Histopathology of Major Salivary Gland Neoplasms

Sam J. Cunningham, MD, PhD
Faculty Advisor: Shawn D. Newlands, MD, PhD
Faculty Advisor: David C. Teller, MD
The University of Texas Medical Branch,
Department of Otolaryngology

Grand Rounds Presentation
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Introduction

- Neoplasms of the major salivary glands constitute minor portion of head and neck neoplasms
- Less than 2% are malignant
- Most neoplasms in parotid 75%, 0.8% in sublingual glands
- Remainder equally distributed between submandibular gland and minor salivary glands

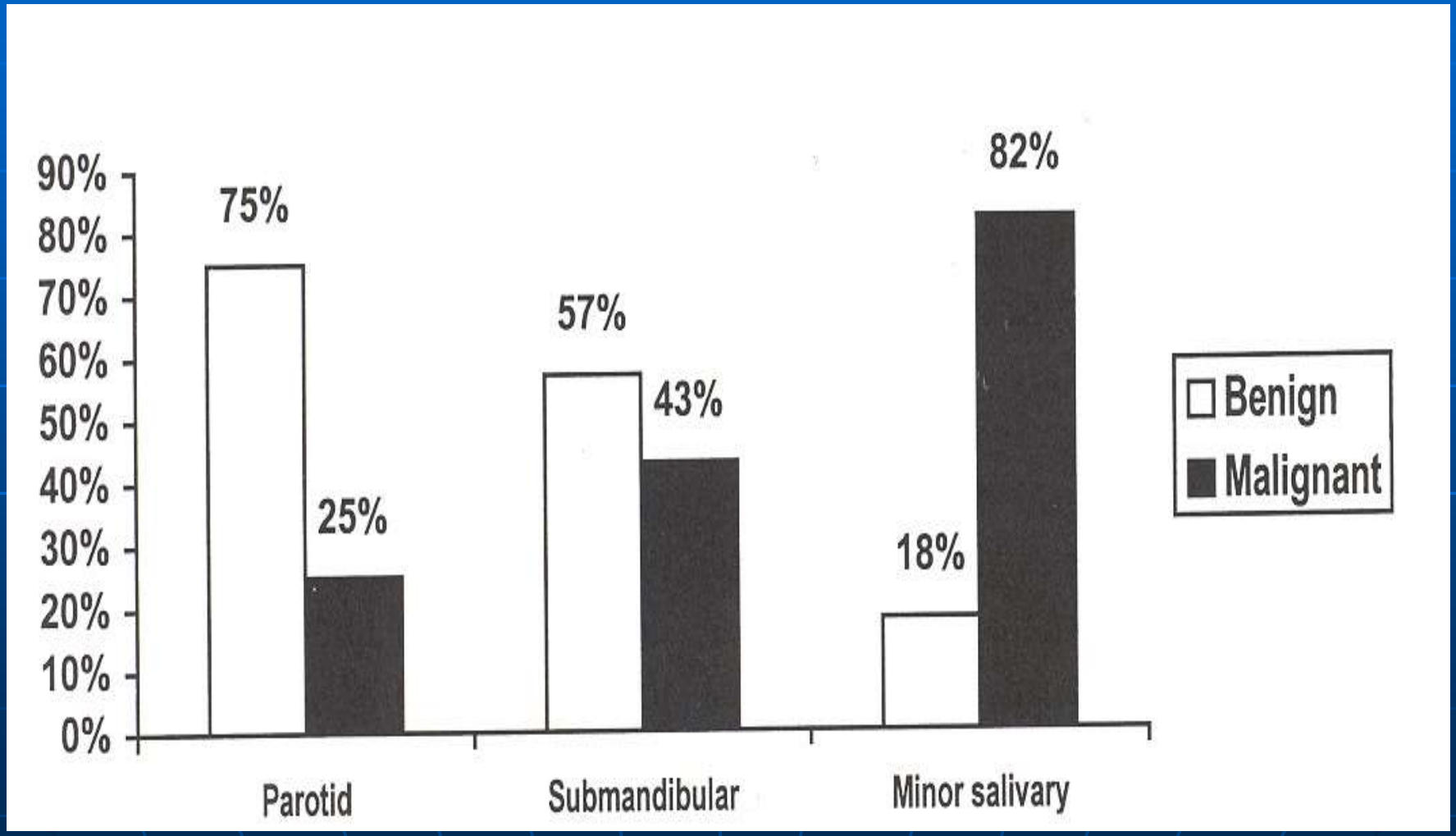
Introduction

- Incidence rises at age 15 and peaks at 65-75.
- Incidence of malignant neoplasms increases after 4^{th} and 5^{th} decades and peaks 65-75 years.
- Benign neoplasms present slightly earlier
- Malignant neoplasms occur most often in men.

Introduction

- Cancers of the salivary glands account for only 6% of H&N cancers
- Only 0.3% of all cancers
- Proportion of malignant and benign varies with the gland of origin.

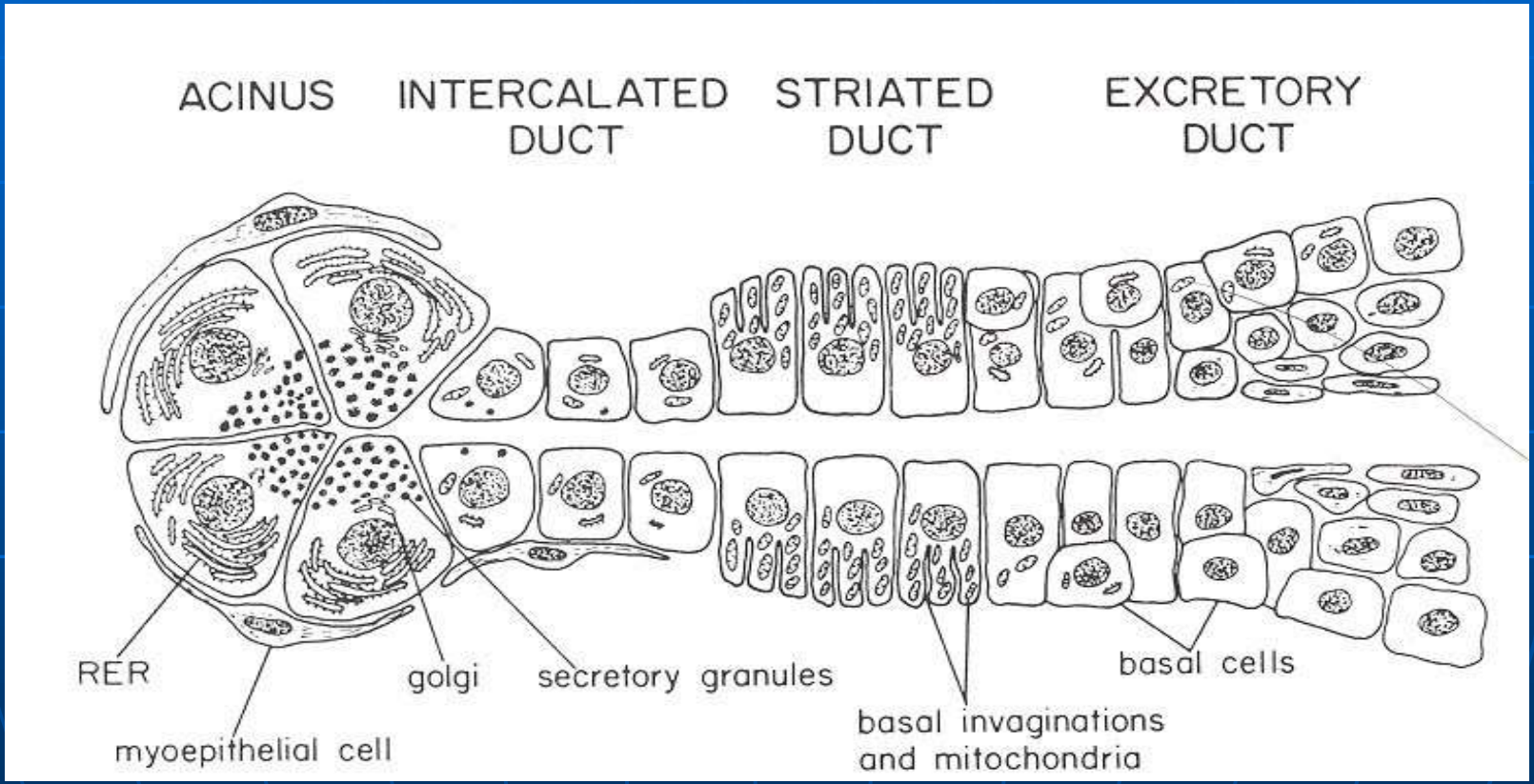
Introduction



Salivary Gland Microanatomy

- Saliva transported from central structure (acini) in complex ductal system to the oral cavity
- System is a bilayer with internal luminal layer and external reserve layer.
- Internal layer forms acini and ductal epithelium
- External layer forms myoepithelium and reserve cells

Salivary Gland Microanatomy



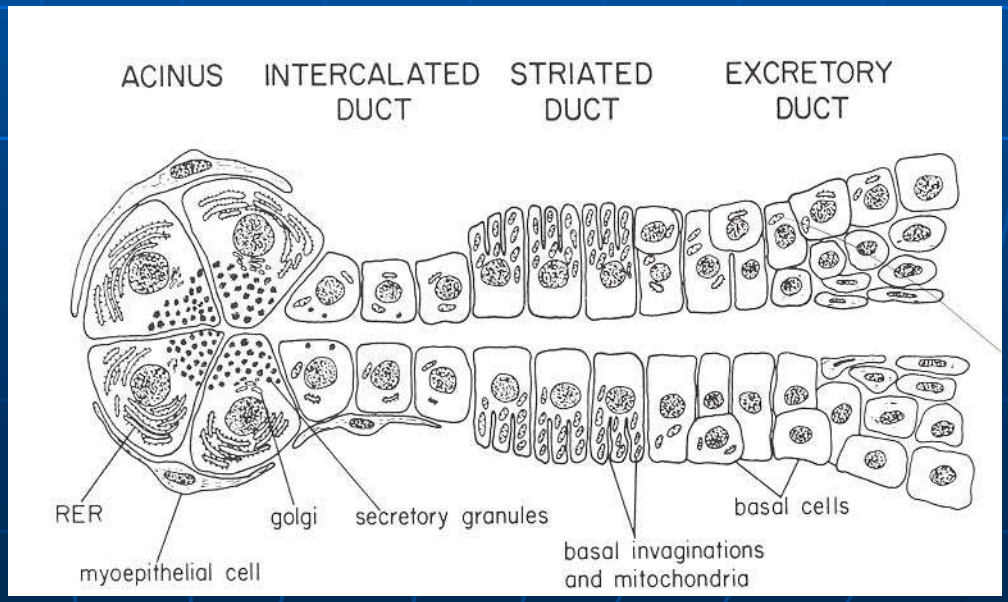
IMMUNOHISTOCHEMICAL STAINING OF THE SALIVARY GLAND UNIT

Site	Positive stains
Acini	Carcinoembryonic antigen Epithelial membrane antigen (serous acini only)
Intercalated duct	Carcinoembryonic antigen Epithelial membrane antigen Cytokeratins S-100 (minor glands only)
Striated duct	Epithelial membrane antigen Cytokeratins S-100 (minor glands only)
Myoepithelial cells	Cytokeratins (serous glands only) S-100 Muscle-specific actin

From Chen JC, et al: Adenoid cystic carcinoma of the salivary glands: An immunohistochemical analysis. *Oral Surg Oral Med Oral Pathol* 1988;65:316-326.[2]

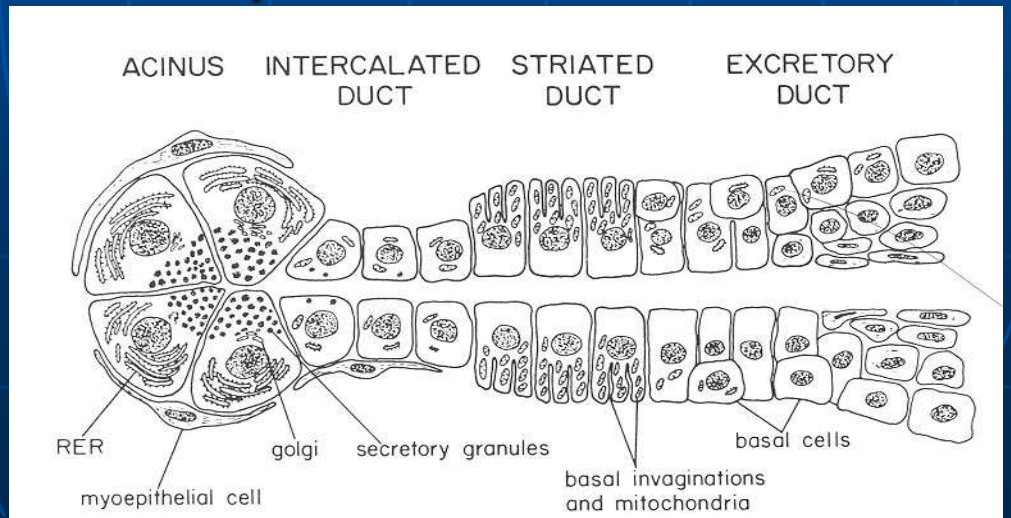
Bicellular Theory

- Intercalated Ducts
  - Pleomorphic adenoma
  - Warthin's tumor
  - Oncocytoma
  - Acinic cell
  - Adenoid cystic
- Excretory Ducts
  - Squamous cell
  - Mucoepidermoid



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



Classification of Salivary Gland Neoplasms

- WHO
  - Adenomas
  - Carcinomas
  - Nonepithelial Tumors
  - Malignant lymphomas
  - Secondary tumors
  - Unclassified tumors
  - Tumor-like lesions

Classification of Salivary Gland Neoplasms

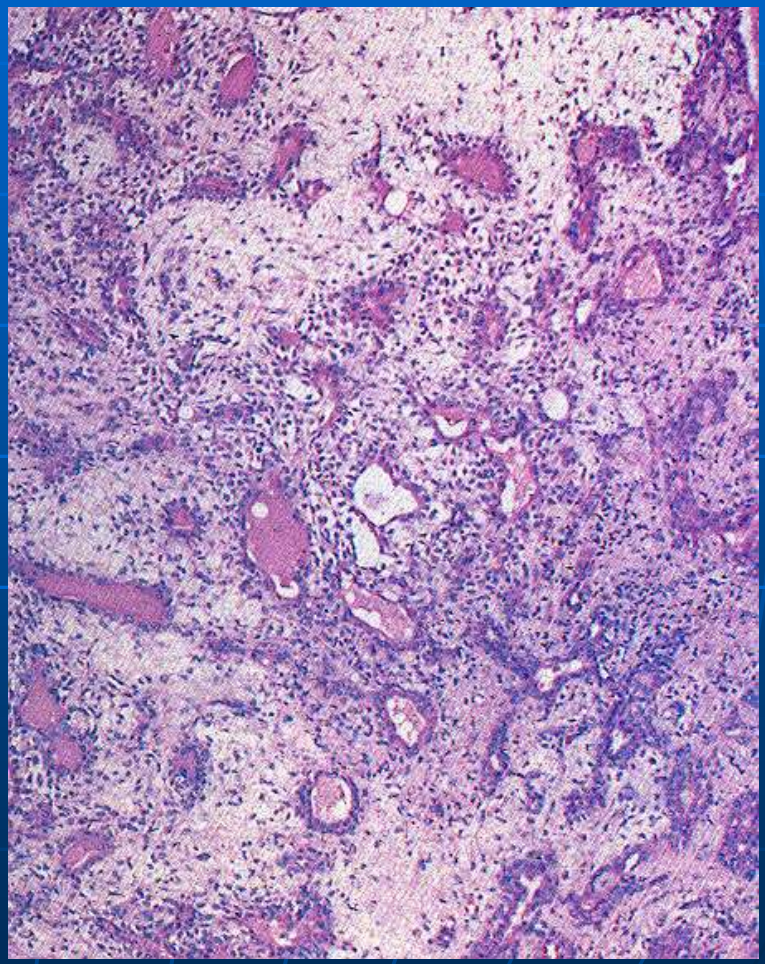
- Armed Forces Institute of Pathology
  - Benign Epithelial Neoplasms
  - Malignant Epithelial Neoplasms
  - Mesenchymal Neoplasms
  - Malignant Lymphomas
  - Metastatic Tumors
  - Nonneoplastic Tumor-like Conditions

Benign Neoplasms

- Pleomorphic Adenoma
- Warthin's Tumor
- Basal Cell Adenoma
- Oncocytoma
- Canalicular Adenoma
- Myoepithelioma

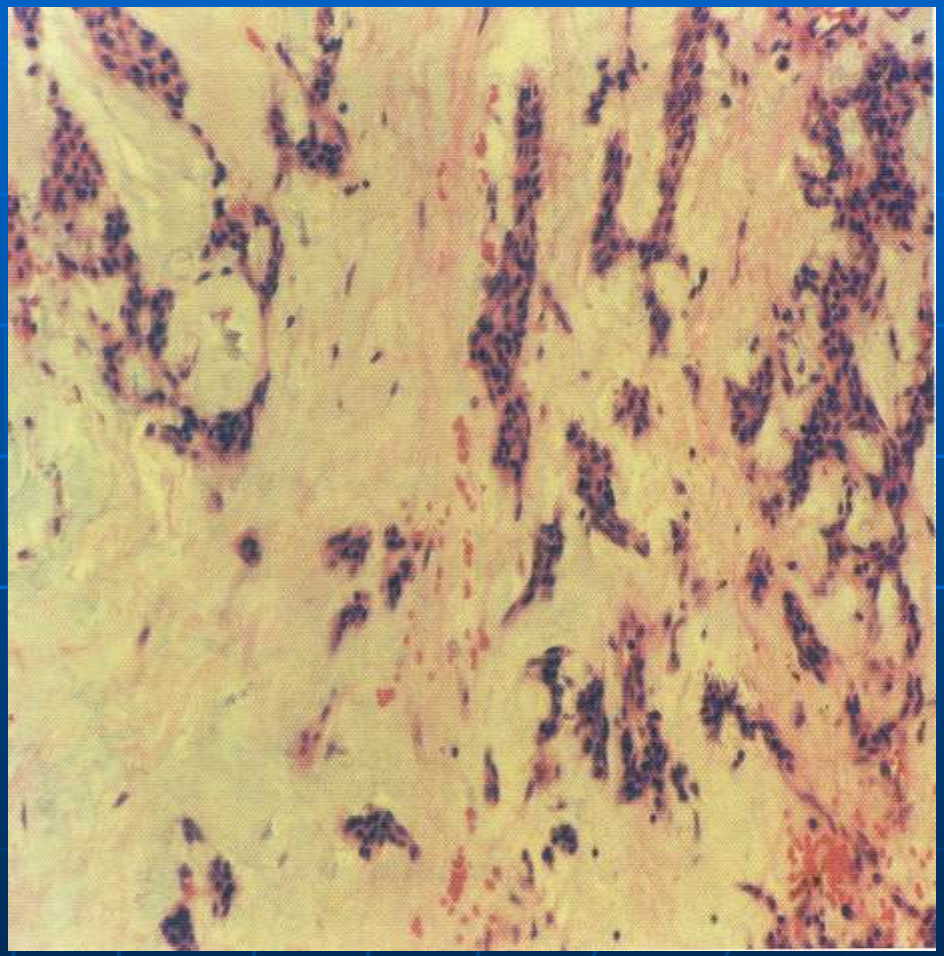
Pleomorphic Adenoma

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



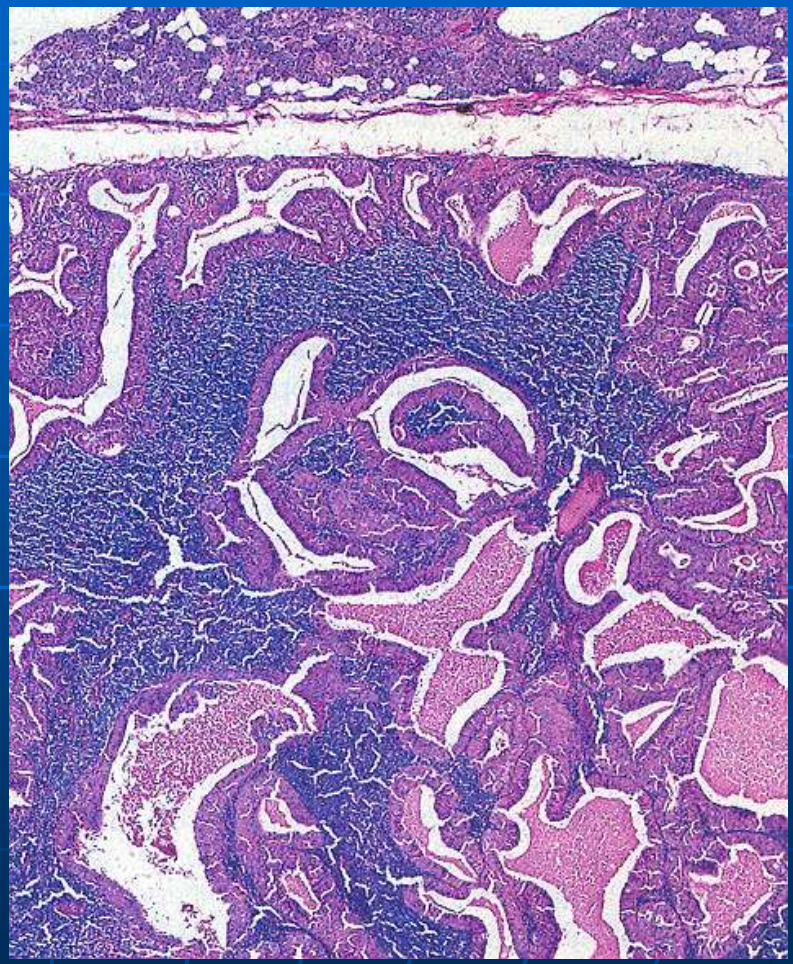
Pleomorphic Adenoma

- Necrosis and mitosis rare
- IHC profile consistent with dual architecture
- Glandular areas stain with CEA and S-100, actin, epithelial membrane antigen
- Mesemchymal areas stain with S-100 and actin only

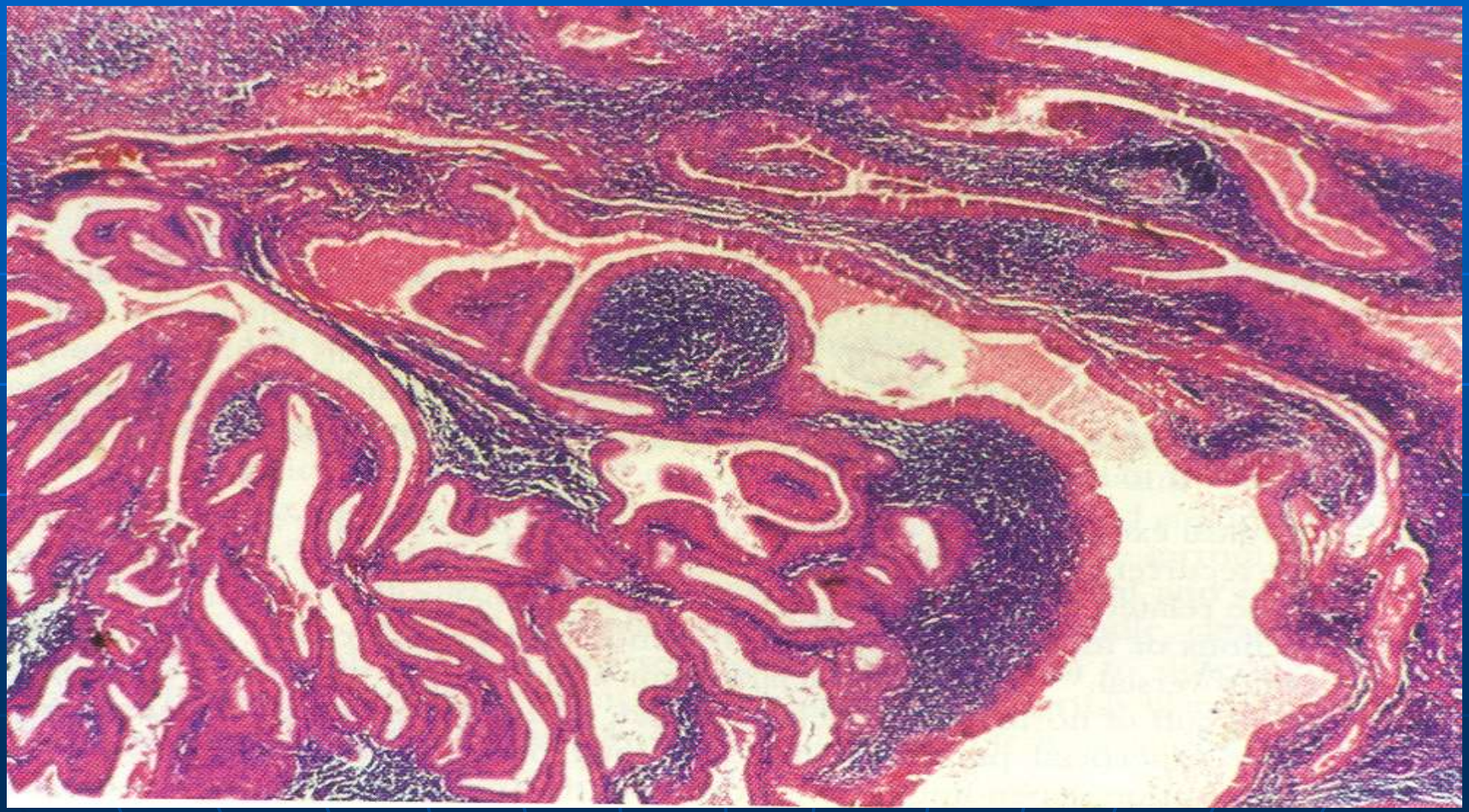


Warthin's Tumor

- 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

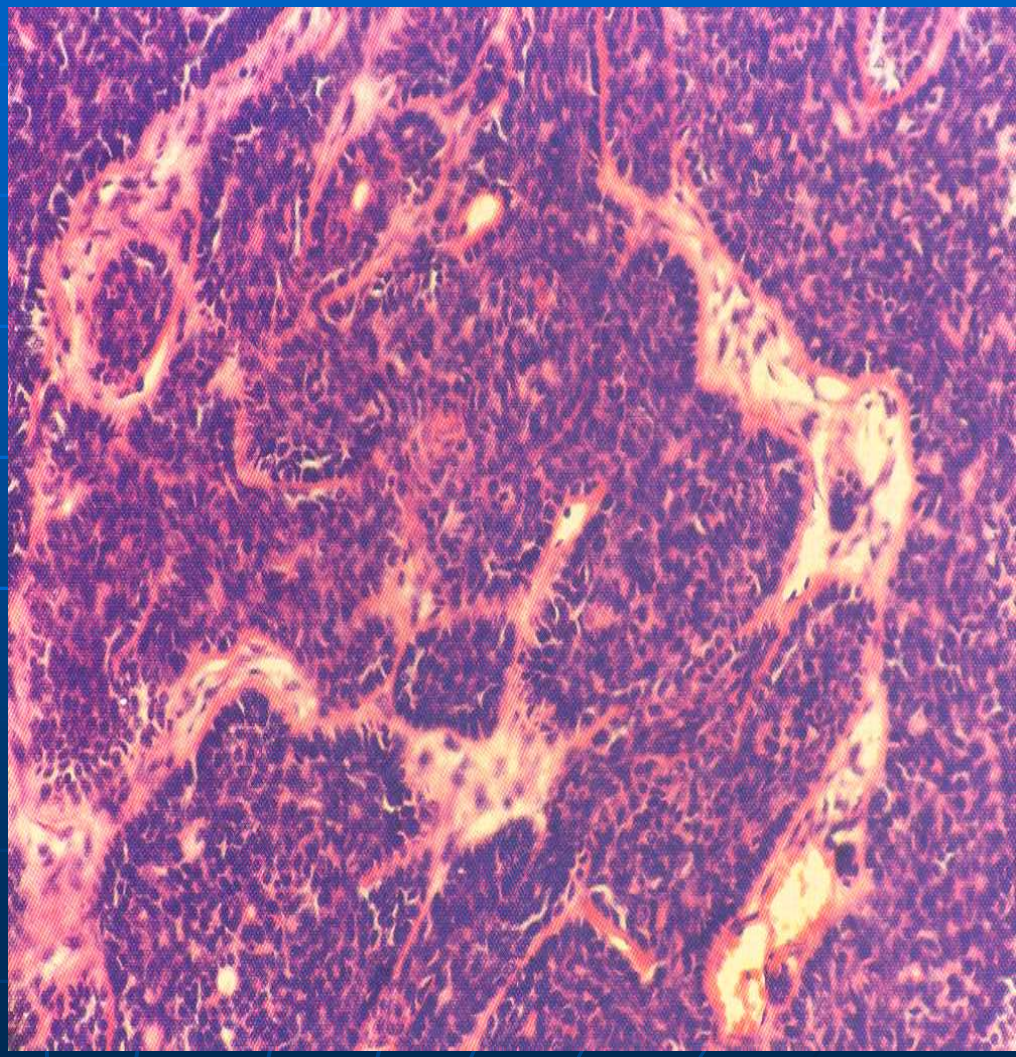


Warthin's Tumor



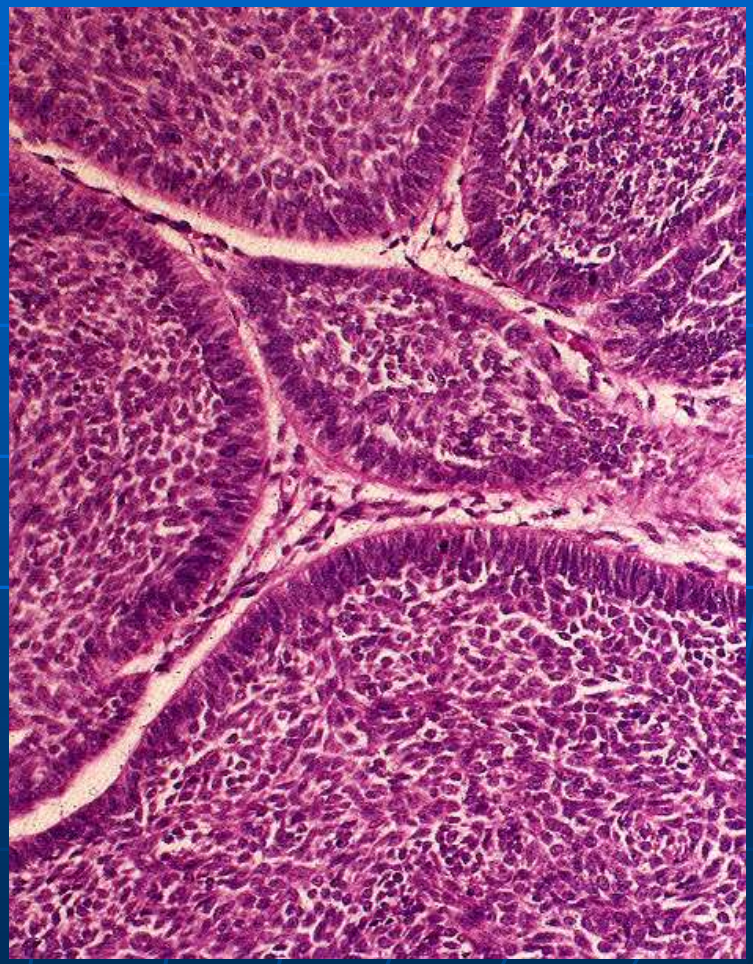
Basal Cell Adenoma

- Solid nests of cells with scant cytoplasm and hyperchromatic nuclei
- Tendency for peripheral pallisading.



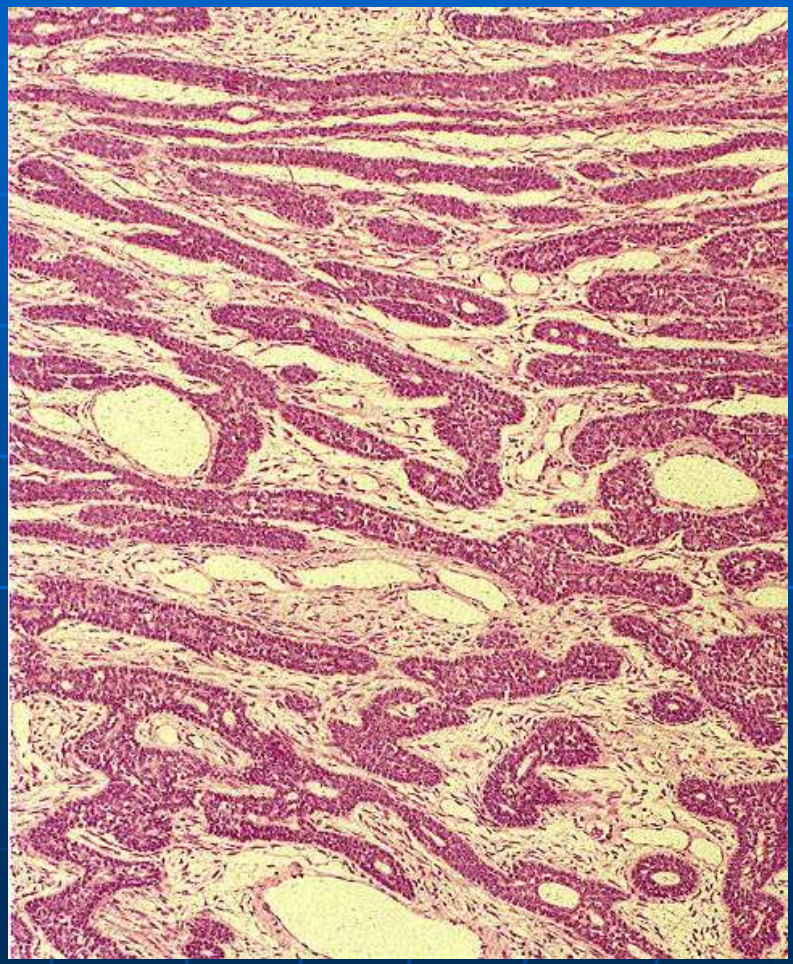
Basal Cell Adenoma

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



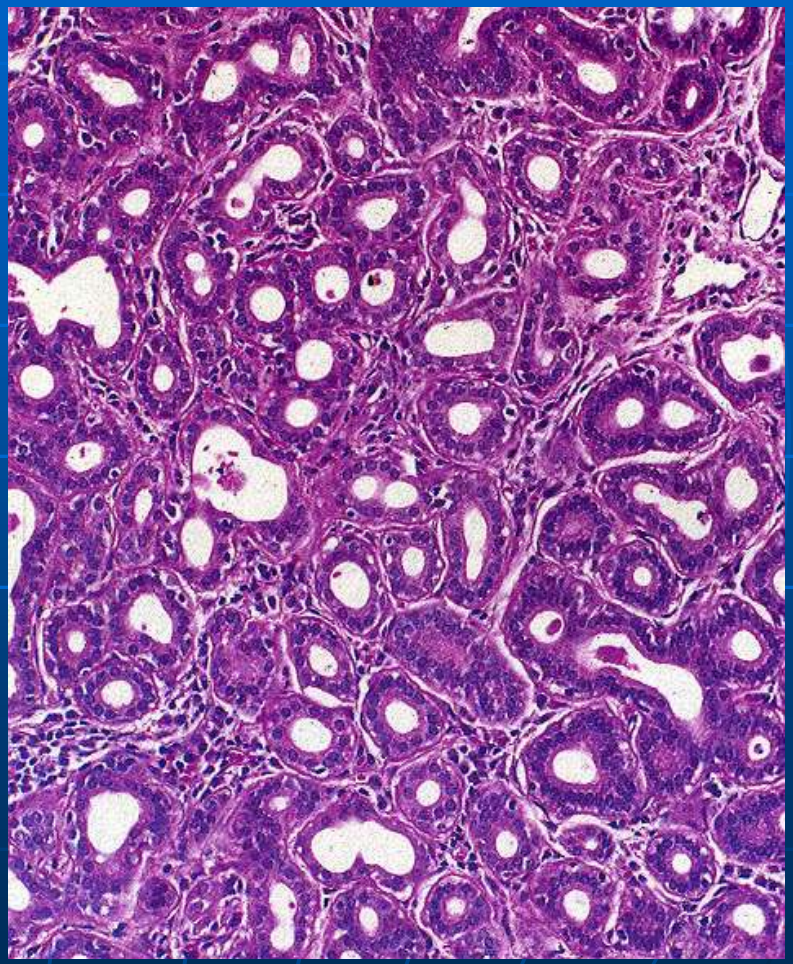
Basal Cell Adenoma

- Trabecular
  - Cells in elongated trabecular pattern
  - Vascular stroma



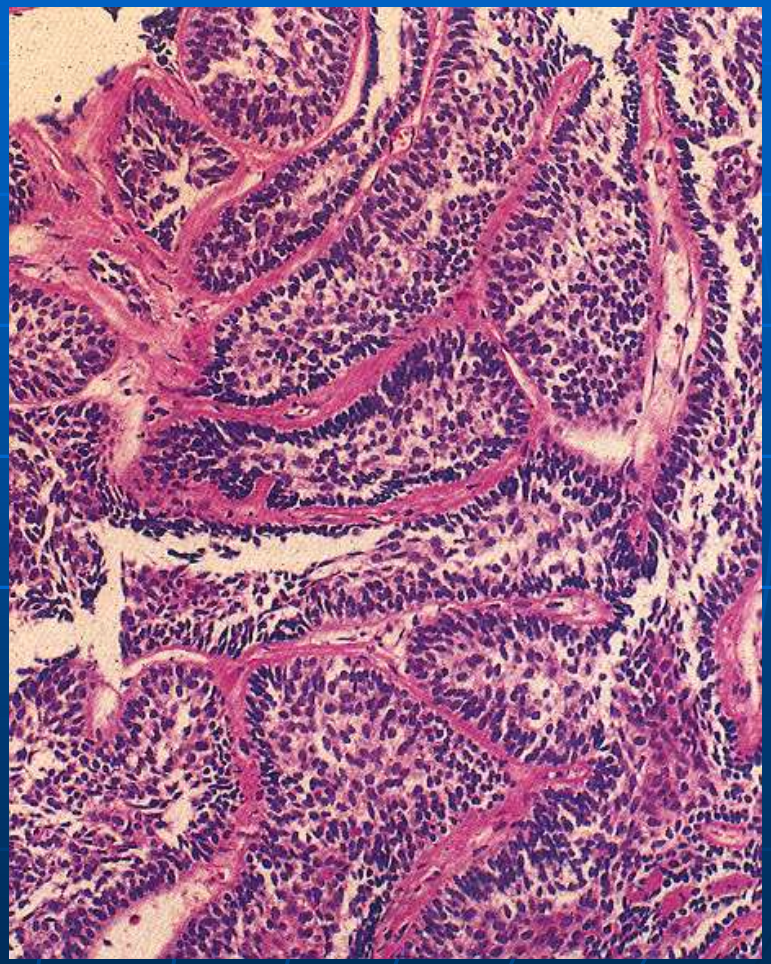
Basal Cell Adenoma

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

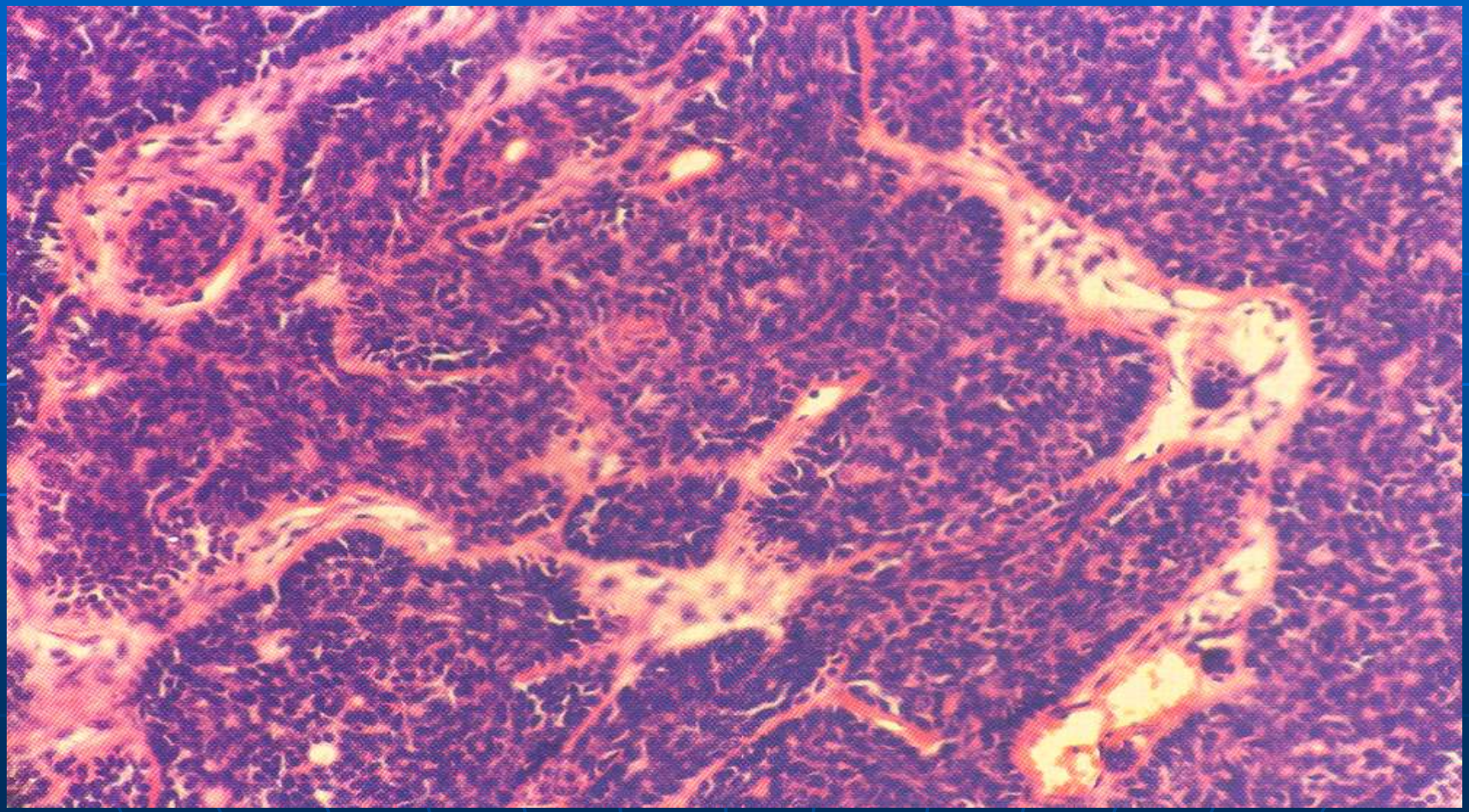


Basal Cell Adenoma

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

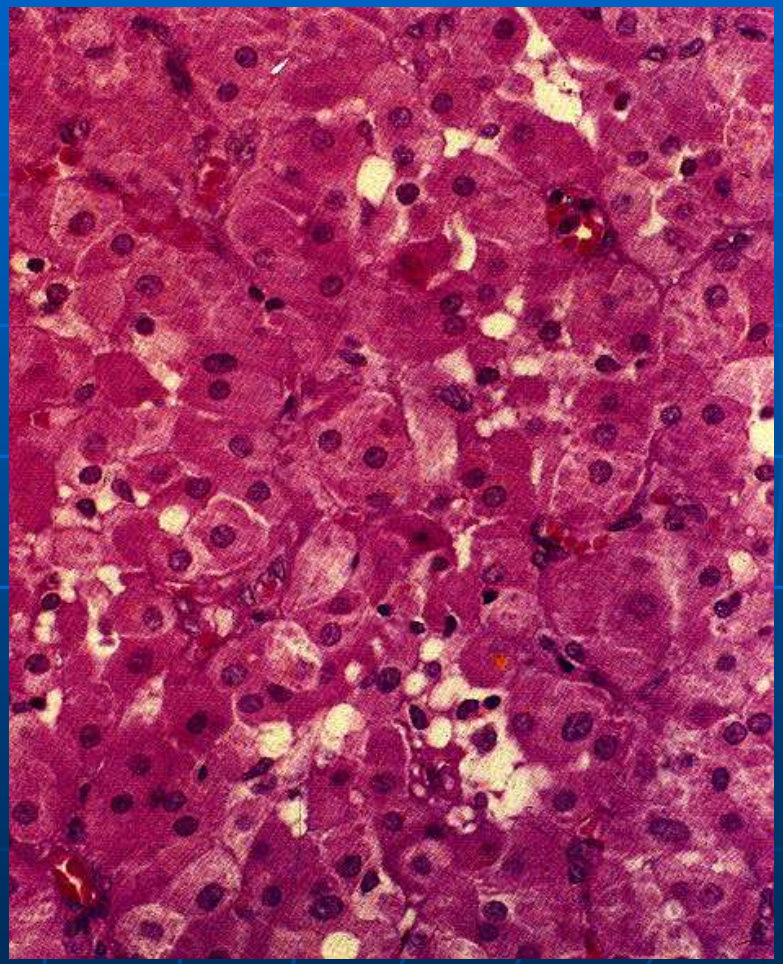


Basal Cell Adenoma



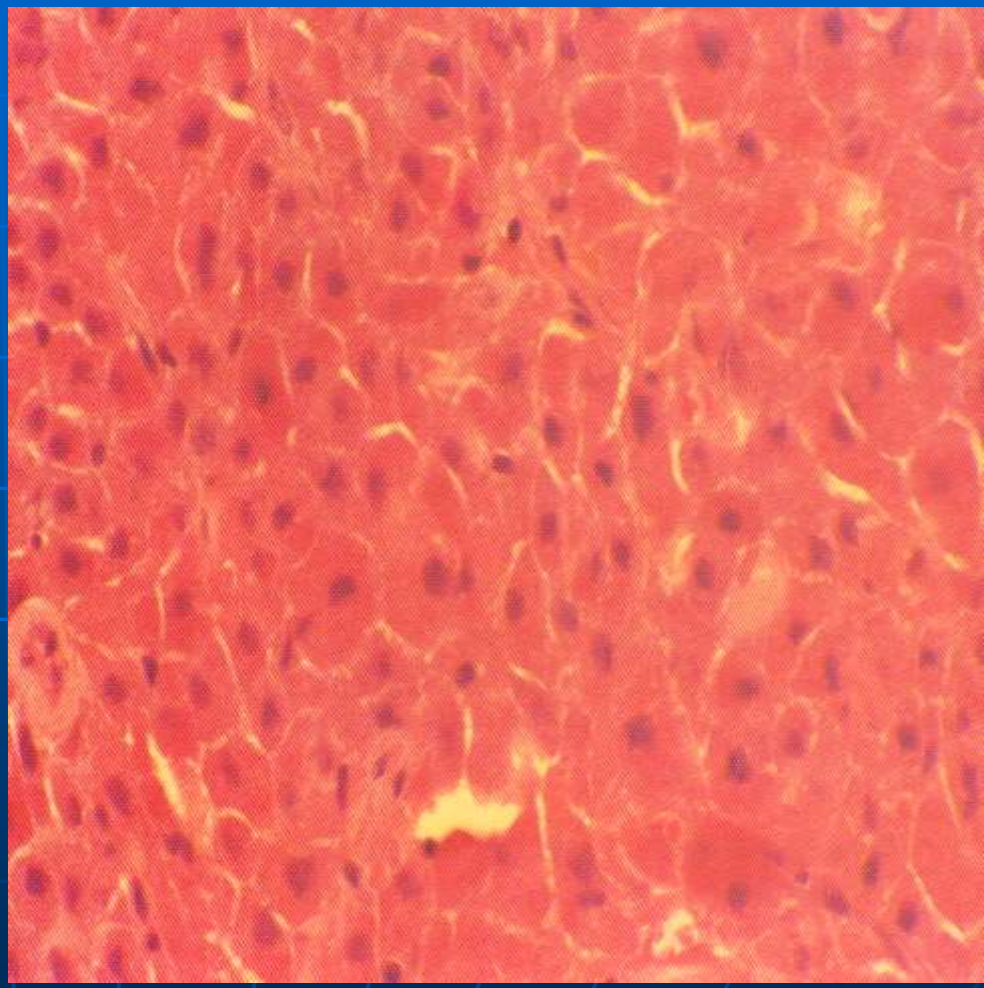
Oncocytoma

- Histology
  - Cords of uniform cells and thin fibrous stroma
  - Large polyhedral cells
  - Distinct cell membrane
  - Granular, eosinophilic cytoplasm
  - Central, round, vesicular nucleus



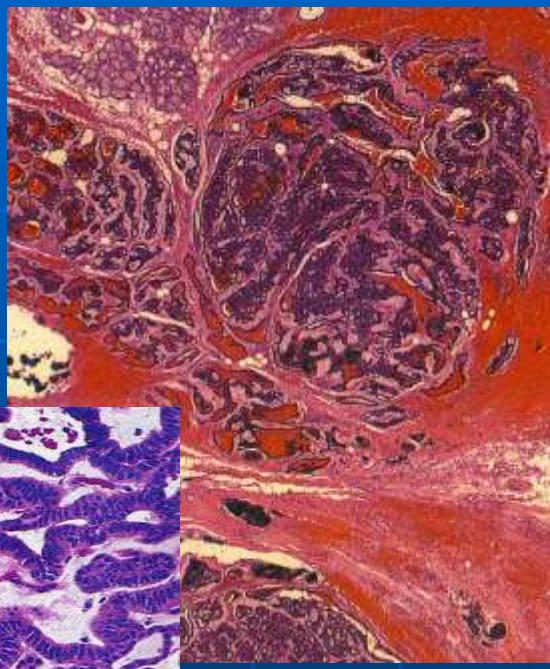
Oncocytoma

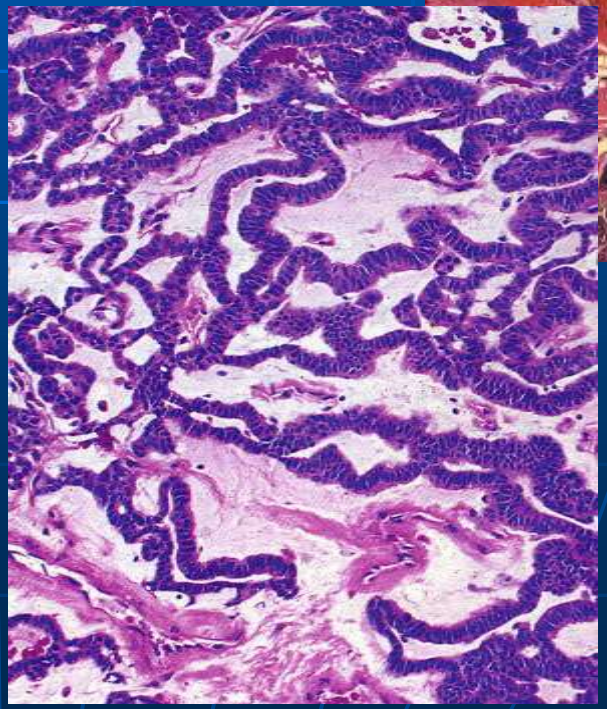
- Positive staining for phosphotungstic acid:hematoxylin, cytokeratin, epithelial membrane antigen
- Negative for S-100 glial fibrillary, smooth muscle actin



Canalicular Adenoma

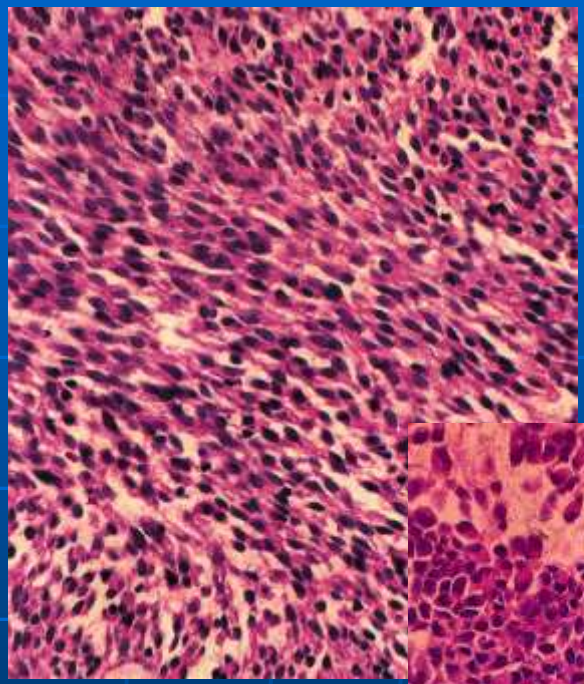
- Histology
  - Well-circumscribed
  - Multiple foci
  - Tubular structures line by columnar or cuboidal cells
  - Vascular stroma

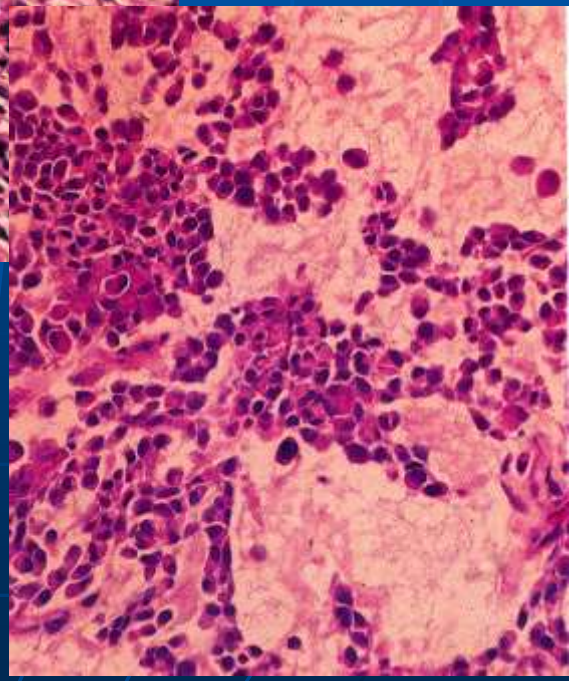




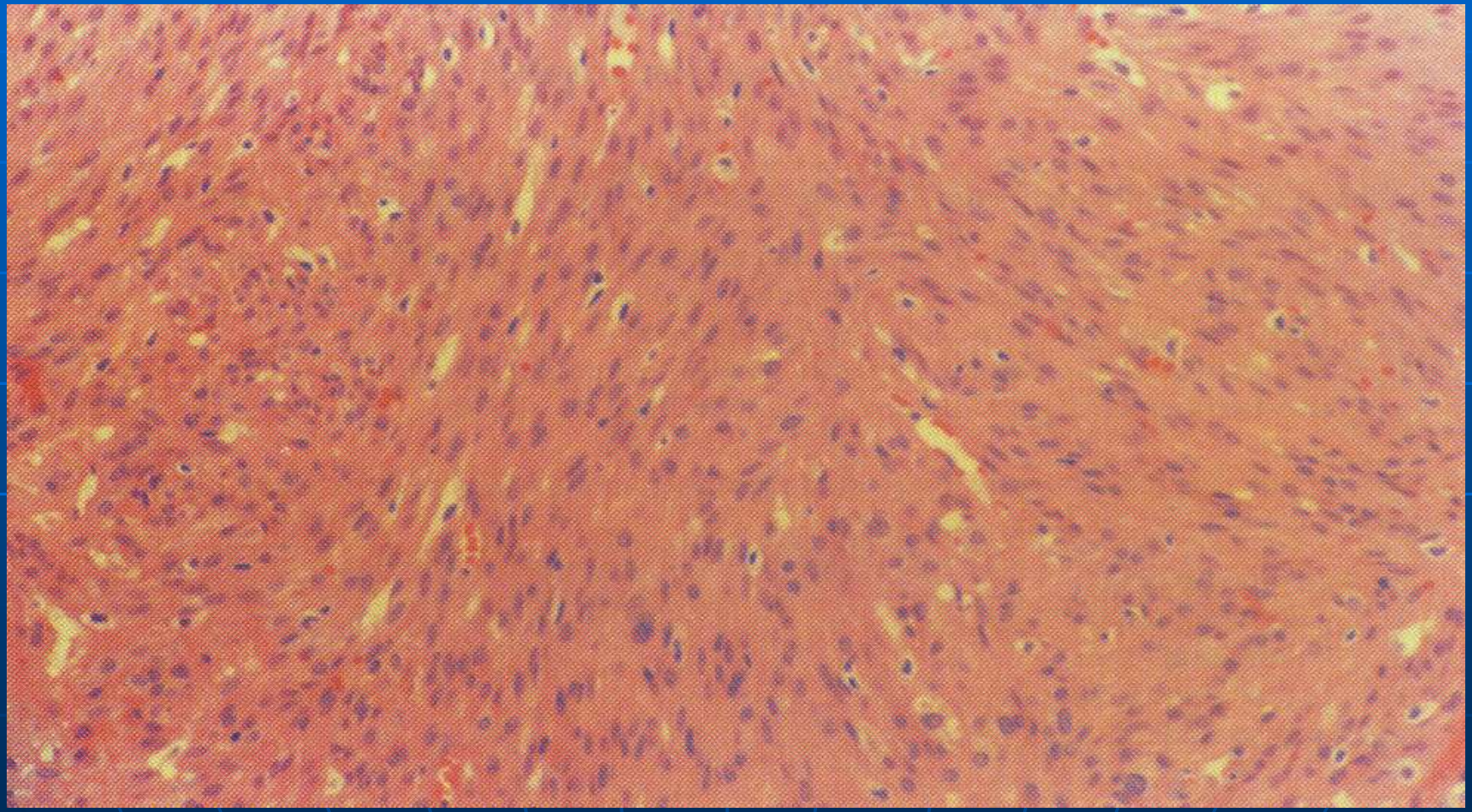
Myoepithelioma

- Histology
  - Spindle cell
    - More common
    - Parotid
    - Uniform, central nuclei
    - Eosinophilic granular or fibrillar cytoplasm
  - Plasmacytoid cell
    - Polygonal
    - Eccentric oval nuclei





Myoepithelioma

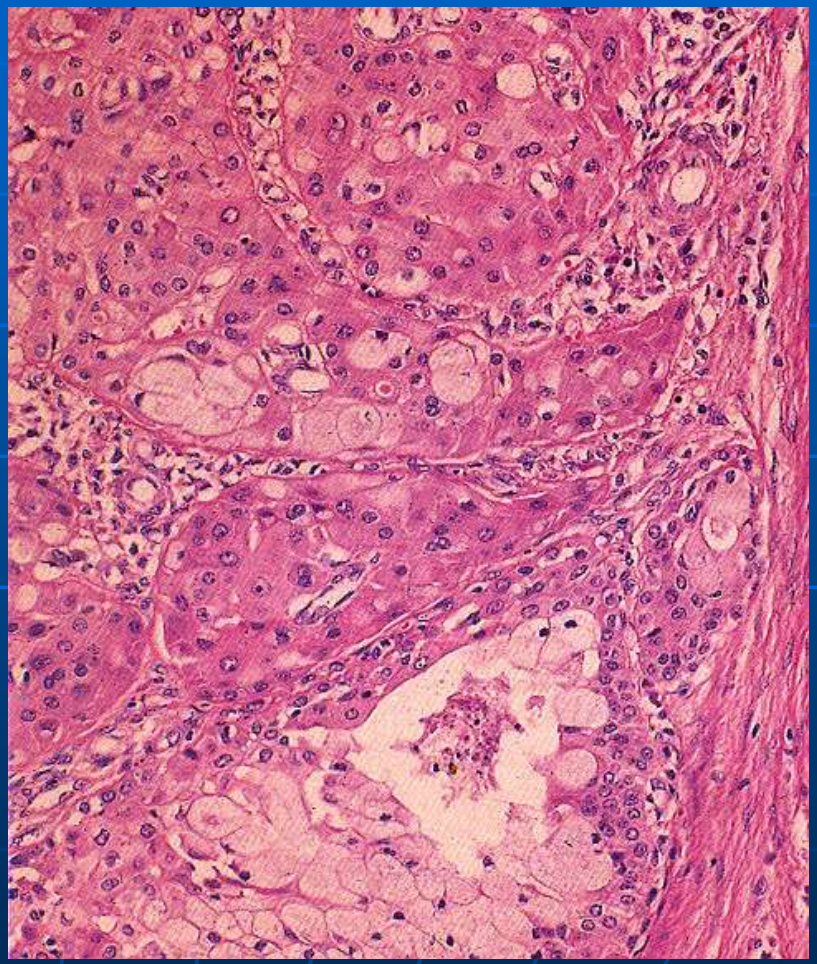


Malignant Neoplasms

- Mucoepidermoid Carcinoma
- Adenoid Cystic Carcinoma
- Polymorphous Low-Grade Adenocarcinoma
- Acinic Cell Carcinoma
- Adenocarcinoma
- Malignant Mixed Tumor
- Epithelial-Myoepithelial Carcinoma
- Salivary Duct Carcinoma
- Squamous Cell Carcinoma
- Undifferentiated Carcinoma

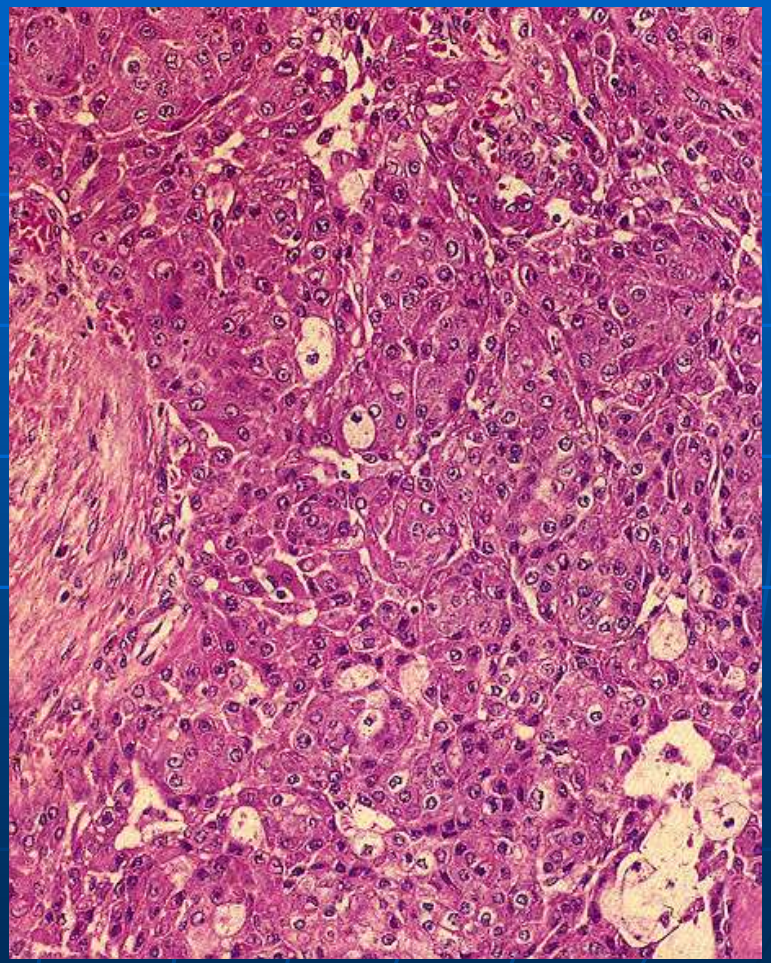
Mucoepidermoid Carcinoma

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



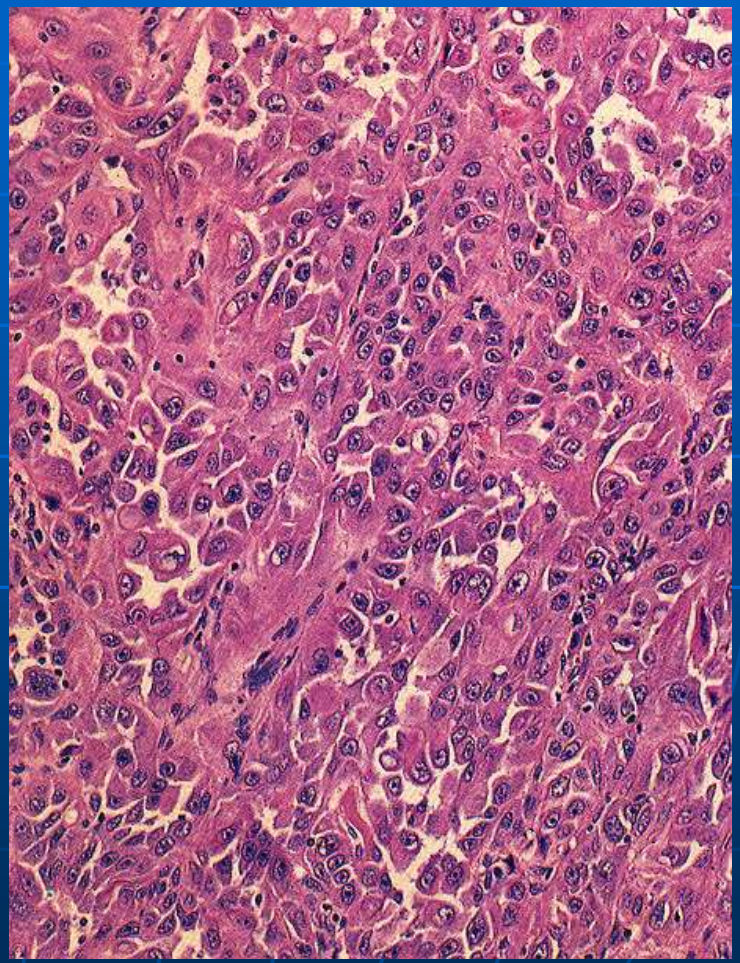
Mucoepidermoid Carcinoma

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

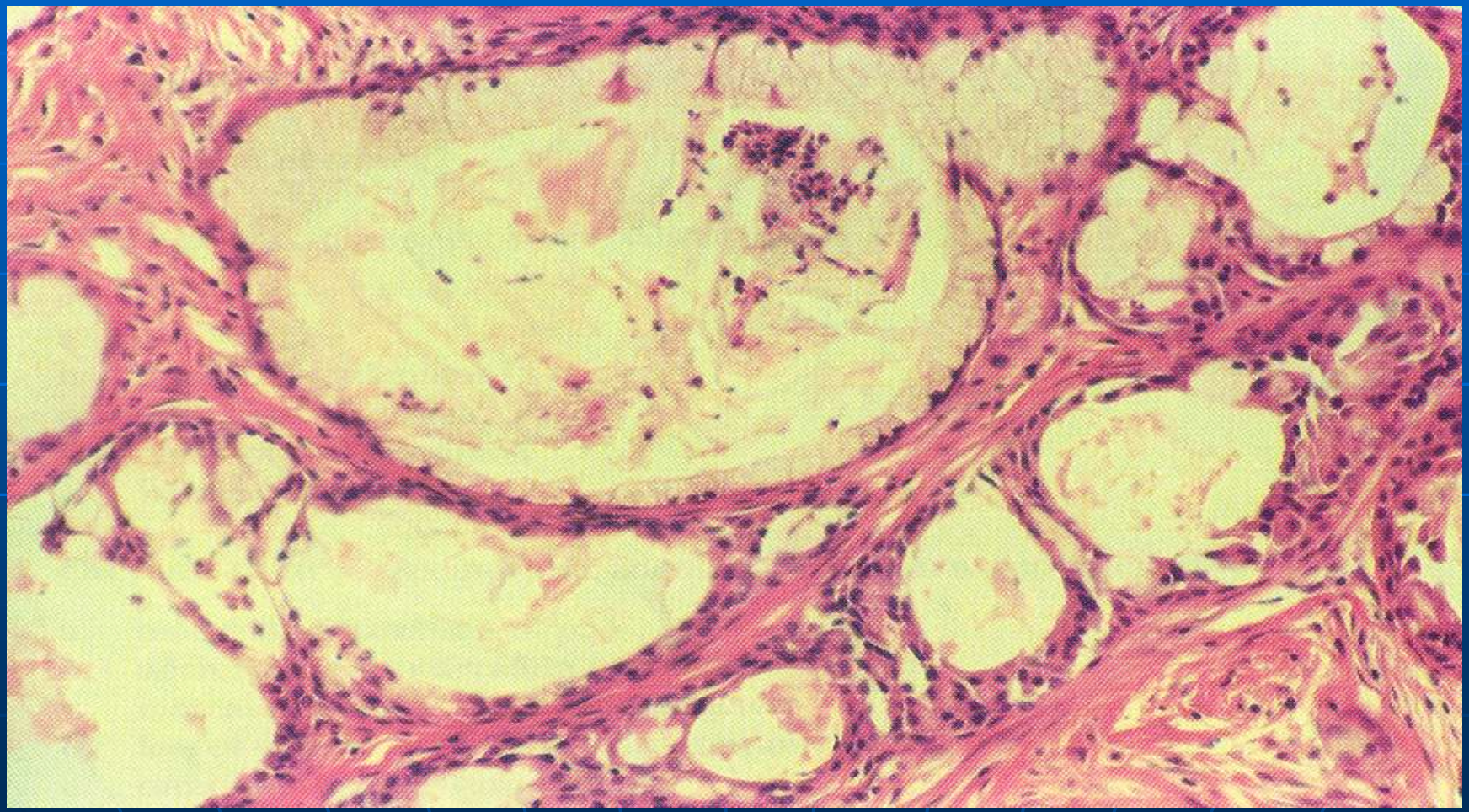


Mucoepidermoid Carcinoma

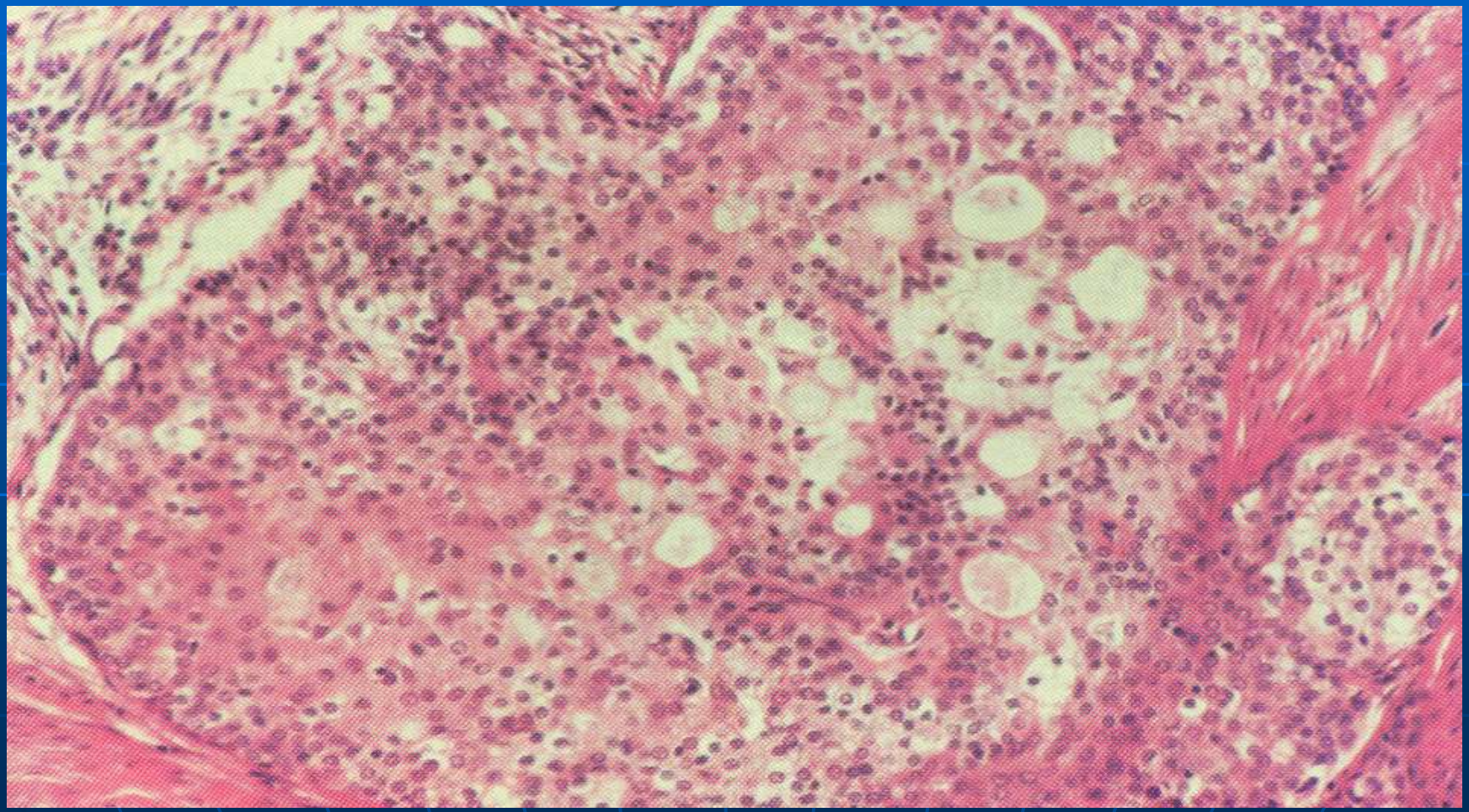
- Histology—High-grade
  - Epidermoid > mucus
  - Solid tumor cell proliferation
  - Mistaken for SCCA
    - Mucin staining



Low Grade Mucoepidermoid Carcinoma

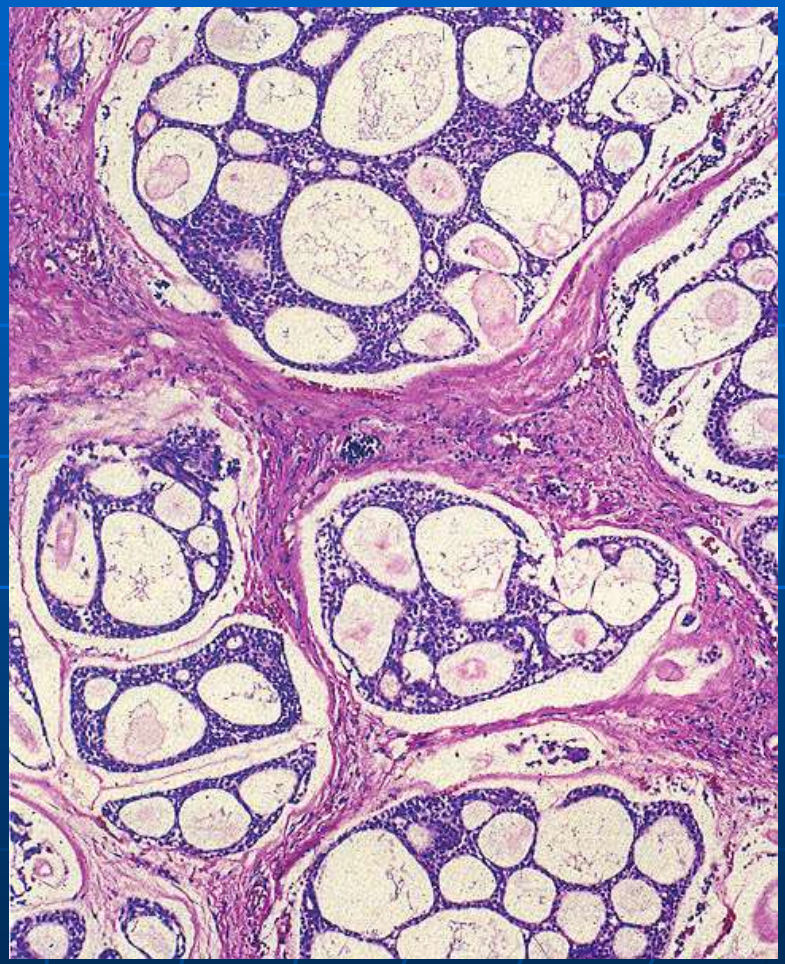


High Grade Mucoepidermoid Carcinoma



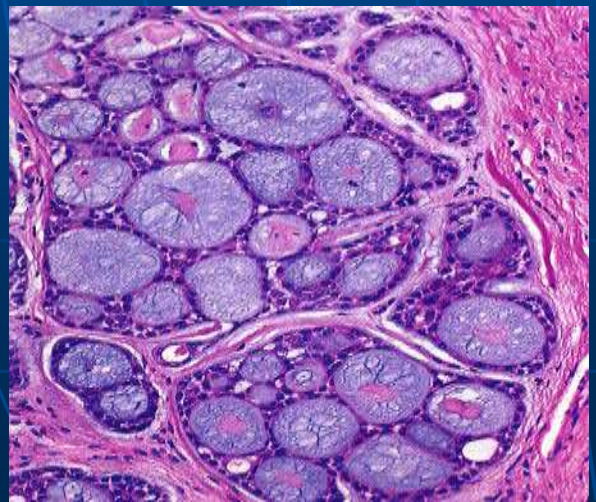
Adenoid Cystic Carcinoma

- Histology—cribriform pattern
  - Most common
  - "swiss cheese" appearance

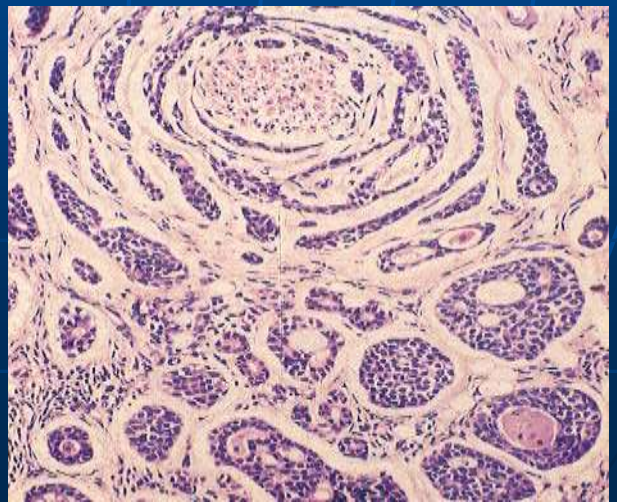


Adenoid Cystic Carcinoma

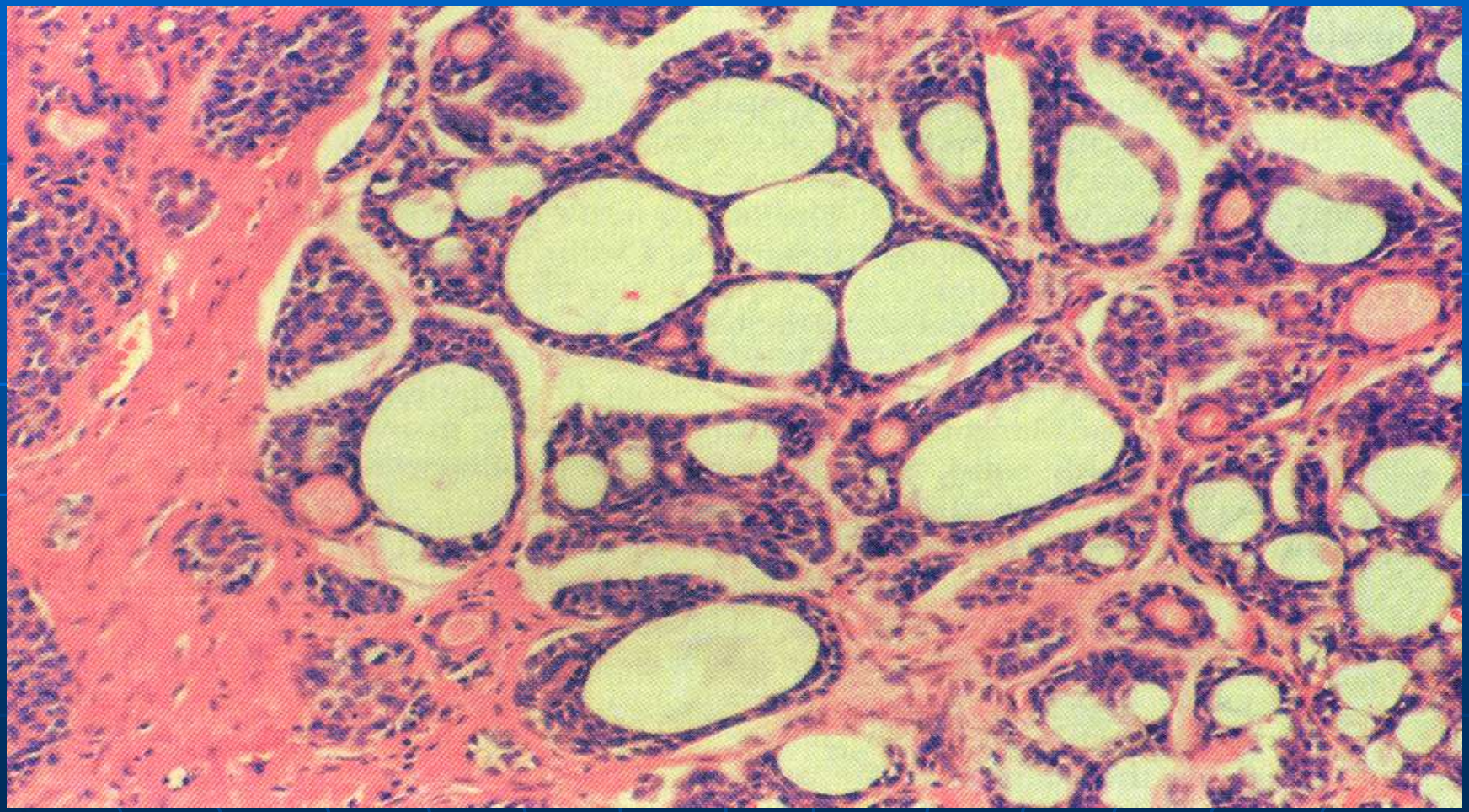
- Histology—tubular pattern
  - Layered cells forming duct-like structures
  - Basophilic mucinous substance



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

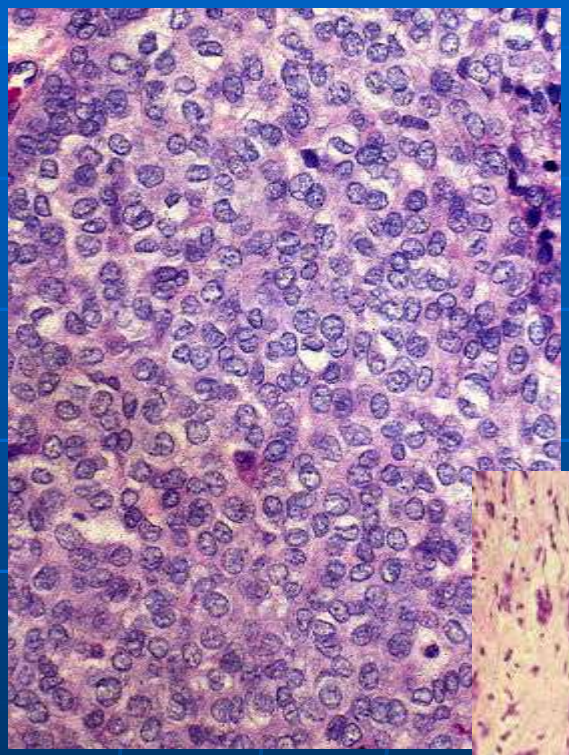


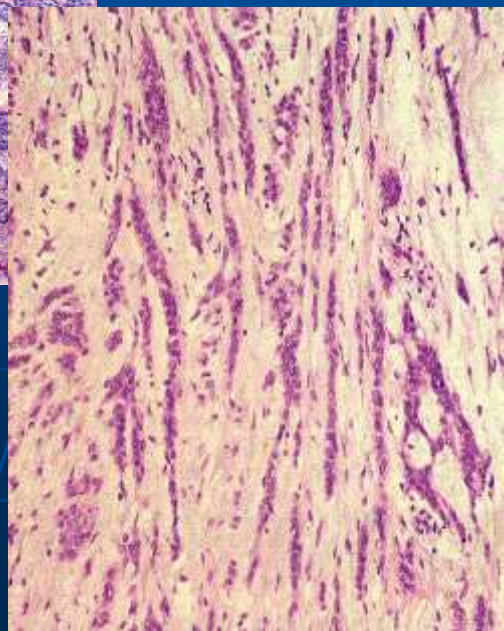
Adenoid Cystic Carcinoma



Polymorphous Low-Grade Adenocarcinoma

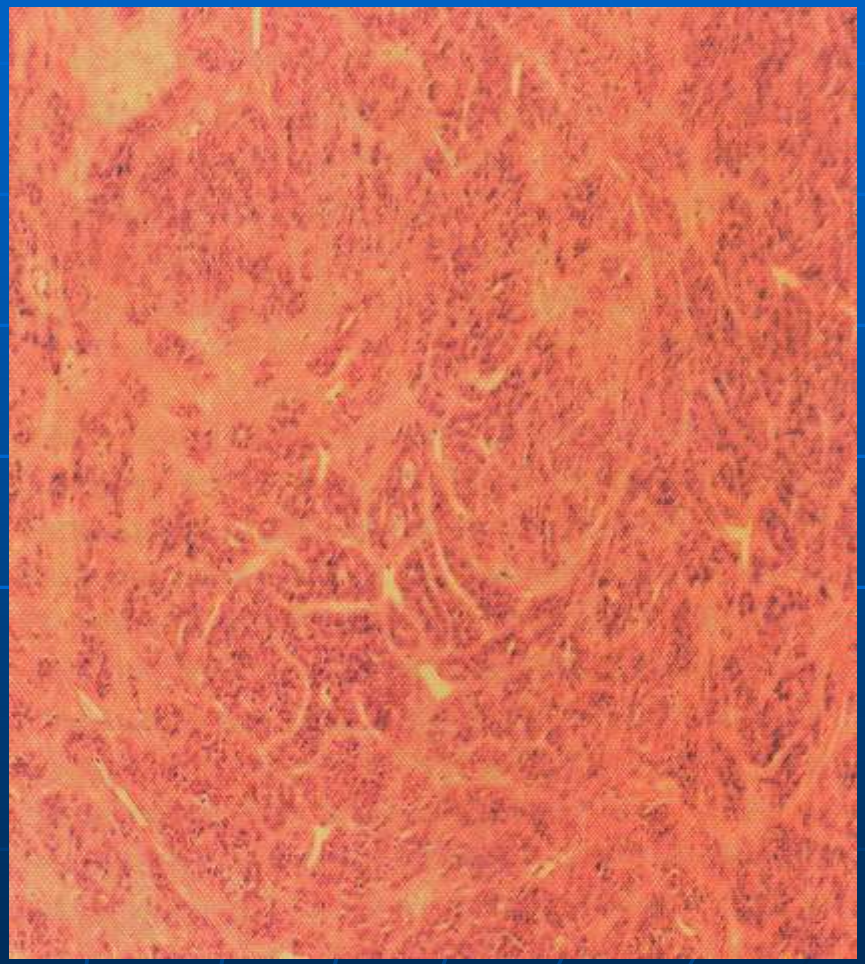
- Histology
  - Isomorphic cells, indistinct borders, uniform nuclei
  - Peripheral "Indian-file" pattern





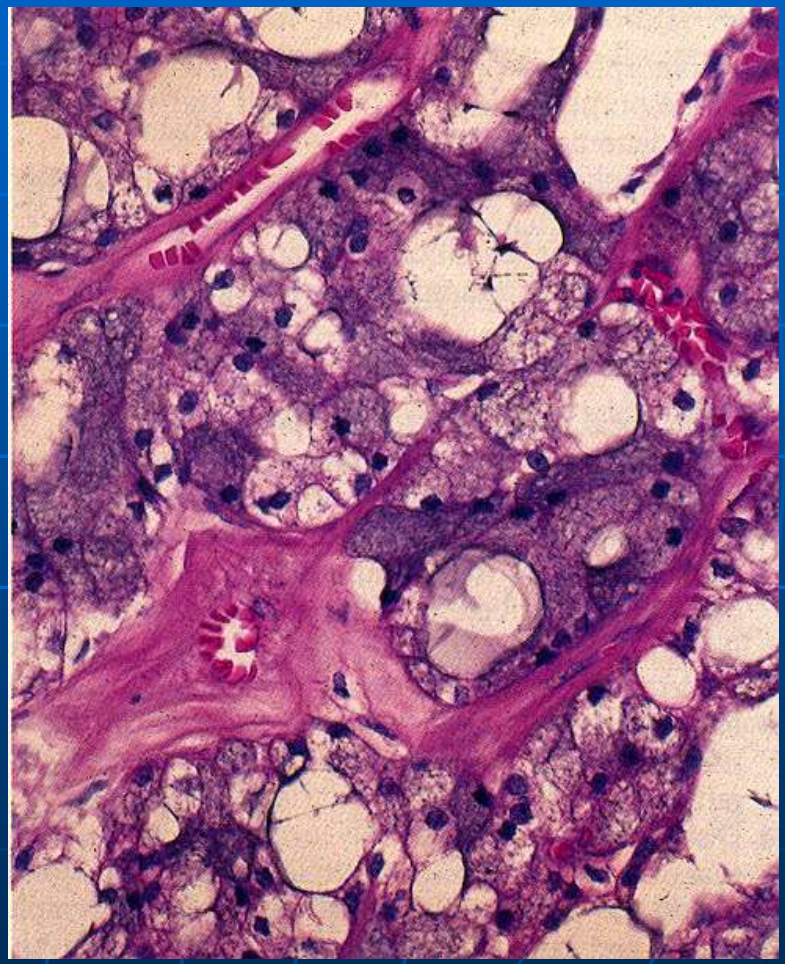
Polymorphous Low-Grade Adenocarcinoma

- Markedly positive staining for S-100, epithelial membrane antigen, and cytokeratins. Less predictable with CEA and muscle-specific actin



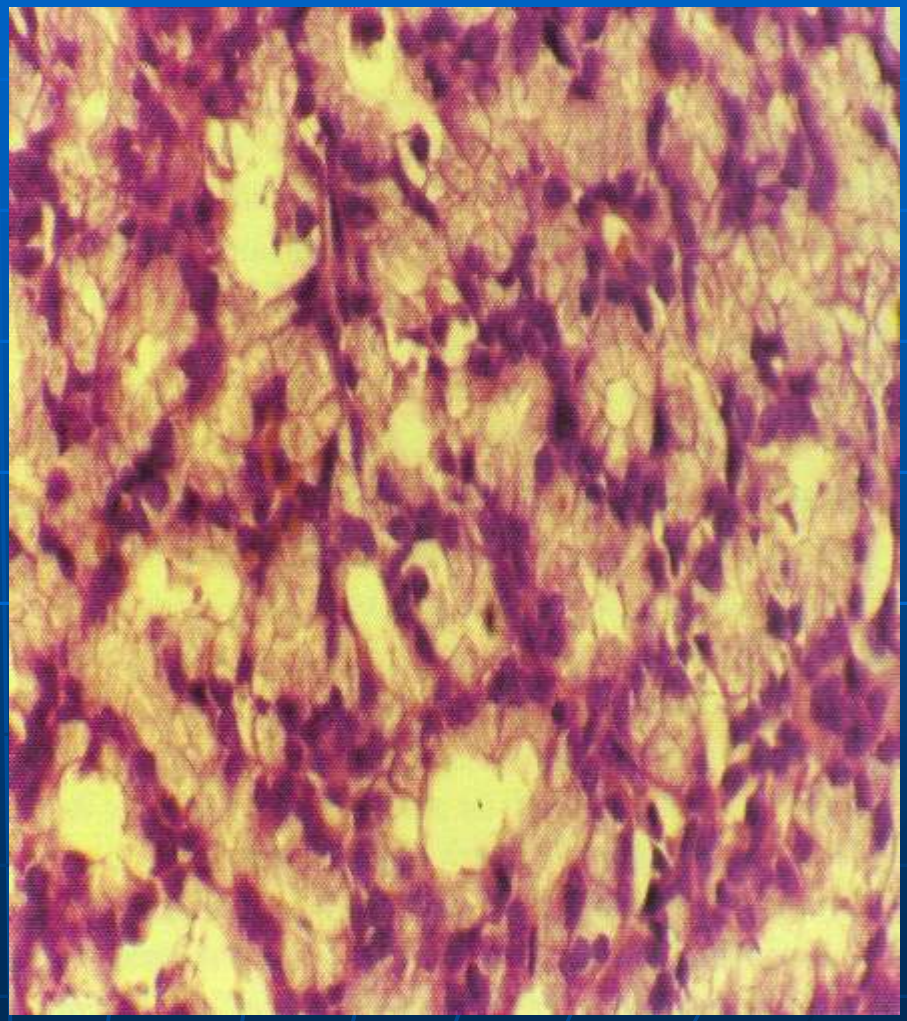
Acinic Cell Carcinoma

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



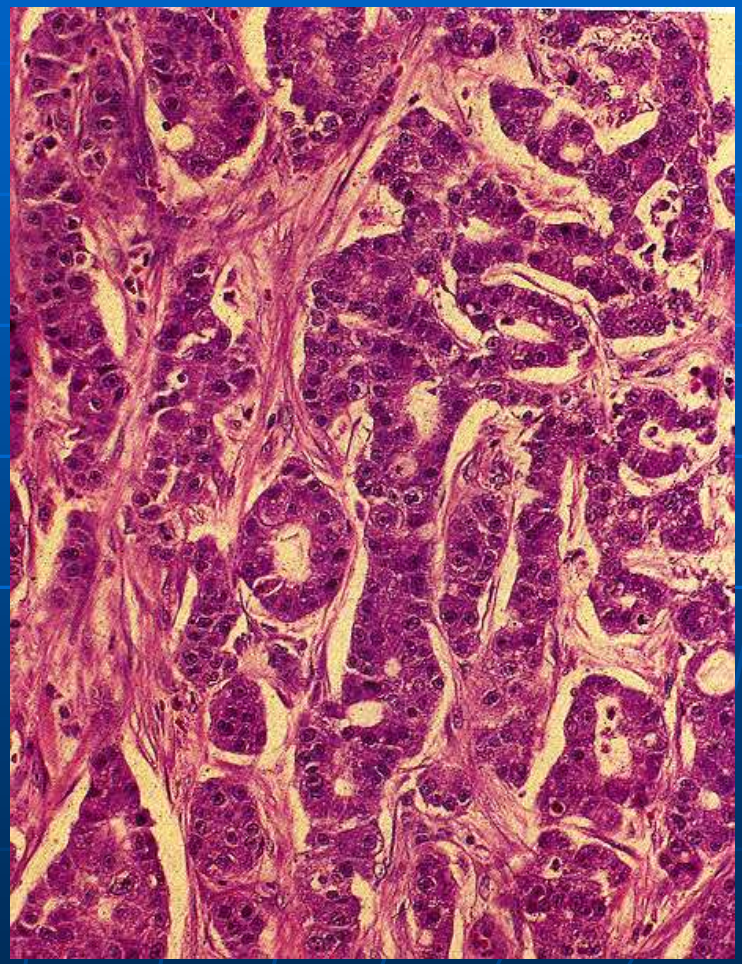
Acinic Cell Carcinoma

- Positive staining with cytokeratins and CEA, mixed results with others
- Vacuolated cells with eccentrically located nuclei and granular, basophilic cytoplasm, scant stroma

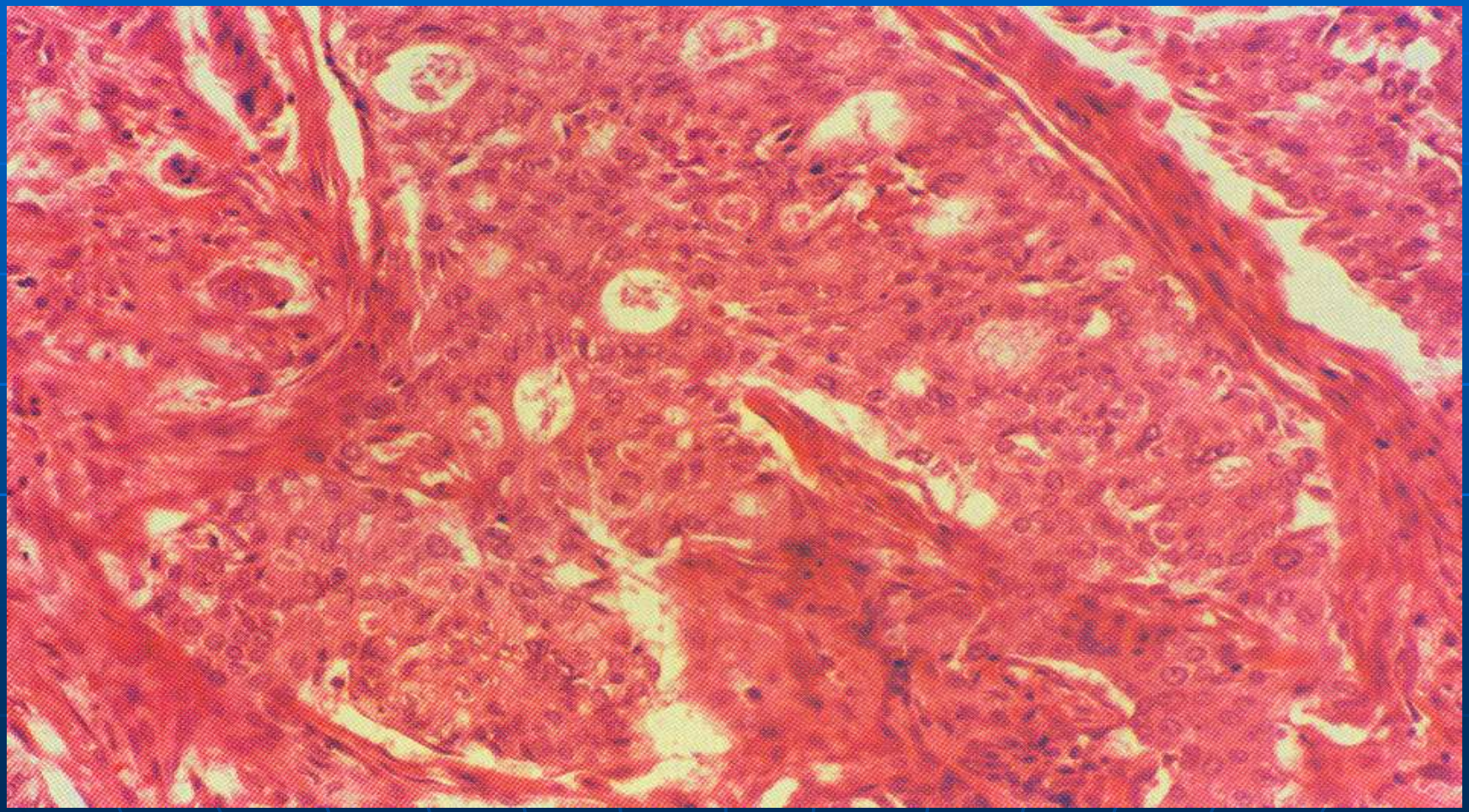


Adenocarcinoma

- Histology
  - Heterogeneity
  - Presence of glandular structures and absence of epidermoid component
  - Requires exclusion of other specific salivary gland carcinomas



Adenocarcinoma

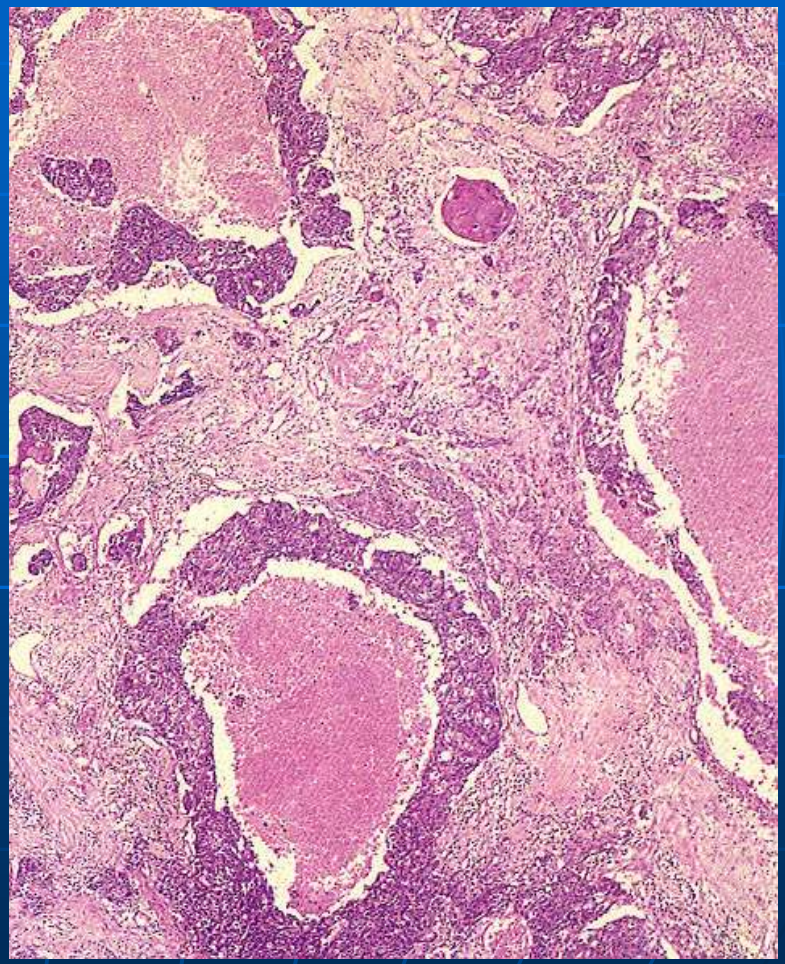


Malignant Mixed Tumors

- 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

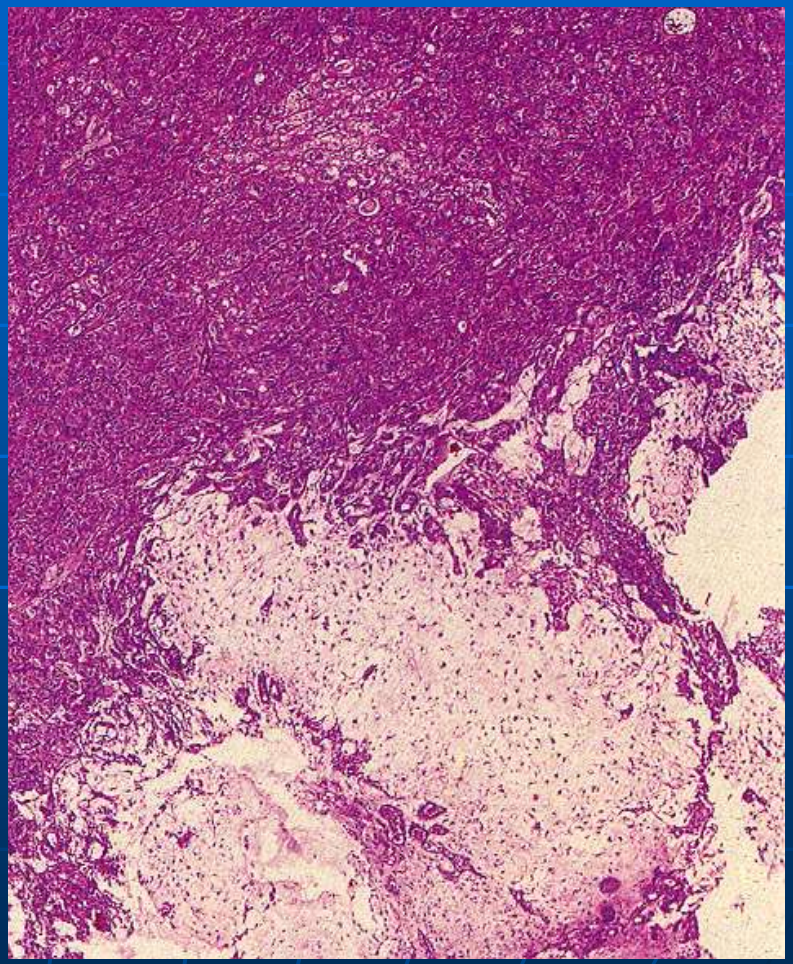
Carcinoma Ex-Pleomorphic Adenoma

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

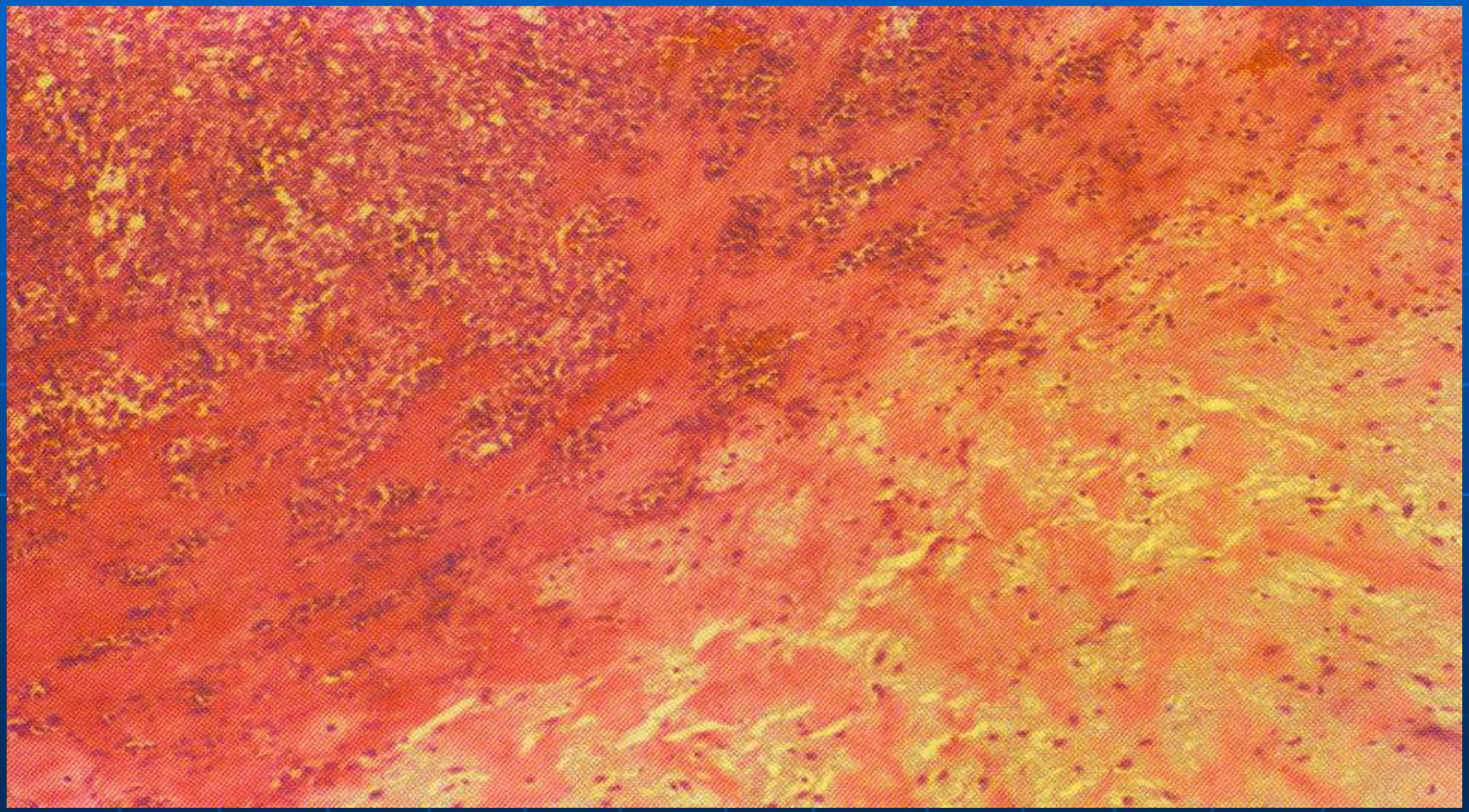


Carcinosarcoma

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

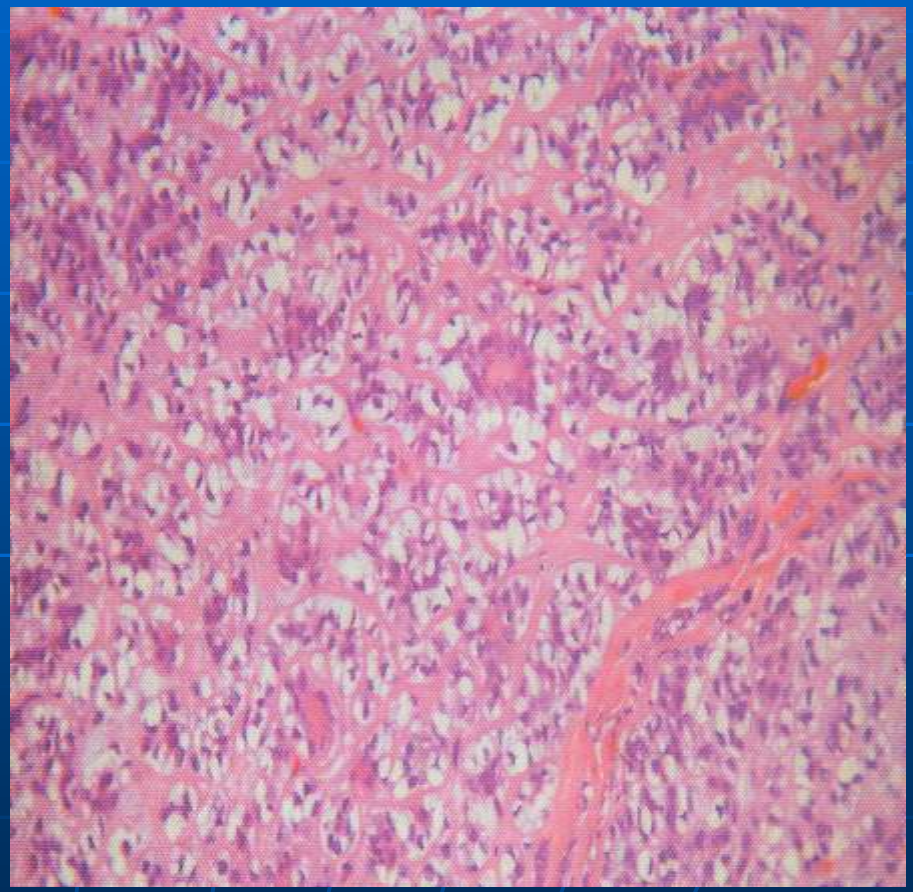


Malignant Mixed Tumor



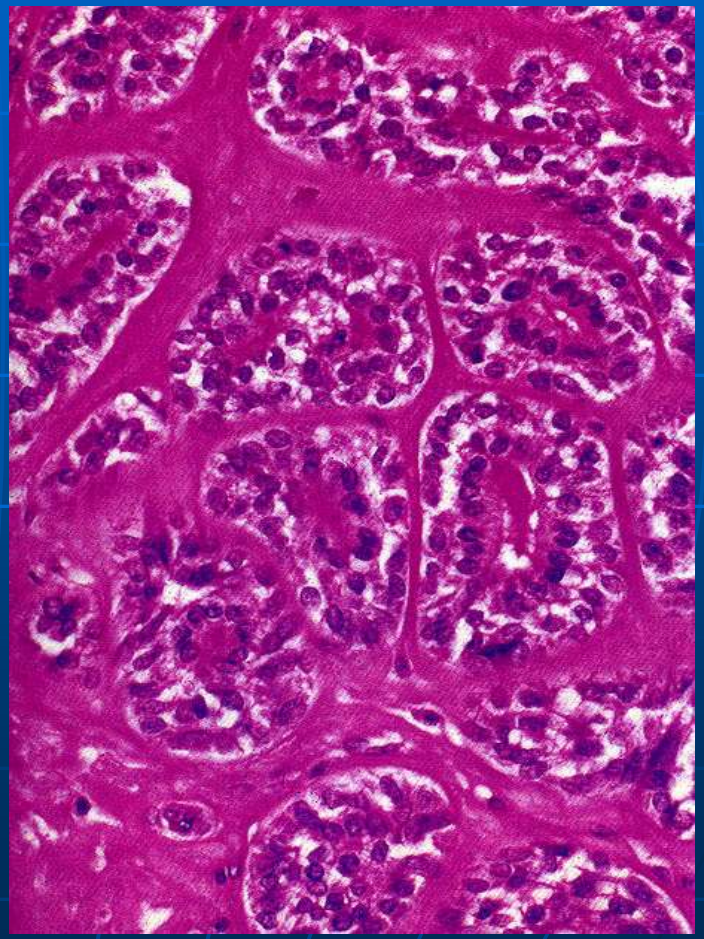
Epithelial-Myoepithelial Carcinoma

- Dual epithelial component
- Irregular, eccentric nuclei w vacuolated cytoplasm
- IHC reveals dual cell origin
- epithelial:cytokeratins
- Myoep:S-100, actin



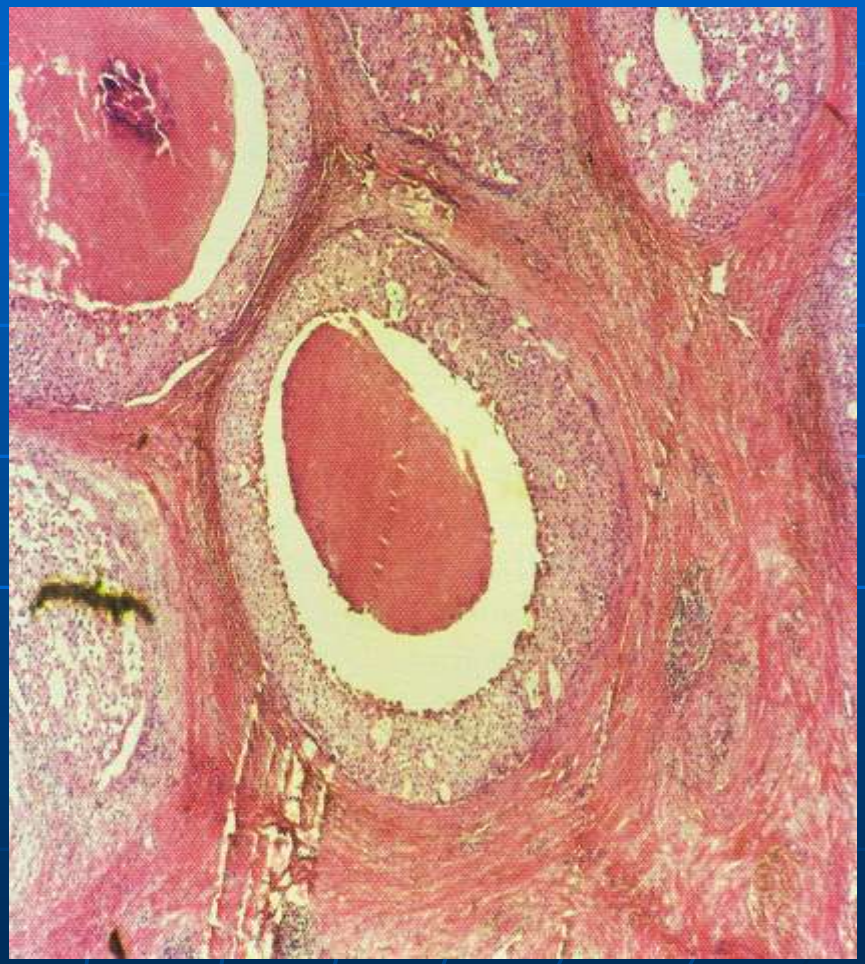
Epithelial-Myoepithelial Carcinoma

- Tumor cell nests
- Two cell types
- Thickened basement membrane



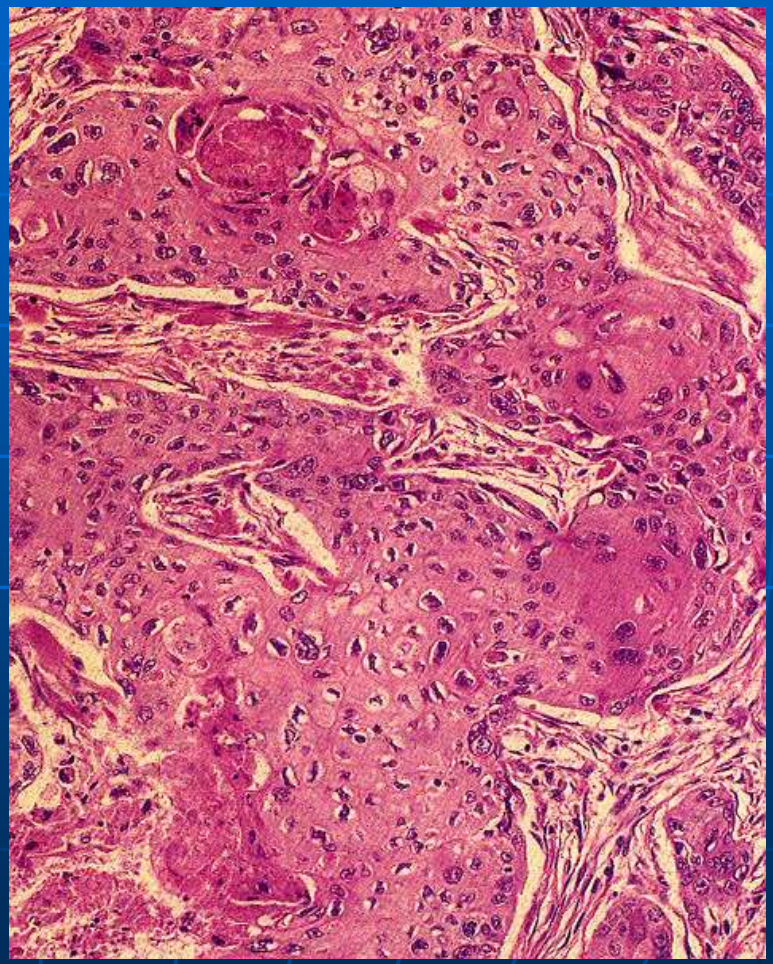
Salivary Duct Carcinoma

- Large polygonal cells w well defined borders
- Pleomorphic nuclei w prominent nucleoli and granular, eosinophilic cytoplasm
- IHC patterns similar to breast CA except neg for estrogen
- CEA, epithelial membrane +
- S-100, cytokeratins -

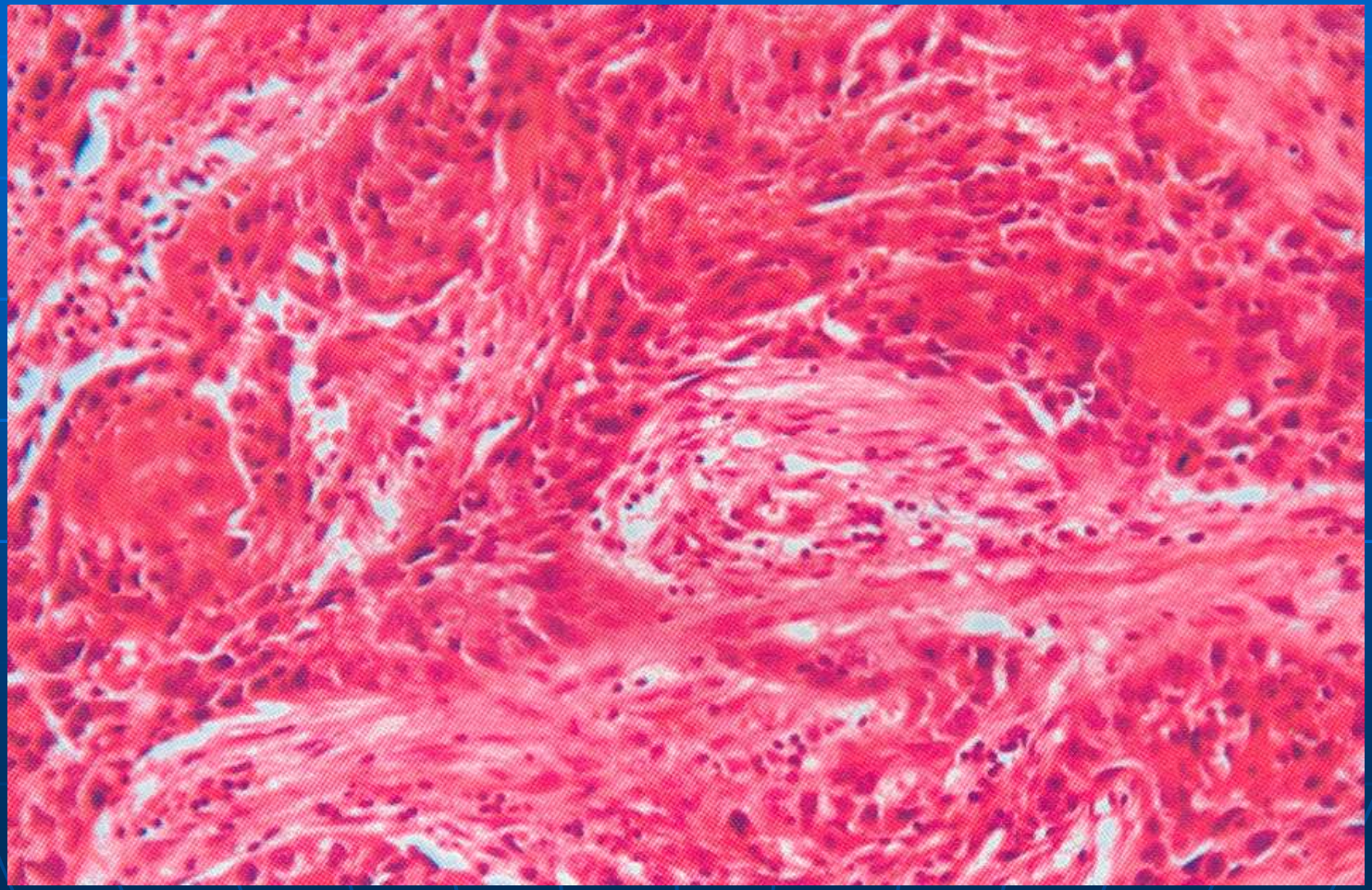


Squamous Cell Carcinoma

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

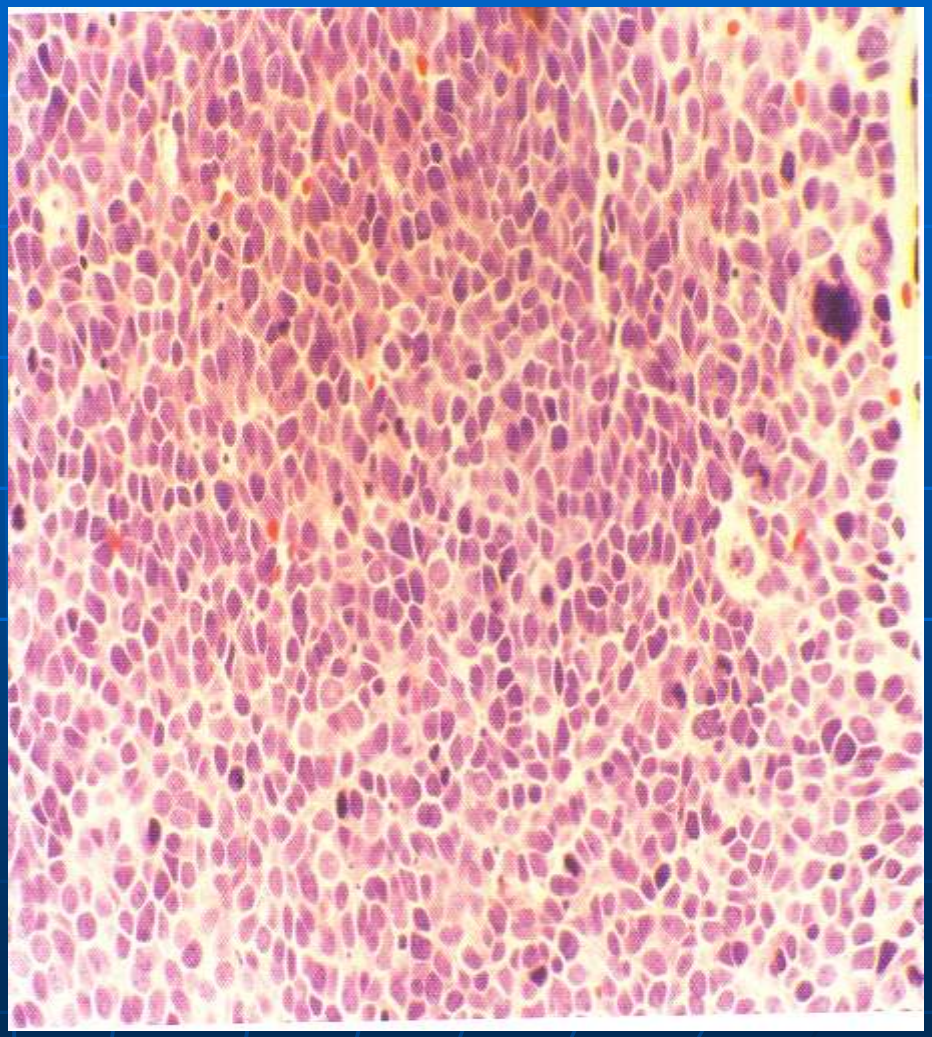


Squamous Cell Carcinoma



Undifferentiated Carcinoma

- High grade, high mitotic activity, scant cytoplasm, hyperchromatic nuclei
- IHC:cytokeratins, epithelial membrane antigen
- +/- neuroendocrine



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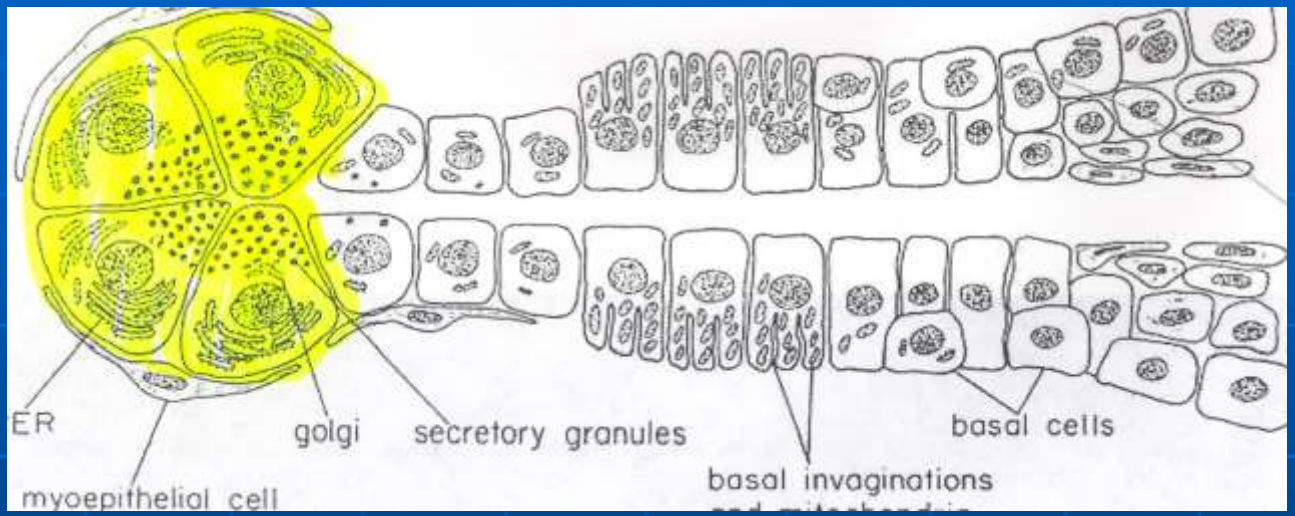
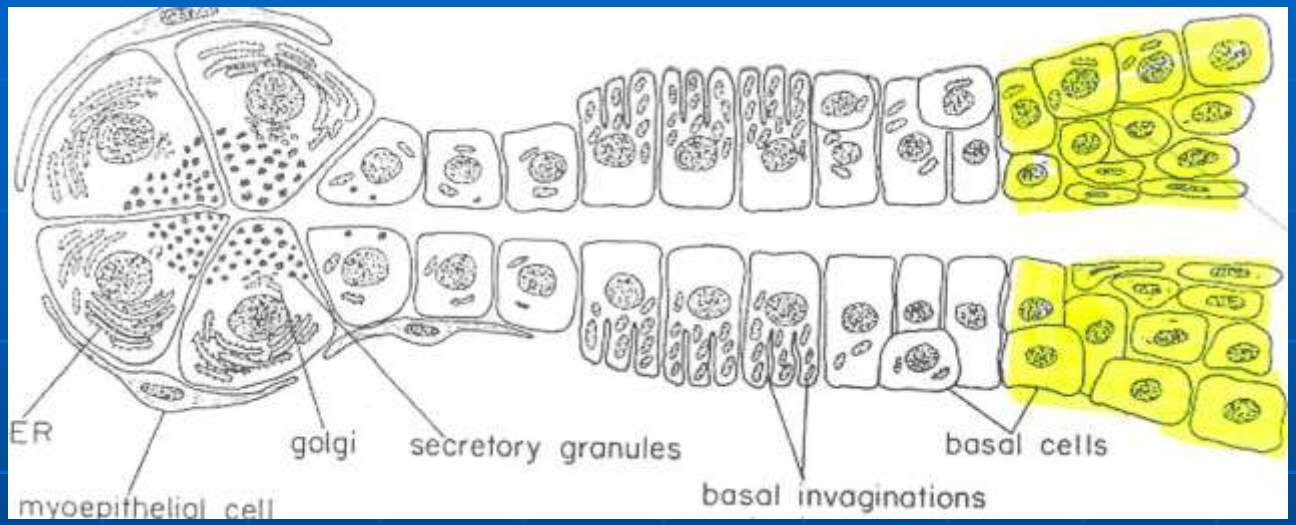
Question 1



The highlighted area represents:

a. the acini
b. the intercalated duct
c. the striated duct
d. the excretory duct

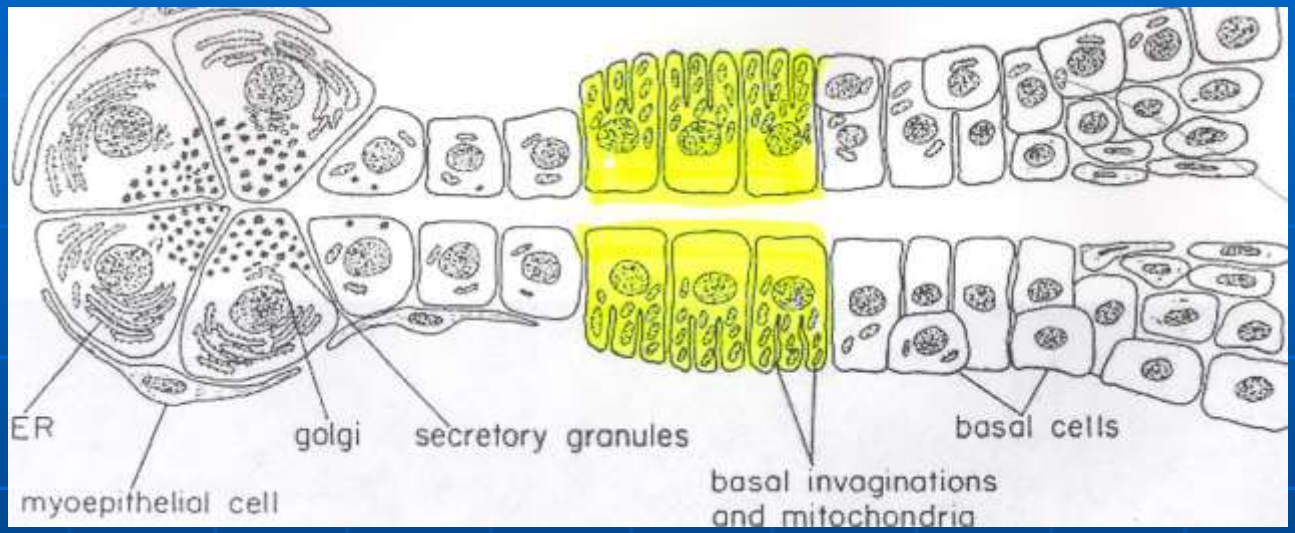
Question 2



The highlighted area represents:

a. the acini
b. the intercalated duct
c. the striated duct
d. the excretory duct

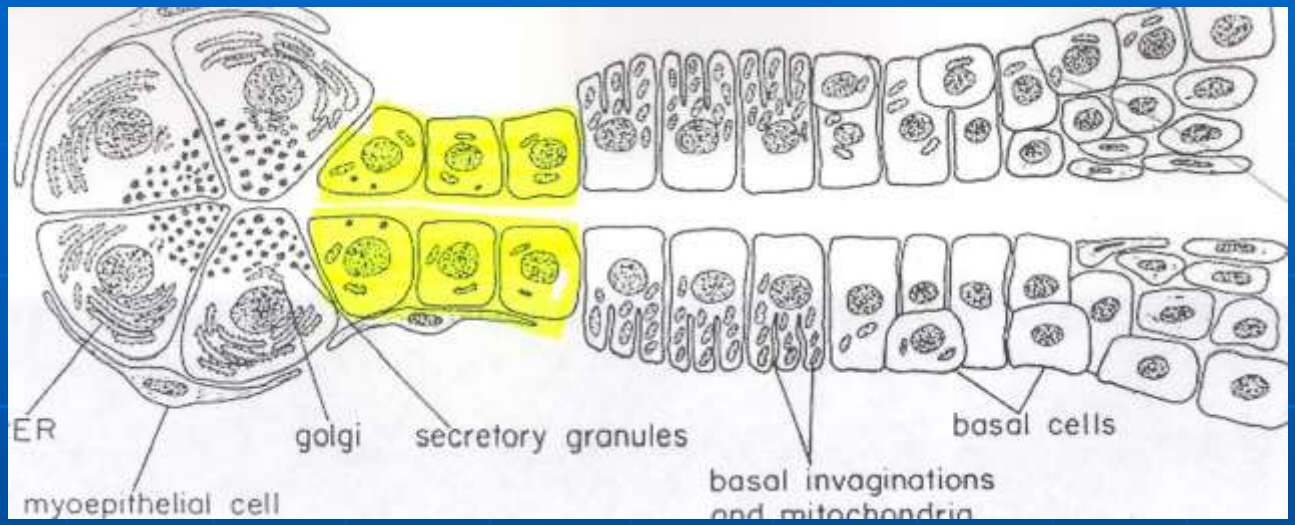
Question 3



The highlighted area represents:

a. the acini
b. the intercalated duct
c. the striated duct
d. the excretory duct

Question 4



The highlighted area represents:

a. the acini
b. the intercalated duct
c. the striated duct
d. the excretory duct

Question 5

The parotid gland neoplasms are:

a.) Mostly Benign

b.) Mostly Malignant

c.) About equal distribution, benign=malignant

Question 6

The submandibular gland neoplasms are:

a.) Mostly Benign

b.) Mostly Malignant

c.) About equal distribution, benign=malignant

Question 7

The sublingual gland neoplasms are:

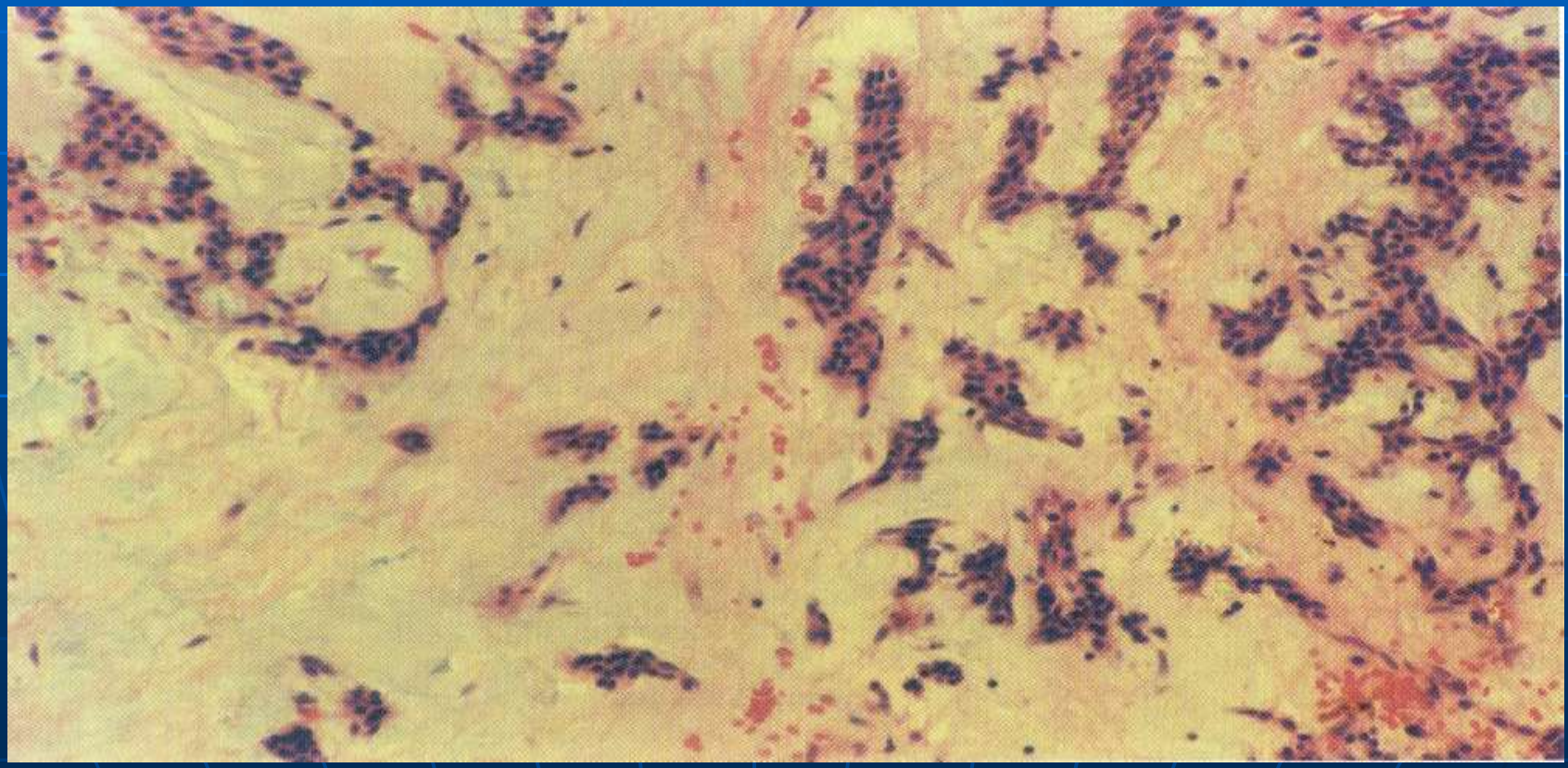
a.) Mostly Benign

b.) Mostly Malignant

c.) About equal distribution, benign=malignant

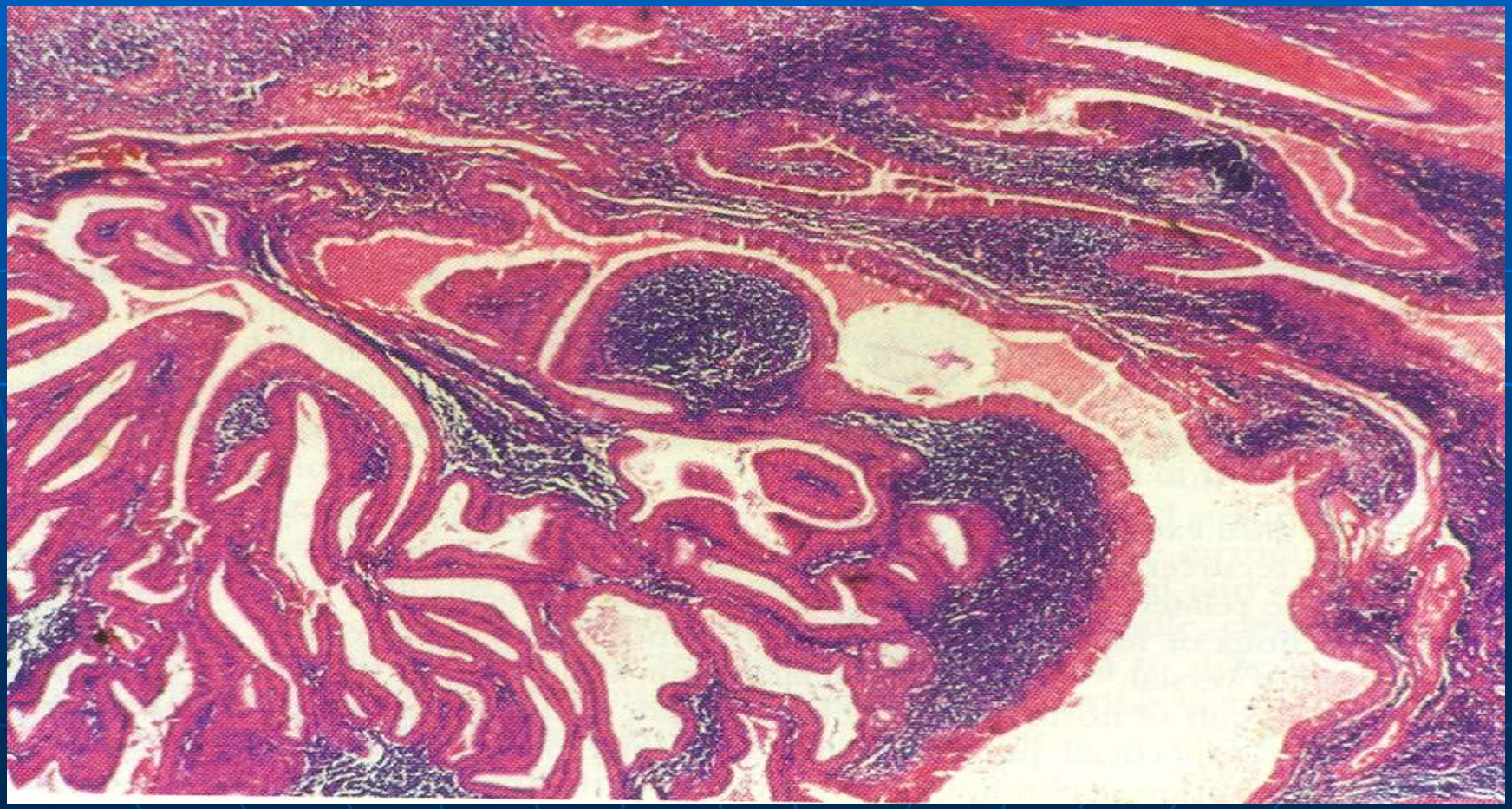
Question 8

Identify the neoplasm:



Question 9

Identify the neoplasm:



Question 10

Identify the neoplasm: