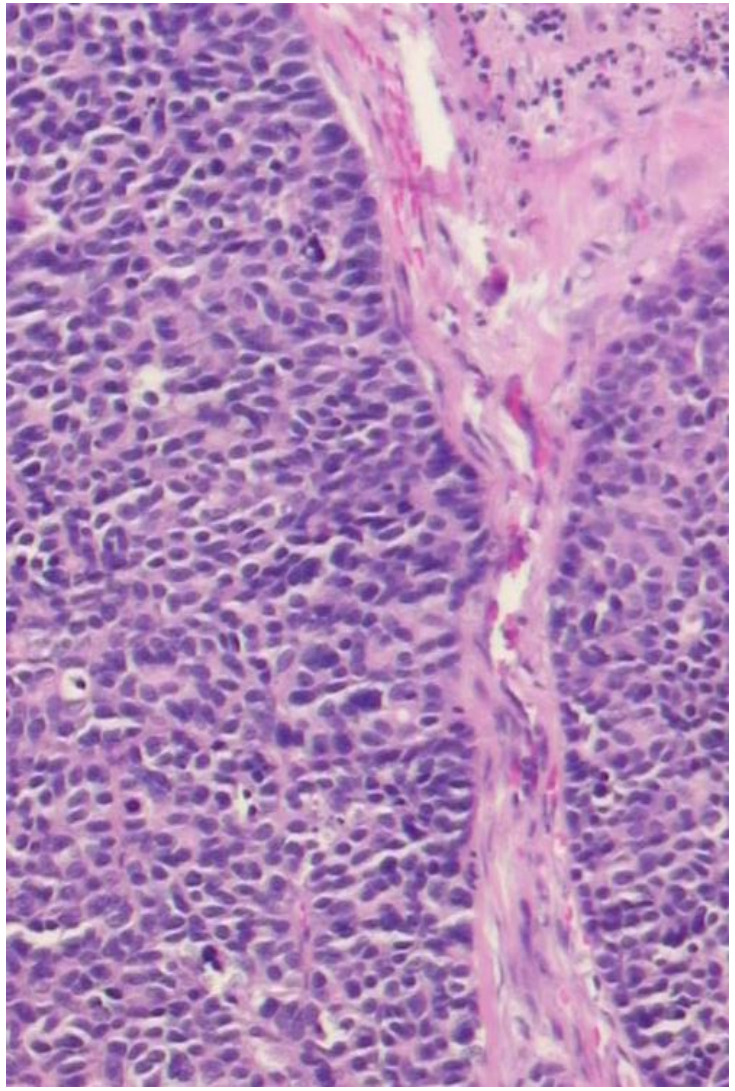
- 1-3% of salivary gland tumors; #2 childhood salivary gland malignancy after mucoepidermoid carcinoma
- Peaks in 20's and 40's
- Usually parotid and minor salivary glands,
- 10-15% metastatize (usually to local lymph nodes),
- 10-30% recur (may be due to inadequate excision) 80-90% recur if incompletely excised
- 5 year survival 90%, 20 year survival 60%
- Less aggressive in minor salivary glands

Micro: *variable patterns* - solid, microcystic, papillary cystic

Variable cell types - uniform acinar (serous) type cells with basophilic granular cytoplasm, clear cells, nonspecific glandular cells; few mitotic figures; NR4A3 gene involvement

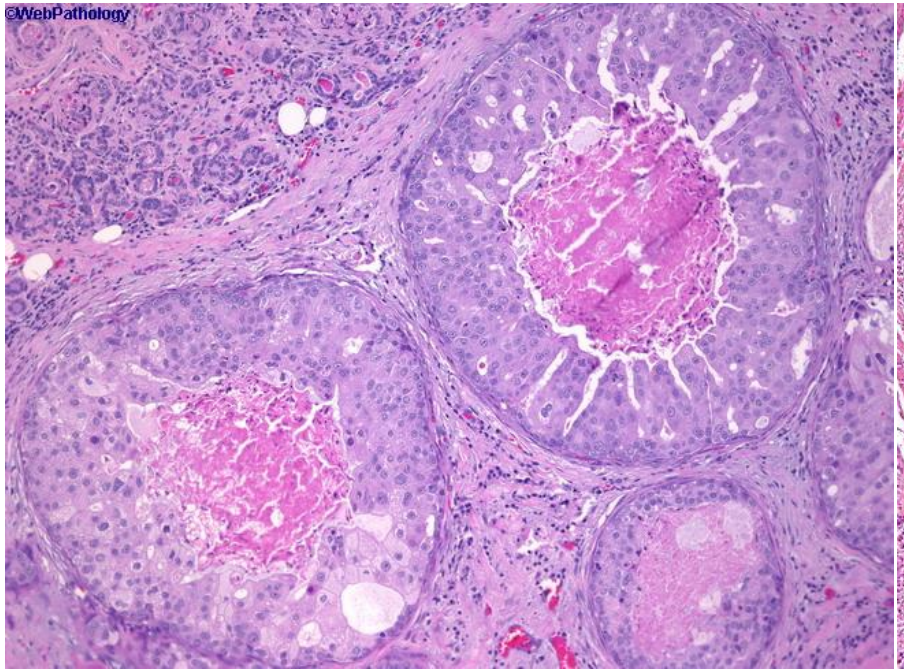
Basal cell adenocarcinoma

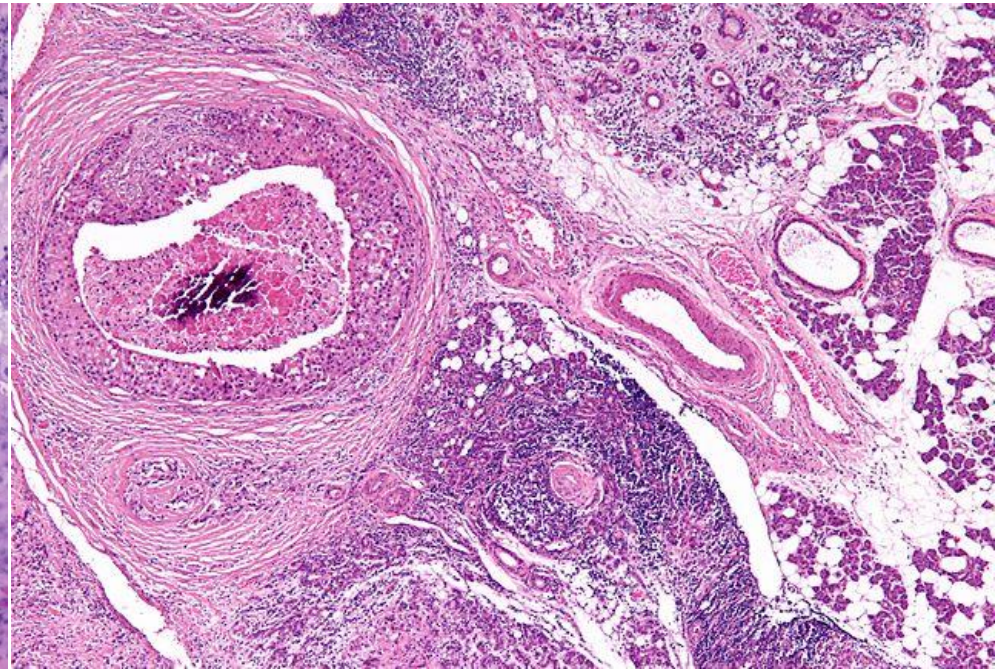
Also called basaloid carcinoma
1-2% of salivary gland carcinomas
Malignant counterpart of basal cell adenoma; 23% arise within basal cell adenomas
10-14% are associated with skin adnexal tumor syndrome
Usually parotid gland, ages 50+
37% recur locally, 8% metastasize (solid pattern) to lymph nodes, 4% to lungs; death from disease in unusual
Associated with dermal cylindromas
Treatment: excision with clear margins
Micro: low grade malignancy; similar to basal cell adenoma but infiltrative with perineurial invasion and vascular invasion; variable cytologic atypia and mitotic activity; solid, trabecular, tubular or membranous patterns; no myxoid matrix



Salivary duct carcinoma

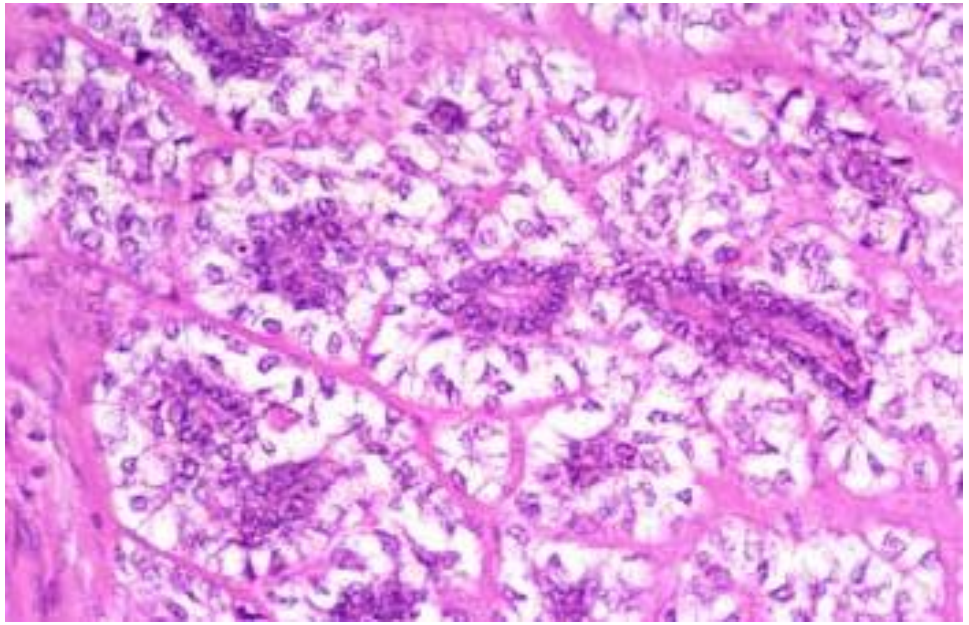
- Uncommon; usually elderly, 75% males
- Usually parotid gland, also submandibular gland
- High grade tumors are aggressive with frequent metastases to regional lymph nodes and distant sites, 70% mortality
- May arise from pleomorphic adenoma or polymorphous low grade adenocarcinoma or de novo
- Aggressive, 60% have nodal or distant metastases; commonly tumor infiltration into soft tissue at diagnosis
- >60% die from tumor, usually within 5 years
- Poor prognostic factors: > 3 cm, metastases, small intraductal component
- Micro: resembles breast carcinoma

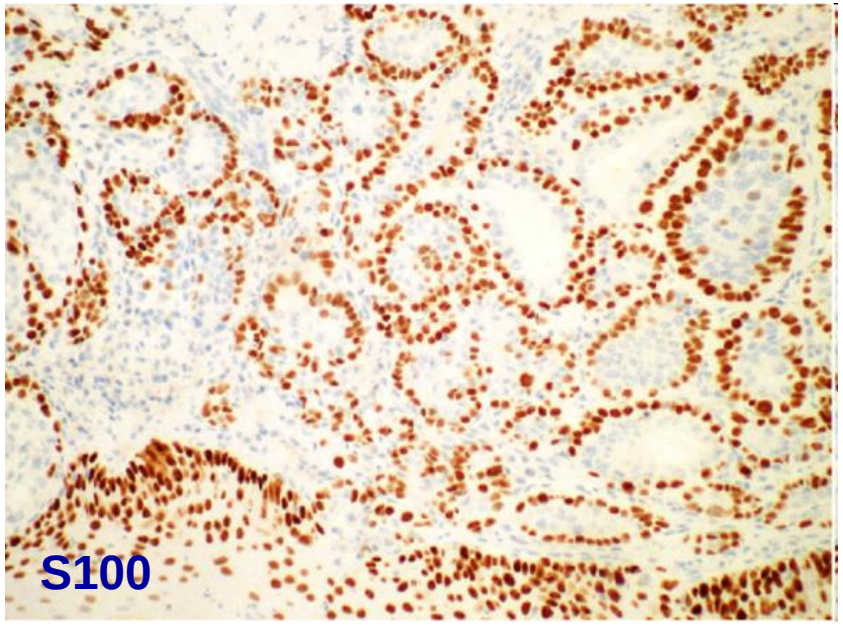




Epithelial myoepithelial carcinoma

- Rare; 80% arise in parotid gland
- Mean age 60 years; 60% in women
- Low grade malignancies with frequent local recurrences; previously often considered to be benign, but with sufficient follow-up, there are rare regional nodal metastases and distant metastases to lung and kidney
- In overtly malignant cases (cytologic atypia and infiltrative), metastases are found in 47% and 29% die of disease after mean 32 months
- Gross: well delineated, firm, infiltration into adjacent tissue; usually 2-3 cm
- Micro: low grade with epithelial and myoepithelial components; there are ducts or tubules with an outer rim of myoepithelial cells and inner, dark ductal cells with scant eosinophilic cytoplasm and round, bland nuclei





Other salivary gland malignant tumors

Clear cell carcinoma
Cystadenocarcinoma
Mucinous carcinoma
Myoepithelial carcinoma
Small cell carcinoma
Lymphoepithelial carcinoma

Soft tissue tumors of salivary glands

Lymphoid tumors

Aspiration cytology

Surgery in centers

Differential diagnostics