

SALIVARY GLAND NEOPLASMS

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LEVEL VI

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Salivary Gland Neoplasms

- Benign Neoplasms
- Malignant Neoplasms
- Controversial Issues

BENIGN NEOPLASMS

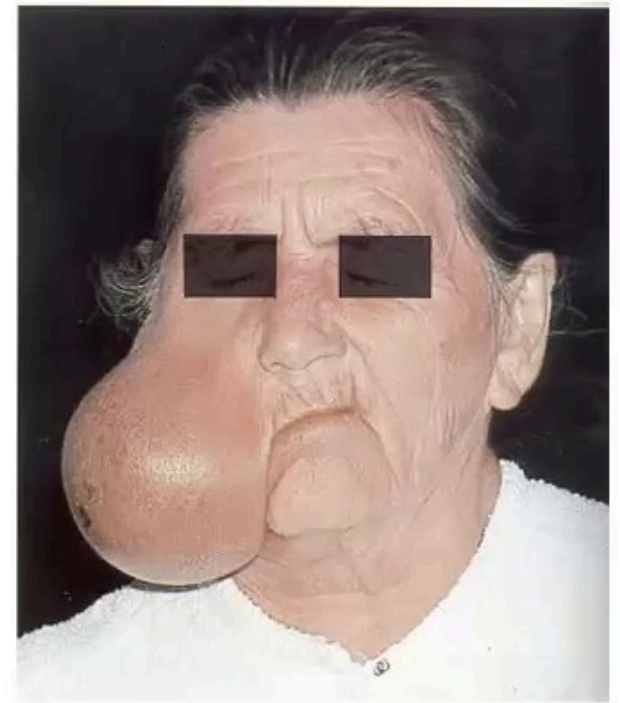
1. Pleomorphic Adenoma
2. Warthin's Tumor
3. Oncocytoma
4. Monomorphic Adenoma : Basal Cell Adenoma, Canalicular Adenoma
5. Myoepithelioma

BENIGN Salivary Gland Neoplasms

- Diverse histopathology
- Relatively uncommon
 - 2% of head and neck neoplasms
- Distribution
 - Parotid: 80% overall; 80% benign
 - Submandibular: 15% overall; 50% benign
 - Sublingual/Minor: 5% overall; 40% benign

Pleomorphic Adenoma

- Most common of all salivary gland neoplasms
 - 70% of parotid tumors
 - 50% of submandibular tumors
 - 45% of minor salivary gland tumors
 - 6% of sublingual tumors
- 4th-6th decades
- F:M = 3-4:1



Pleomorphic Adenoma

- Slow-growing, painless mass
- Parotid: 90% in superficial lobe, most in tail of gland
- Minor salivary gland: lateral palate, submucosal mass
- Solitary vs. synchronous/metachronous neoplasms

Pleomorphic Adenoma

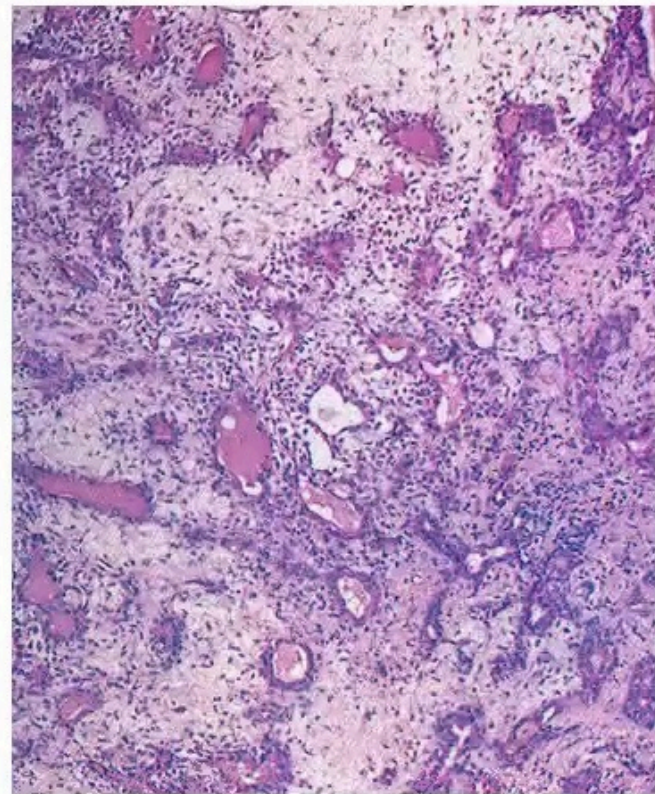
- Gross pathology
 - Smooth
 - Well-demarcated
 - Solid
 - Cystic changes
 - Myxoid stroma



Pleomorphic Adenoma

- **Histology**

- Mixture of epithelial, myoepithelial and stromal components
- Epithelial cells: nests, sheets, ducts, trabeculae
- Stroma: myxoid, chondroid, fibroid, osteoid
- No true capsule
- Tumor pseudopods



Pleomorphic Adenoma

- Treatment: complete surgical excision
 - Parotidectomy with facial nerve preservation
 - Submandibular gland excision
 - Wide local excision of minor salivary gland

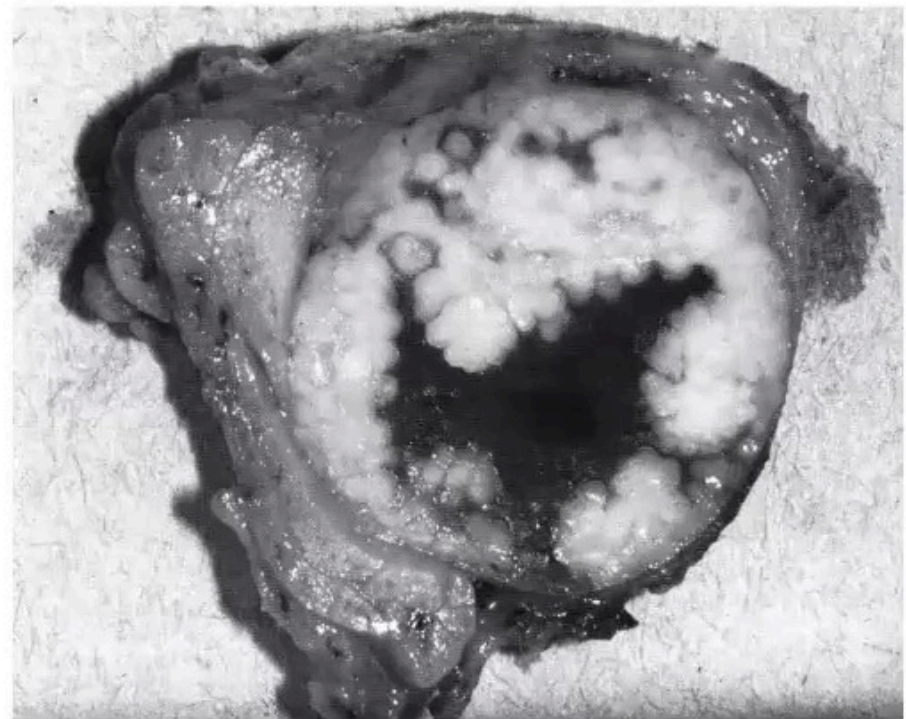
- Avoid enucleation and tumor spill

Warthin's Tumor

- AKA: papillary cystadenoma lymphomatosum
- 6-10% of parotid neoplasms
- Older, Caucasian, males
- 10% bilateral or multicentric
- 3% with associated neoplasms
- Presentation: slow-growing, painless mass

Warthin's Tumor

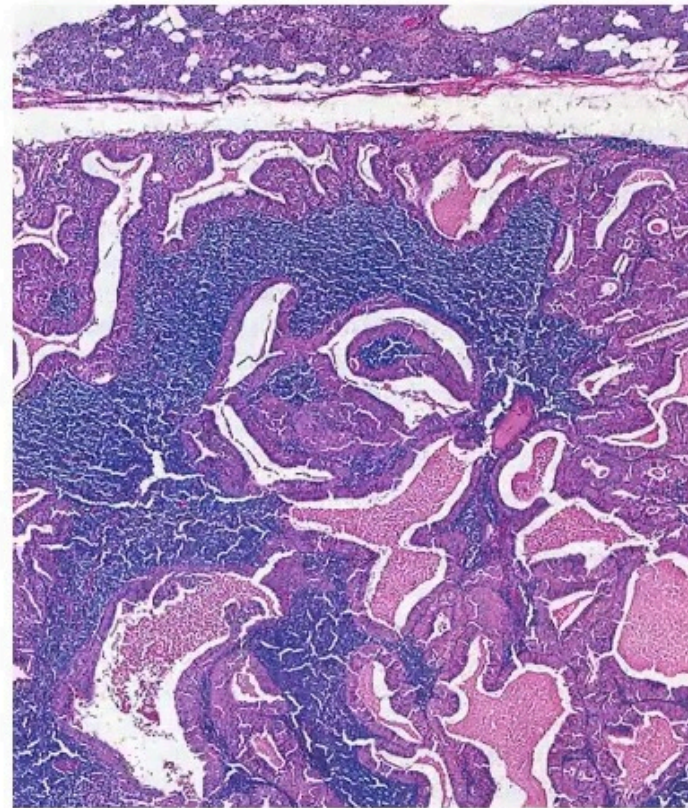
- Gross pathology
 - Encapsulated
 - Smooth/lobulated surface
 - Cystic spaces of variable size, with viscous fluid, shaggy epithelium
 - Solid areas with white nodules representing lymphoid follicles



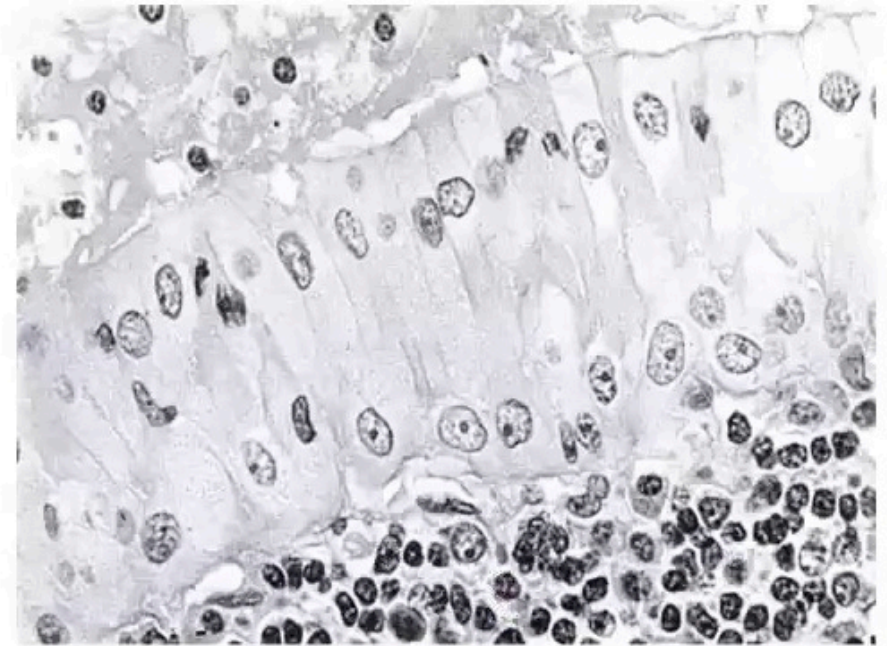
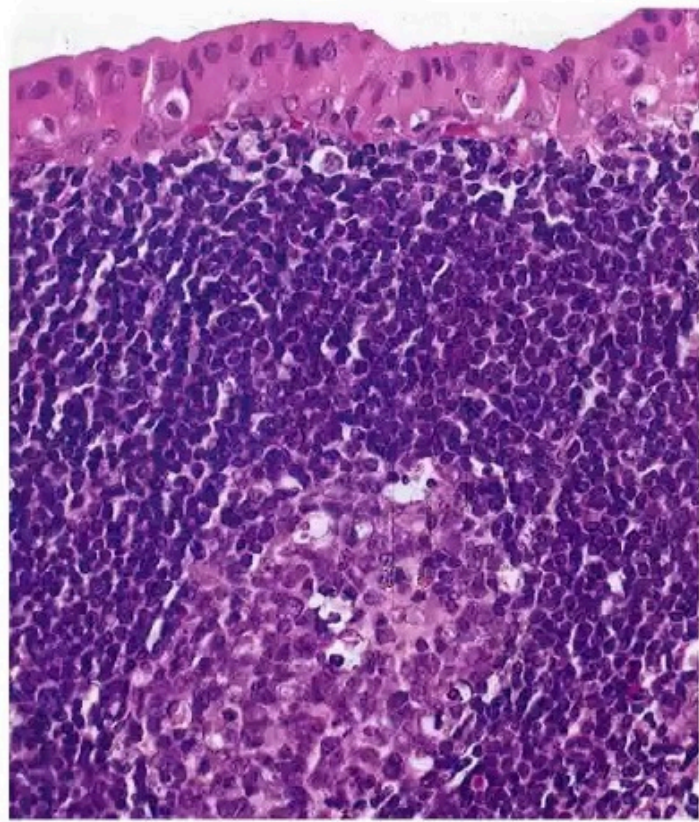
Warthin's Tumor

- Histology

- Papillary projections into cystic spaces surrounded by lymphoid stroma
- Epithelium: double cell layer
 - Luminal cells
 - Basal cells
- Stroma: mature lymphoid follicles with germinal centers



Warthin's Tumor



Oncocytoma

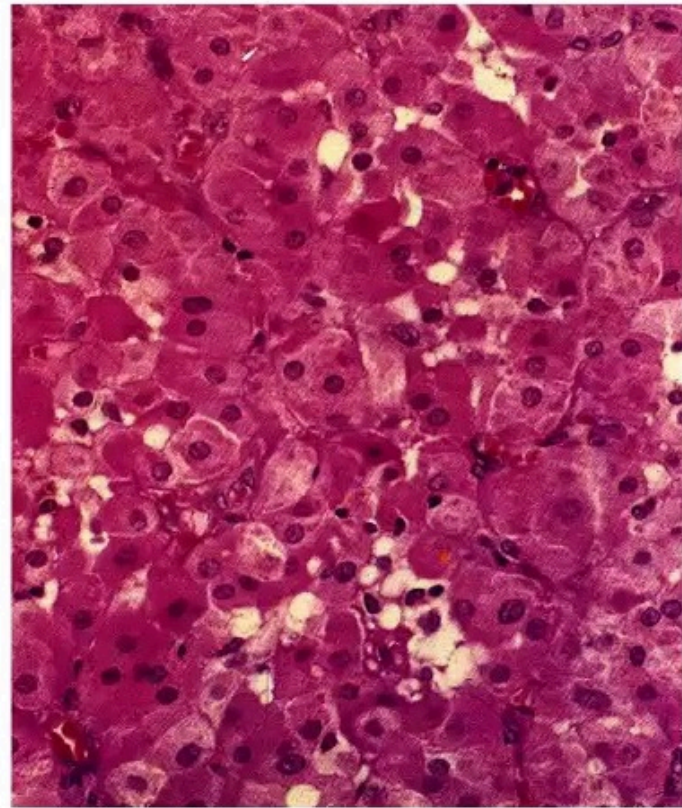
- Rare: 2.3% of benign salivary tumors
- 6th decade
- M:F = 1:1
- Parotid: 78%
- Submandibular gland: 9%
- Minor salivary glands: palate, buccal mucosa, tongue

Oncocytoma

- Presentation
 - Enlarging, painless mass
- Technetium-99m pertechnetate scintigraphy
 - Mitochondrial hyperplasia

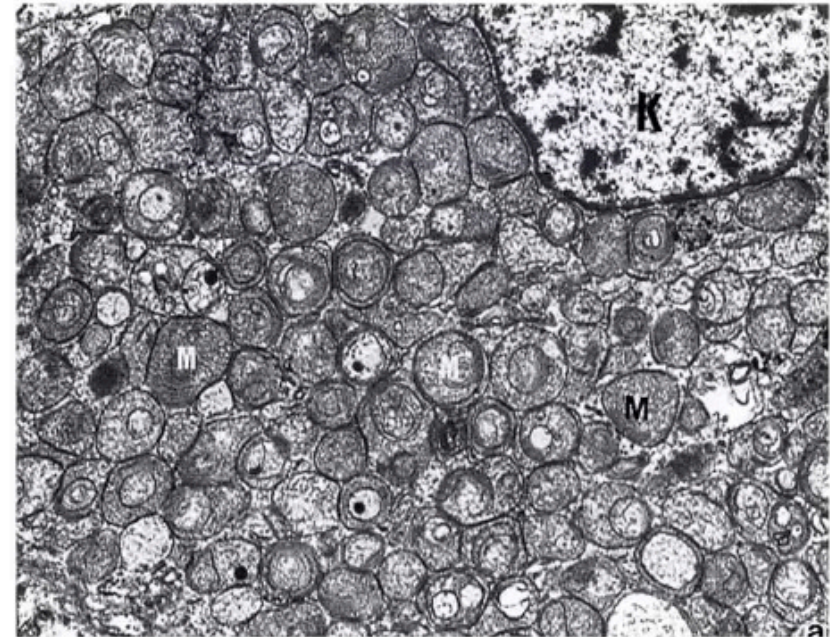
Oncocytoma

- Gross
 - Encapsulated
 - Homogeneous, smooth
 - Orange/rust color
- Histology
 - Cords of uniform cells and thin fibrous stroma
 - Large polyhedral cells
 - Distinct cell membrane
 - Granular, eosinophilic cytoplasm
 - Central, round, vesicular nucleus



Oncocytoma

- Electron microscopy:
 - Mitochondrial hyperplasia
 - 60% of cell volume

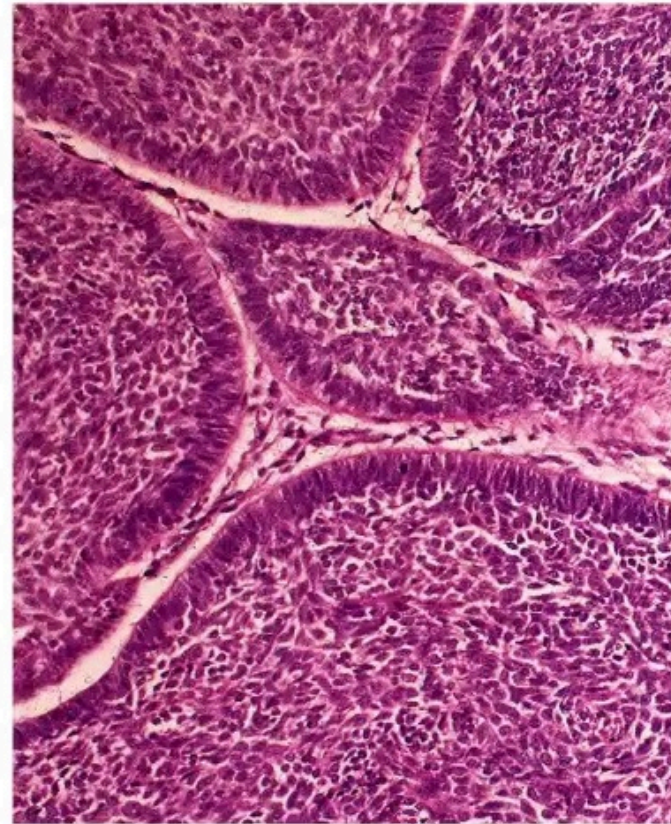


Monomorphic Adenomas

- Types: Basal cell, canalicular, sebaceous, glycogen-rich, clear cell
- Basal cell is most common: 1.8% of benign epithelial salivary gland neoplasms
- 6th decade
- M:F = approximately 1:1
- Caucasian > African American
- Most common in parotid

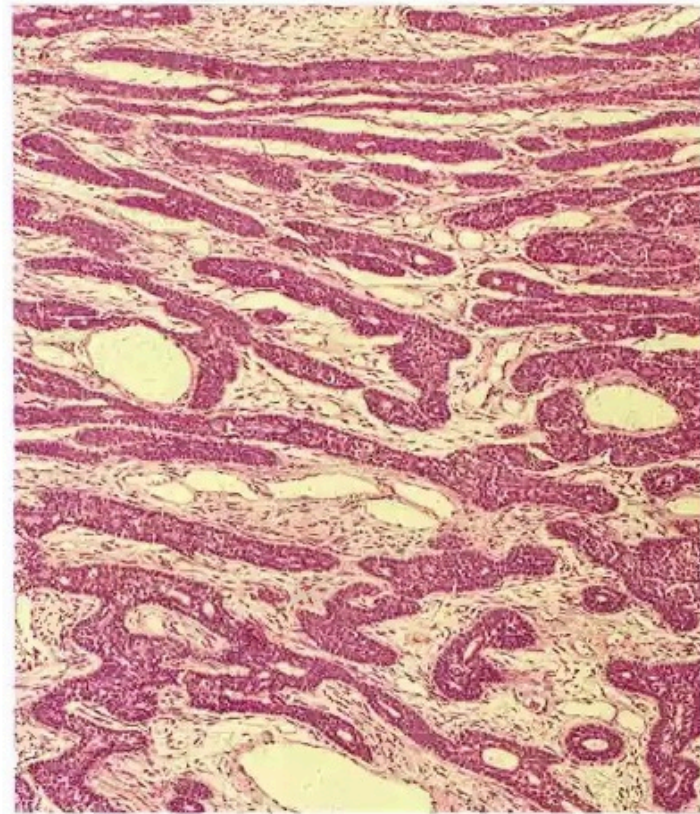
Basal Cell Adenoma

- Solid
 - Most common
 - Solid nests of tumor cells
 - Uniform, hyperchromatic, round nuclei, indistinct cytoplasm
 - Peripheral nuclear palisading
 - Scant stroma



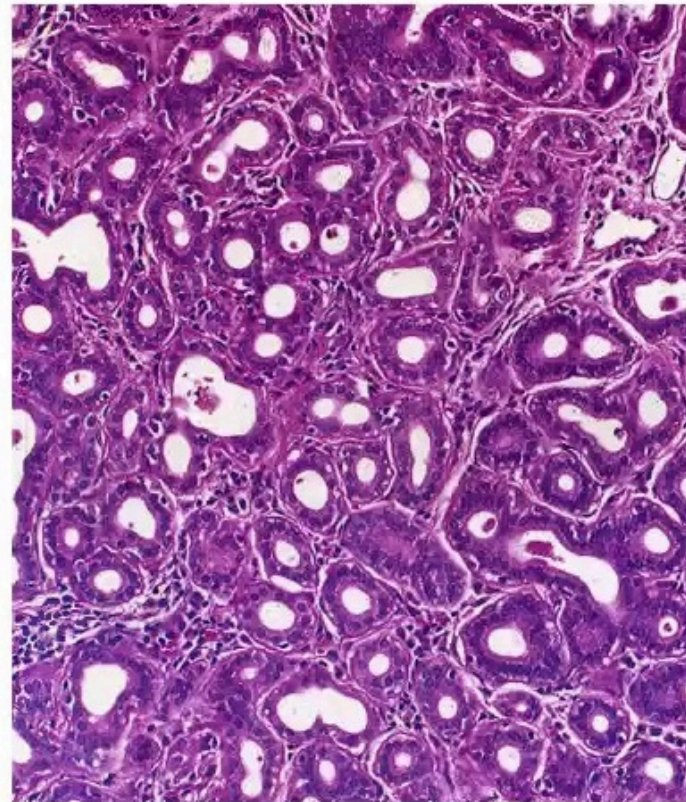
Basal Cell Adenoma

- Trabecular
 - Cells in elongated trabecular pattern
 - Vascular stroma



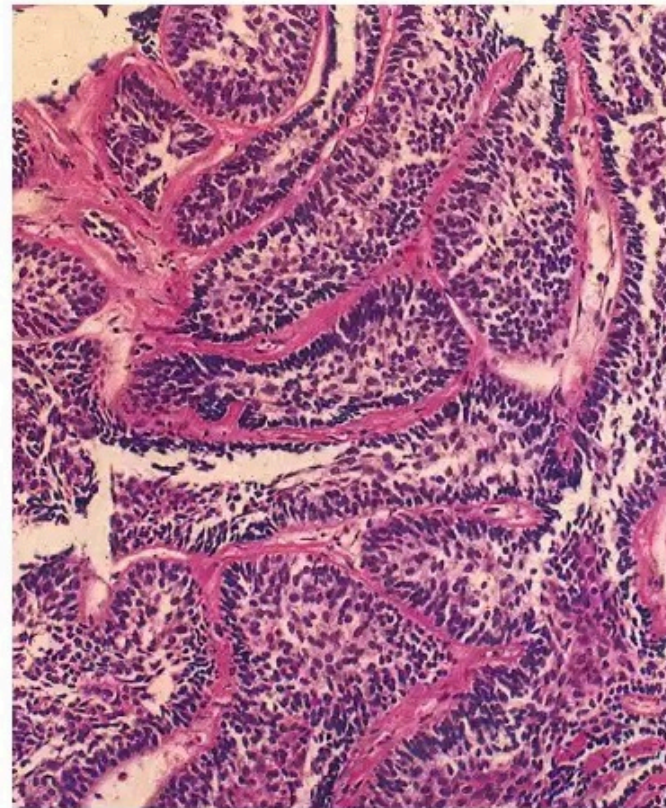
Basal Cell Adenoma

- Tubular
 - Multiple duct-like structures
 - Columnar cell lining
 - Vascular stroma



Basal Cell Adenoma

- Membranous
 - Thick eosinophilic hyaline membranes surrounding nests of tumor cells
 - “jigsaw-puzzle” appearance

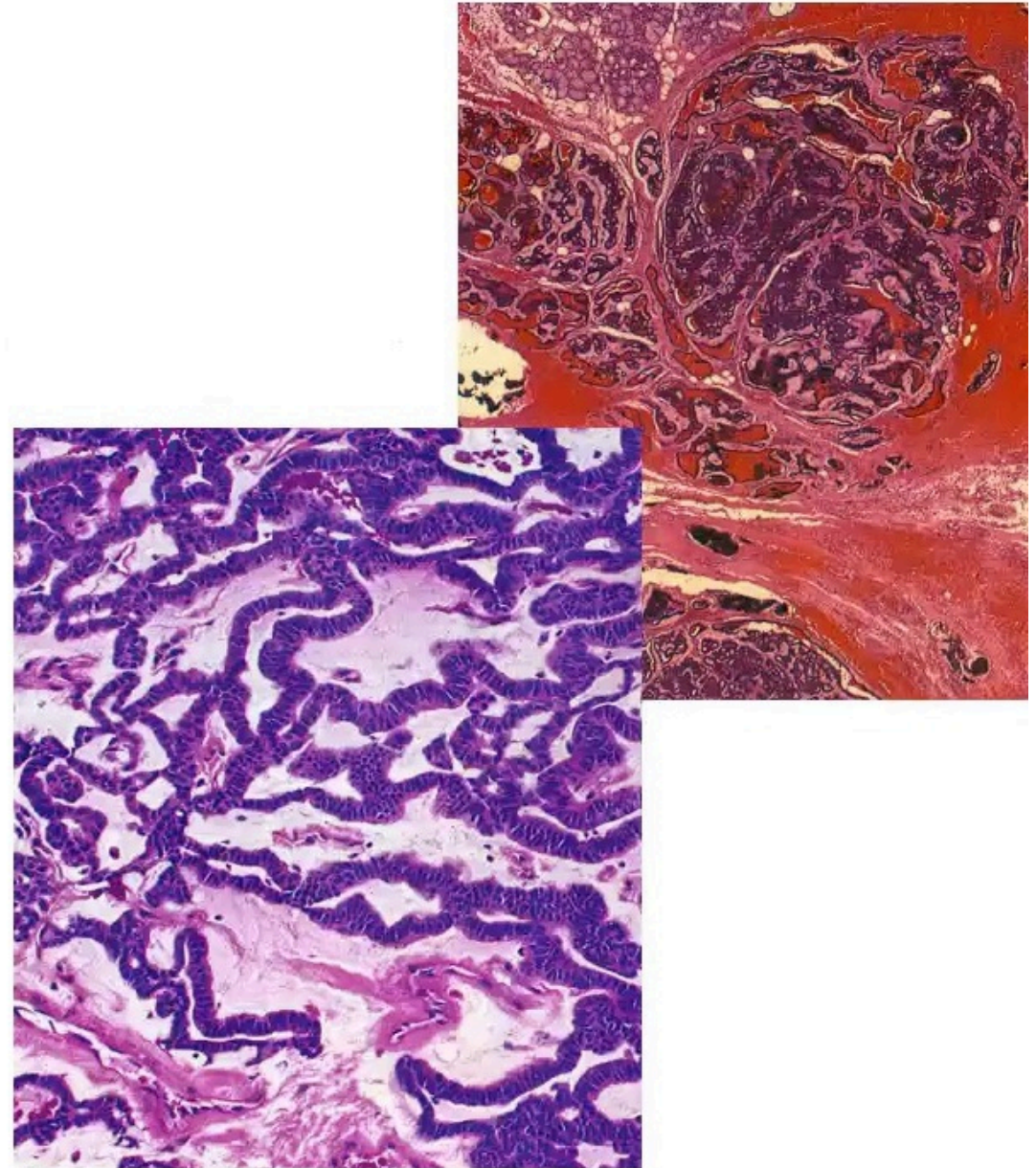


Monomorphic Adenomas

- Canalicular adenoma
 - 7th decade
 - F:M – 1.8:1
 - Most common in minor salivary glands of the upper lip (74%)
 - Painless submucosal mass

Canalicular Adenoma

- Histology
 - Well-circumscribed
 - Multiple foci
 - Tubular structures lined by columnar or cuboidal cells
 - Vascular stroma



Myoepithelioma

- <1% of all salivary neoplasms
- 3rd-6th decades
- F>M
- Minor salivary glands > parotid > submandibular gland
- Presentation: asymptomatic mass

Myoepithelioma

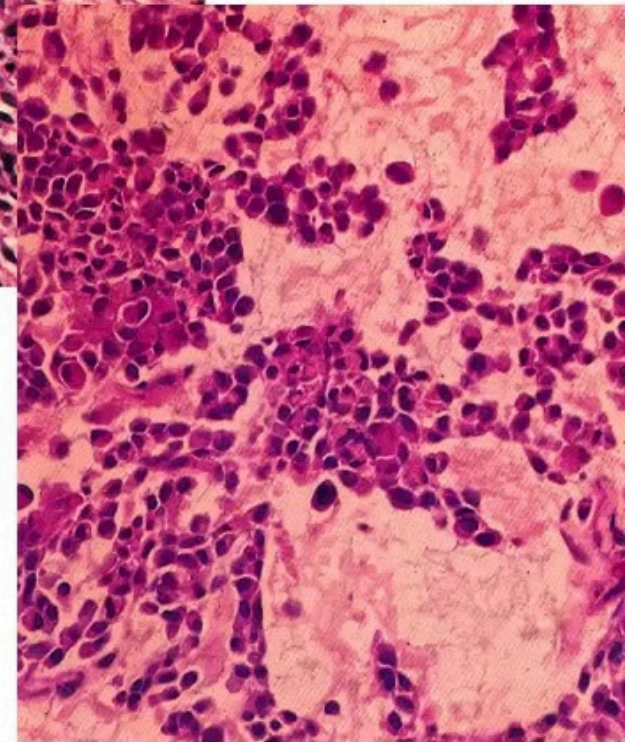
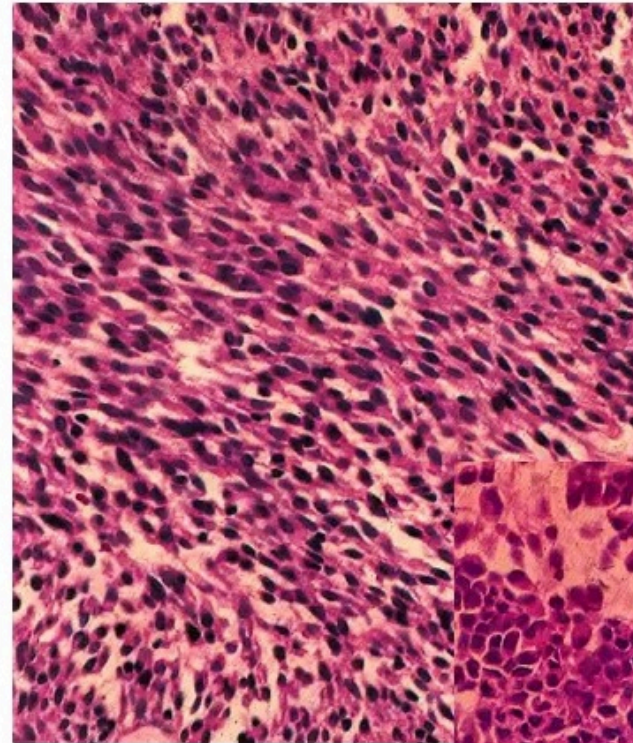
- Histology

- Spindle cell

- More common
 - Parotid
 - Uniform, central nuclei
 - Eosinophilic granular or fibrillar cytoplasm

- Plasmacytoid cell

- Polygonal
 - Eccentric oval nuclei



MALIGNANT NEOPLASMS

1. Mucoepidermoid Carcinoma
2. Adenoid Cystic Carcinoma
3. Acinic Cell Carcinoma
4. Adenocarcinoma
5. Malignant Mixed Tumors: Carcinoma Ex-Pleomorphic Adenoma, Carcinosarcoma
6. Squamous Cell Carcinoma
7. Polymorphous Low-Grade Adenocarcinoma
8. Clear Cell Carcinoma
9. Epithelial-Myoepithelial Carcinoma
10. Undifferentiated Carcinoma

MALIGNANT TUMORS

Mucoepidermoid Carcinoma

- Most common salivary gland malignancy in children
- 5-9% of salivary neoplasms
- Parotid 45-70% of cases
- Palate 18%
- 3rd-8th decades, peak in 5th decade
- F>M
- Caucasian > African American

Mucoepidermoid Carcinoma

- Presentation
 - Low-grade: slow growing, painless mass
 - High-grade: rapidly enlarging, +/- pain
- **Minor salivary glands: may be mistaken for benign or inflammatory process
 - Hemangioma
 - Papilloma
 - Tori

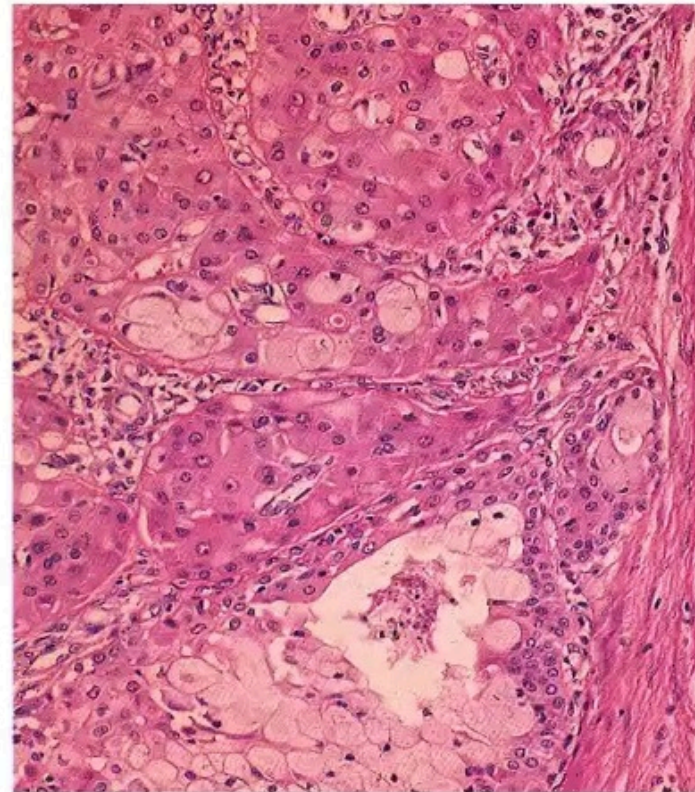
Mucoepidermoid Carcinoma

- Gross pathology
 - Well-circumscribed to partially encapsulated to unencapsulated
 - Solid tumor with cystic spaces



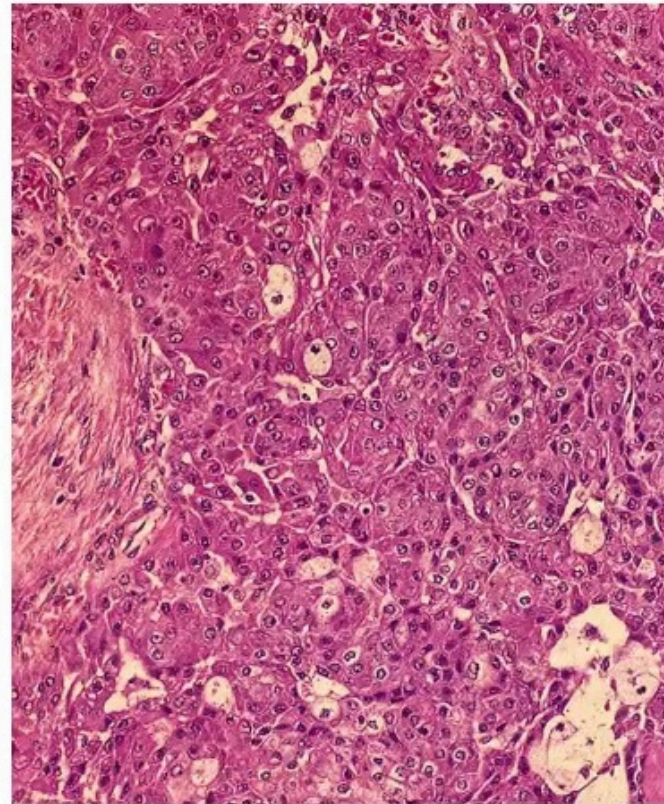
Mucoepidermoid Carcinoma

- Histology—Low-grade
 - Mucus cell > epidermoid cells
 - Prominent cysts
 - Mature cellular elements



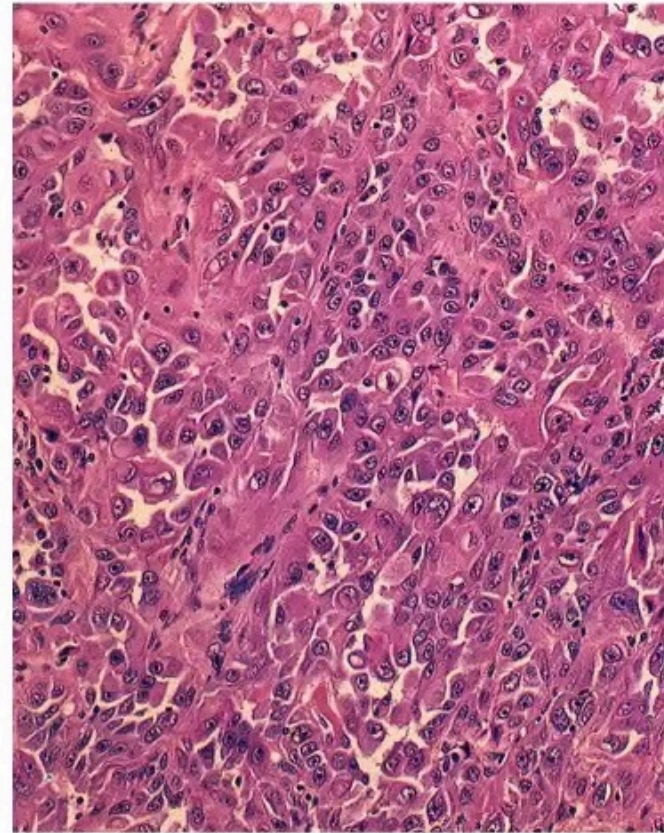
Mucoepidermoid Carcinoma

- Histology—Intermediate-grade
 - Mucus = epidermoid
 - Fewer and smaller cysts
 - Increasing pleomorphism and mitotic figures



Mucoepidermoid Carcinoma

- Histology—High-grade
 - Epidermoid > mucus
 - Solid tumor cell proliferation
 - Mistaken for SCCA
 - Mucin staining



Mucoepidermoid Carcinoma

- Treatment
 - Influenced by site, stage, grade
 - Stage I & II
 - Wide local excision
 - Stage III & IV
 - Radical excision
 - +/- neck dissection
 - +/- postoperative radiation therapy

Adenoid Cystic Carcinoma

- Overall most common malignancy
- Most common in submandibular, sublingual and minor salivary glands
- M = F
- 5th decade
- Presentation
 - Asymptomatic enlarging mass
 - Pain, paresthesias, facial weakness/paralysis

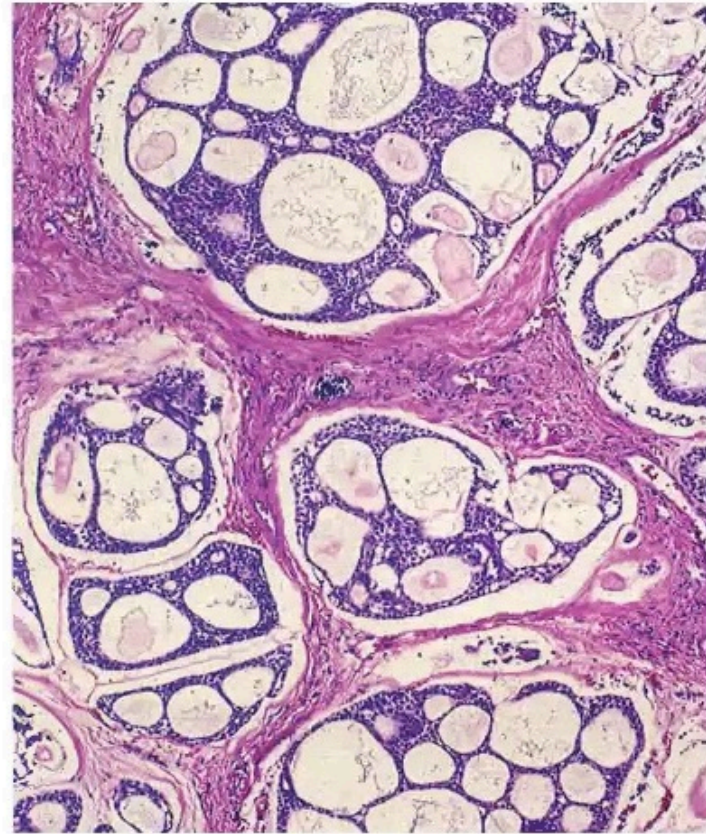
Adenoid Cystic Carcinoma

- Gross pathology
 - Well-circumscribed
 - Solid, rarely with cystic spaces
 - infiltrative



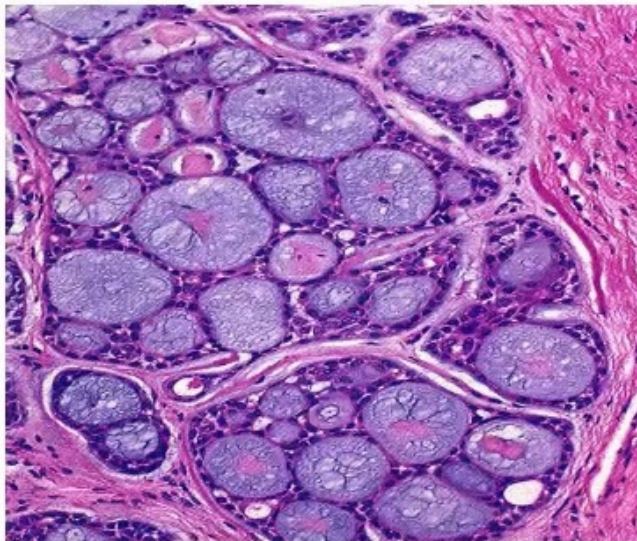
Adenoid Cystic Carcinoma

- Histology—cribriform pattern
 - Most common
 - “swiss cheese” appearance

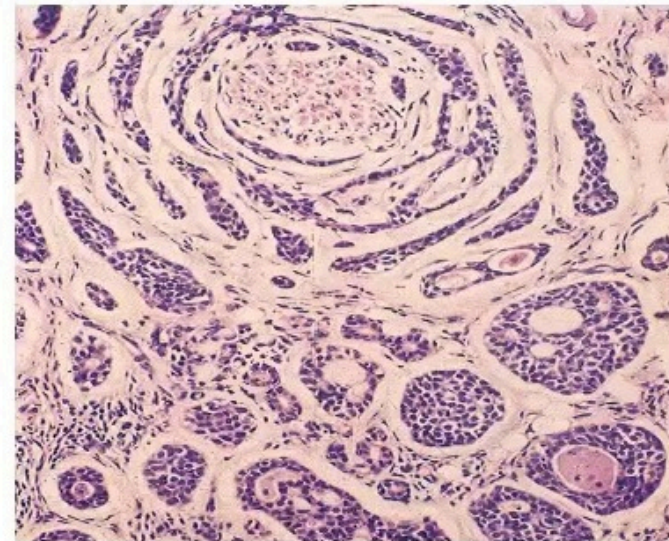


Adenoid Cystic Carcinoma

- Histology—tubular pattern
 - Layered cells forming duct-like structures
 - Basophilic mucinous substance



- Histology—solid pattern
 - Solid nests of cells without cystic or tubular spaces



Adenoid Cystic Carcinoma

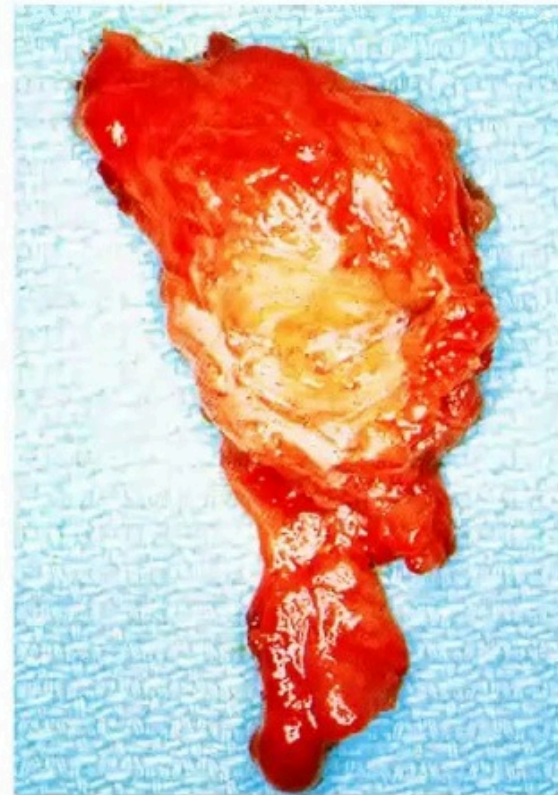
- Treatment
 - Complete local excision
 - Tendency for perineural invasion: facial nerve sacrifice
 - Postoperative XRT
- Prognosis
 - Local recurrence: 42%
 - Distant metastasis: lung
 - Indolent course: 5-year survival 75%, 20-year survival 13%

Acinic Cell Carcinoma

- 2nd most common parotid and pediatric malignancy
- 5th decade
- F>M
- Bilateral parotid disease in 3%
- Presentation
 - Solitary, slow-growing, often painless mass

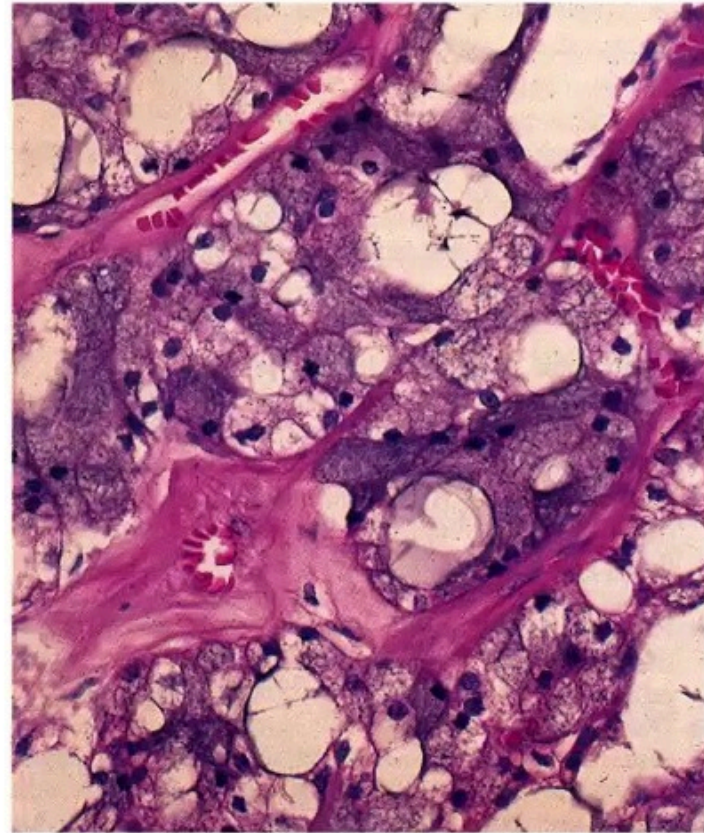
Acinic Cell Carcinoma

- Gross pathology
 - Well-demarcated
 - Most often homogeneous



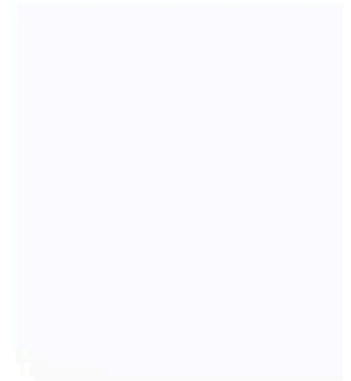
Acinic Cell Carcinoma

- Histology
 - Solid and microcystic patterns
 - Most common
 - Solid sheets
 - Numerous small cysts
 - Polyhedral cells
 - Small, dark, eccentric nuclei
 - Basophilic granular cytoplasm



Acinic Cell Carcinoma

- Treatment
 - Complete local excision
 - +/- postoperative XRT
- Prognosis
 - 5-year survival: 82%
 - 10-year survival: 68%
 - 25-year survival: 50%



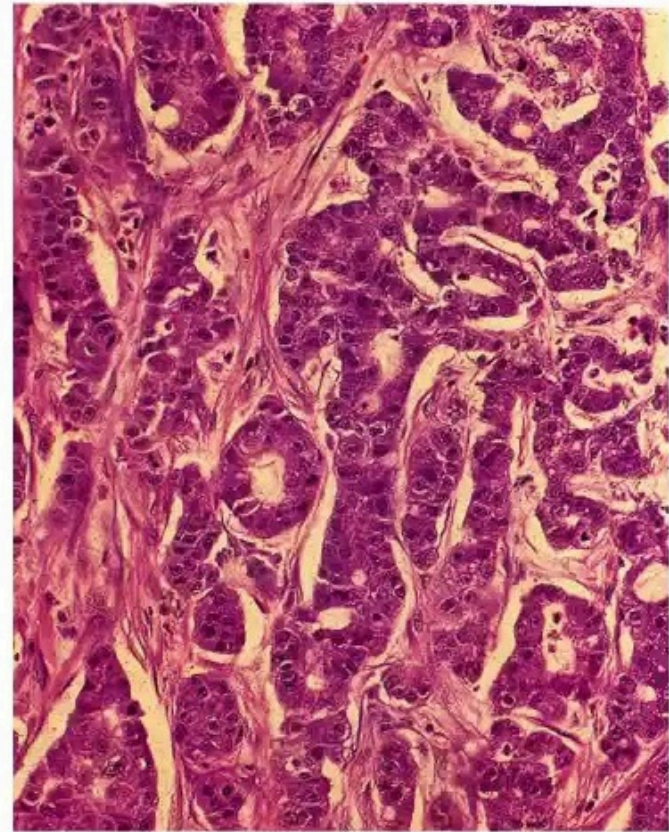
Adenocarcinoma

- Rare
- 5th to 8th decades
- F > M
- Parotid and minor salivary glands
- Presentation:
 - Enlarging mass
 - 25% with pain or facial weakness



Adenocarcinoma

- Histology
 - Heterogeneity
 - Presence of glandular structures and absence of epidermoid component
 - Grade I
 - Grade II
 - Grade III



Adenocarcinoma

- Treatment

- Complete local excision
- Neck dissection
- Postoperative XRT

- Prognosis

- Local recurrence: 51%
- Regional metastasis: 27%
- Distant metastasis: 26%
- 15-year cure rate:
 - Stage I = 67%
 - Stage II = 35%
 - Stage III = 8%

Malignant Mixed Tumors

- Carcinoma ex-pleomorphic adenoma
 - Carcinoma developing in the epithelial component of preexisting pleomorphic adenoma
- Carcinosarcoma
 - True malignant mixed tumor—carcinomatous and sarcomatous components
- Metastatic mixed tumor
 - Metastatic deposits of otherwise typical pleomorphic adenoma

Carcinoma Ex-Pleomorphic Adenoma

- 2-4% of all salivary gland neoplasms
- 4-6% of mixed tumors
- 6th-8th decades
- Parotid > submandibular > palate
- Risk of malignant degeneration
 - 1.5% in first 5 years
 - 9.5% after 15 years
- Presentation
 - Longstanding painless mass that undergoes sudden enlargement

Carcinoma Ex-Pleomorphic Adenoma

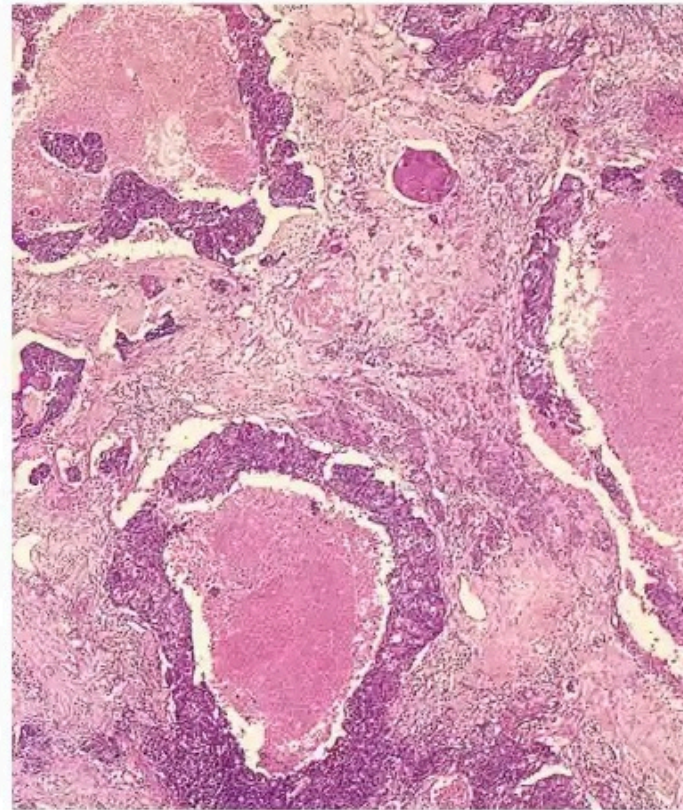
- Gross pathology
 - Poorly circumscribed
 - Infiltrative
 - Hemorrhage and necrosis



Carcinoma Ex-Pleomorphic Adenoma

- **Histology**

- Malignant cellular change adjacent to typical pleomorphic adenoma
- Carcinomatous component
 - Adenocarcinoma
 - Undifferentiated



Carcinoma Ex-Pleomorphic Adenoma

- Treatment
 - Radical excision
 - Neck dissection (25% with lymph node involvement at presentation)
 - Postoperative XRT
- Prognosis
 - Dependent upon stage and histology

Carcinosarcoma

- Rare: <.05% of salivary gland neoplasms
- 6th decade
- M = F
- Parotid
- History of previously excised pleomorphic adenoma, recurrent pleomorphic adenoma or recurring pleomorphic treated with XRT
- Presentation

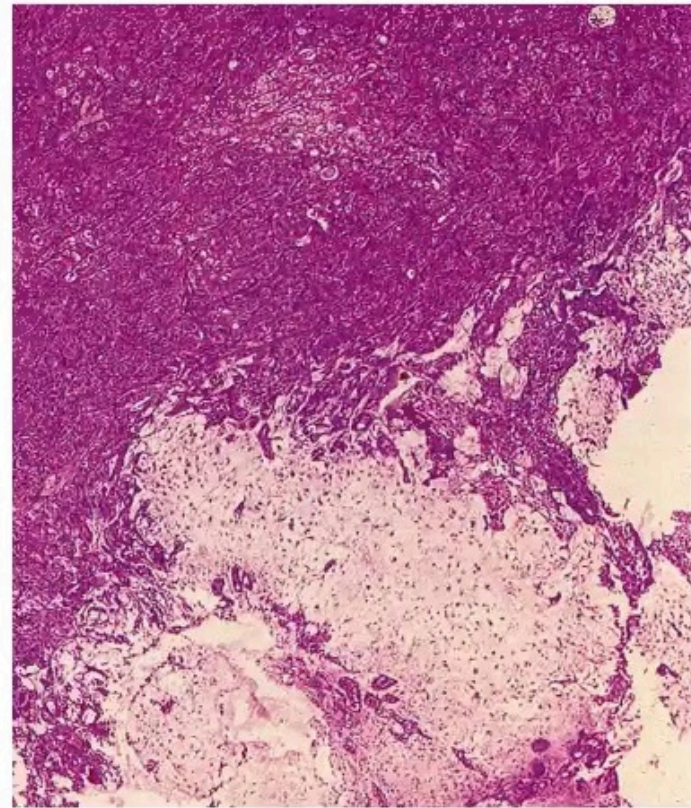
Carcinosarcoma

- Gross pathology
 - Poorly circumscribed
 - Infiltrative
 - Cystic areas
 - Hemorrhage, necrosis
 - Calcification



Carcinosarcoma

- **Histology**
 - Biphasic appearance
 - Sarcomatous component
 - Dominant
 - chondrosarcoma
 - Carinomatous component
 - Moderately to poorly differentiated ductal carcinoma
 - Undifferentiated



Carcinosarcoma

- Treatment
 - Radical excision
 - Neck dissection
 - Postoperative XRT
 - Chemotherapy (distant metastasis to lung, liver, bone, brain)
- Prognosis
 - Poor, average survival less than 2 ½ years

Squamous Cell Carcinoma

- 1.6% of salivary gland neoplasms
- 7th-8th decades
- M:F = 2:1
- MUST RULE OUT:
 - High-grade mucoepidermoid carcinoma
 - Metastatic SCCA to intraglandular nodes
 - Direct extension of SCCA

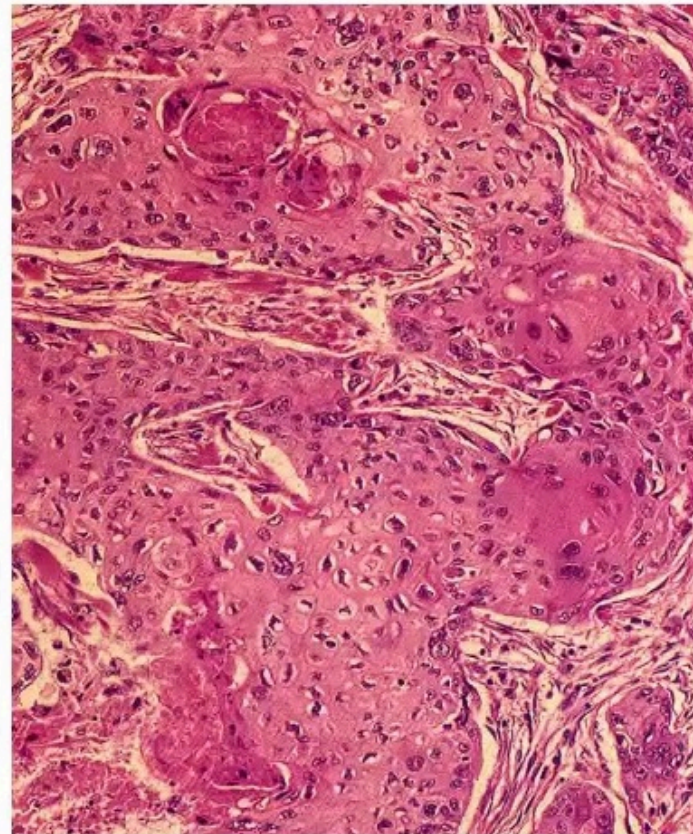
Squamous Cell Carcinoma

- Gross pathology
 - Unencapsulated
 - Ulcerated
 - fixed



Squamous Cell Carcinoma

- Histology
 - Infiltrating
 - Nests of tumor cells
 - Well differentiated
 - Keratinization
 - Moderately-well differentiated
 - Poorly differentiated
 - No keratinization

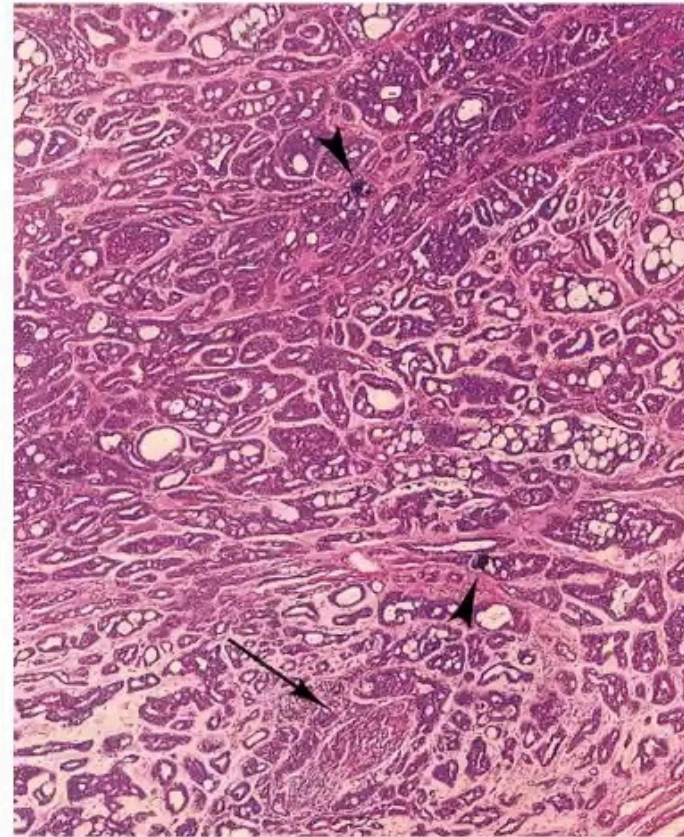


Squamous Cell Carcinoma

- Treatment
 - Radical excision
 - Neck dissection
 - Postoperative XRT
- Prognosis
 - 5-year survival: 24%
 - 10-year survival: 18%

Polymorphous Low-Grade Adenocarcinoma

- 2nd most common malignancy in minor salivary glands
- 7th decade
- F > M
- Painless, submucosal mass
- Morphologic diversity
 - Solid, glandular, cribriform, ductular, tubular, trabecular, cystic



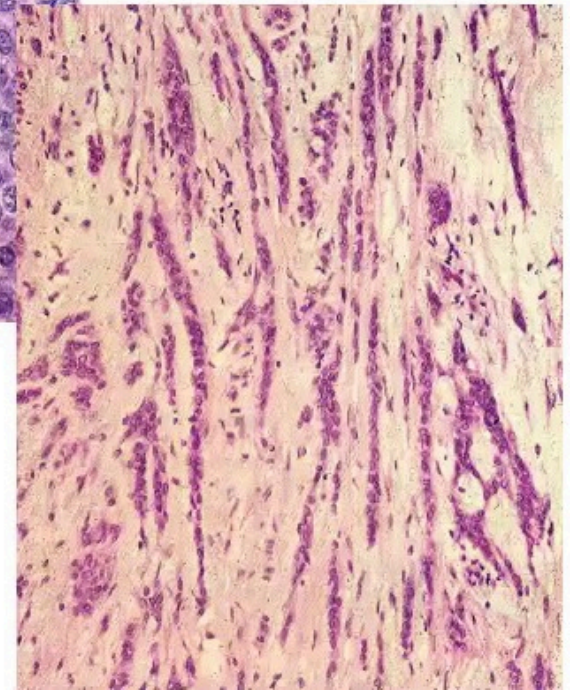
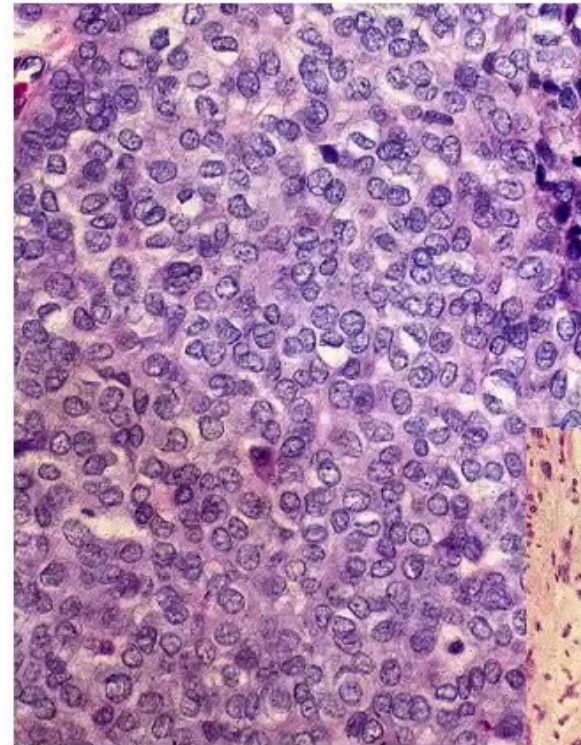
Polymorphous Low-Grade Adenocarcinoma

- **Histology**

- Isomorphic cells, indistinct borders, uniform nuclei
- Peripheral “Indian-file” pattern

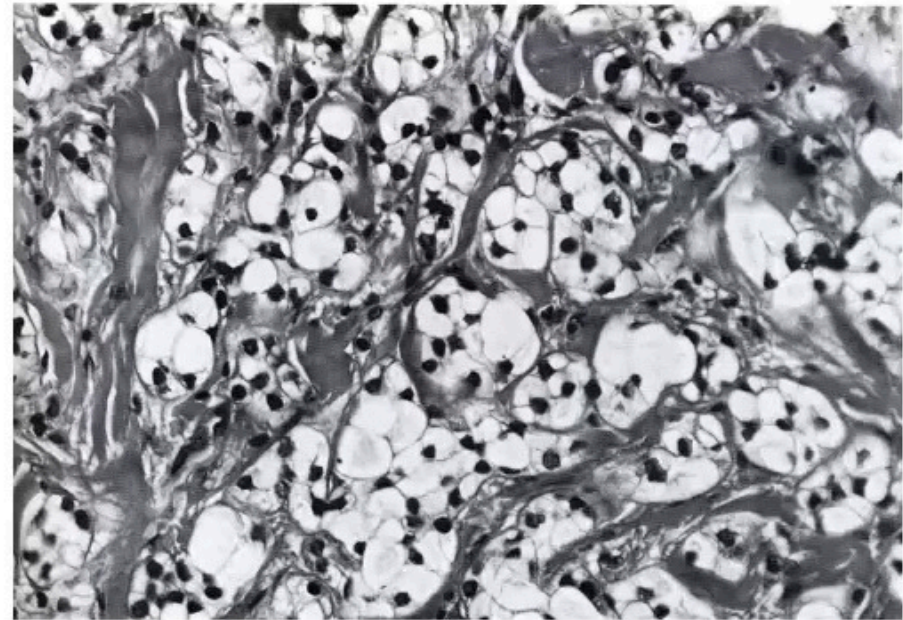
- **Treatment**

- Complete yet conservative excision



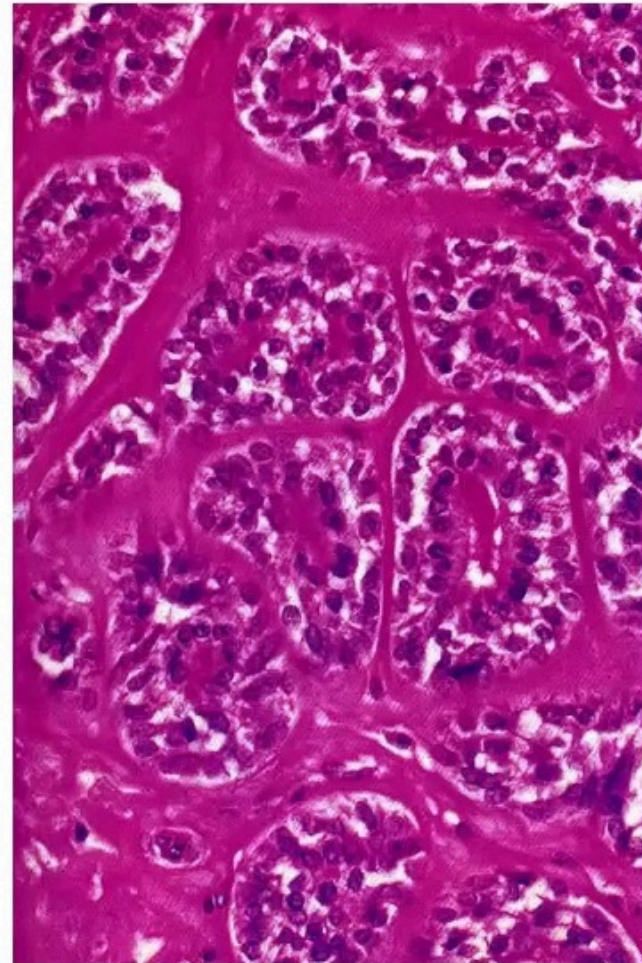
Clear Cell Carcinoma

- AKA glycogen-rich
- Palate and parotid
- 6th-8th decade
- M = F
- Histology
 - Uniform, round or polygonal cells
 - Peripheral dark nuclei
 - Clear cytoplasm
- Treatment
 - Complete local excision



Epithelial-Myoepithelial Carcinoma

- < 1% of salivary neoplasms
- 6th-7th decades, F > M, parotid
- ? Increased risk for 2nd primary
- Histology
 - Tumor cell nests
 - Two cell types
 - Thickened basement membrane
- Treatment
 - Surgical excision



Undifferentiated Carcinoma

- **Lymphoepithelial**

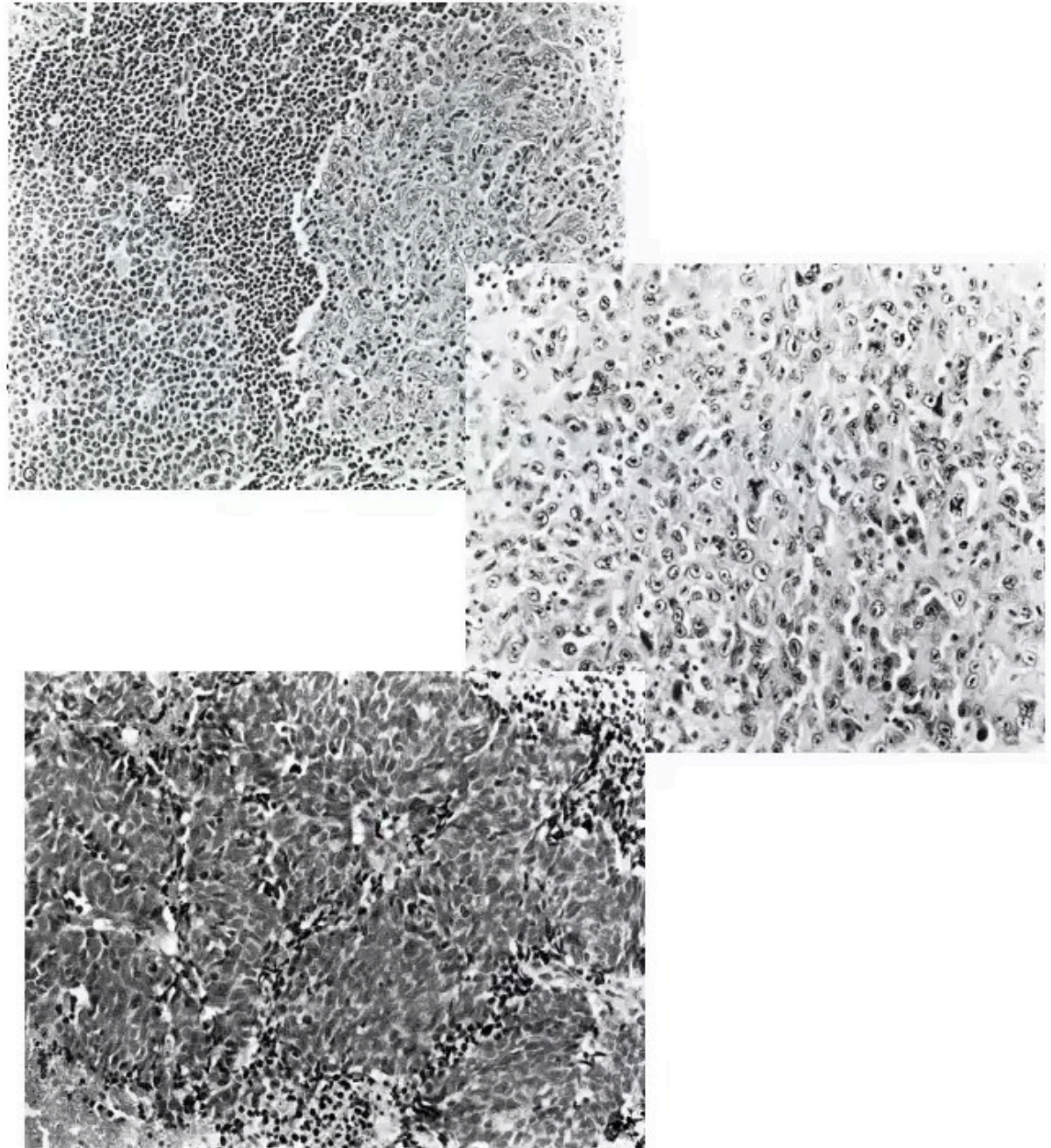
- Eskimos: parotid, F > M, familial
- Asian: submandibular, M > F

- **Large-cell**

- Bimodal peaks
- M > F
- Parotid

- **Small-cell**

- 6th-7th decades
- M:F = 1.6:1
- parotid



Controversial Issues

- **Management of the N0 Neck:**

- Recurrence in the neck = low likelihood of salvage
- Parotid: clinical neck disease, 16%
 - N- disease = 74% 5-year survival
 - N+ disease = 9% 5-year survival
- Submandibular: clinical neck disease, 8%
 - N- disease = 41% 5-year survival
 - N+ disease = 9% 5-year survival

Management of the N0 Neck

- **Increase risk of occult neck metastasis:**
 - **High-grade malignancies
 - **Advanced primary tumor stage (T3-T4)
 - High risk histology
 - Undifferentiated, SCCA, adenocarcinoma, high-grade mucoepidermoid, salivary duct carcinoma
 - Tumor size > 3cm
 - Patient > 54 years of age
 - Facial paralysis
 - Extracapsular, perilymphatic spread

Management of the N0 Neck

- **Neck Dissection**

- Advantages

- Pathologic staging

- Improved counseling and prediction of prognosis

- Disadvantages

- Longer OR time, increase complications, increased cost

- Functional deficits, cosmetic effects

- Type

- Parotid: levels II-IV

- Submandibular: levels I-III

Management of the N0 Neck

- **Radiation Therapy**

- Advantage

- Avoids surgical sequelae

- Disadvantages

- Radiation effect on normal tissue
 - Radiation induced malignancies

- Proponents argument: the same factors that increase the risk of occult neck disease also increase the risk for local recurrence and necessitate postoperative XRT to the primary so it is reasonable to treat the neck with XRT as well

Fine-Needle Aspiration Biopsy - Facts

- Efficacy is well established
- Accuracy = 84-97%
- Sensitivity = 54-95%
- Specificity = 86-100%
- Safe, well tolerated

Fine-Needle Aspiration Biopsy

- **Opponents argument (advise against):**
 - Doesn't change management
 - Surgery regardless of reported diagnosis
 - Obscuring final pathologic diagnosis
 - Frequency of “inadequate” sampling, requires multiple biopsies, prolongs course until definitive treatment, increases cost

Fine-Needle Aspiration Biopsy

- **Proponent's argument (advise for/recommend):**
 - Important to distinguish benign vs. malignant nature of neoplasm
 - Preoperative patient counseling
 - Surgical planning
 - Differentiate between neoplastic and non-neoplastic processes
 - Avoid surgery in large number of patients

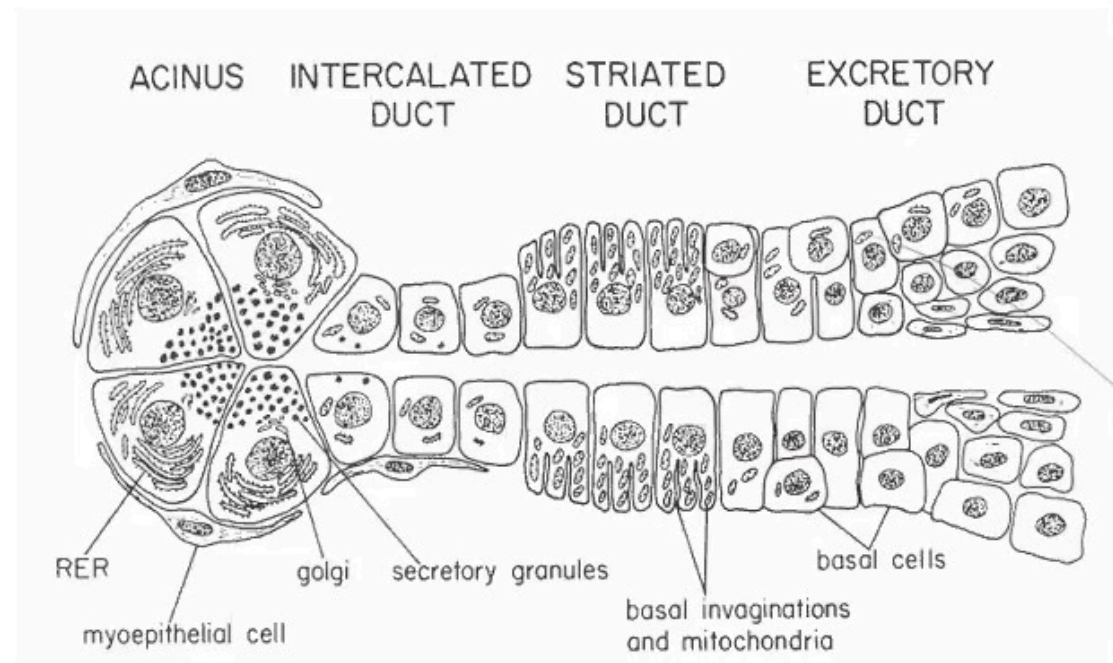
Tumorigenesis: Bicellular Theory

- Intercalated Ducts

- Pleomorphic adenoma
- Warthin's tumor
- Oncocytoma
- Acinic cell
- Adenoid cystic

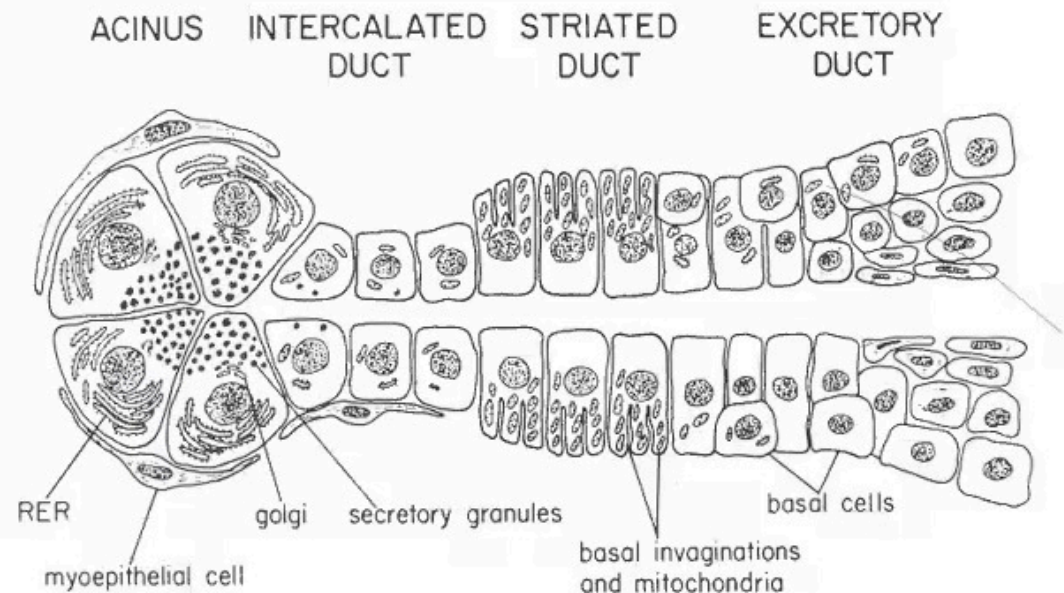
- Excretory Ducts

- Squamous cell
- Mucoepidermoid



Tumorogenesis: Multicellular Theory

- Striated duct—oncocytic tumors
- Acinar cells—acinic cell carcinoma
- Excretory Duct—squamous cell and mucoepidermoid carcinoma
- Intercalated duct and myoepithelial cells—pleomorphic tumors



Tumorigenesis

- Contradictory evidence:
 - Luminal cells are readily capable of replication
 - Acinar cells participate in gland regeneration
 - Immunohistochemical staining of S-100 protein
 - Present in many salivary gland neoplasms
 - Not present in normal ductal cells

Conclusions

- Hugely diverse histopathology
- Accurate pathologic diagnosis does influence management
- Relatively rare malignancies
- Utilize preoperative studies when indicated