Salivary Gland Neoplasms for Dummies!

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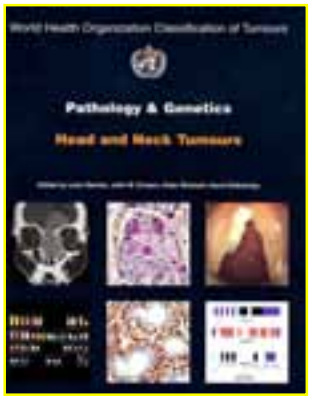
World Health Organization Blue Book



- Published 2005
- 130 contributing authors
- 28 countries
- 37 member Working Group
- 890 color illustrations
- 430 pages
- 2918 references
- $110.00

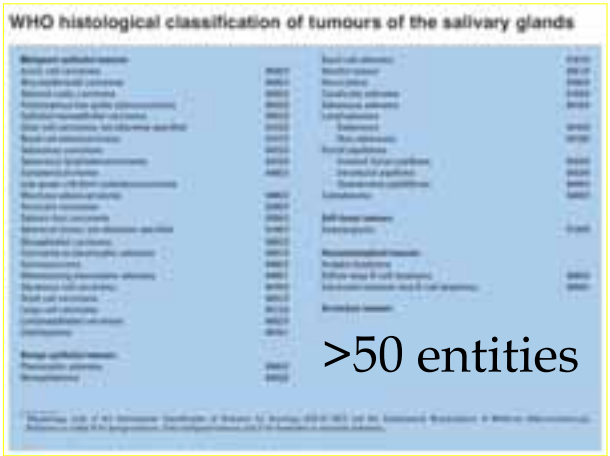
World Health Organization Blue Book
Pathology and Genetics of Head and Neck Tumours

Highly templated style

- Definition
- Epidemiology
- Etiology
- Localization
- Clinical features
- Radiographic findings
- Tumour spread and staging
- Macroscopy
- Histopathology
- Ancillary studies (histochemical, immunohistochemical, ultrastructural, molecular, and genetic)
- Differential diagnosis
- Precursor lesions
- Histogenesis
- Prognosis and predictive factors
- Methods of treatment

Chapters

1. Nasal Cavity and Paranasal Sinuses
2. Nasopharynx
3. Hypopharynx, Larynx and Trachea
4. Oral Cavity and Oropharynx
5. Salivary Glands
6. Odontogenic Tumors
7. Ear
8. Paraganglionic System



General Considerations

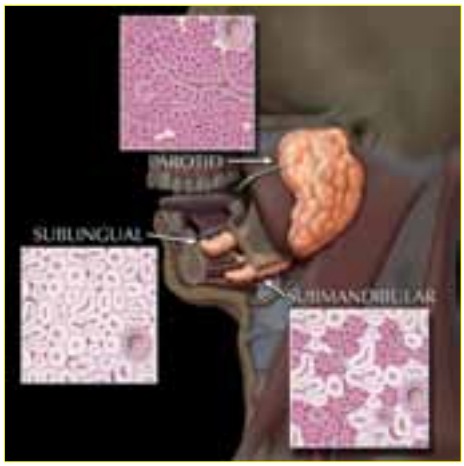
- 1% of all tumors (considered under-reported)
- Most common in adults
- Increased frequency in females with Warthin tumor
- Fine needle aspiration first line screening test
- Little known about etiology
- Site helps separate benign and malignant
- Clinic stage is important
- Molecular techniques slow to catch on

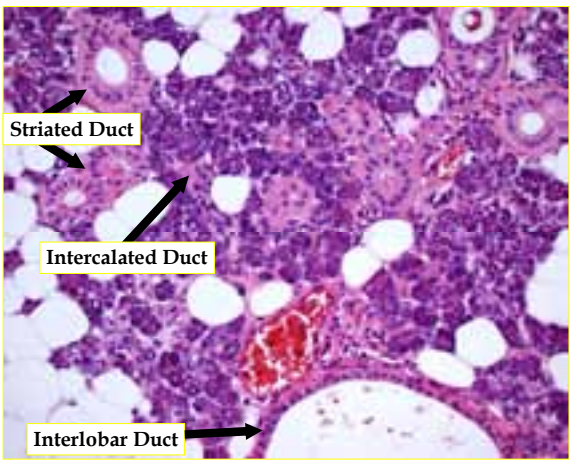
Genetics

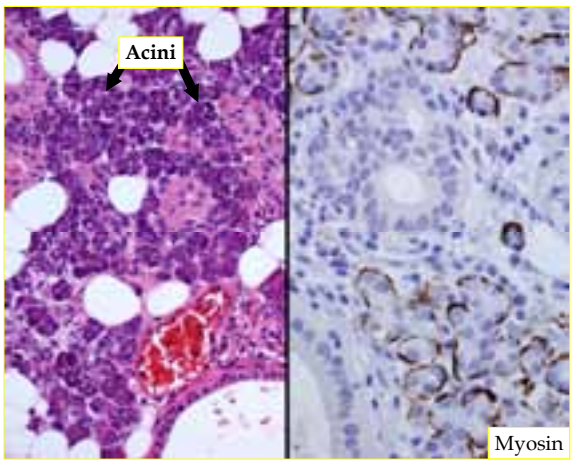
- Pleomorphic adenoma
  - ➔8q12 (*PLAG1*) (40%) (increased *PLAG1*)
  - ➔12q14-15 (HMGA2) (8%)
- Mucoepidermoid carcinoma
  - ➔t(11;19)(q21;p13): MECT1-MAML2
  - ➔About 70% of low grade tumors

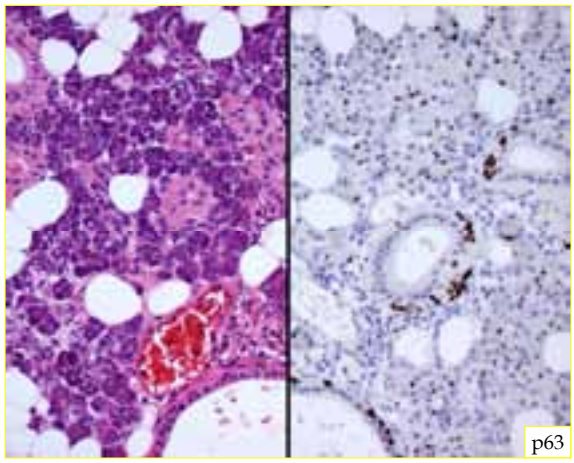
Immunohistochemistry

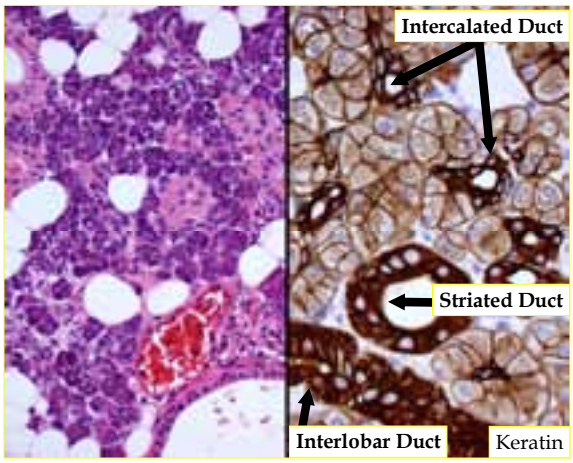
- Ductal cell differentiation
  - ➔Keratin (AE1/AE3), CAM5.2, EMA, CEA
- Myoepithelial cell differentiation
  - ➔Smooth muscle actin, p63, S-100 protein, calponin, GFAP, caldesmon, myosin, MSA
  - ➔Keratin (AE1/AE3), CAM5.2, CK14



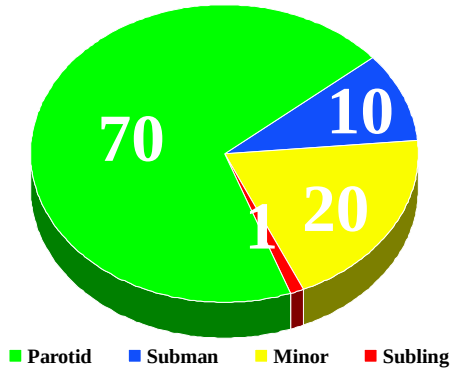




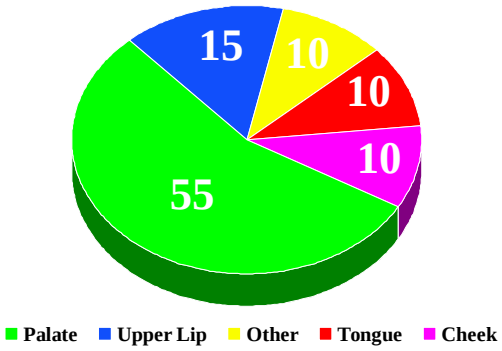




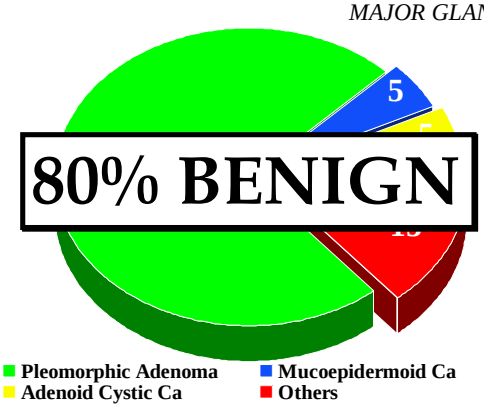
Tumor Site Distribution



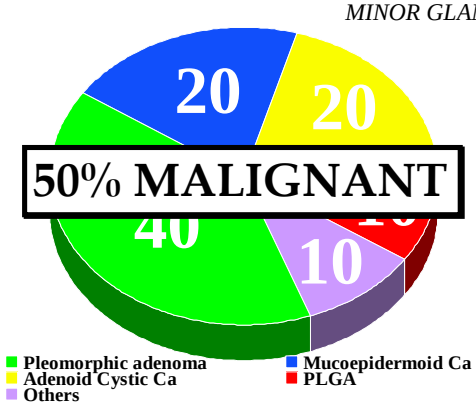
Tumor Site Distribution
Minor Salivary Glands Only



Tumor Type Distribution
MAJOR GLANDS



Tumor Type Distribution
MINOR GLANDS



Differential Diagnosis By Anatomic Site

- Upper lip
  - ➔Pleomorphic adenoma (mixed tumor)
  - ➔Canalicular adenoma
- Lower lip
- Floor of mouth
- Palate
- Parotid

Differential Diagnosis By Anatomic Site

- Upper lip
- Lower lip
  - ➔Mucocele
  - ➔Mucoepidermoid carcinoma
  - ➔Pleomorphic adenoma (mixed tumor)
- Floor of mouth
- Palate
- Parotid

Differential Diagnosis By Anatomic Site

- Upper lip
- Lower lip
- Floor of mouth (sublingual & submandibular)
  - ➔Mucoepidermoid carcinoma
  - ➔Adenoid cystic carcinoma
  - ➔Pleomorphic adenoma (mixed tumor)
- Palate
- Parotid

Differential Diagnosis By Anatomic Site

- Upper lip
- Lower lip
- Floor of mouth
- Palate
  - ➔Pleomorphic adenoma (mixed tumor)
  - ➔Mucoepidermoid carcinoma
  - ➔Polymorphous low-grade adenocarcinoma
  - ➔Adenoid cystic carcinoma
- Parotid

Differential Diagnosis By Anatomic Site

- Upper lip
- Lower lip
- Floor of mouth
- Palate
- Parotid
  - ➔Pleomorphic adenoma (mixed tumor)
  - ➔Warthin tumor
  - ➔Mucoepidermoid carcinoma
  - ➔Acinic cell adenocarcinoma

Benign versus Malignant

- Rate of growth
  - ➔Benign: slow, steady growth (low mitoses)
  - ➔Malignant: rapid increase in size (high mitoses)
    - ✓Very worrisome if longstanding lesion suddenly develops rapid growth

Benign versus Malignant

- ◆Relationship with surrounding structures
  - ➔Fixation
    - ✓Benign: Freely movable (palate excluded)
    - ✓Malignant: Adherent to surrounding tissue
  - ➔Ulceration
    - ✓Benign: Overlying epithelium intact
    - ✓Malignant: Ulceration of overlying epithelium
  - ➔Paresthesia (due to nerve invasion by tumor)
    - ✓Benign: No change in sensation
    - ✓Malignant: Paresthesia common

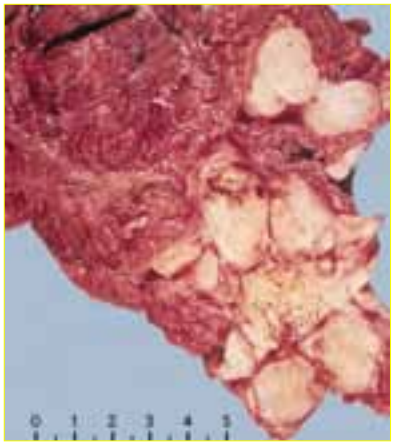
Benign versus Malignant

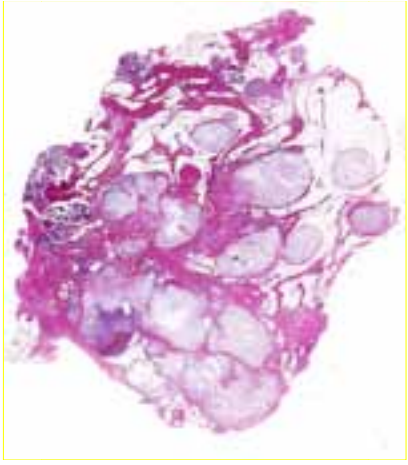
- ◆Circumscription
  - ➔Benign: Encapsulated; well circumscribed
  - ➔Malignant: Poorly circumscribed; infiltrative

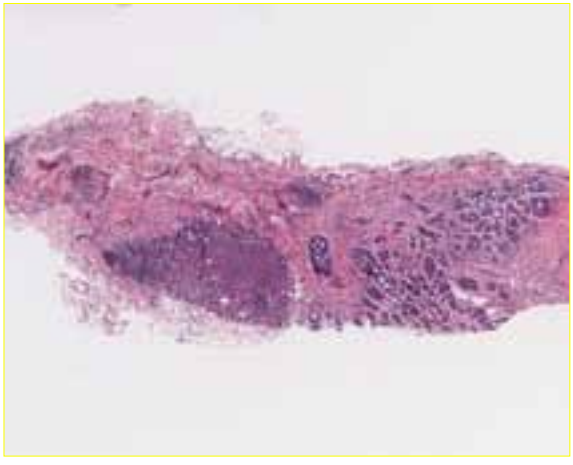
. . . BUT — Be aware of multifocality and minor salivary gland location

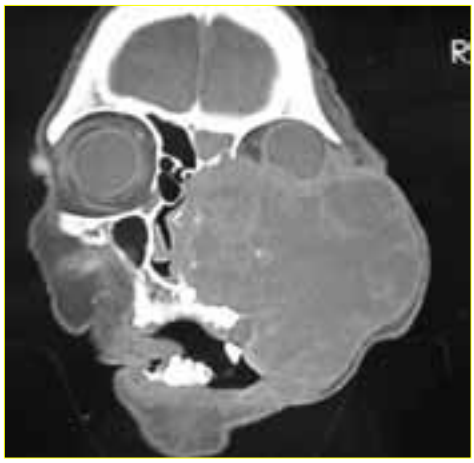
Multifocal, Multilobular, & Without a Capsule

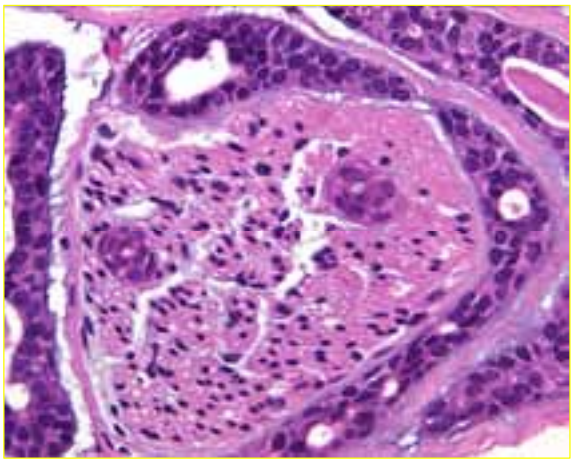
- ◆Pleomorphic adenoma
- ◆Basal cell adenoma
- ◆Canalicular adenoma
- ◆Warthin tumor
- ◆Cystadenomas
- ◆Oncocytic lesions
  - ➔Oncocytoma vs. nodular hyperplasia

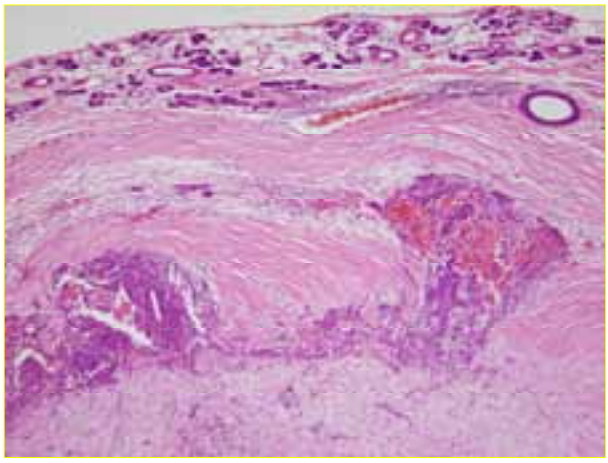






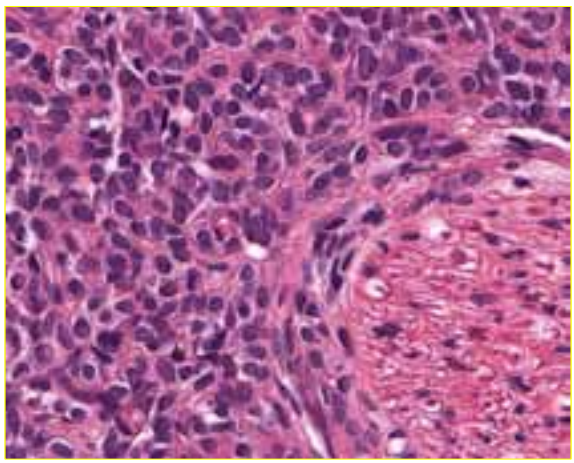


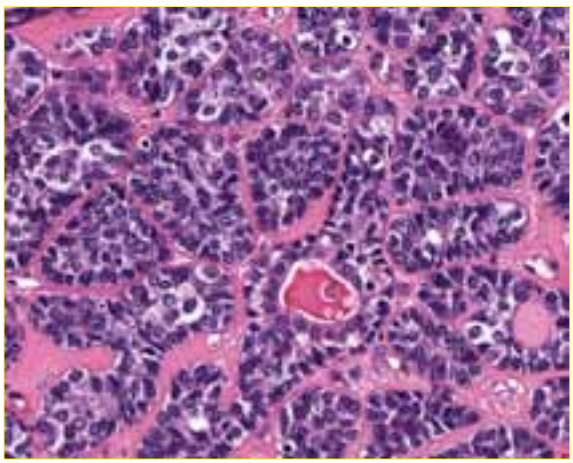


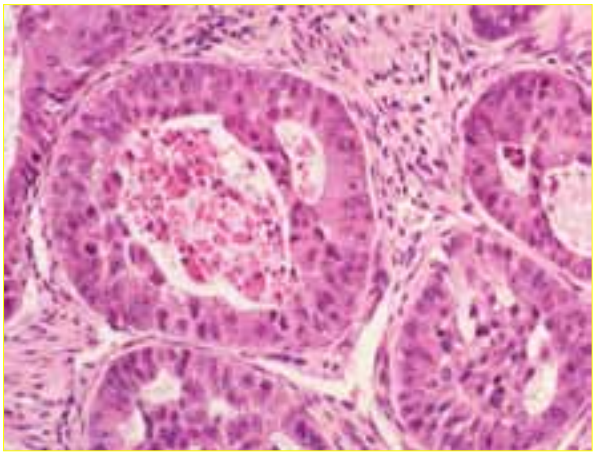


Benign versus Malignant

- ◆Cytological atypia
  - ➔But malignant tumors are frequently bland
  - ➔Profoundly pleomorphic
    - ✓Salivary duct carcinoma







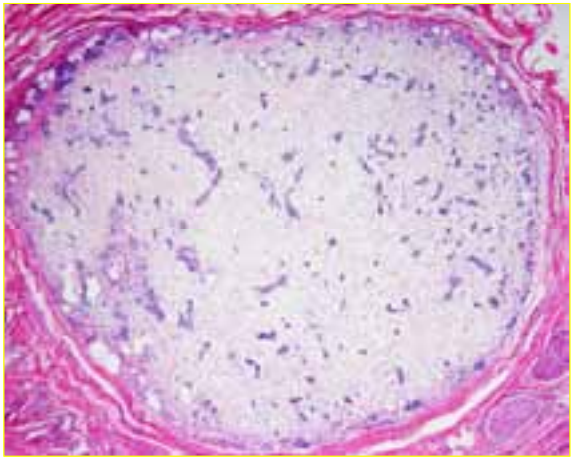
Pleomorphic Adenoma
Clinical

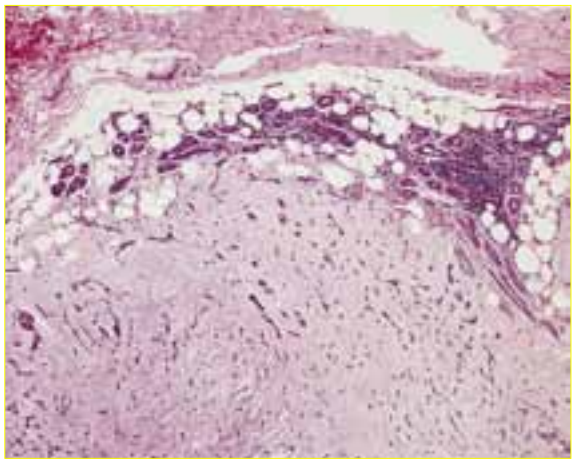
- Most common salivary gland neoplasm
- Age: 30 – 60 years
- Sex: F~M
- Site: Parotid most common site
  - 75% superficial lobe; 25% deep lobe
  - Palate next most common
- Slow growing, painless, lobular mass
  - ➔Can reach huge size

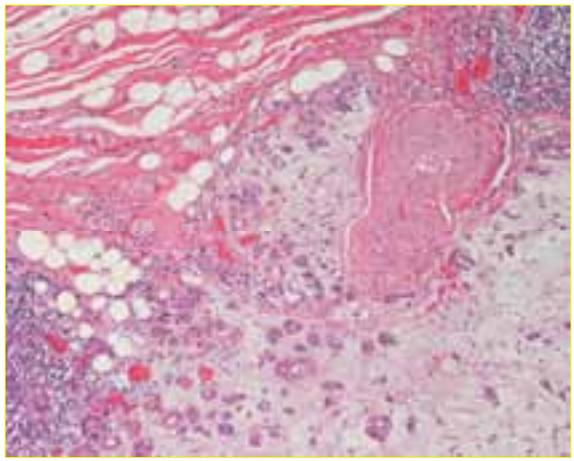
Pleomorphic Adenoma
Macroscopic

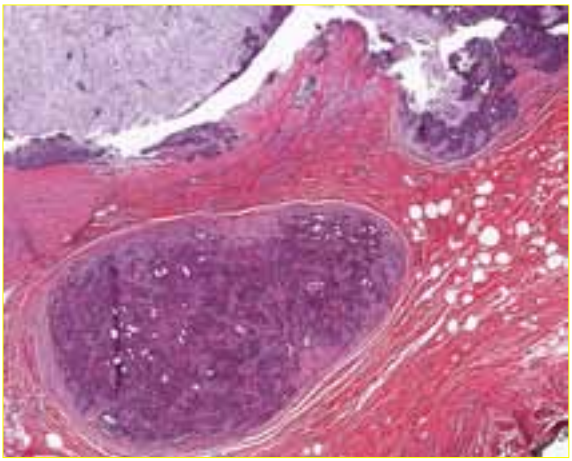
Tumor is epithelial (ductal), basal, and myoepithelial with mesenchymal component (myxoid, chondroid, hyaline, osseous)

- Tumor may be multinodular
- Tumor has “pseudopods” that bulge outwards
- Margins are difficult to assess
  - ➔Tumor without parotid tissue surrounding it
  - ➔The capsule may rest on the nerve(s)



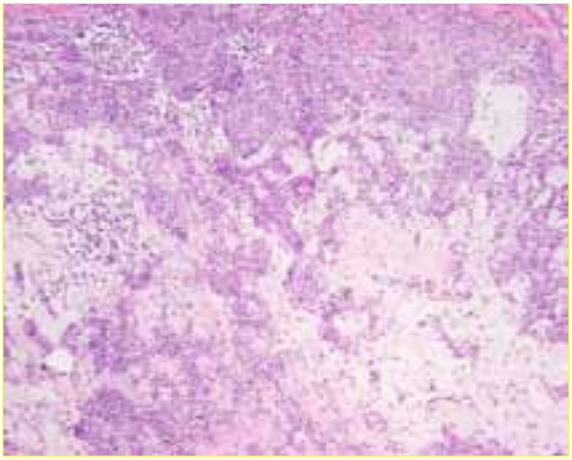


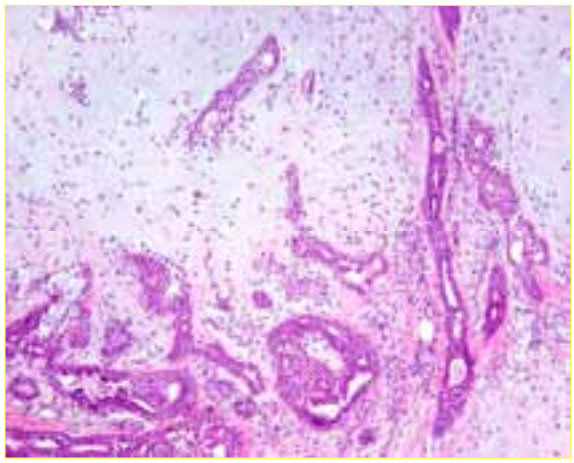


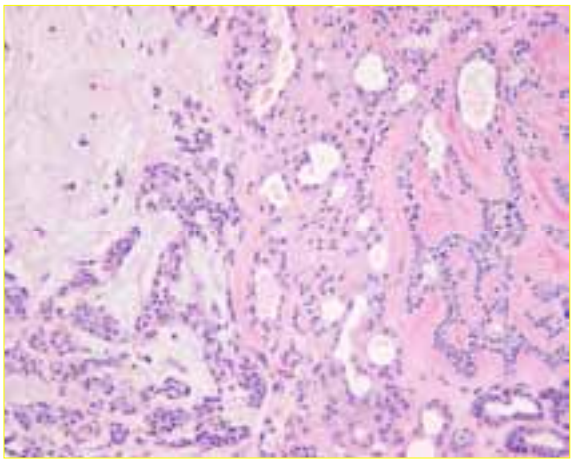


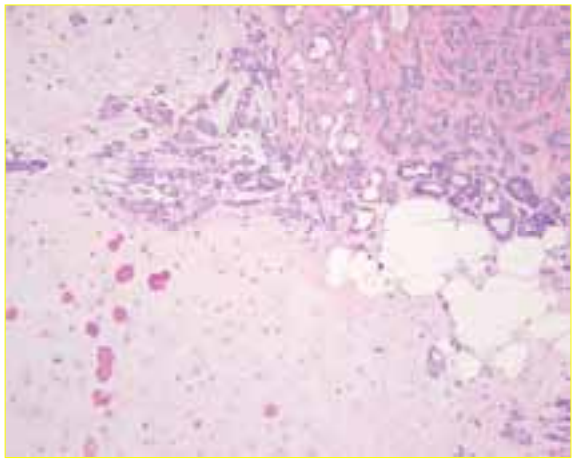
Pleomorphic Adenoma

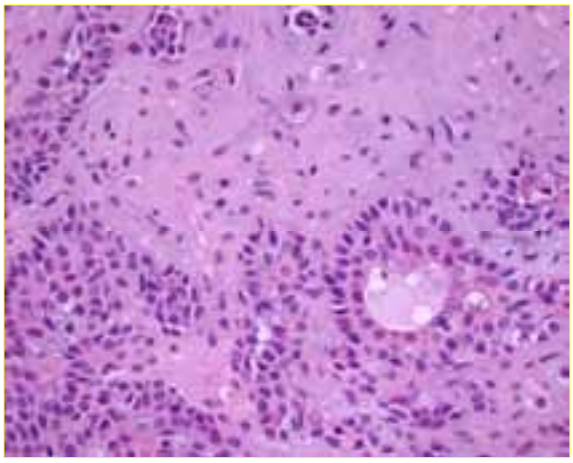
- Remarkably variable histology
  - ➔Solid, tubular, trabecular, cystic
  - ➔Cells literally "melt" into the chondroid or myxoid background stroma
  - ➔Stroma may be heavily fibrotic/hyalinized
  - ➔Spindled, epithelioid, *glandular*, & plasmacytoid cells
  - ➔Squamous metaplasia is common
  - ➔Increased mitotic figures s/p FNA

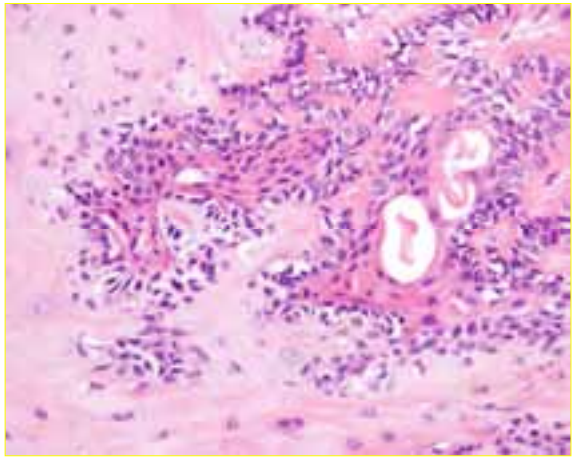


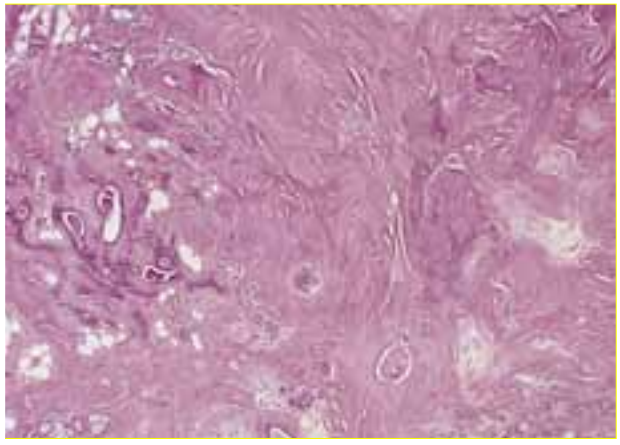


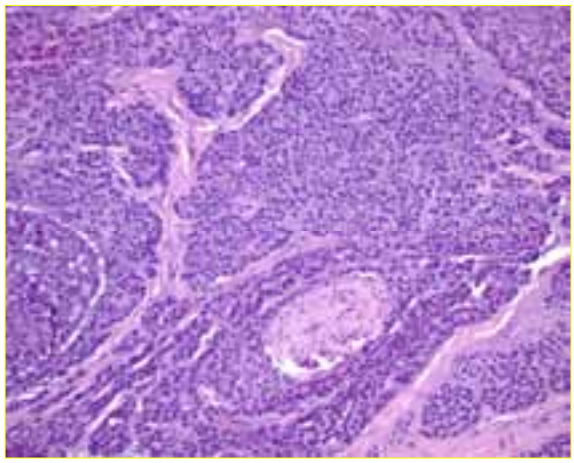












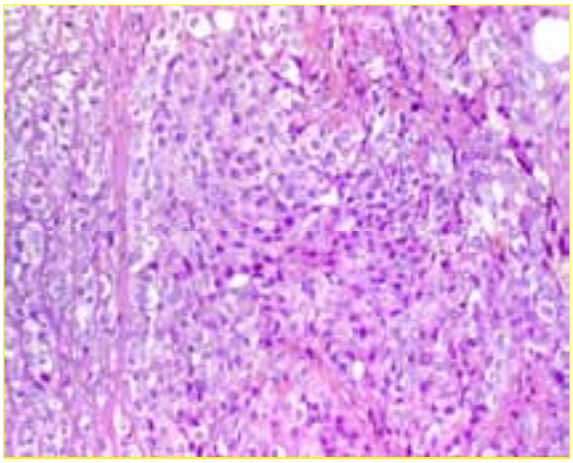
Myoepithelioma

A benign epithelial tumor composed of spindle, plasmacytoid, epithelioid, and clear myoepithelial cells

- Age: Mean 45 years
- Sex: Equal
- Site: Parotid gland and palate
- Encapsulated

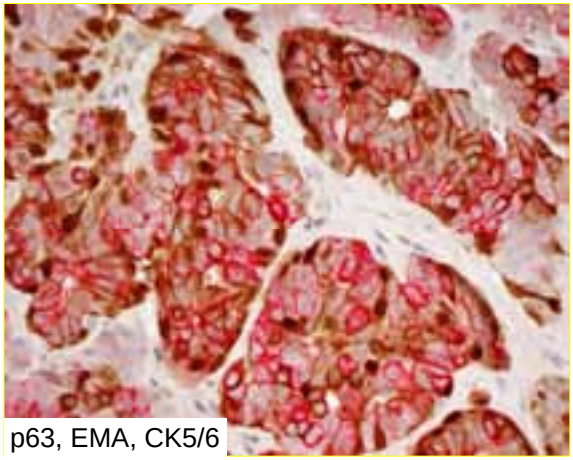
Myoepithelioma

- Similar to PA: **except**
  - **No** myxochondroid matrix
  - **No** ductal elements
- Plasmacytoid cells in a mucoid stroma and/or interlacing fascicles of spindled cells
- Immunohistochemistry
  - Positive: CK5/6, p63, SMA, SMMHC, caldesmon, calponin
  - Rare S100 protein positive cells
  - Negative with GFAP



Immunohistochemistry

- Epithelial
  - Keratin, EMA, CK5/6, CK7
- Myoepithelial
  - Smooth muscle actin, muscle specific actin, p63, GFAP, S-100 protein, calponin
- Pleomorphic adenoma with 12q chromosomal abnormalities show increased risk of developing carcinoma



p63, EMA, CK5/6

Pleomorphic Adenoma

- Recurrence vs. Recrudescence vs. Residual
- "Benign" metastasis
- Malignant transformation can be seen in long standing tumors

Pleomorphic Adenoma

Past Management

- Local anaesthetic
- Direct incision over lump
- Remove some/any parotid tissue
- High recurrence rate
  - ➔*70% Lanier 1972*

Present management

- General anaesthesia
- Remove ALL parotid tissue (superficial and/or deep lobes)
- <2% recurrence 10 yr

Carcinoma Ex-Pleomorphic Adenoma
Demographics

- About 6-10% of PA develop carcinoma
  - ➔Represents about 12% of all salivary malignancies
  - ➔About 4% of all salivary gland tumors
- Must have pre-existing PA
  - ➔Only clinical history is some cases
  - ➔Long history of PA or frequent recurrences
    - ✓Risk of 1.5% at 5 years; 10% at 15 years

Carcinoma Ex-Pleomorphic Adenoma
Clinical

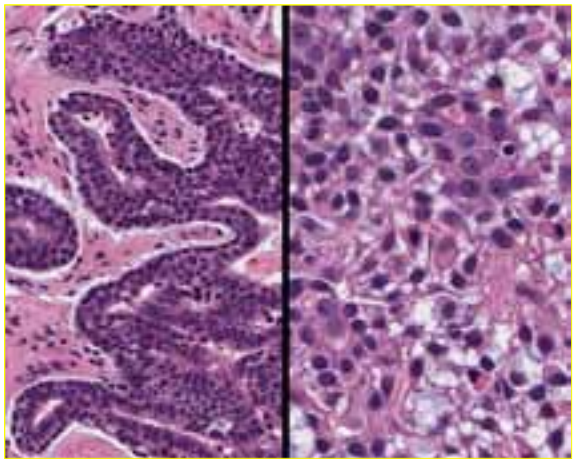
- Age: Elderly (usually >60 yrs)
- Sex: M = F
- Site: Majority in major glands
  2/3 in parotid
- Sudden enlargement, with/without nerve symptoms

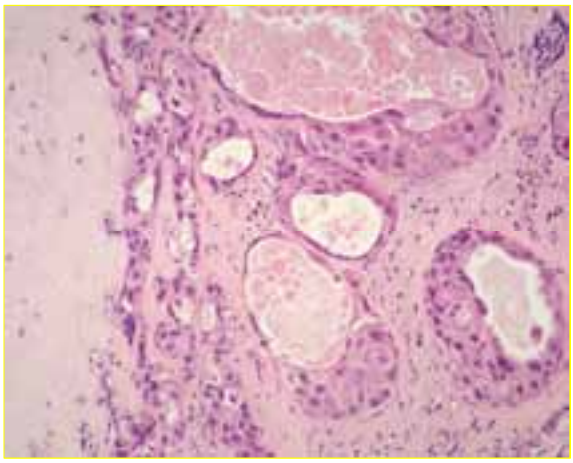
Carcinoma Ex-Pleomorphic Adenoma
Pathology

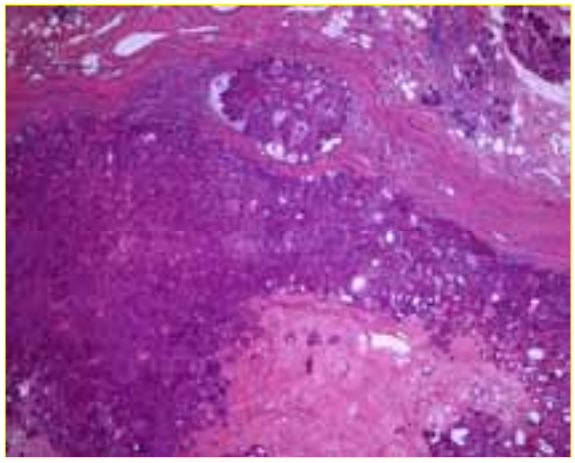
- Large tumors
  - ➔Must have adequate sampling
- Malignant component adjacent to benign
- Often poorly differentiated carcinoma
  - ➔Salivary duct carcinoma common
- Infiltrative pattern
- Remarkable cytological atypia
- Scarring and sclerosis is common
  - ➔Presence in PA requires additional evaluation

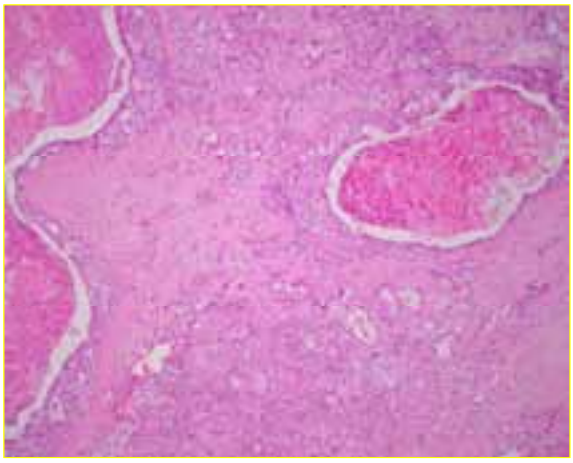
Carcinoma Ex-Pleomorphic Adenoma
Classification

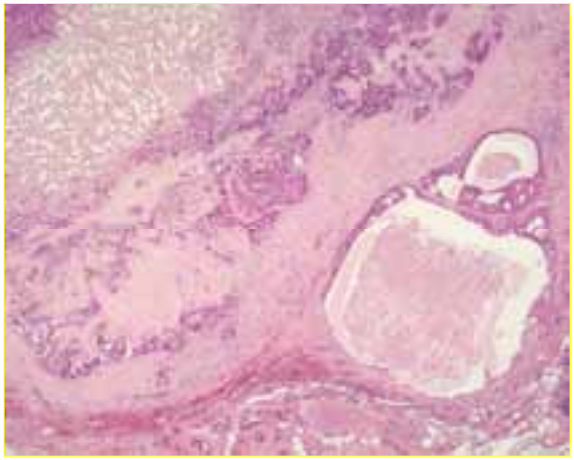
- Subclassified (prognostic significance)
  - ➔Non-invasive = Excellent
    - ✓Intracapsular, *in situ*, dysplastic PA
  - ➔Minimally invasive (< 1.5 mm) = Good
  - ➔Invasive (>1.5 mm) = Poor
- Recurrences (40-50%), usually within 5 yrs
- Up to 70% show regional and/or distant metastases
  - ➔Lungs, bone, brain or liver

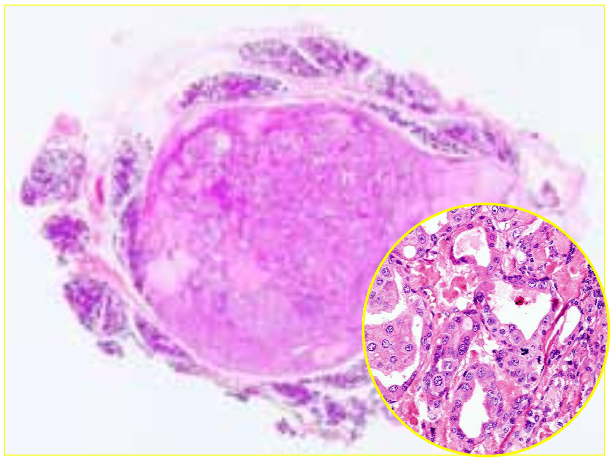


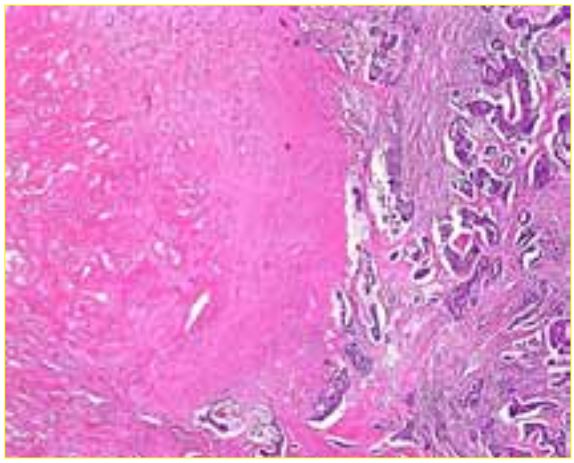


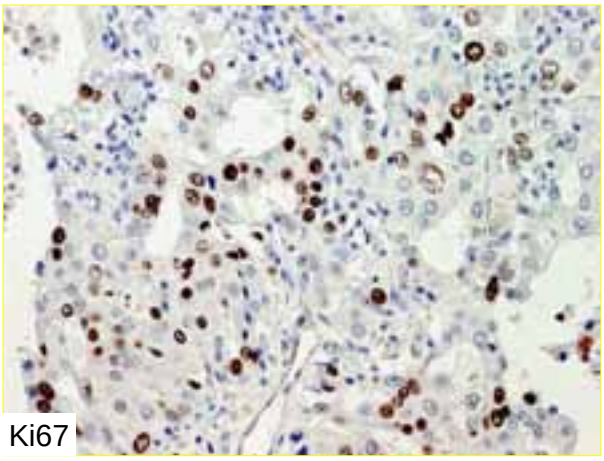












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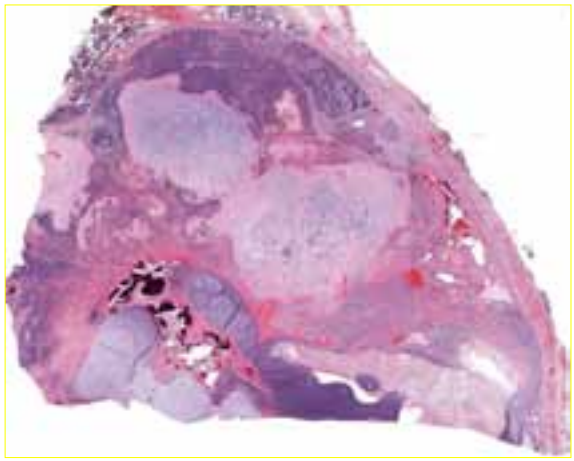
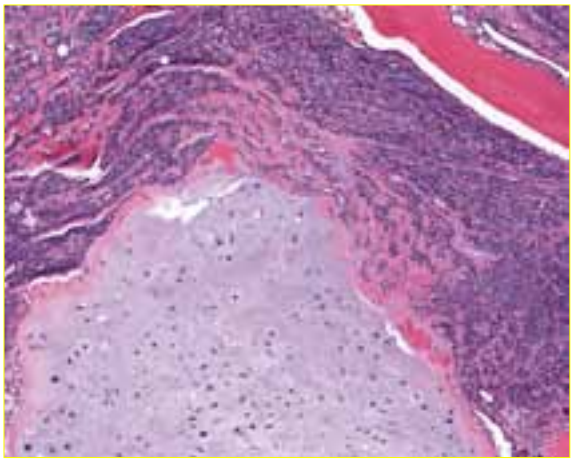
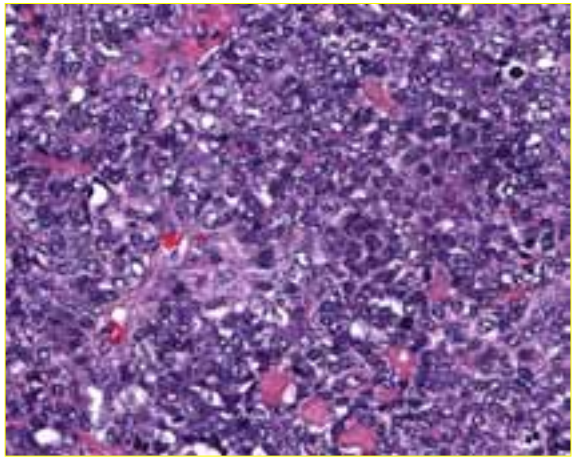
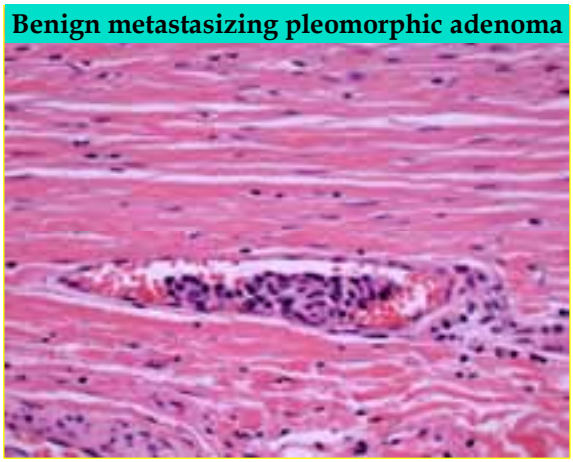








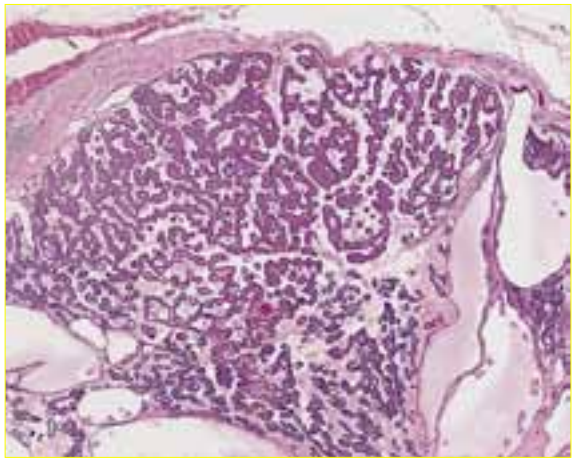
Carcinoma Ex-Pleomorphic Adenoma
Prognostic Factors

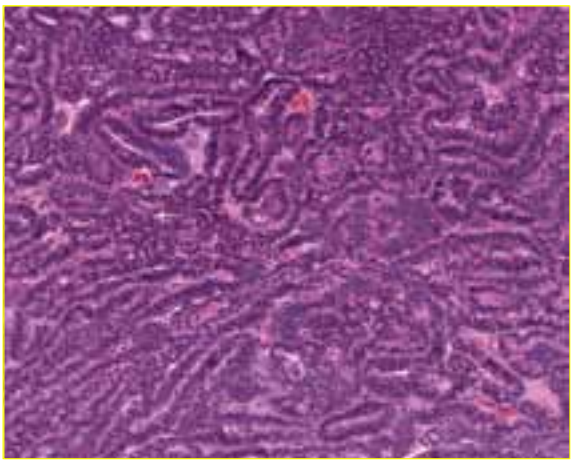
- ◆Pathologic stage
- ◆Size
- ◆Histologic grade and type
- ◆Proportion of carcinoma
- ◆Extent of invasion
- ◆Ki-67 labeling index

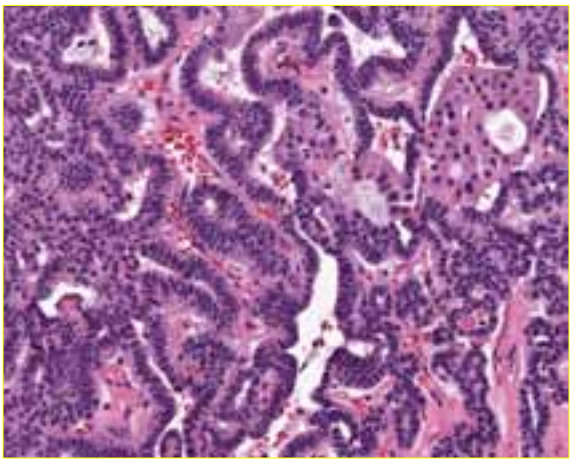
Canalicular adenoma

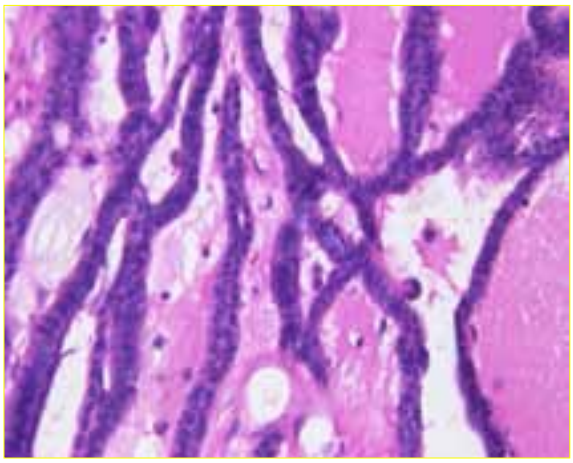
Benign salivary gland neoplasm composed of bilayered strands of basaloid cells that branch and anastomose to form variably sized channels (canaliculi)

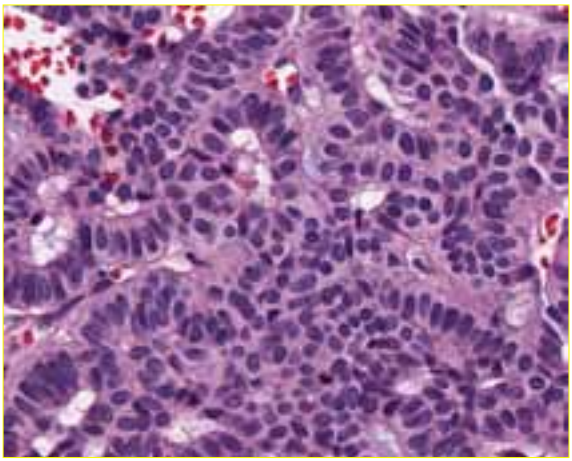
- ◆Age: >50 years
- ◆Sex: F > M
- ◆Site: Predilection for the **upper lip**
- ◆Minor salivary glands (exclusively)
- ◆~20% of are multifocal











Basal Cell Adenoma
Demographics

Benign epithelial tumor comprised of a relatively uniform, monomorphous proliferation of basaloid cells

- Not cell origin—only phenotype
  - ➔Both duct luminal and myoepithelial cells present
- Don't use "*Monomorphic adenoma*"
- About 4% of salivary gland tumors
- Age: peak, 60 years
- Sex: F > M
- Site: 80% parotid gland (superficial lateral)
  6% upper lip

Basal Cell Adenoma
Clinical

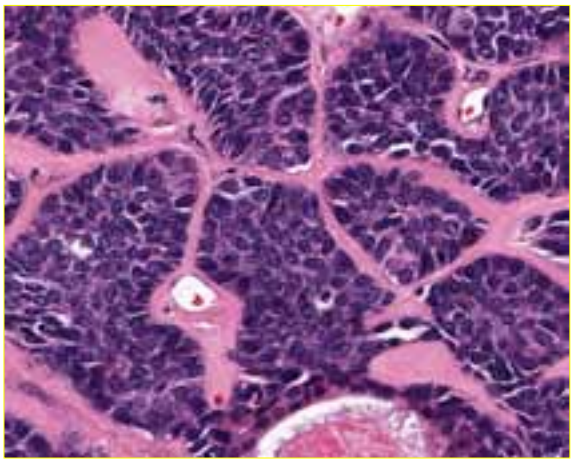
- Membranous type basal cell adenomas associated with dermal cylindromas
  - ➔Face and scalp
  - ➔Same molecular alterations at chromosome region 16q12-13
- Usually single and encapsulated
  - ➔Exception: membranous type is multinodular

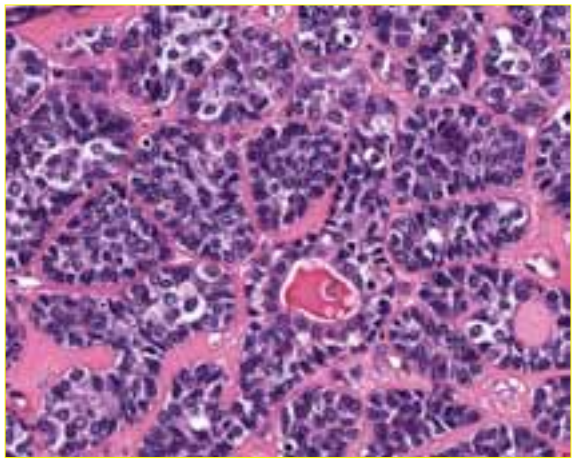
Basal Cell Adenoma
Histology

- Circumscribed and encapsulated
  - ➔Except membranous type
- Variable number of basal, ductal, and myoepithelial cells, but . . .
- **Basaloid cells** (not "basal") predominant
- Monotonous architecture
- Absence of myxochondroid matrix
- No spindled and plasmacytoid cells

Basal Cell Adenoma
Histology

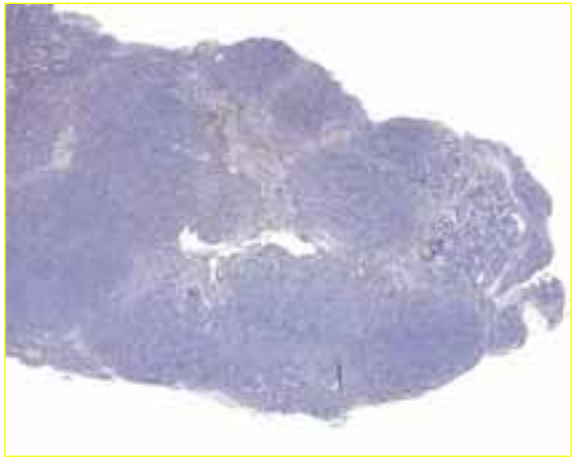
- Small, uniform cuboidal cells with indistinct cell borders, and round to oval nuclei
- Cytoplasm is usually limited, giving "basophilic" appearance
- Larger and smaller cells:
  - Larger cells are central
  - Smaller cells cluster at the periphery near stromal interface
- Palisaded alignment

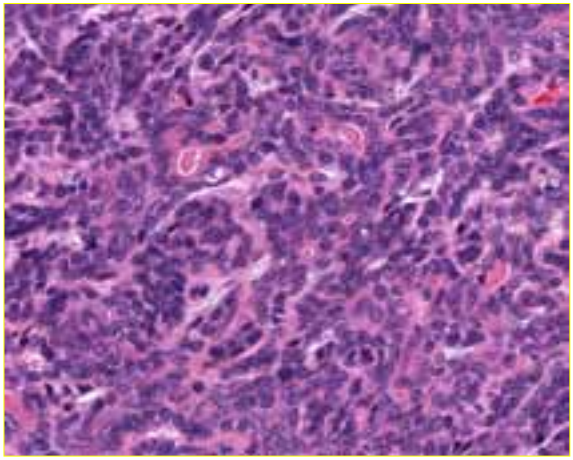


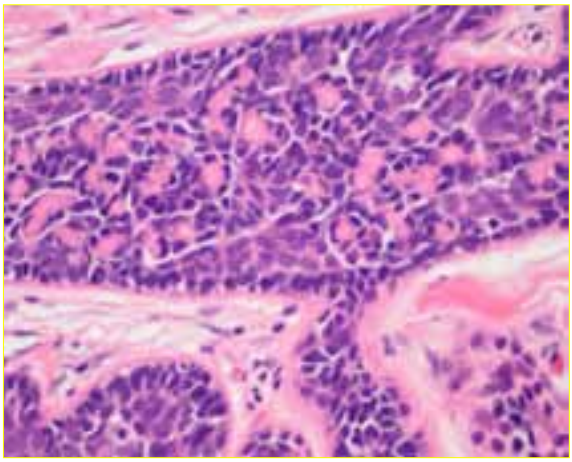


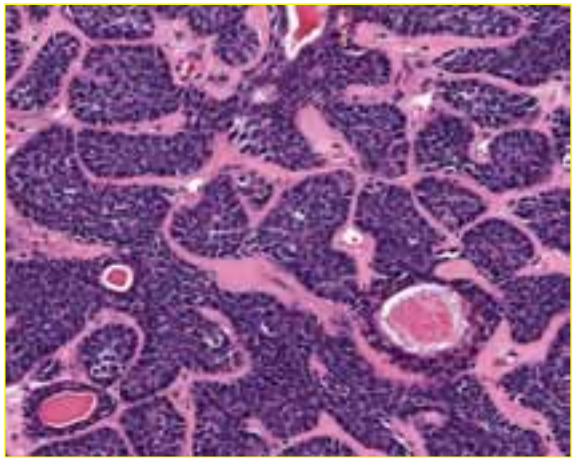
Basal Cell Adenoma
Subtypes

- Four subtypes:
  - Solid
    - ✓Collagenous stroma separates clusters of basaloid epithelial cells
  - Trabecular and tubular
    - ✓Interlacing, narrow bands of basaloid cells
    - ✓Palisading of the epithelial nuclei along the stromal interface
  - Membranous
    - ✓Large quantities of densely collagenous, eosinophilic, PAS positive, hyaline material separate tumor nests
    - ✓"Jigsaw puzzle"-like
    - ✓Intracellular droplets may coalesce



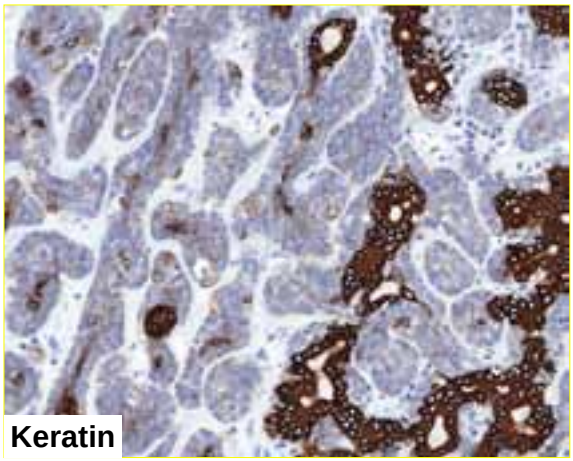


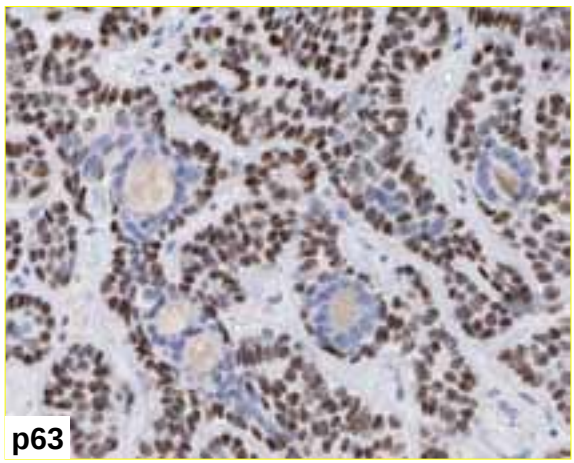


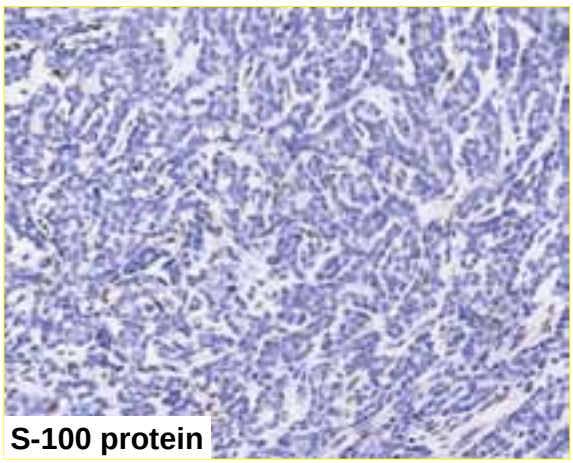


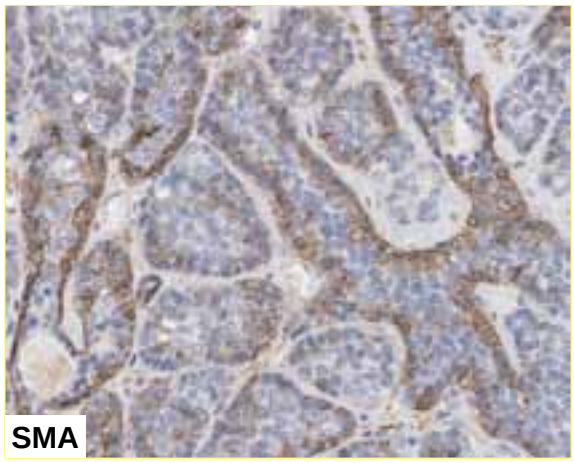
Basal Cell Adenoma
Immunohistochemistry

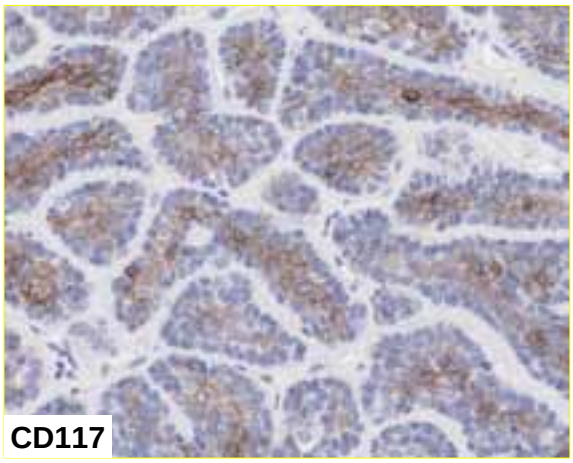
- ◆Cytokeratin positive
  - ➔Most intense in the duct-luminal cells
- ◆CEA and EMA positive luminal cells
- ◆Peripheral cells positive with smooth muscle actin (SMA), myosin, p63 and S100 protein
- ◆CD117 and bcl-2 are reactive in most tumors











Basal Cell Adenoma
Differential Diagnosis

Criteria	Cellular Pleomorphic Adenoma	Basal cell AdenoCA	Adenoid Cystic Ca
Growth	Encapsulated	Invasive	Invasive
Cribriform pattern	-	-	+++
Cells	Plasmacytoid	Basaloid	Ductal/myoepi.
Stroma relationship	Blending	Abrupt	Surrounded
Mitosis	+	++	+++
Necrosis	-	+	+++
Nuclei	Round	Basal	Angular
Perineural invasion	-	+	+++
Matrix	Myxochondroid	Fibrosis	Reduplicated BM

Basal Cell Adenoma
Prognosis and Treatment

- Excellent prognosis
- Surgery with rim of normal tissue
- Membranous type tends to be multinodular, and associated with a higher recurrence rate (up to 25%)
  - ➔Parotidectomy recommended
- Malignant transformation may develop
  - ➔Higher for membranous type

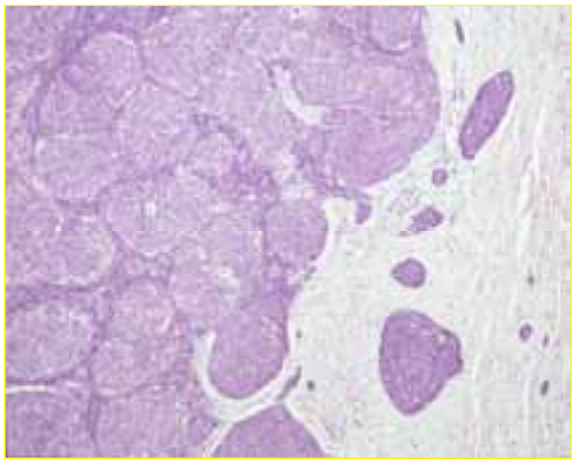
Basal Cell Adenocarcinoma
Clinical

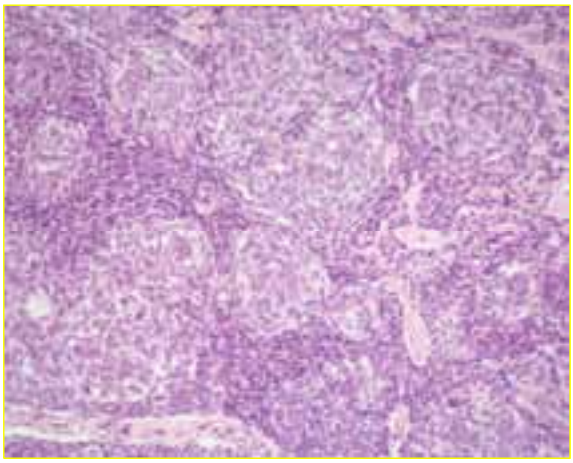
Malignant counterpart of basal cell adenoma showing infiltrative growth

- < 1% of all salivary tumors
- Age: 60 years (mean)
- Sex: M = F
- Site: ~90% parotid (superficial lobe)
- High recurrence rate
  - ➔Up to 40%

Basal Cell Adenocarcinoma
Pathology

- Invasion/infiltration into salivary gland tissue, soft tissue, nerves and vessels
- Same patterns and growth as basal cell adenoma
- Foci of squamous metaplasia
- Nuclear atypia usually minimal
- Mitotic index usually low
- Same immunohistochemistry as basal cell adenoma





Adenoid Cystic Carcinoma
Demographics

Malignant epithelial tumor of modified myoepithelial (abluminal) and ductal (luminal) differentiated cells

- ◆About 5% of all salivary gland tumors
- ◆12% of all malignant tumors
- ◆Age: Peak incidence 6th decade
- ◆Sex: F > M (3:2)
- ◆Site: Parotid most common site
  Half develop in minor salivary glands
  Most common malignant oral SGT

Adenoid Cystic Carcinoma
Clinical

- ◆Slowly growing swellings or nodules
- ◆Tenderness, pain, and facial nerve paralysis frequently develop
  - ➔Related to high incidence of nerve invasion
- ◆Palate tumors frequently have ulceration
- ◆Small tumors are often mobile
- ◆Fixation difficult to assess in palate tumors

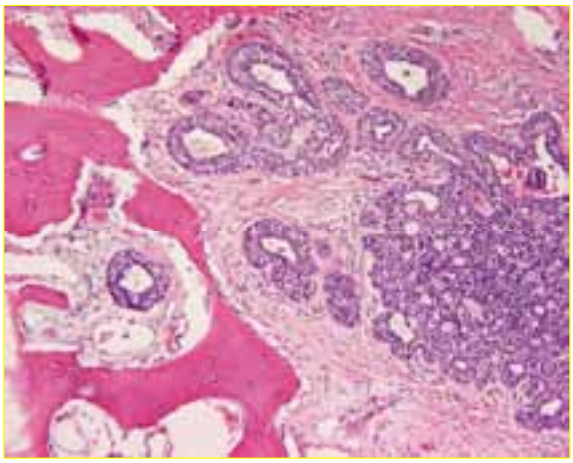
Adenoid Cystic Carcinoma
Macroscopic

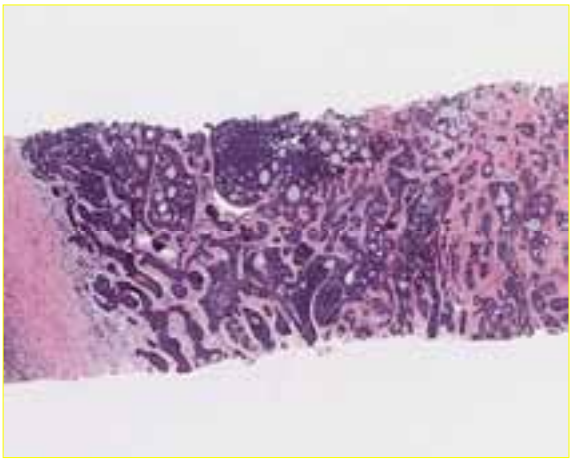
- ◆Poorly circumscribed and unencapsulated
- ◆Small tumors appear well circumscribed, but this is deceiving
- ◆Tumors are firm, white to gray-white
- ◆Multiple frozen section examinations requested due to insidious neural invasion

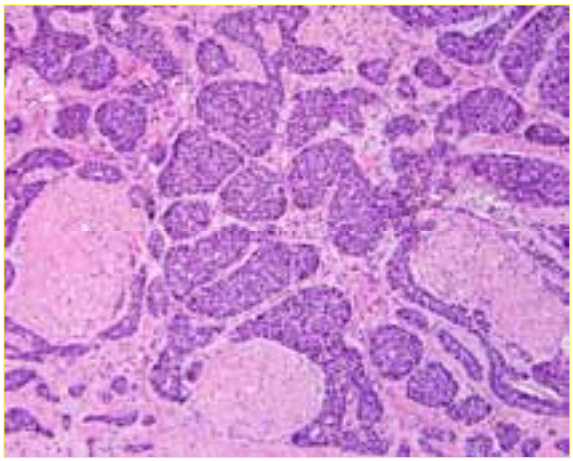
Adenoid Cystic Carcinoma
Histology

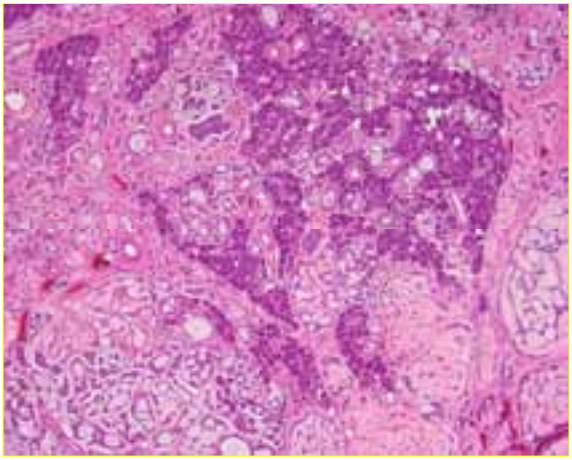
Luminal ductal cells and *abluminal* modified myoepithelial cells

- ◆Tracking nerves is a hallmark (peri- or intraneural)
- ◆"*Encapsulated*" tumors (minor salivary glands) can be difficult to diagnosis
- ◆Histomorphologically polymorphous but cytomorphologically uniform
- ◆Myoepithelial-type cells with indistinct cell borders, high N:C ratio with angular, basophilic nuclei



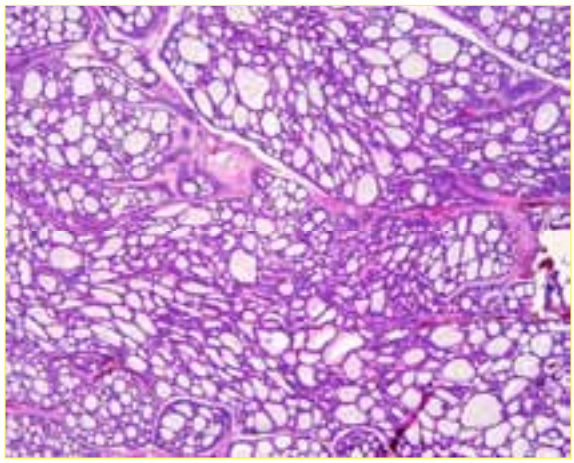


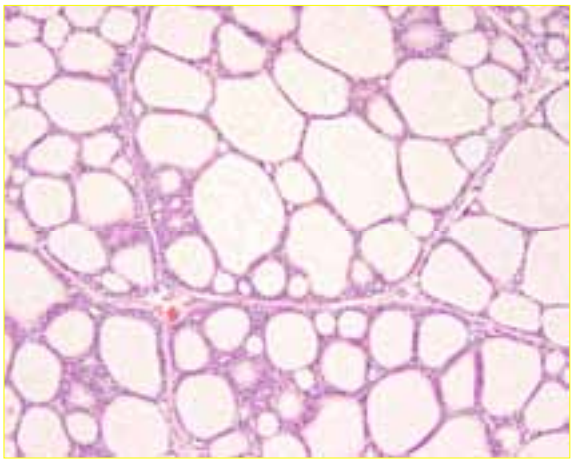


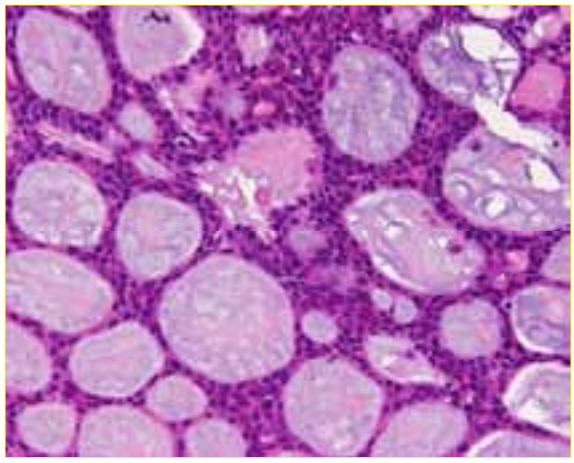


Adenoid Cystic Carcinoma
Histology

- ◆Three major patterns
- ◆Frequent overlap: use dominant pattern, has prognostic significance:
  - ➔Cribriform
    - ✓Most common
    - ✓Punched out, sieve, Swiss cheese-like but in fact …
    - ✓Surround, blend and are in direct continuity with pseudocystic structures of basophilic glycosaminoglycans or hyalinized basal lamina material
    - ✓True glandular lumens lined by cuboidal ductal cells



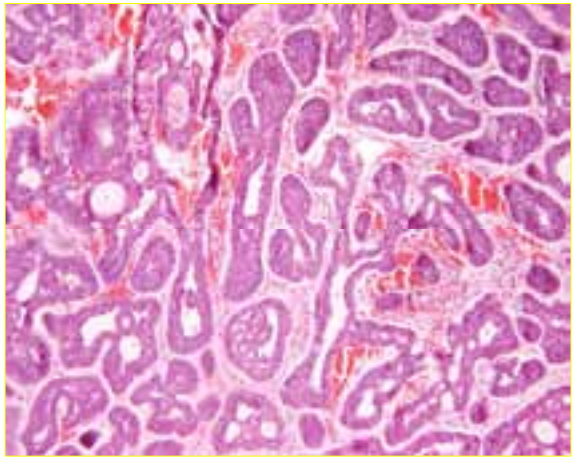


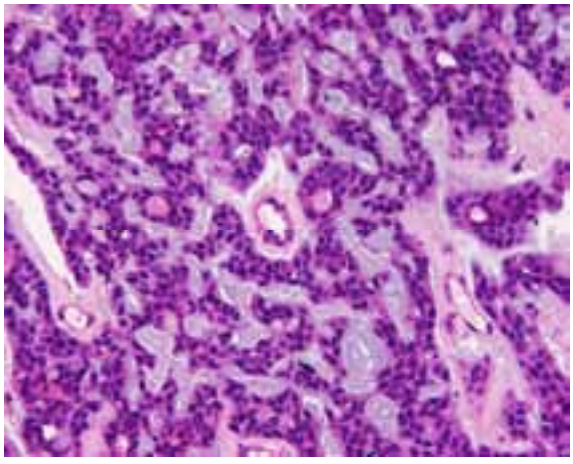


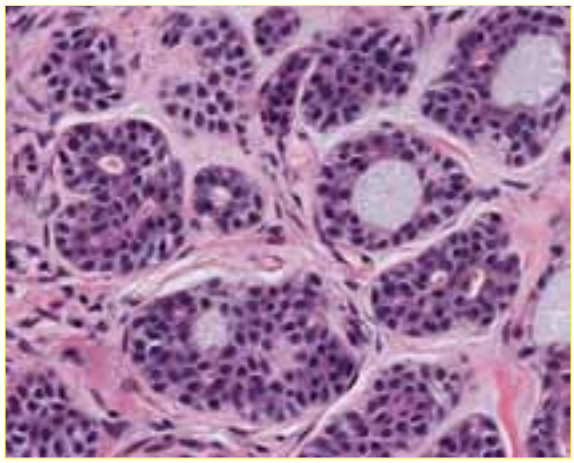
Adenoid Cystic Carcinoma
Histology

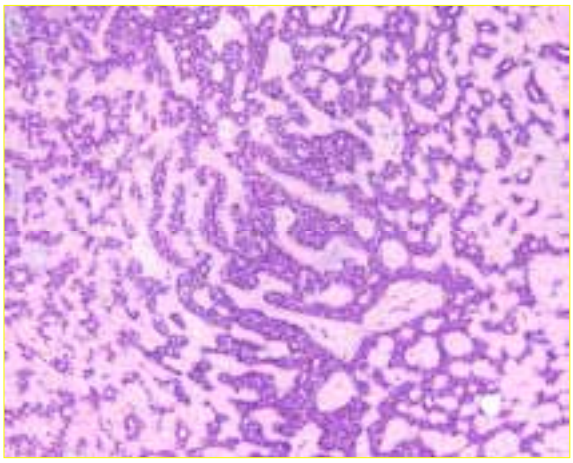
➔Tubular

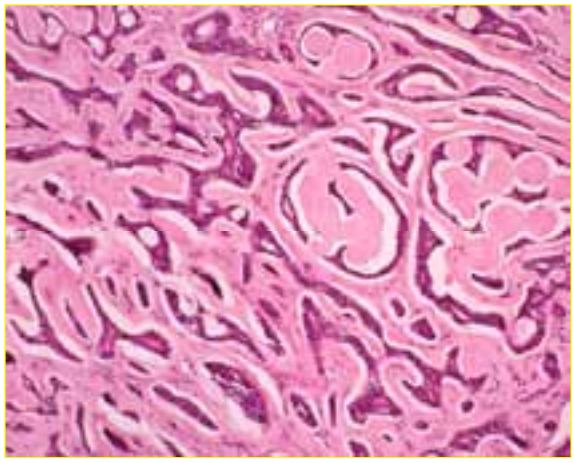
- ✓Ductal cells predominate
- ✓Surrounded by myoepithelial-type cells
- ✓Separated by stroma, although the continuity is more easily visible in this tumor type
- ✓Heavily hyalinized stroma may create "stranded" appearance





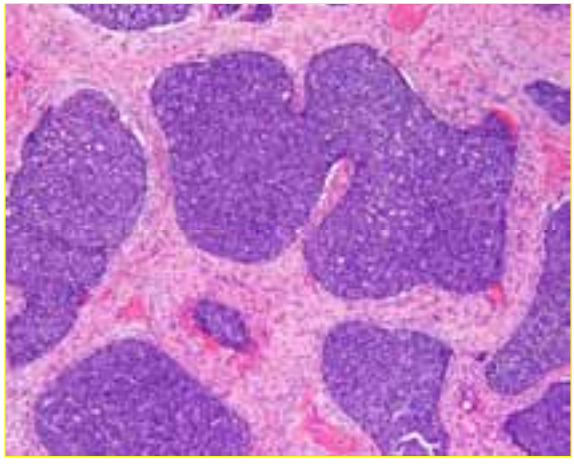


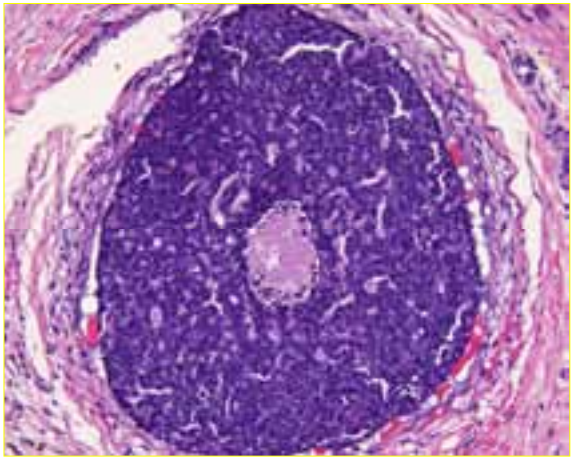


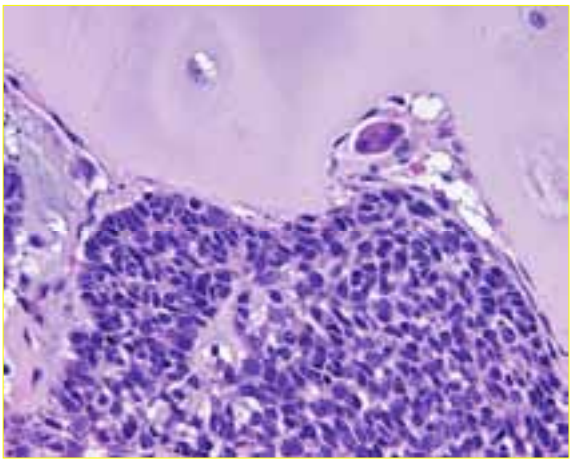


Adenoid Cystic Carcinoma
Histology

➔Solid (30% or higher)
- ✓About 15% of all ACC
- ✓Lacks stroma
- ✓Slightly larger cells with less angular nuclei
- ✓Basaloid myoepithelial cells predominant
- ✓Increased mitotic figures (5/10 HPFs)
- ✓Necrosis may be present (pyknosis, apoptosis and comedonecrosis)

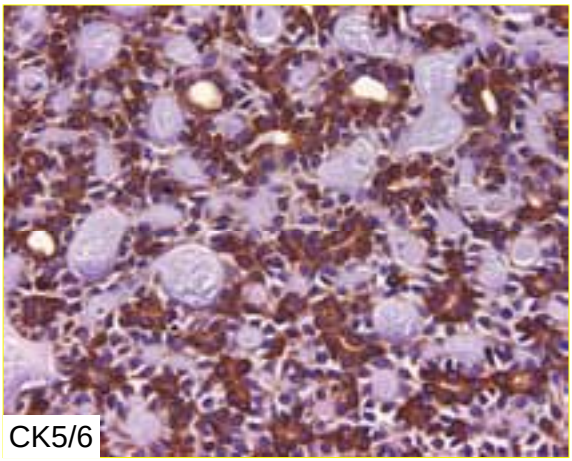




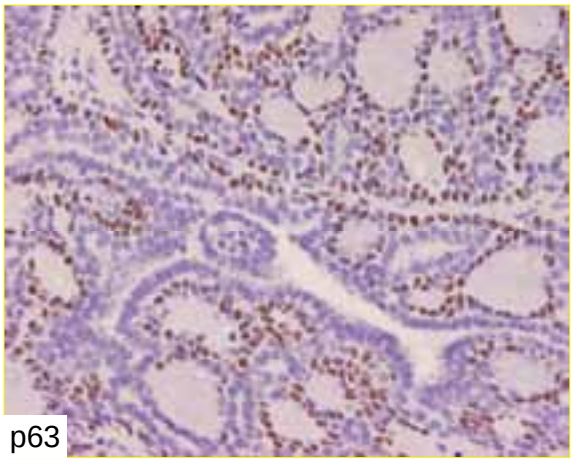


Adenoid Cystic Carcinoma
Immunohistochemistry

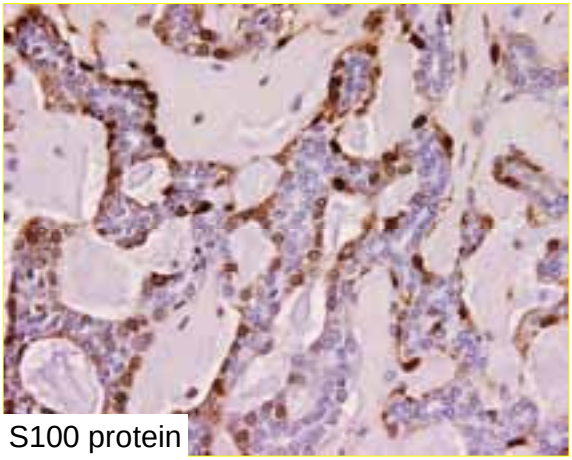
- ◆Dual population of ductal and myoepithelial cells
- ◆Ductal cells:
  - ➔More intensely reactive with keratins (pankeratin, CK7, CK19)
  - ➔Variable reactivity with CEA(p) and EMA
- ◆Abluminal myoepithelial cells:
  - ➔Keratin, vimentin, muscle specific actin, smooth muscle actin, SMMHC, p63, calponin
- ◆S-100 protein positive
- ◆CD117 positive (80%)—especially solid variant
  - ➔Not helpful for differential
- ◆MUC1 positive
- ◆Limited to absent GFAP



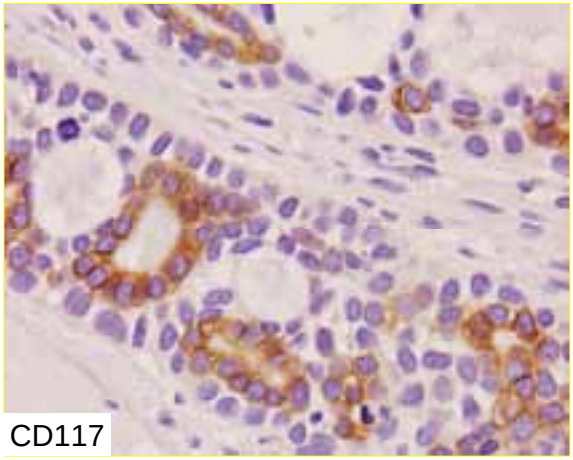
CK5/6



p63



S100 protein



CD117

Adenoid Cystic Carcinoma
Grading

	Grade 1 (45%)	Grade 2 (35%)	Grade 3 (20%)
Circumscription	Good	Deceptive	Never
Necrosis	No	+/-	+
Bone Invasion	No	+/-	+
Perineural invasion*	+/-	+	+++
Dominant pattern	Tubular	Cribriform	Solid
Pleomorphism	+/-	+	++
Mitoses	Rare	Few	Many
Recurrence	50%	80%	100%
15-year survival	39%	26%	5%

Adenoid Cystic Carcinoma
Molecular Alterations

- About 50% have loss of chromosome 12q12
- About 30% have translocations between 9p13-23 and 6q
- LOH at 6q23-25: associated with a poorer prognosis
- Alteration *p53*: associated with tumor recurrence and progression to solid type

Adenoid Cystic Carcinoma
Differential Diagnosis

- Cribriform/tubular growth pattern
  - ➔Polymorphous low grade adenocarcinoma:
    - ✓Exclusively minor salivary gland, "onion-skin", lacks reduplicated basement membrane, cytologically bland with vesicular chromatin
- Ductal and myoepithelial type cells
  - ➔Pleomorphic adenoma
    - ✓Lacks invasion, blends with myxochondroid matrix, plasmacytoid cells
  - ➔Epithelial-myoepithelial carcinoma
    - ✓Biphasic pattern
- Basaloid pattern
  - ➔Basal cell adenoma, adenocarcinoma, solid variant of adenoid cystic carcinoma

Adenoid Cystic Carcinoma
Differential Diagnosis – Basaloid Pattern

Criteria	Basal cell Adenoma	Basal cell AdenoCA	Solid Adenoid Cystic Ca
Growth	Encapsulated	Invasive	Invasive
Peripheral palisading	+++	++	+/-
Atypia	+	++	+++
Mitosis	+	++	+++
Necrosis	-	+	+++
Squamous areas	+	++	-
Perineural invasion	-	+	+++
Vascular involvement	-	+	+++
Biological behavior	Benign	Low-grade	High-grade

Adenoid Cystic Carcinoma
Prognosis and Management

- Indolent, but relentless, progressive growth
- Worse prognosis with increasing clinical stage
  - ➔Tumor size, lymph node metastasis, distant metastasis
  - ➔10-year survival
    - ✓Stage I 75%
    - ✓Stage II 43%
    - ✓Stage III & IV 15%

Adenoid Cystic Carcinoma
Prognosis and Management

- Up to 40% occult lymph node metastasis at presentation
- Late onset of metastases (lungs, bone)
- Overall survival:
  - ➔5-year ~80%
  - ➔10-year ~45%
  - ➔15-year ~30%

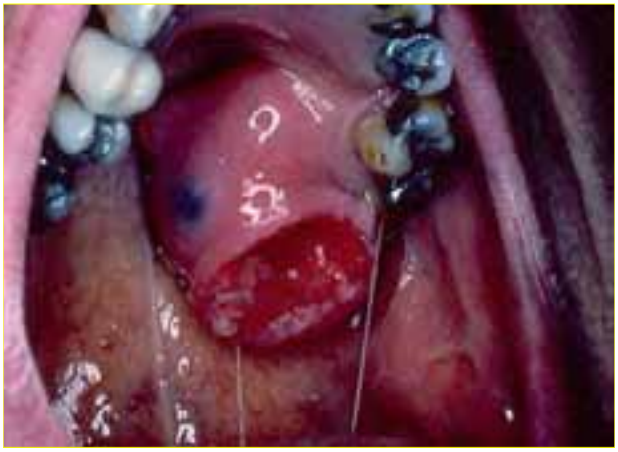
Adenoid Cystic Carcinoma
Prognosis and Management

- ◆Worse outcome (recurrence or prognosis):
  - ➔Solid histologic pattern (15-year: 5%)
  - ➔Higher grade tumors
  - ➔Perineural invasion associated with higher recurrence rate (conflicting results)
  - ➔Sinonasal primaries (worst prognosis)
    - ✓Palate have the best prognosis
  - ➔Increased Ki-67 index (>5-10%)
- ◆Radical surgery is treatment of choice
  - ➔Surgical margin status affects recurrence not overall survival
- ◆Postoperative radiation therapy is commonly used

Polymorphous Low Grade Adenocarcinoma
Clinical

A malignant epithelial tumor characterized by morphological diversity, cytological uniformity, and a low metastatic potential

- ◆**PLGA exclusively in minor glands**
- ◆Age: 50-70 years
- ◆Sex: F > M (2:1)
- ◆Site: Palate (60%), junction of hard & soft
  Upper lip, buccal mucosa, retromolar, and posterior tongue
- ◆Slow growing mass
  - ➔Ulceration, bleeding and pain uncommon

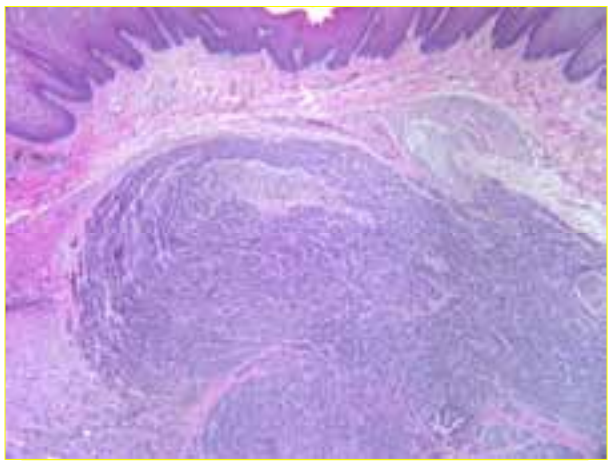


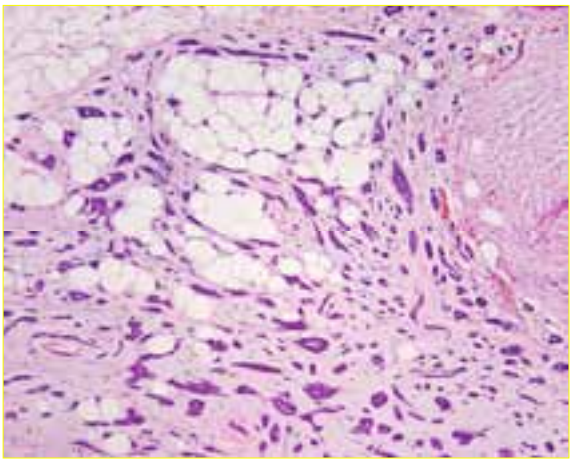
Polymorphous Low Grade Adenocarcinoma
Macroscopic

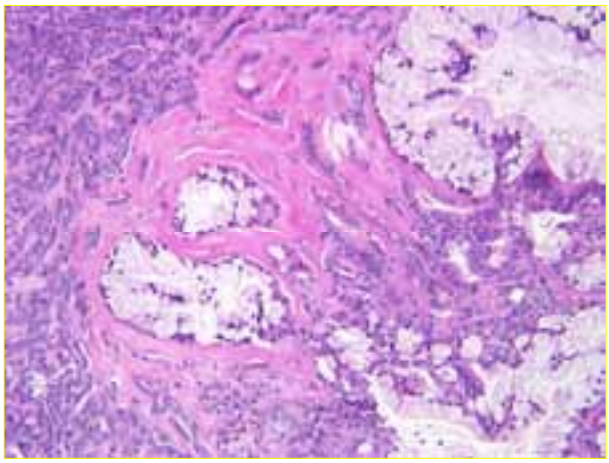
- ◆2nd most common intraoral salivary gland malignancy
- ◆Circumscribed but not encapsulated
- ◆Size:
  - ➔Up to 4 cm
  - ➔Mean: 2 cm
- ◆Firm to solid, ovoid masses
- ◆Close to surface epithelium

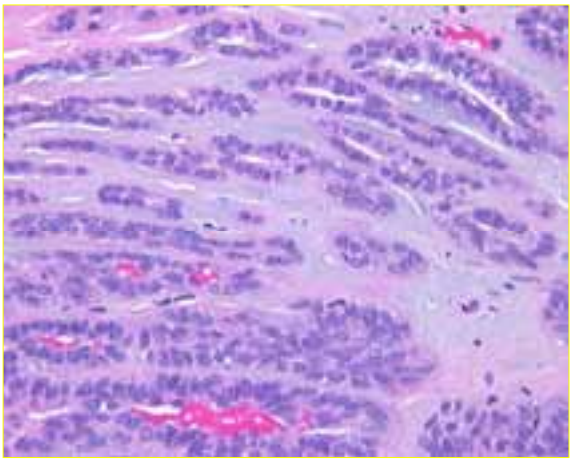
Polymorphous Low Grade Adenocarcinoma
Microscopic

- ◆Intact surface
- ◆Prominent “targetoid” perineural infiltration
- ◆Fat invasion
- ◆Normal salivary gland incarcerated by tumor
- ◆Background “slate-grey” myxoid degenerated stromal hyalinization



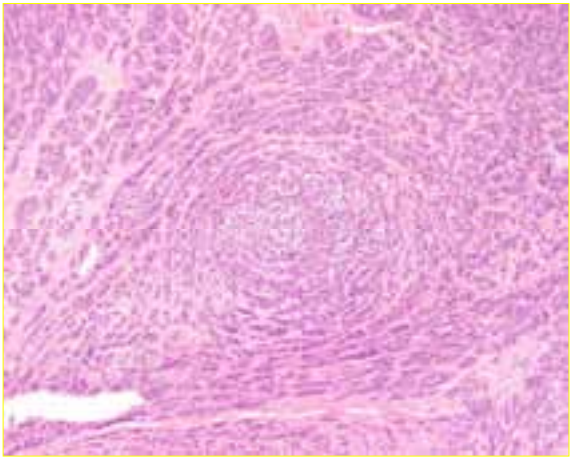


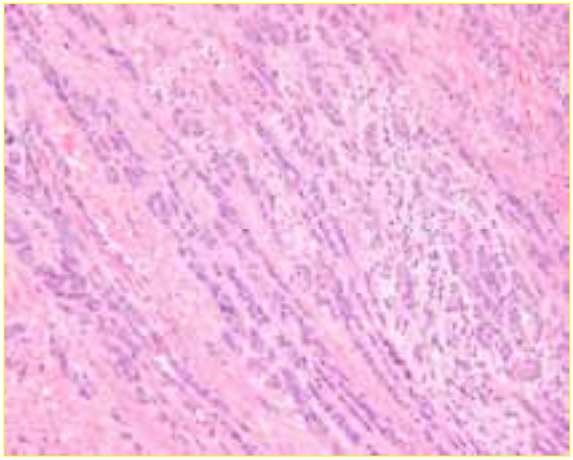


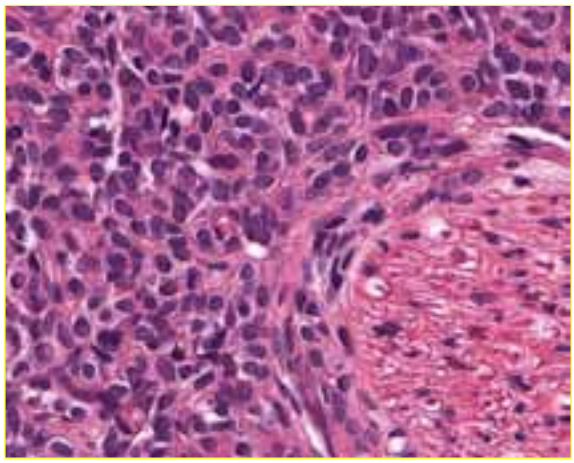


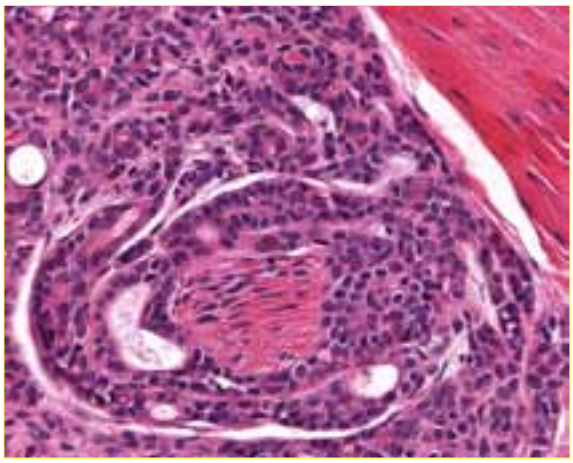
Polymorphous Low Grade Adenocarcinoma
Microscopic

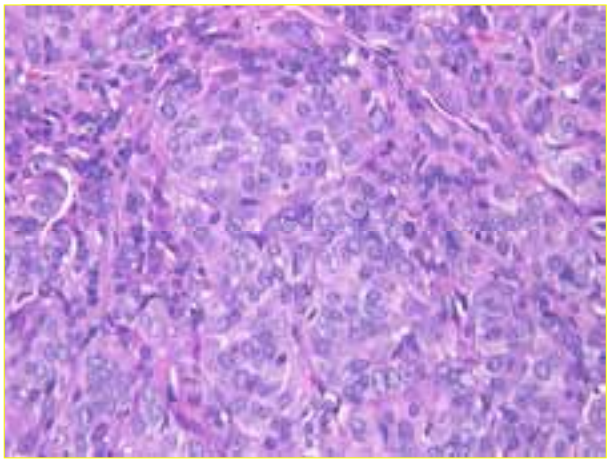
- Wide variety of patterns
  - Lobules, nests, tubules
  - Linear, single cell (*Indian filing*), concentric targetoid pattern around a nerve
  - Swirling, "*Eye-of-the-storm"* appearance
- Cytologically bland
  - Small to medium polygonal cells
  - Abundant pale cytoplasm without distinct border
  - Round nuclei with "vesicular" open nuclear chromatin
  - Mitotic figures are nearly absent











Polymorphous Low Grade Adenocarcinoma
Immunohistochemistry

- Positive:
  - ➔Cytokeratin
  - ➔S100 protein
  - ➔CK5/6
  - ➔p63
  - ➔Glial fibrillary acidic protein (GFAP)
  - ➔Actin
  - ➔bcl-2
  - ➔CD117 (variably positive)

Polymorphous Low Grade Adenocarcinoma
Differential Diagnosis

- Small, incisional biopsy and frozen artifacts make separation difficult
- Pleomorphic adenoma
  - ➔Circumscribed (but palate tumors are often unencapsulated)
  - ➔Plasmacytoid appearance
  - ➔Chondroid matrix
- Adenoid cystic carcinoma
  - ➔Destructive growth
  - ➔Smaller cells with hyperchromatic, angular nuclei

Polymorphous Low Grade Adenocarcinoma
Prognosis and Management

- Excellent (>95% 10-year survival)
- Local recurrence (around 10%)
  - ➔Higher frequency in palate tumor
  - ➔Women develop recurrences more often than men
- Regional lymph node metastases up to 15%
- Complete, but conservative surgery
  - ➔May be more extensive due to neural invasion
- Neck dissection for proven regional metastases