

**SALIVARY GLAND PATHOLOGY**

# **NEOPLASTIC DISEASE**

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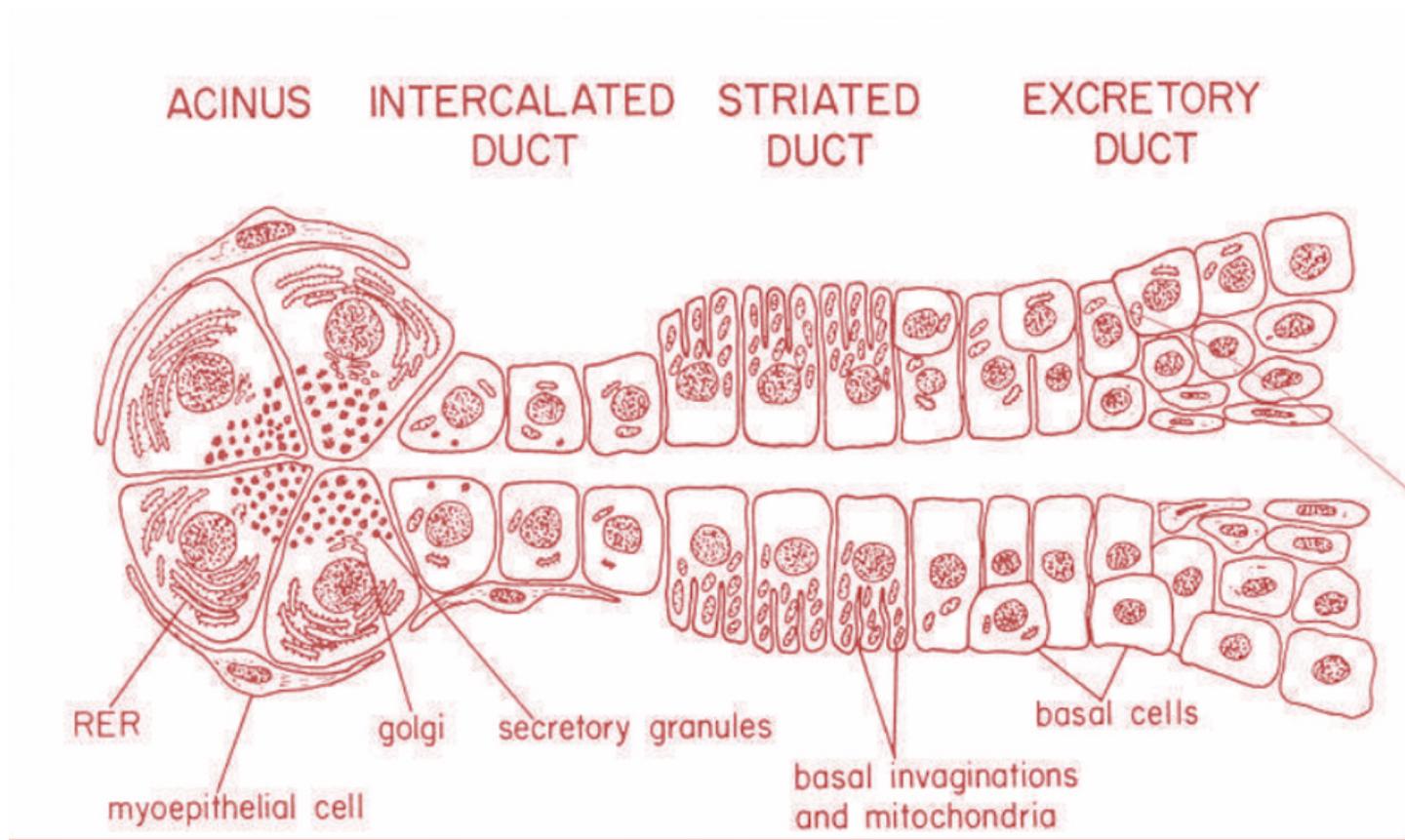


## **Learning Objectives:**

By the end of the lecture , you will identify:

1. WHO classification of SGTs
2. Types of SGTs.
3. Tissue of Origin of each tumor
4. TNM system and Clinical staging
5. Management

# SALIVARY GLAND DUCT & ACINUS



# WHO Classification of SGTs: 2005

## 1. Adenomas:

- 1.1 Pleomorphic adenoma
- 1.2 Myoepithelioma
- 1.3 Basal cell adenoma
- 1.4 Warthin's tumor (Adenolymphoma)
- 1.5 Oncocytoma
- 1.6 Canalicular adenoma
- 1.7 Sebaceous adenoma

## Lymphadenoma (Sebaceous & non-sebaceous)

- 1.8 Ductal papilloma
  - 1.8.1 Inverted ductal papilloma
  - 1.8.2 Intraductal papilloma
  - 1.8.3 Sialoadenoma papilliferum
- 1.9 Cystadenoma
  - 1.9.1 Papillary cystadenoma
  - 1.9.2 Mucinous cystadenoma

## Hemangioma (Hematolymphoid tumor & Hodgkin's lymphoma)

Diffuse large B-cell lymphoma (secondary tumor)

- WHO Classification of SGTs:

## **2. Carcinoma**

**2.1 Acinic cell carcinoma**

**2.2 Mucoepidermoid carcinoma**

**2.3 Adenoid cystic carcinoma**

**2.4 Polymorphous low grade adenocarcinoma (terminal duct adenocarcinoma)**

**2.5 Epithelial-myoepithelial carcinoma**

**2.6 Basal cell adenocarcinoma**

**2.7 Sebaceous Carcinoma**

**2.8 Papillary cystadenocarcinoma**

**2.9 Mucinous adenocarcinoma**

**2.10 Oncocytic carcinoma**

**2.11 Salivary duct carcinoma**

**2.12 Myoepithelial carcinoma**

**2.13 Adenocarcinoma**

**2.14 Carcinoma in Pleomorphic adenoma**

**2.15 Squamous cell carcinoma**

**2.16 Small cell carcinoma**

**2.17 Undifferentiated carcinoma**

**2.18 Other carcinoma ( Carcinosarcoma, large cell carcinoma, lymphoepithelial carcinoma, sialoblastoma)**

**3. Non epithelial tumor**

**4. Malignant lymphoma**

**5. Secondary tumor**

**6. Unclassified tumors**

**7. Tumor like lesions**

**7.1 Sialoadenosis**

**7.2 Oncocytosis**

**7.3 Necrotizing Sialometaplasia**

**7.4 Benign lymphoepithelial lesion**

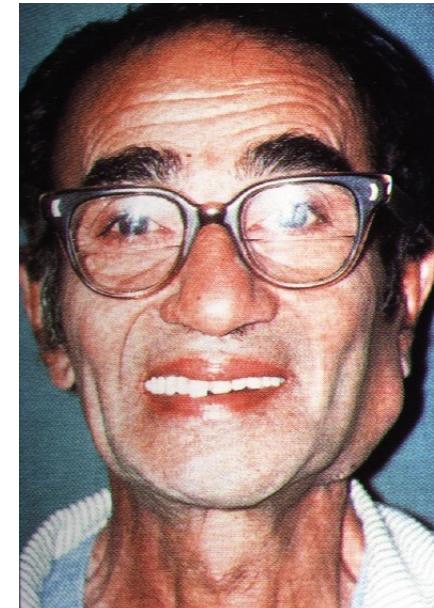
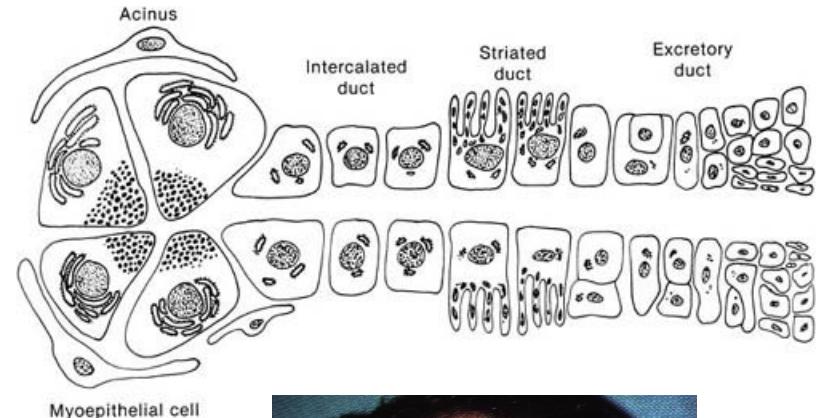
**7.5 Salivary gland cysts**

**7.6 chronic sclerosing sialadenitis of Submandibular gland**

**7.7 Cystic lymphoid hyperplasia in AIDS**

# TUMOR ORIGIN

- **Pleomorphic adenomas** originate from the **intercalated duct** cells and **myoepithelial** cells
- **Oncocytic tumors** originate from the **striated duct** cells
- **Acinous cell tumors** originate from the **acinar** cells,
- **Mucoepidermoid tumors** and **squamous cell carcinomas** develop in the **excretory duct** cells.



# CLINICAL FEATURES

## Benign SGTs

- No Pain
- Slow growing
- Soft, rubbery
- not fixed
- Smaller in size
- facial nerve not involved
- Pseudo-encapsulated
- Ulceration not common
- local invasion

## Malignant SGTs

- Pain
- Fast growing
- Hard
- Fixed
- Larger in size
- facial nerve commonly involved
- Non encapsulated
- Ulceration is common
- Spread to LNs , metastasis to lung, liver, brain & bone

# PLEOMORPHIC ADENOMA

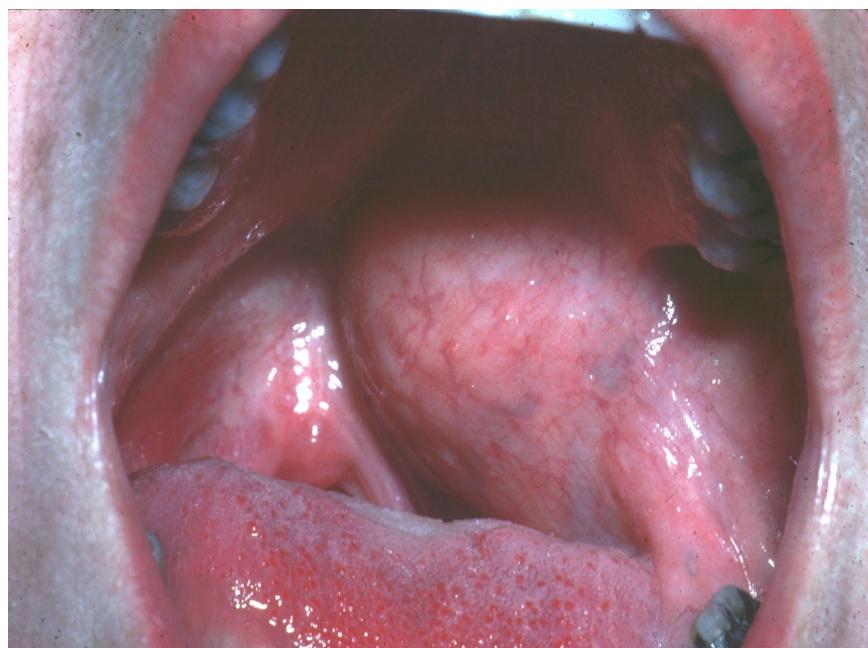
- **Commonest** salivary gland neoplasm
- **Site**
  - Parotid (60-70% of parotid tumors),
  - Palate (50% of minor gland tumors), followed by upper lip &buccal mucosa
- **Age**
  - any age but adults ++ (**4<sup>th</sup>-6<sup>th</sup>** decades)
- **Sex**
  - males slightly more than females
- **Presenting signs**
  - Few mm to several cm of **non-ulcerated**, slow growing, **painless mobile** **swelling**. ( except that in hard palate)



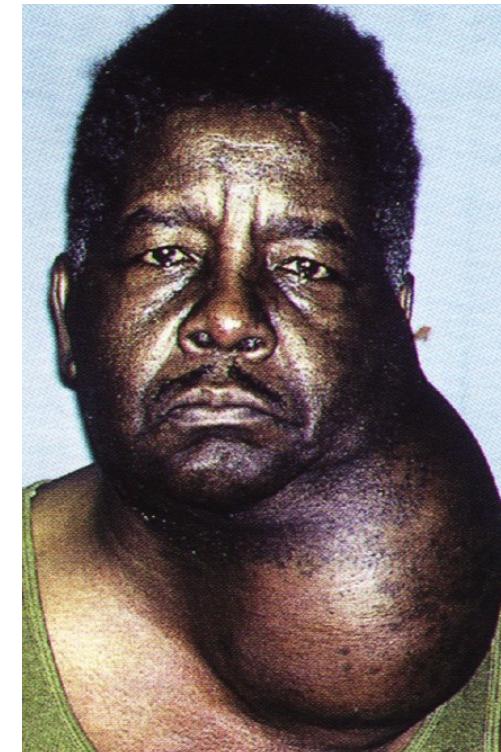
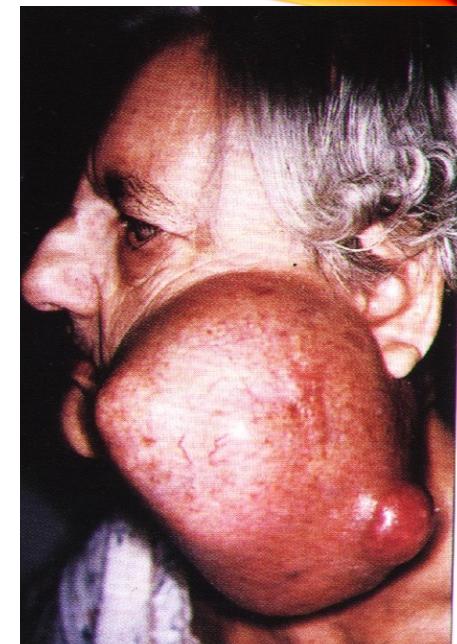
A



B



- Slow-growing, painless mass
- Parotid: 90% in superficial lobe, most in tail of gland
- Minor salivary gland: lateral palate, submucosal mass



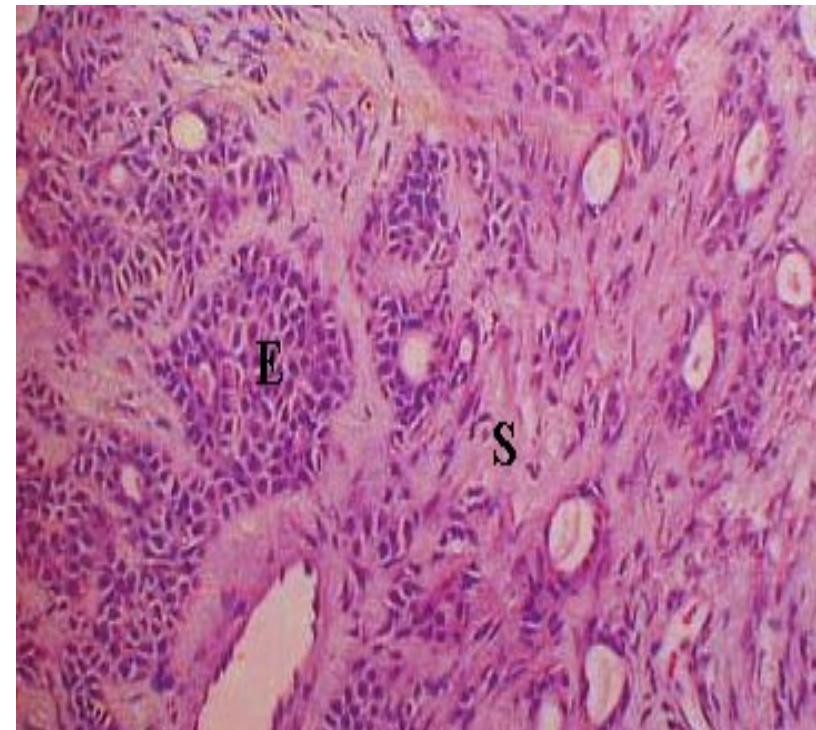
## Gross pathology

- – Smooth
- – Well-demarcated
- – Solid
- – Cystic changes
- – Myxoid stroma



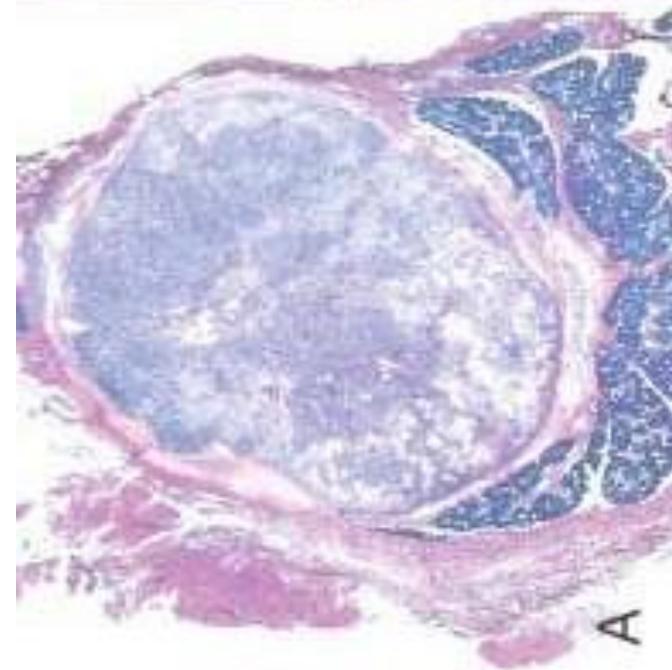
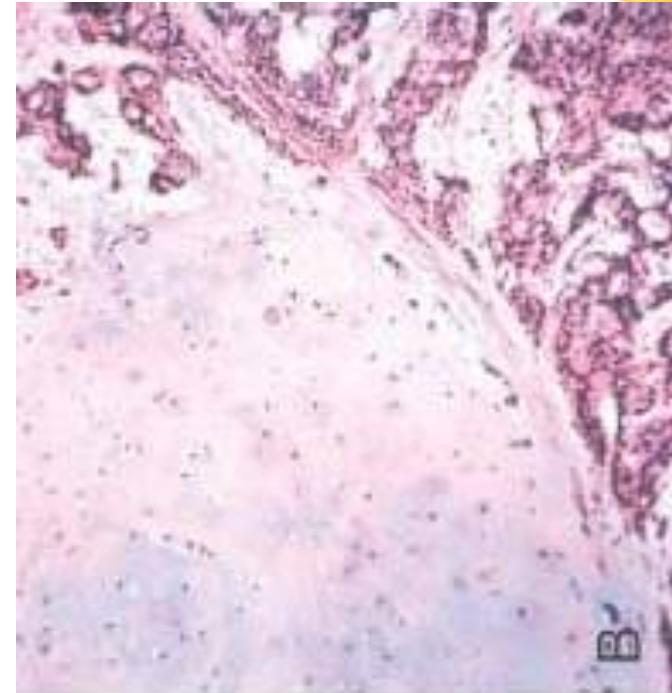
# PLEOMORPHIC ADENOMA

- PA contains both **epithelial** (E) and **stromal** (S) components.
- **Epithelial Components**
  - Tubular and **cord-like** or **solid sheet** arrangements
  - Mitoses are **rare**



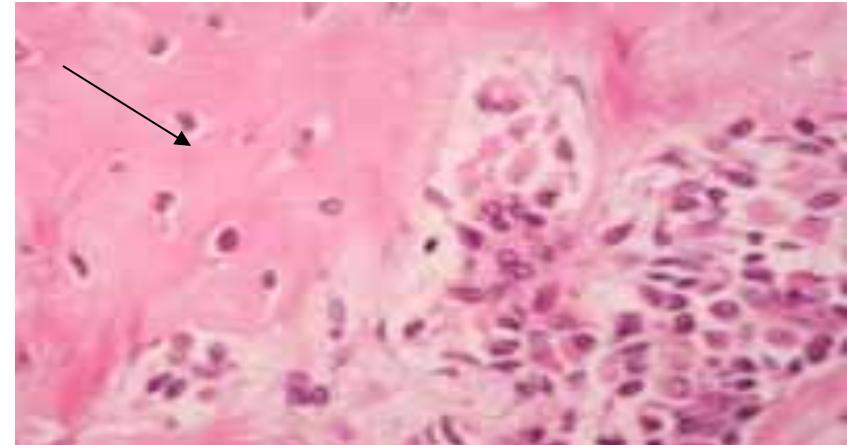
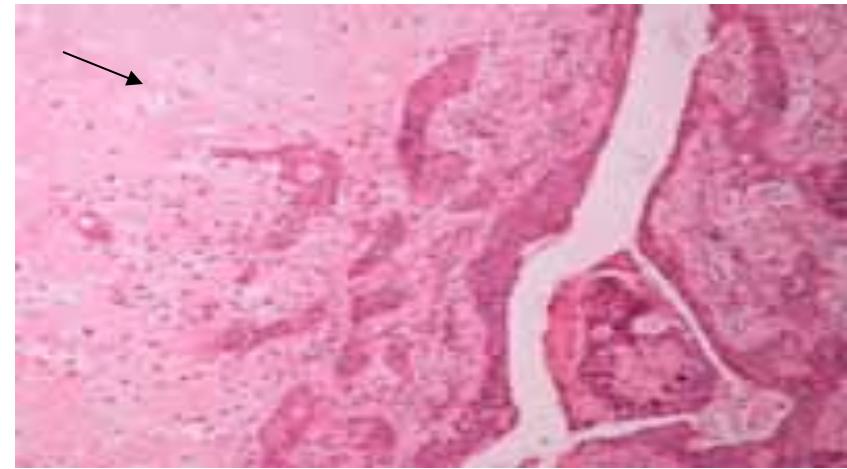
# PLEOMORPHIC ADENOMA

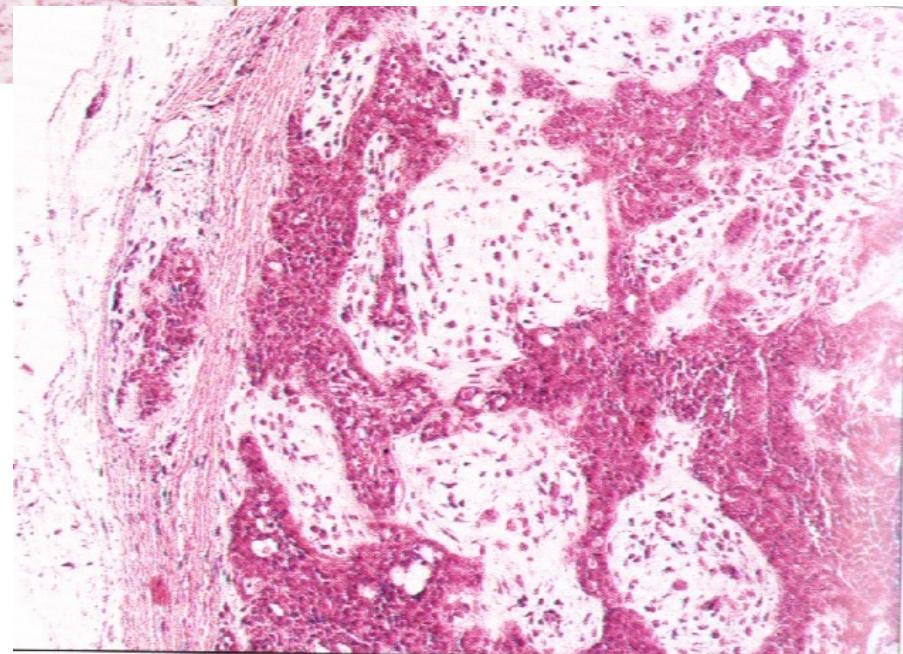
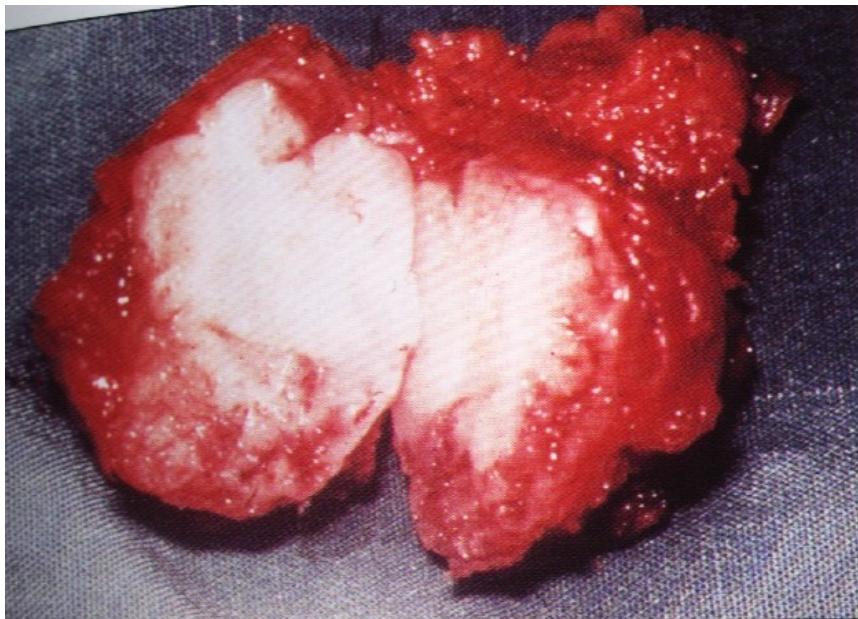
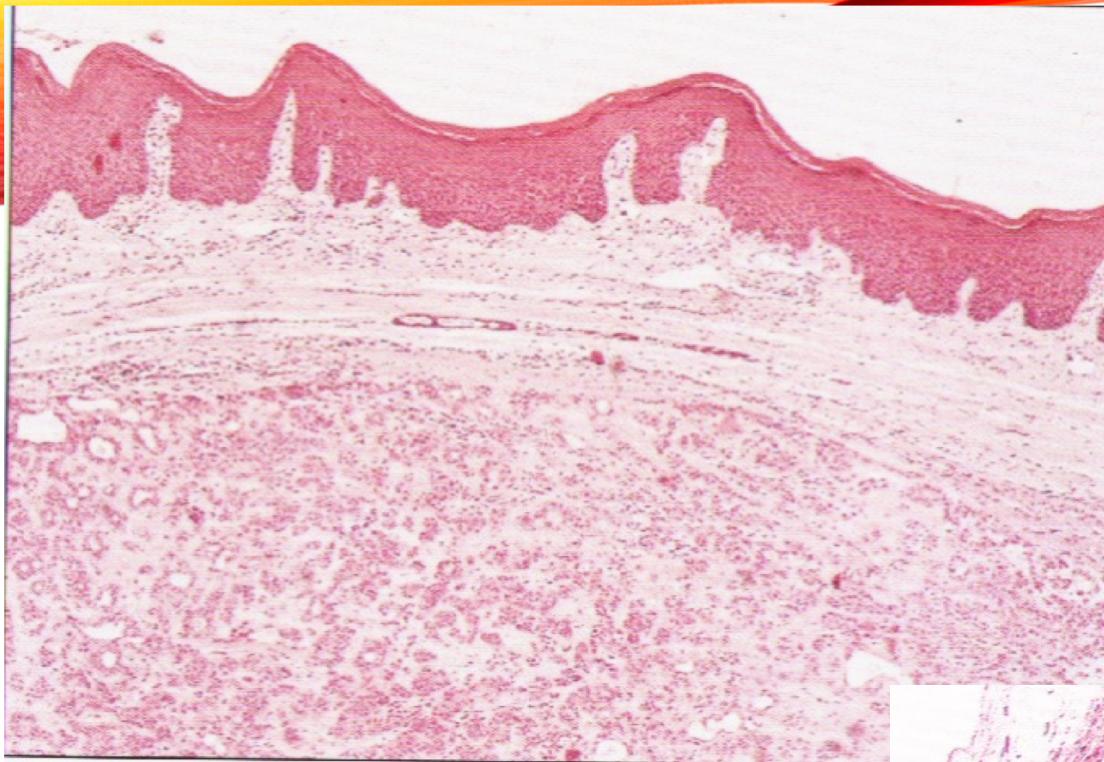
- **Stromal or “mesenchymal” Components**
  - Can be quite **variable**
  - Attributable to the myoepithelial cells
  - Most tumors show **chondroid** (cartilaginous) differentiation
  - **Osseous** metaplasia not uncommon
  - Relatively hypocellular and composed of **pale blue** to slightly eosinophilic tissue.



# PLEOMORPHIC ADENOMA

- The diverse microscopic pattern of this lesion is one of its most characteristic features.
- Islands of cuboidal cells arranged in duct-like structures is a common finding.
- **Loose chondromyxoid stroma**, hyalinized connective tissue, **cartilage**(arrows) and even **osseous** tissue are observed.
- This neoplasm is **pseudo-encapsulated**, although tumor islands may be found within the fibrous capsule which is **continuous** with main tumor mass & likely to contribute to **recurrence.(tumor pseudopodes)**





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# PLEOMORPHIC ADENOMA

## Behavior

- Benign, slow growing
- Recurrences common due to incomplete removal
- Low risk of malignant transformation



## Management

- Careful excision [parotidectomy with VII preservation]
- Submandibular gland excision
- Wide local excision of minor SG
- Follow-up
- With each recurrence there is an increased possibility of malignant transformation.
- Radioresistant, radiotherapy is contraindicated.



## Signs of Malignant Transformation:

- Weakness in the distribution of facial nerve.
- may appear fixed to underlying bone
- Palpable regional LNs
- Ulceration
- Difficulty in mastication, talking & breathing
- Irregular nodular lesion
- recurrent lesion however occurs as multiple nodules.



# WARTHIN'S TUMOR

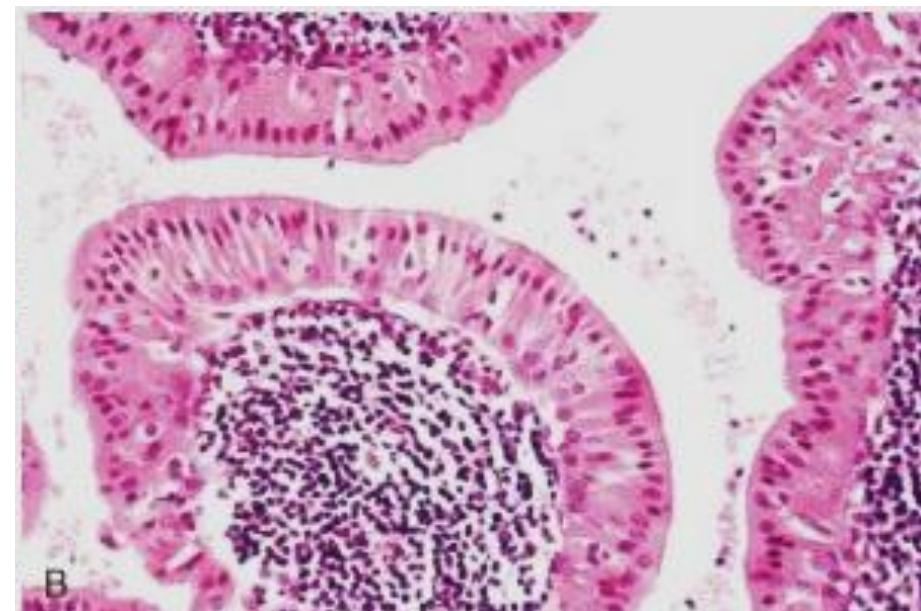
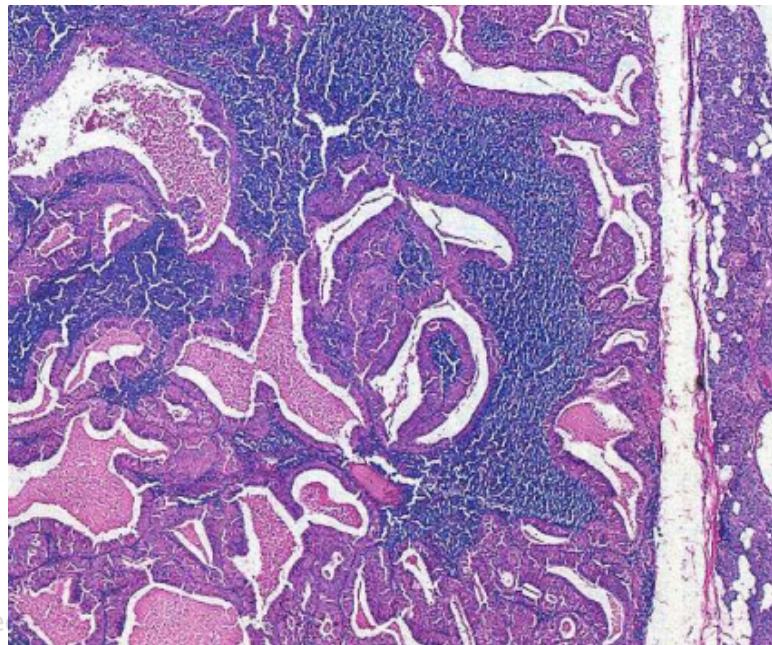
- Warthin's tumor (Adenolymphoma; benign papillary cystadenoma lymphomatosum)
- Second most common benign tumor of the parotid gland.
- Exclusive in parotid gland mainly the tail
- Predominant in males
- It accounts for 6-10% of all parotid gland tumors
- Bilateral in 10% of the cases
- May contain mucoid brown fluid in FNA
- Positive correlation with cigarette smoking & EBV.
- Dough to cystic mass in the inferior pole of parotid gland adjacent to posterior angle of mandible.
- Encapsulated with smooth lobulated surface & round outline

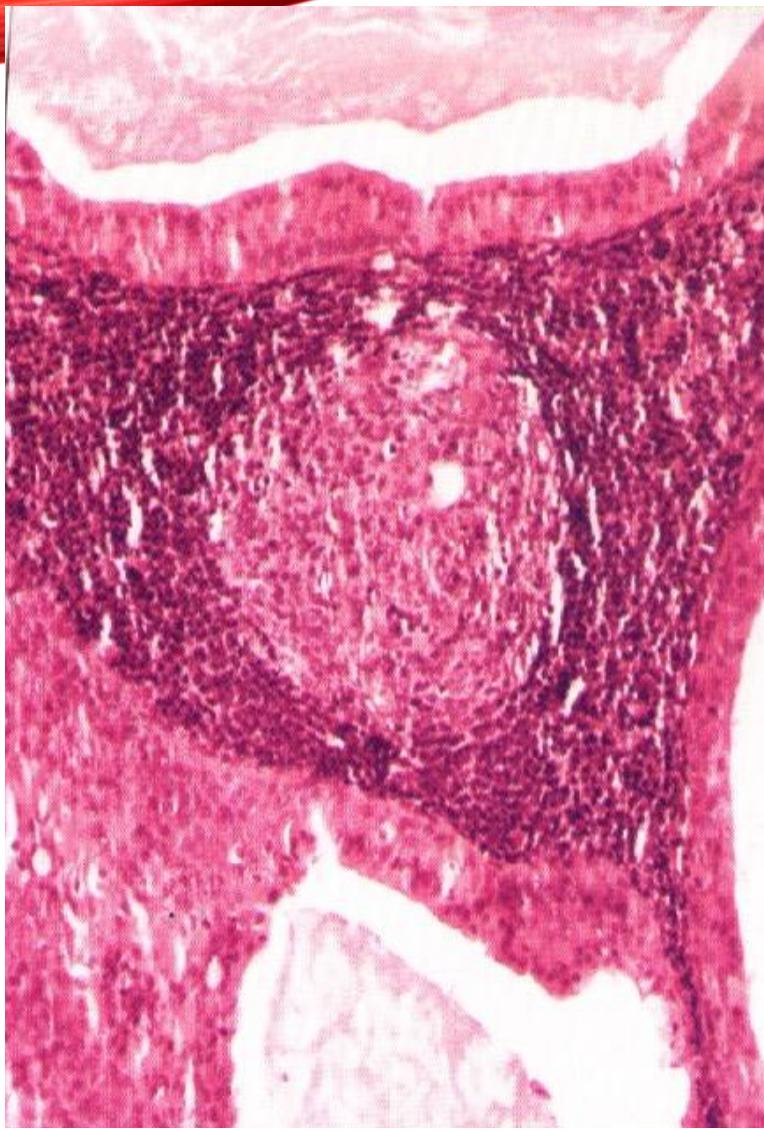


# WARTHIN'S TUMOR

- **Epithelial Component**

- Consists of numerous cystic spaces with irregular outline containing papillary fronds which demonstrate 2 layers of **oncocytic epithelial cells**.(luminal & basal cells)
- The lining cells overlie lymphoid tissue with germinal center
- Cytoplasm stains deep pink and shows granularity b/c of an abundance of mitochondria
- Occasionally undergoes squamous metaplasia (may mistakenly diagnose SCC on FNA)



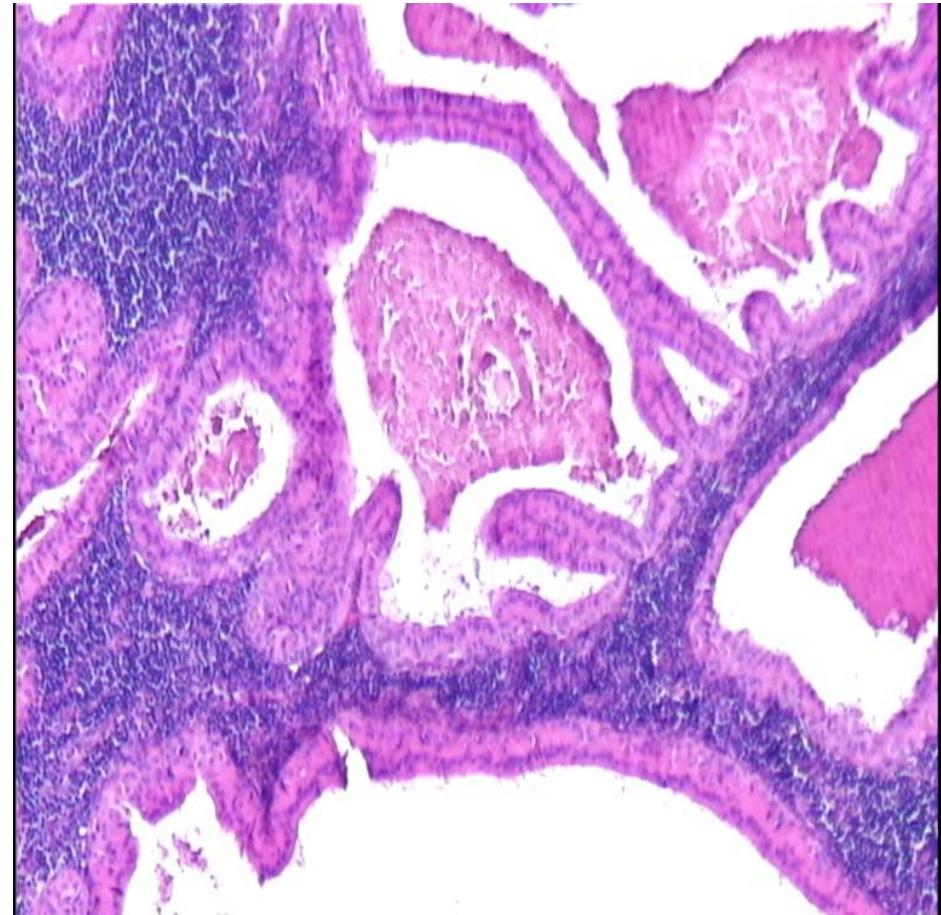


# WARTHIN'S TUMOR

- Lymphoid Component
  - Abundance .
  - Occasional germinal centres will be seen
  - Lymphoid tissue forms the core or papillary structures
- Both **lymphoid** and **oncocytic epithelial** elements must be present to diagnose Warthin's.

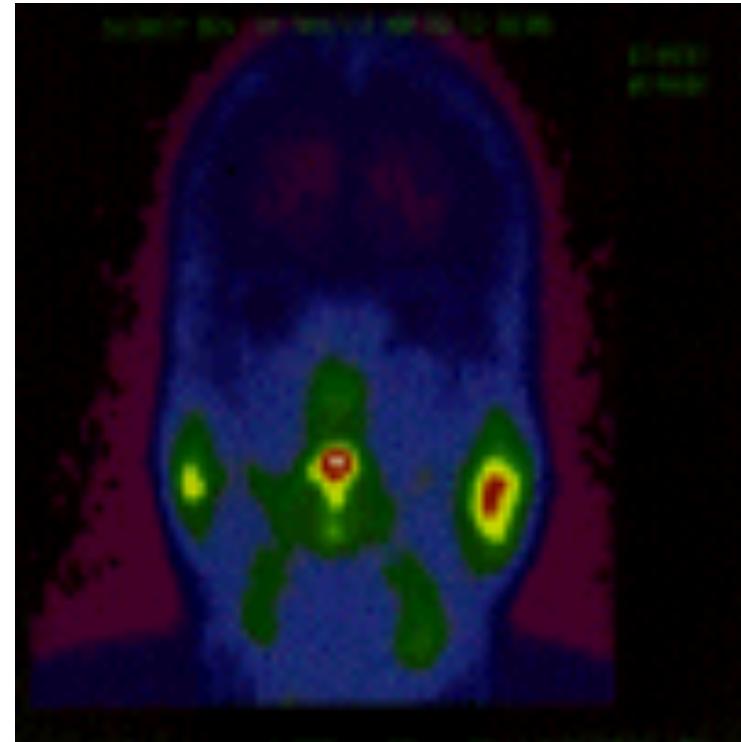
## Treatment:

- surgical excision
- Seldom recurrence
- Rare malignant transformation



# WARTHIN'S TUMOR

- Oncocytes selectively incorporate technetium Tc 99m and appear as hot spots on a radionucleotide scan.



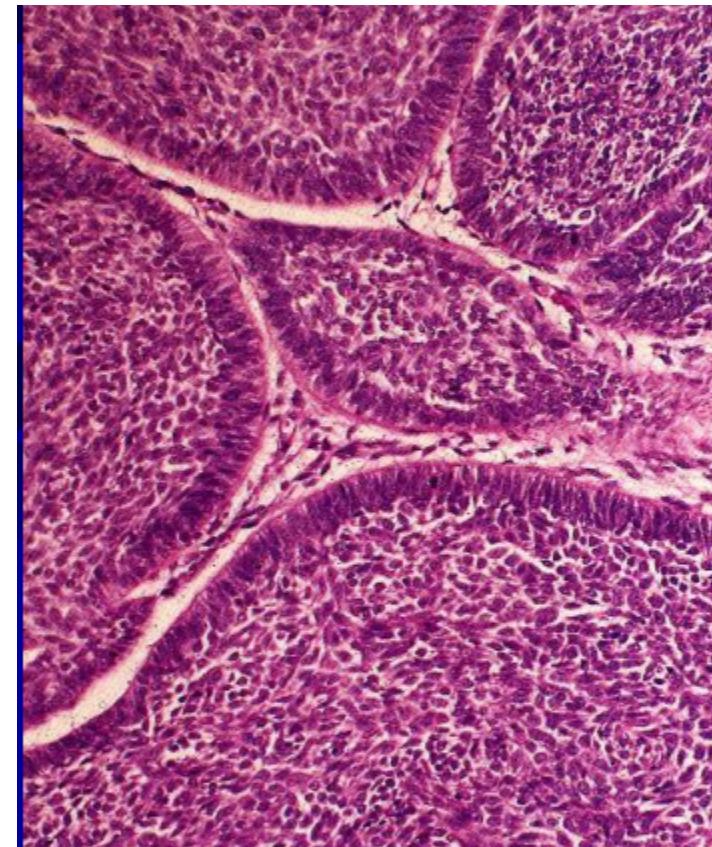
# MONOMORPHIC ADENOMA

- Similar to Pleomorphic Adenoma except no mesenchymal stromal component
  - Predominantly an epithelial component
- More common in minor salivary glands (upper lip)
- 12% bilateral
- Rare malignant potential
- **Types:**
  - Basal Cell Adenoma
  - Canicular Adenoma
  - Myoepithelioma Adenoma

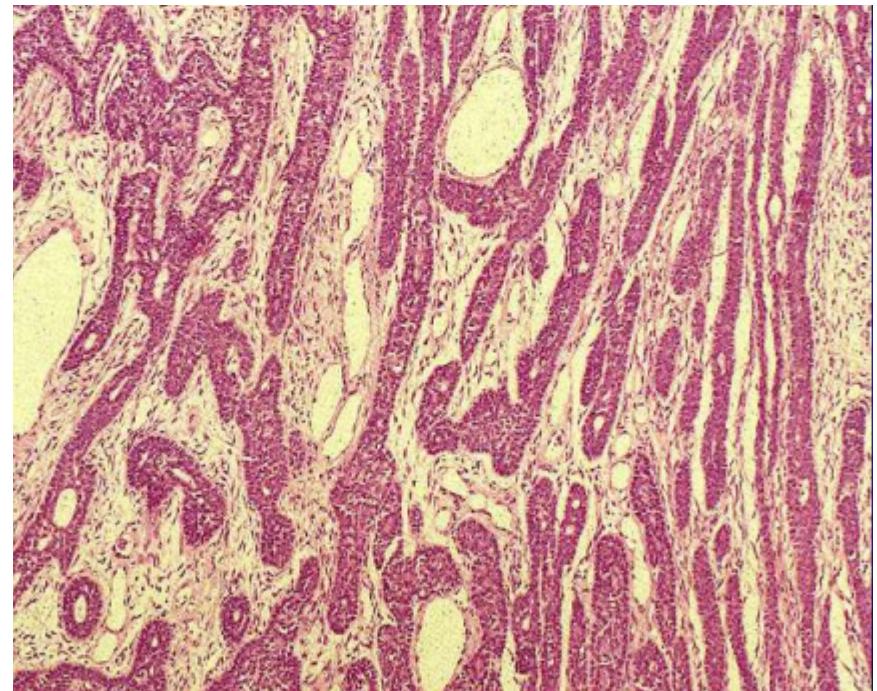
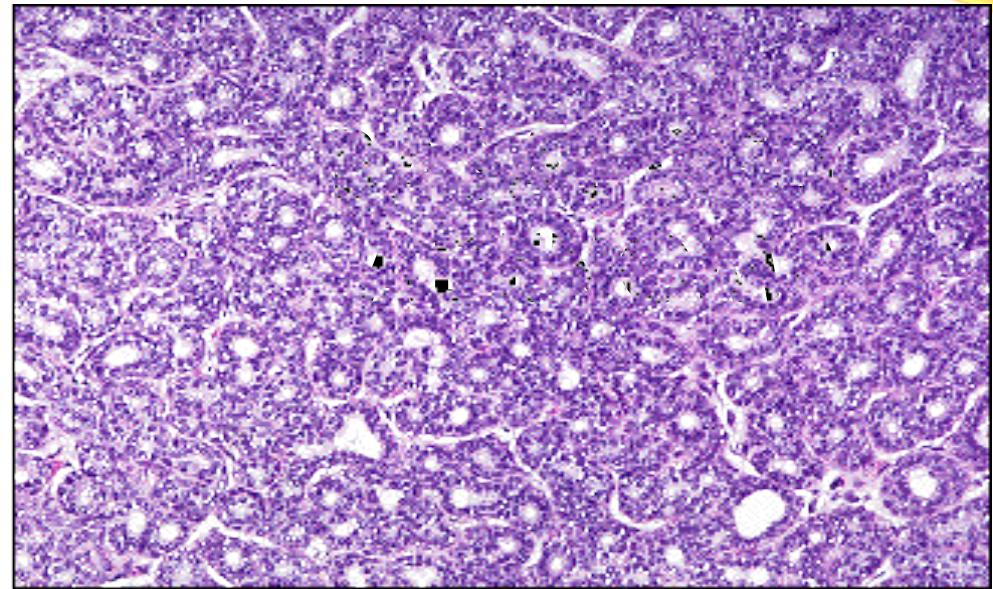


# BASAL CELL ADENOMA

- 1-2% of all Salivary Glands Adenoma
- 70% within Parotid gland
- Upper lip is the most common IO site.
- Slowly growing painless solitary swelling.
- Firm on palpation
- Wide age range ( 35-80 years) with male predilection.



- A monomorphic adenoma
- It is composed of uniform **basaloid epithelial cells** with a monomorphous pattern.
- The arrangement of tumor cells may be **trabecular, tubular or solid.**
- Histologically, these tumors are distinguished from pleiomorphic adenomas by their **absence of chondromyxoid stroma** and the presence of a uniform epithelial pattern.



# CANALICULAR ADENOMA

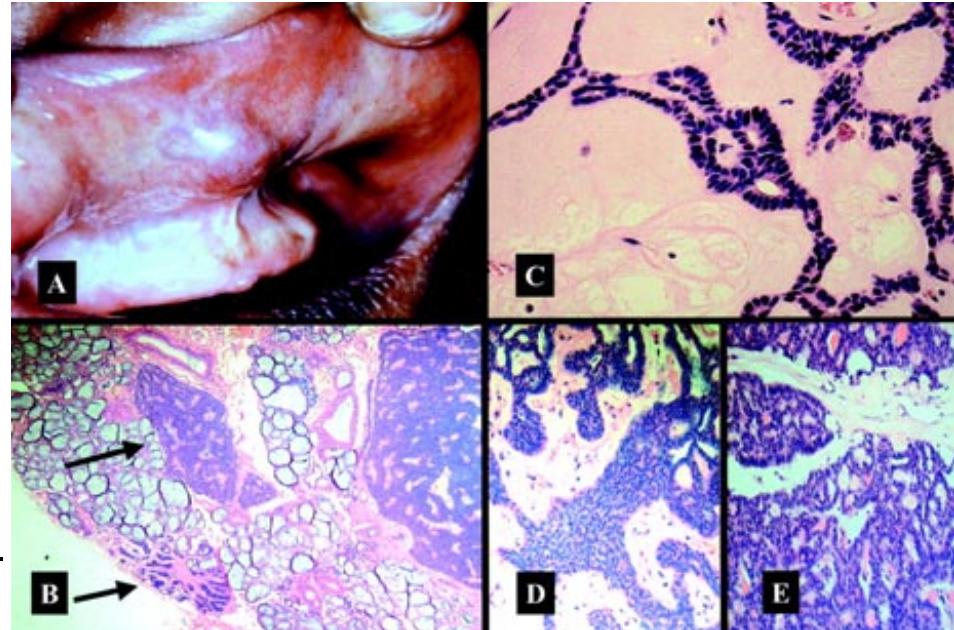
- Almost exclusively within oral cavity ( upper lip)
- Narrow age range ( older than 50 yrs) with female predilection.
- Freely movable , asymptomatic ( few mm – 2-3 cm)

## Histopathology

- Bilayer strands of basaloid cells that branch & anastamose within delicate highly vascular stroma.
- Individual cells: cuboidal to colouminar with moderate- abundant eosinophilic cytoplasm
- Encapsulated

## Treatment

Excision ( 20% are multifocal ---- recurrence)



# MYOEPITHELIOMA

- Benign, composed entirely of myoepithelial cells
- Most of them arise within **MSG, parotid gland, SMG**
- Circumscribed, painless masses.
- Wide age range with equal gender preponderance.

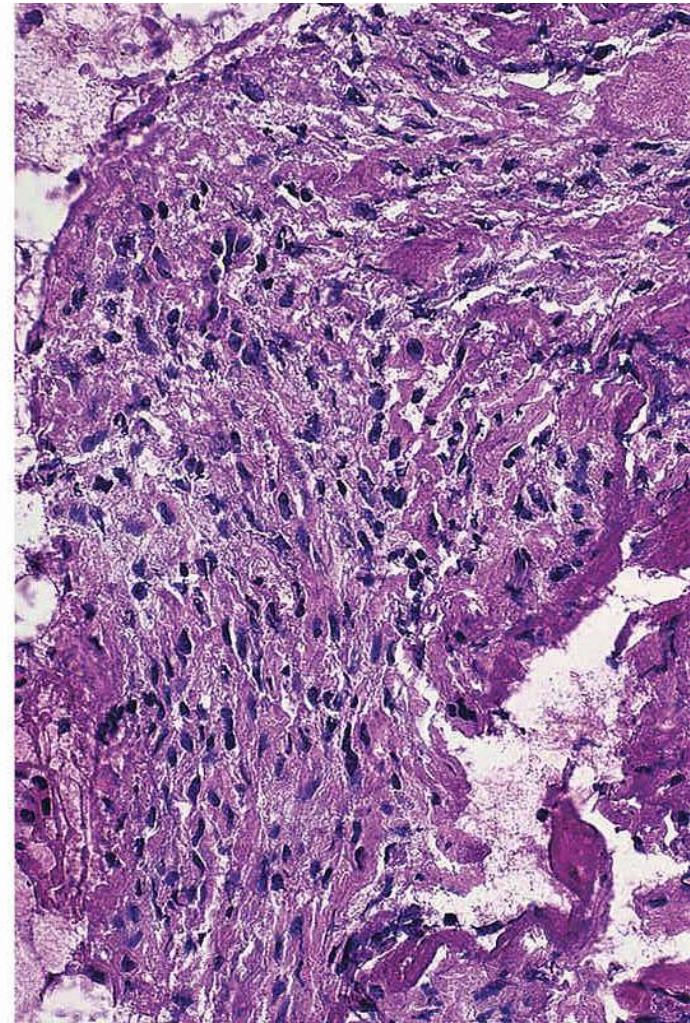
## Histopathology

- Sheets of plasmacytoid or spindle cells
- 70% of cases contain spindle cells & 20% composed of plasmacytoid.

## Treatment

Conservative surgical Excision

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# ONCOCYTIC TUMOR

- Include: **Oncocytoma & oxyphilic adenoma**
- Rare, predominant in parotid gland
- Solid, ovoid encapsulated lesion
- ***Rare in Oral cavity***
- Slow growth rate

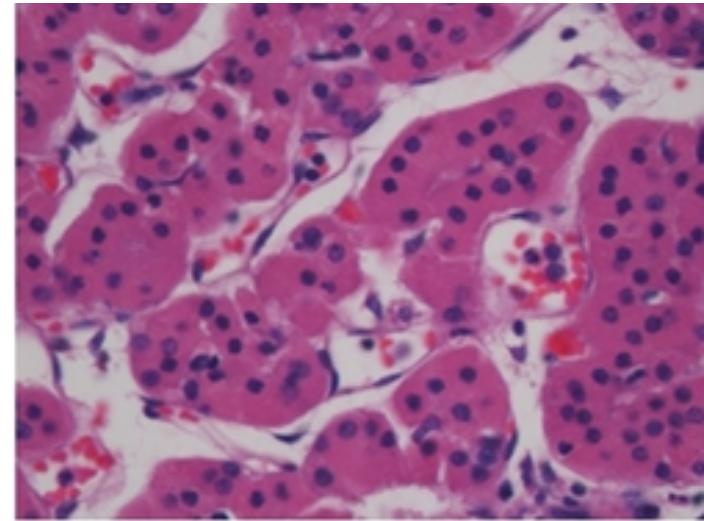
## Histopathology

Sheets of polyhydral cells with granular eosinophilic cytoplasm & centrally placed vesicular nucleous

## Treatment

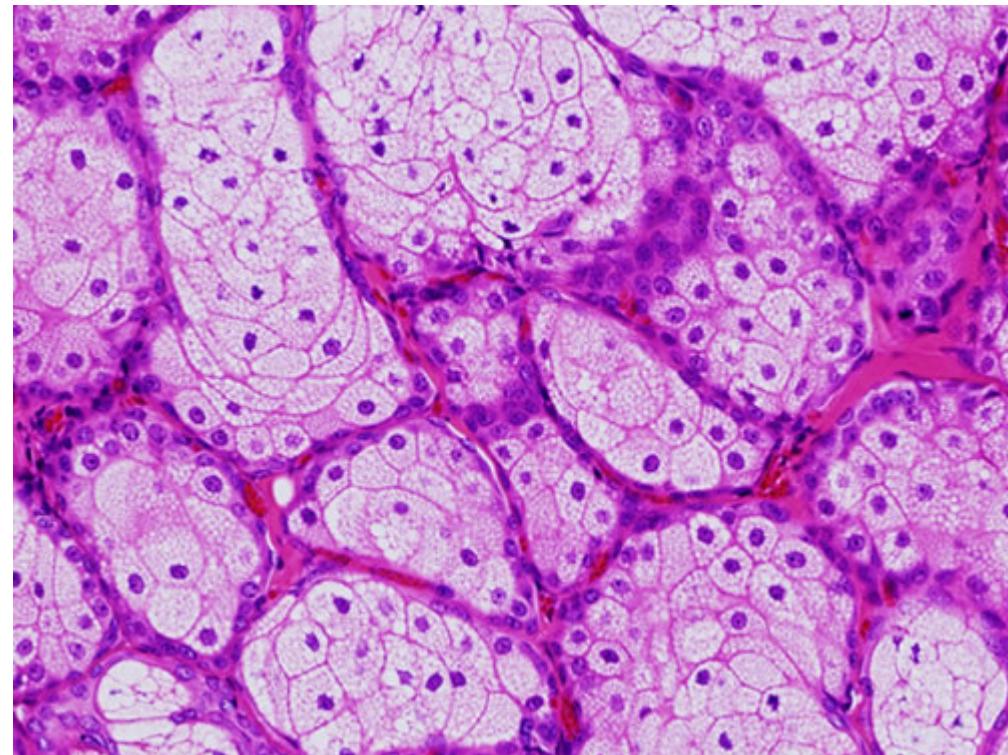
SF parotidectomy

Malignant transformation could be seen



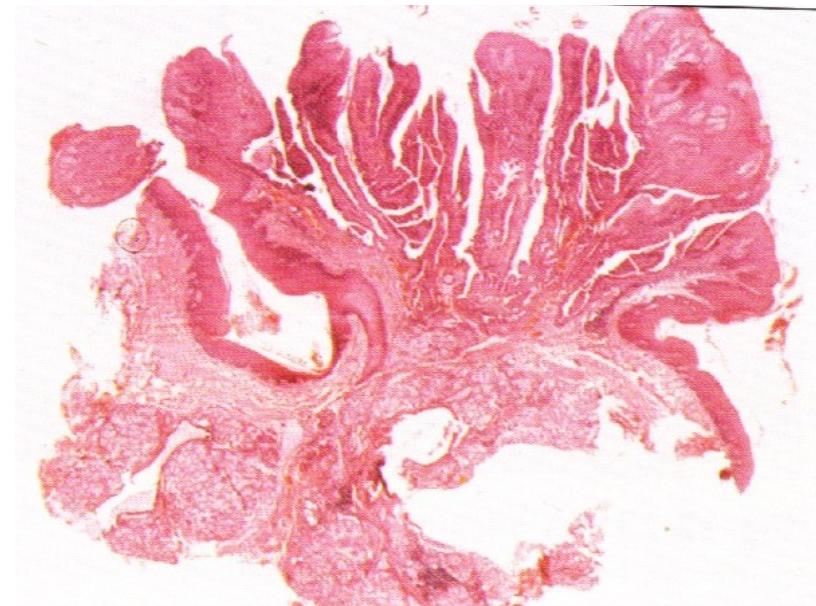
# SEBACEOUS ADENOMA

- Originate in intralobular ducts
- Rare, composed mainly of sebaceous gland-derived cells



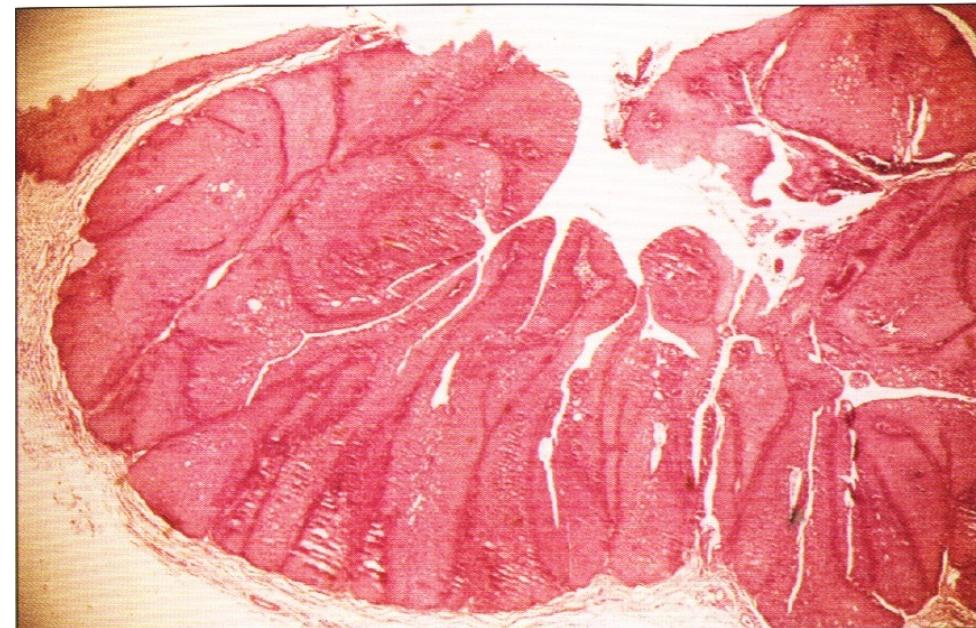
# DUCTAL PAPILLOMAS

- Include: **Sialoadenoma Papilleferus**, Inverted ductal papilloma & Intraductal Papilloma
- All arise within interlobular & excretory duct .
- ***Sialoadenoma Papilleferus***: Rare, majority reported IO ( buccal mucosa & palate), resemble ***squamous cell papilloma***



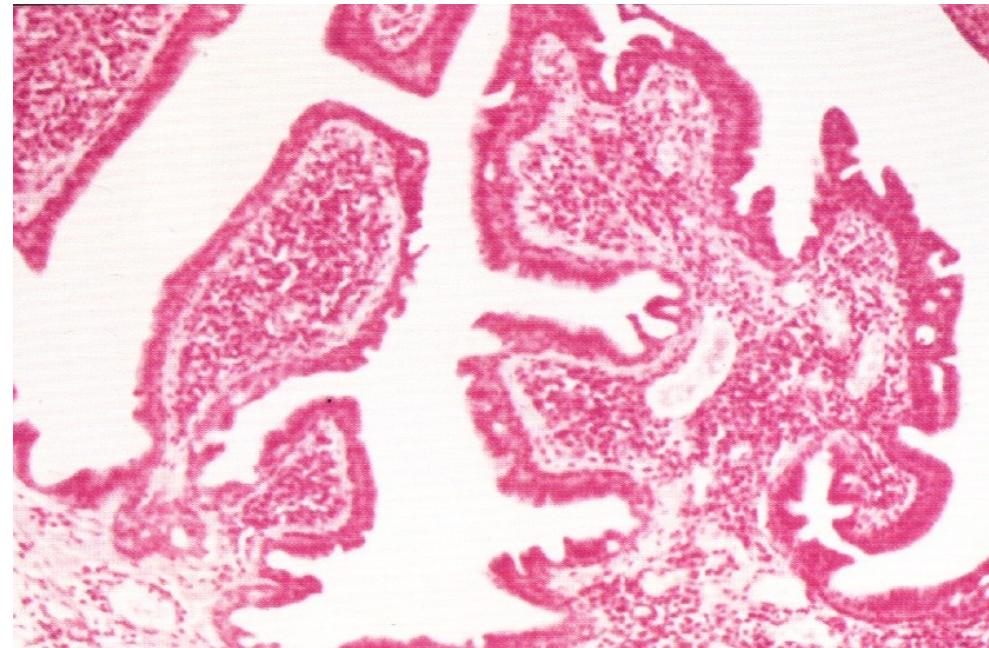
# DUCTAL PAPILLOMAS

- *Inverted ductal papilloma:* Proliferation of squamoid epith. With multiple , thick bulbous papillary projection that fill the ductal lumen

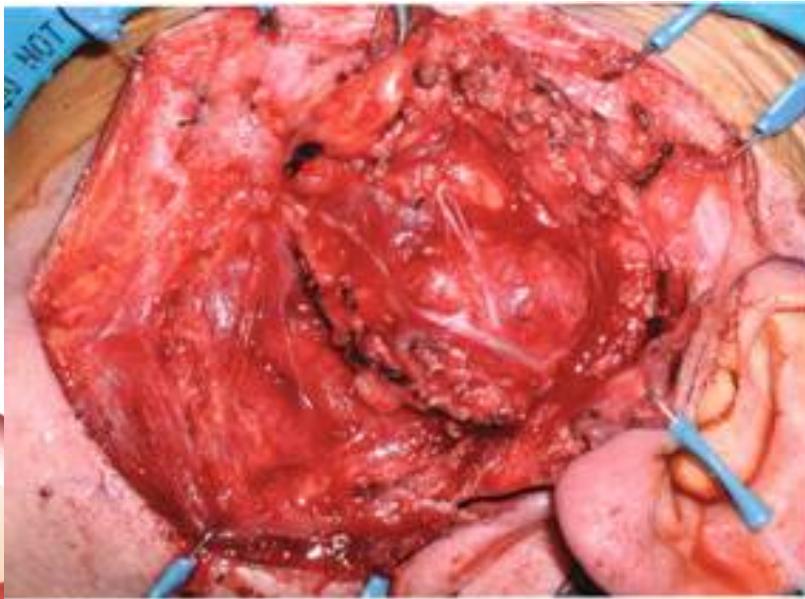


# DUCTAL PAPILLOMAS

- *Intraductal Papilloma*: arise from greater depth within ductal system,  
Presenting as salivary obstruction .



# MALIGNANT SALIVARY GLAND TUMORS



# MUCOEPIDERMOID CARCINOMA

- Most common salivary malignancy accounting for **29% to 43%** of tumors.
- Parotid 45-70% of cases, Palate 18%
- Histologically classified into **low (slowly growing, painless) and high grade (rapidly growing +/- Pain)**.
- Partially encapsulated.
- A higher grade correlates with a poorer outcome
- Low-grade tumors have a protracted course & higher percentage of mucinous cells
- Epithelial cells predominate in high-grade. The presence of four or more mitotic figures per 10 high-power fields, neural invasion, necrosis, intracystic component <20%, and cellular anaplasia indicate high-grade behavior.

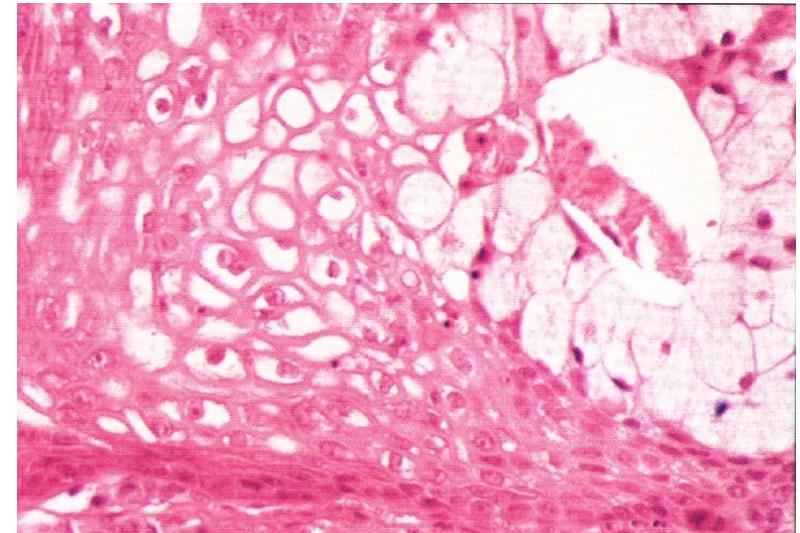
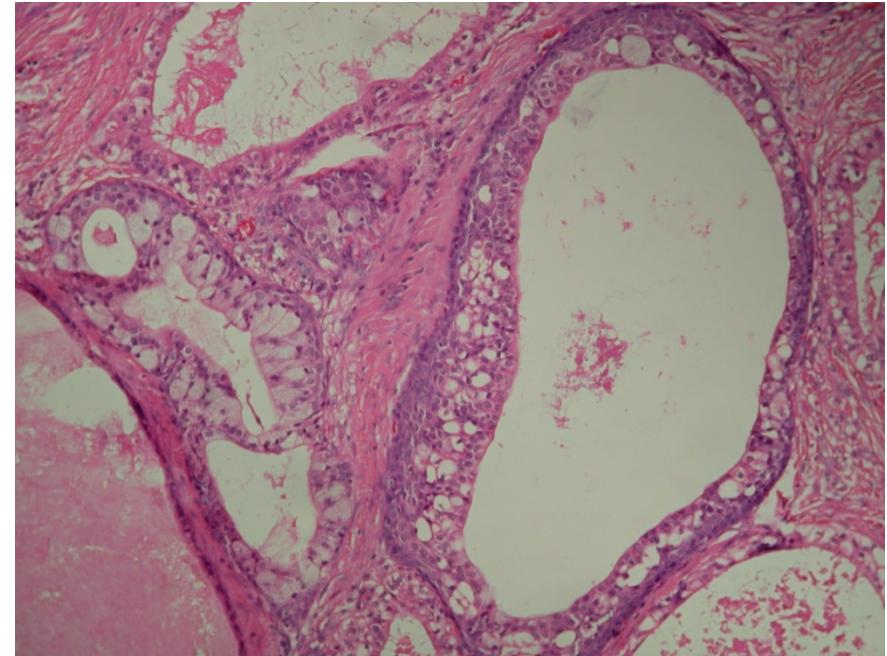
# MUCOEPIDERMOID CARCINOMA

## General features

- parotid>submandibular=minor glands
- any age but adults ++
- Sex
  - females > males

## Histopathology

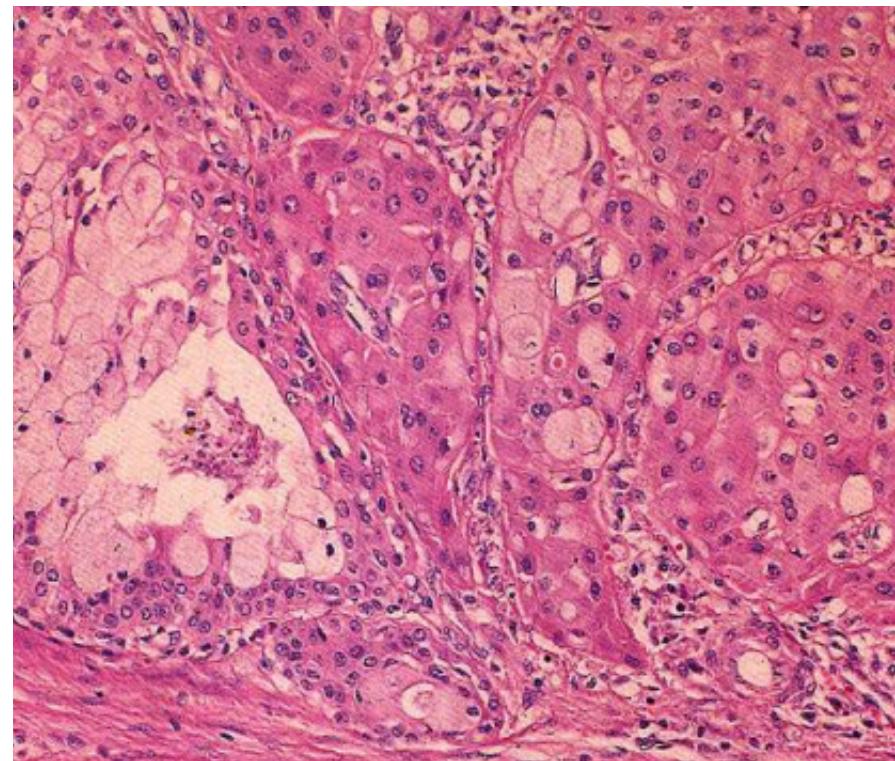
- Epidermoid epithelial cells
- Intermediate epithelial cells
- Mucous secreting epithelial cells



## Histopathology:

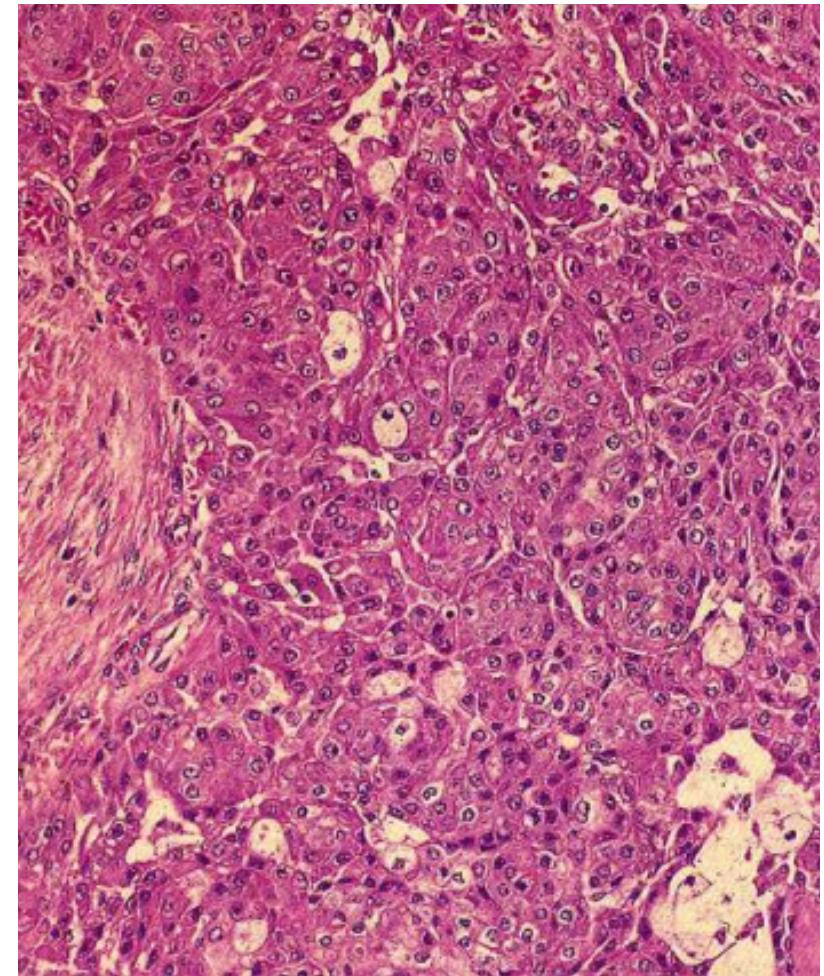
### Low Grade:

Composed of numerous mucus secreting cells arranged around microcystic structure with large & numerous intermediate cells and few epidermoid cells with minimal cellular atypia.



## **Intermediate grade:**

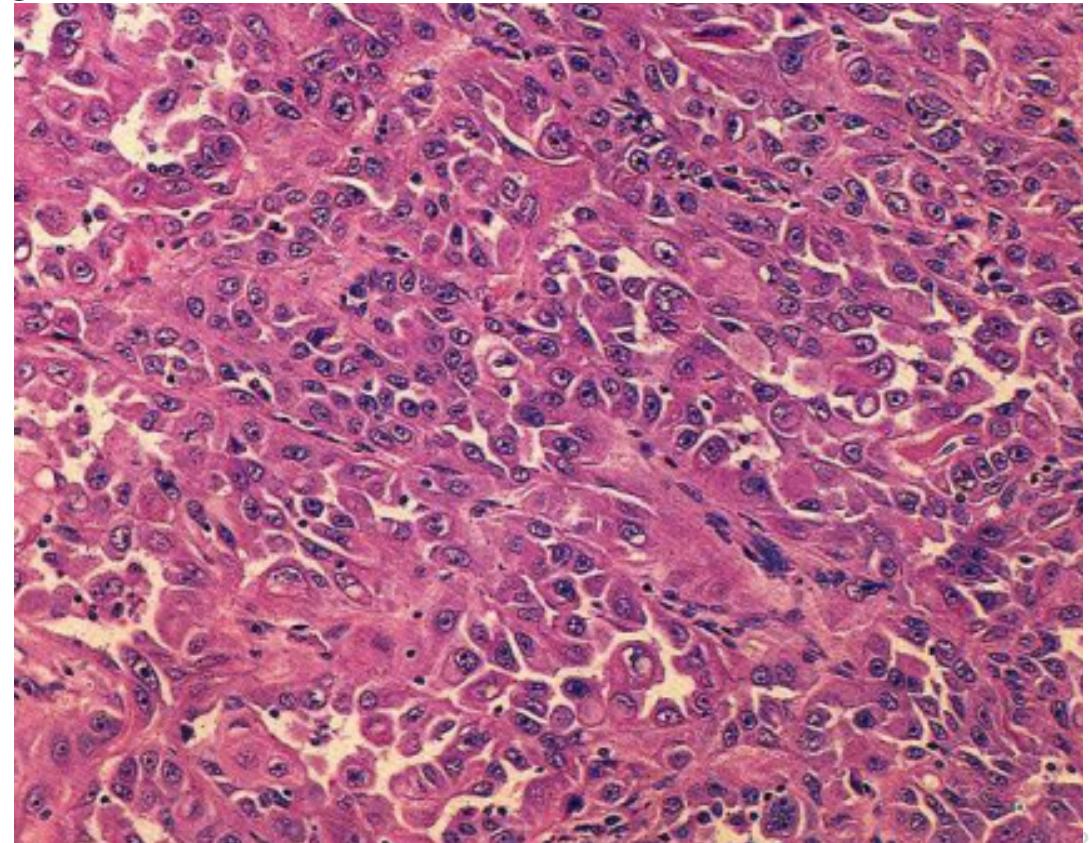
Contains mucus cells & microcystic spaces ,but not as numerous as in low grade



## **High Grade:**

Clusters of proliferating epidermoid cells that are more solid with few mucous cells.

Mistaken for SCC (mucin Staining).



## Prognosis

Related to histo grade ( low grade has benign clinical course but with wide metastasis, while high grade has aggressive course with local & distant metastasis into cervical lymph nodes)

IO tumors has poorer prognosis.

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

- Adenoid cystic carcinoma is the second most common malignancy overall and the first most malignancy of the submandibular gland
- Adenoid cystic carcinoma is characterized by slow growth, neurotropism, local recurrence, and distant metastasis.
- Exhibits a predilection for neurotropic spread, often leading to recurrences at the skull base after surgical and radiation treatment



## General features

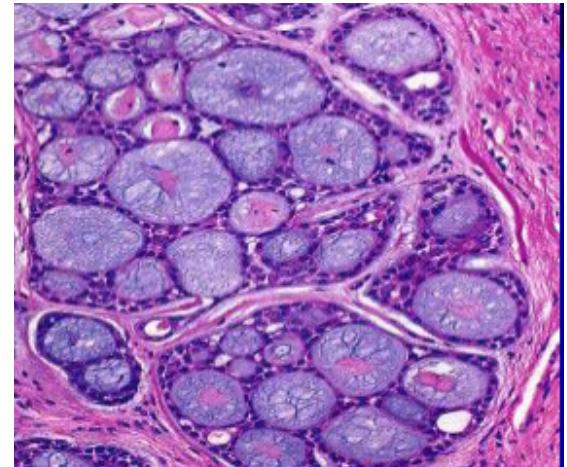
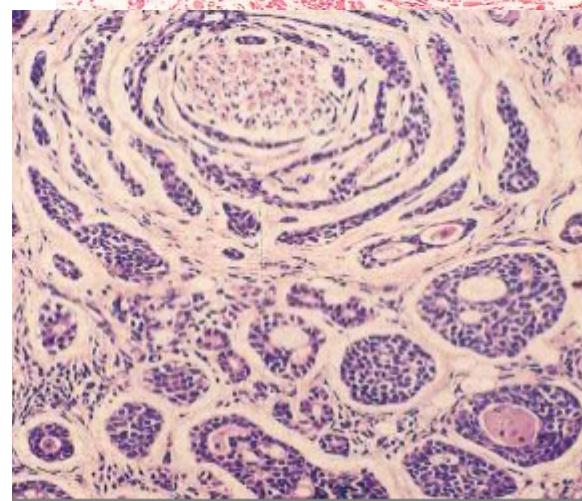
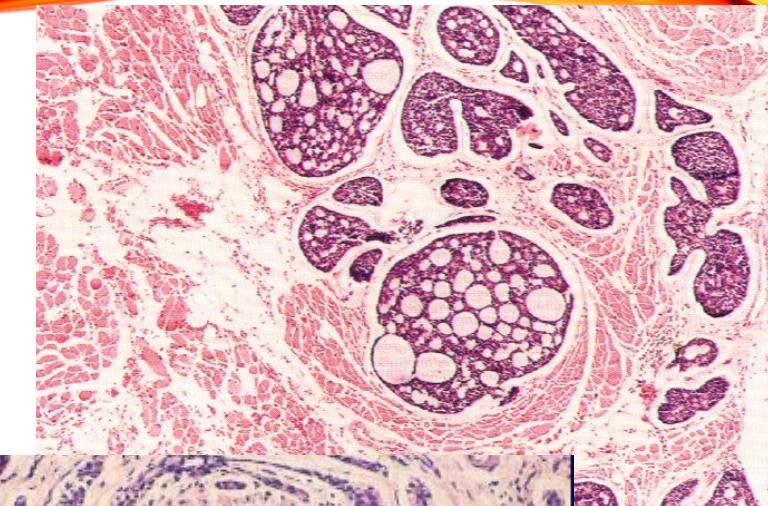
- Adults; Females>males
- 5% of major gland tumours, but 25% of minor gland tumours
- Slow growing, may ulcerate or be painful

## Histopathology

- solid islands, cords, strands of darkly staining epithelial cells in a delicate fibrous connective tissue stroma, however much variation
- notable feature is **perineural invasion**

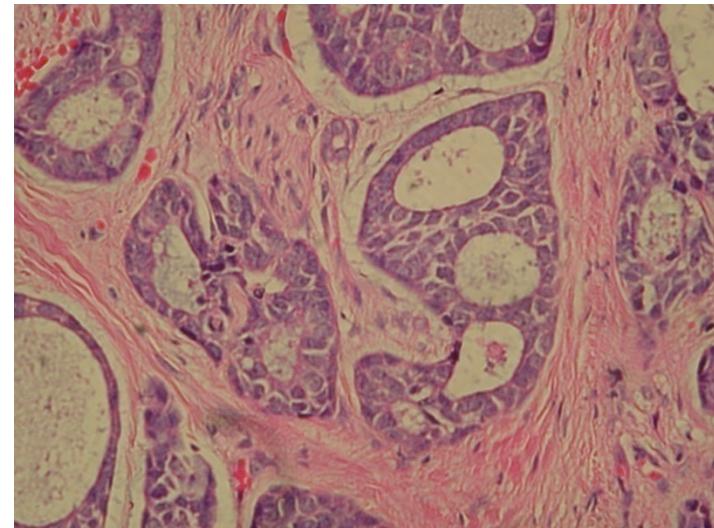
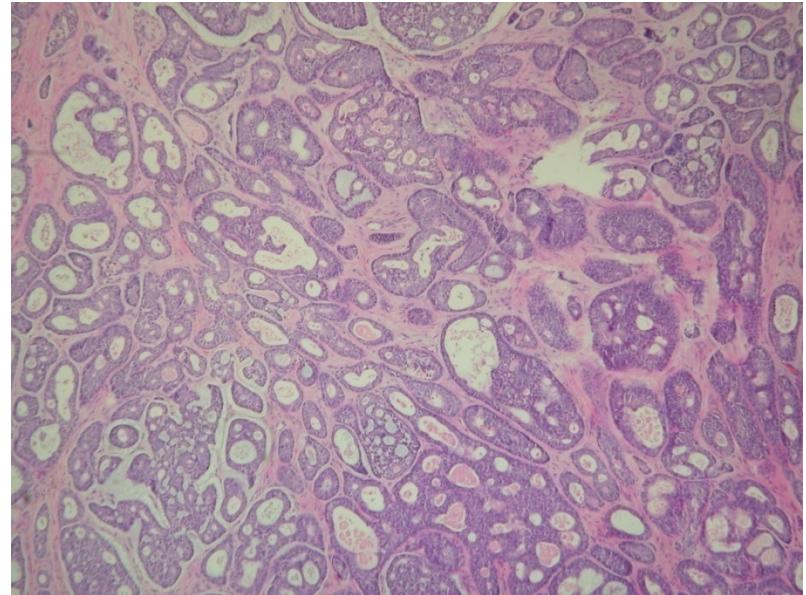


- Three distinct histologic patterns, cribriform, tubular, or solid, although the histologic patterns may coexist in the same tumor
- The **cribriform pattern** has a glandular architecture and is reported to have the best prognosis.
- The **solid pattern** is more epithelial in nature and is associated with a poorer prognosis.
- The **tubular pattern** has a clinical prognosis of intermediate nature between the other two patterns.



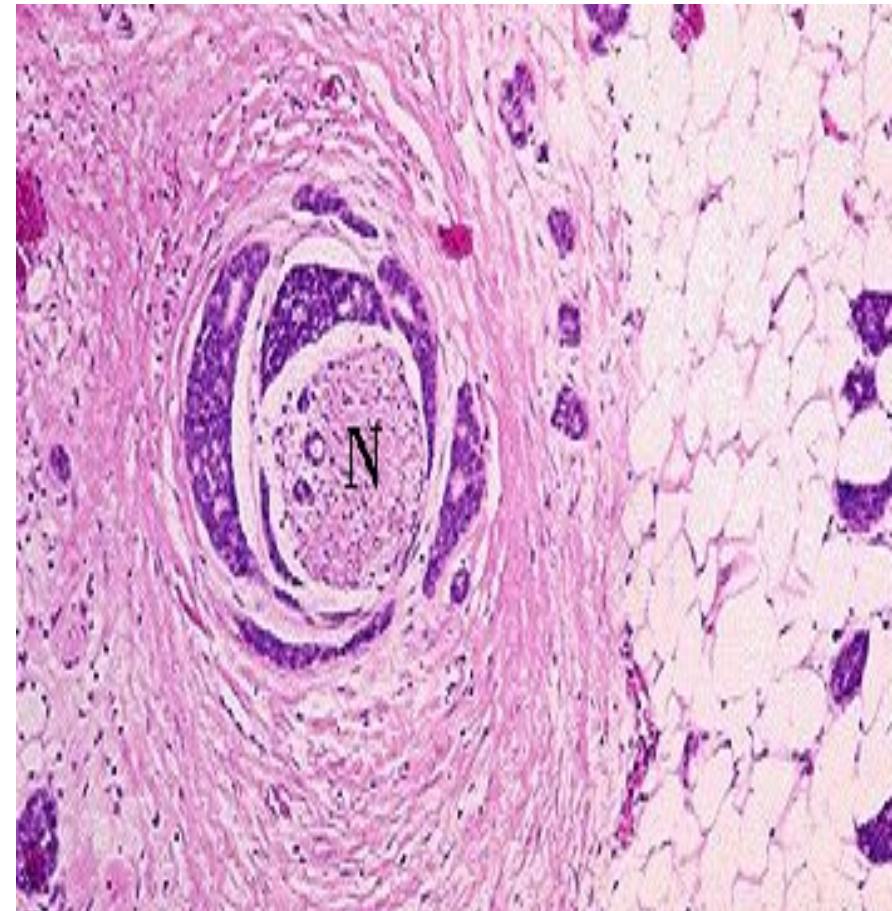
# ADENOID CYSTIC CARCINOMA:

- **Cribiform pattern** is the best recognized pattern characterized by pseudocystic spaces containing mucin (**Swiss cheese pattern**).
- **Tubular Form** : Composed of smallest islands of cells with distinct duct like structure centrally
- **Solid Pattern** shows little duct formation with large islands of small-medium cells with areas of central necrosis indicate aggressive form of the disease



# ADENOID CYSTIC CARCINOMA

- Nerve (N) invaded by adenoid cystic carcinoma  
(the blue area surrounding the nerve).
- Spread may occur by emboli along the nerve lymphatics



## Treatment:

- – Complete local excision
- – Tendency for perineural invasion: (facial nerve sacrifice).
- – Postoperative XRT

## Prognosis :

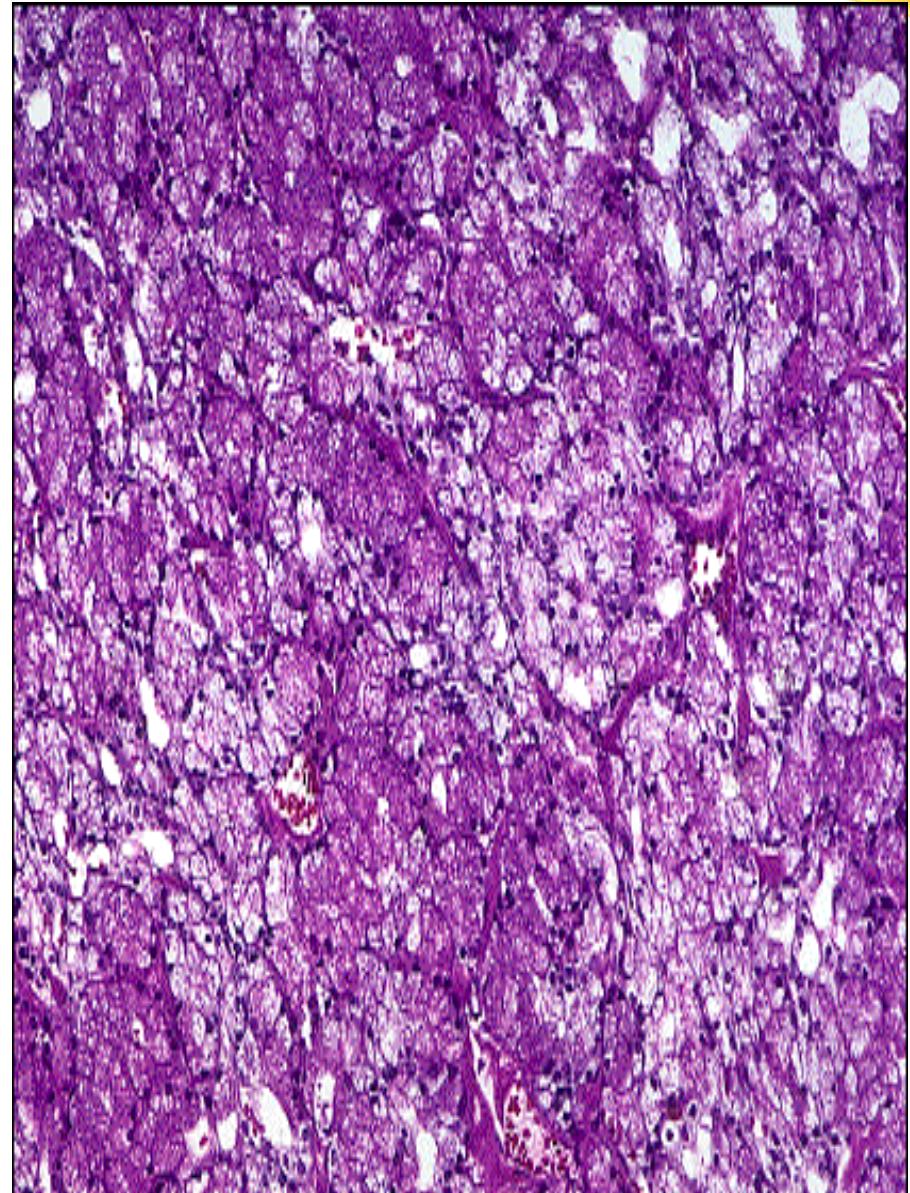
- – Local recurrence: 42% .
- – Distant metastasis: lung
- – Indolent course: 5-year survival 75%, 20-year survival 13%

# ACINIC CELL CARCINOMA

- This tumor has a low-grade behavior and has the best survival rate of any salivary malignancy
- Parotid gland was the most common site of origin
- Second most common parotid and pediatric malignancy
- Gross pathology:
  - Well-demarcated
  - Most often homogeneous



- The acinic cell adenocarcinoma occurs mainly in the parotid gland, also known as **blue dot tumor**.
- Classic multicystic pattern.
- Stained by PAS.
- Cells heavily stained.
- Origin: Intercalated duct & reserve cells
- I O : Palate & buccal mucosa.
- Slowly growing, painful



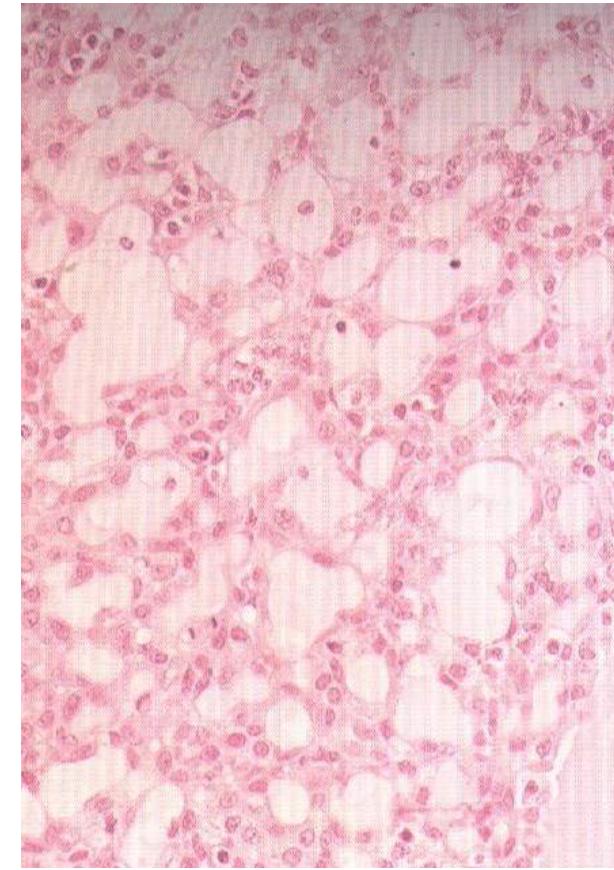
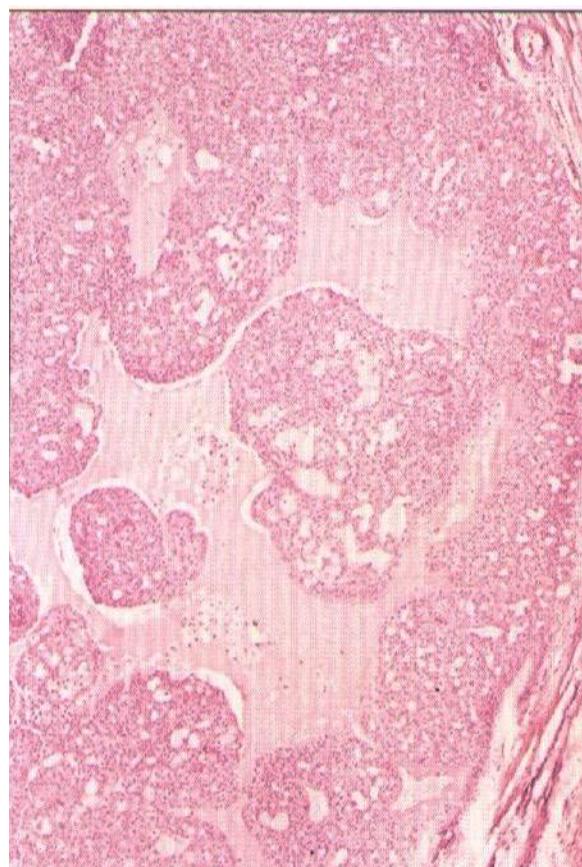
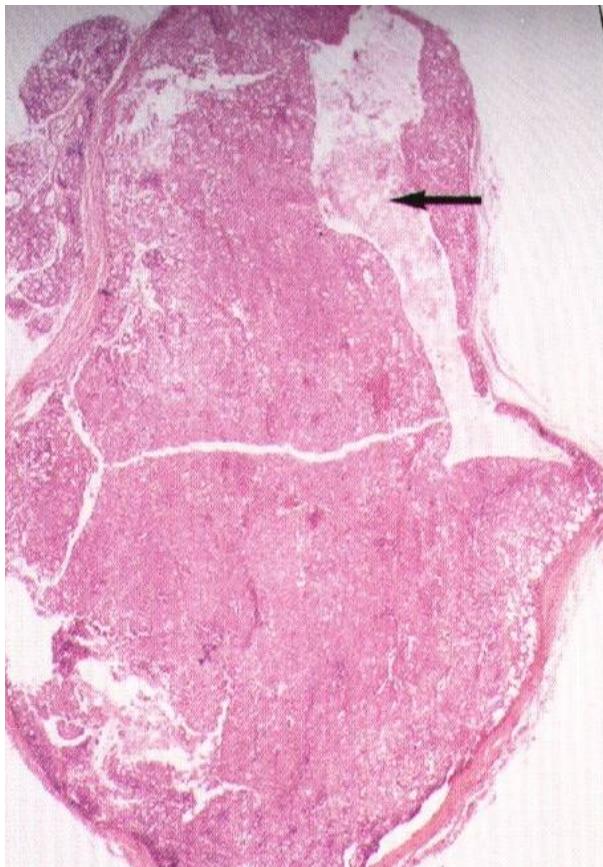
- This lesion is characterized by a benign histomorphologic picture but by occasional malignant behavior.
- These lesions are treated by surgical excision
- Bilateral involvement occurs in 3% of patients, making acinic cell carcinoma the second-most common neoplasm, after Warthin's tumor, to exhibit bilateral presentation.

Treatment:

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

## Histopathology: Three patterns:

- Solid ( most common), Papillary, Follicular
- Tumor cells are uniform & well-differentiated similar to that found in normal acinic cells.



## **Malignant Mixed Tumors**

- **Carcinoma ex-pleomorphic adenoma** Carcinoma developing in the epithelial component of preexisting pleomorphic adenoma

- **Carcino-sarcoma**

True malignant mixed tumor

—carcinomatous and sarcomatous components

- **Metastatic mixed tumor**

Metastatic deposits of otherwise typical pleomorphic adenoma

# CARCINOMA EX-PLEOMORPHIC ADENOMA

- Malignant degeneration can occur in 3% to 7% of pleomorphic adenomas. The risk of malignant degeneration is estimated at 1.5% in the first 5 years and 9.5% after 15 years.
- Histologic findings include those of benign pleomorphic adenoma with carcinomatous degeneration.
- A typical clinical history includes a longstanding salivary mass that begins to rapidly enlarge, often to substantial size, although many patients have no history of a prior tumor.
- Fixation of mass to surrounding tissue, ulceration & regional lymphadenopathy.
- Local recurrence

- 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

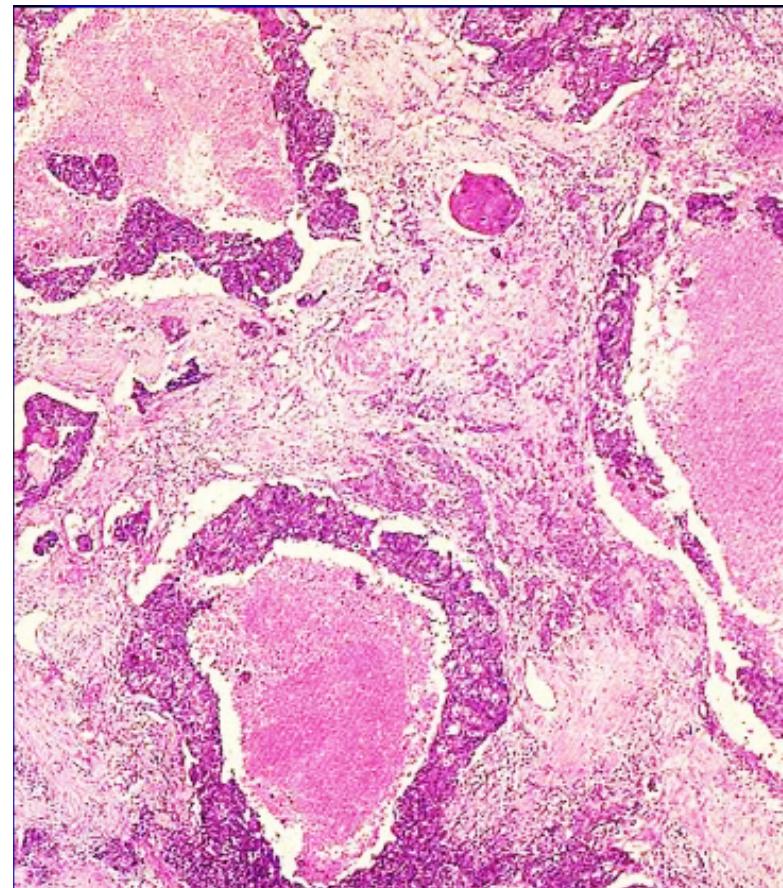
- ***Treatment :***

- Radical excision

- Neck dissection (25% with lymph node involvement at presentation)
- Postoperative XRT

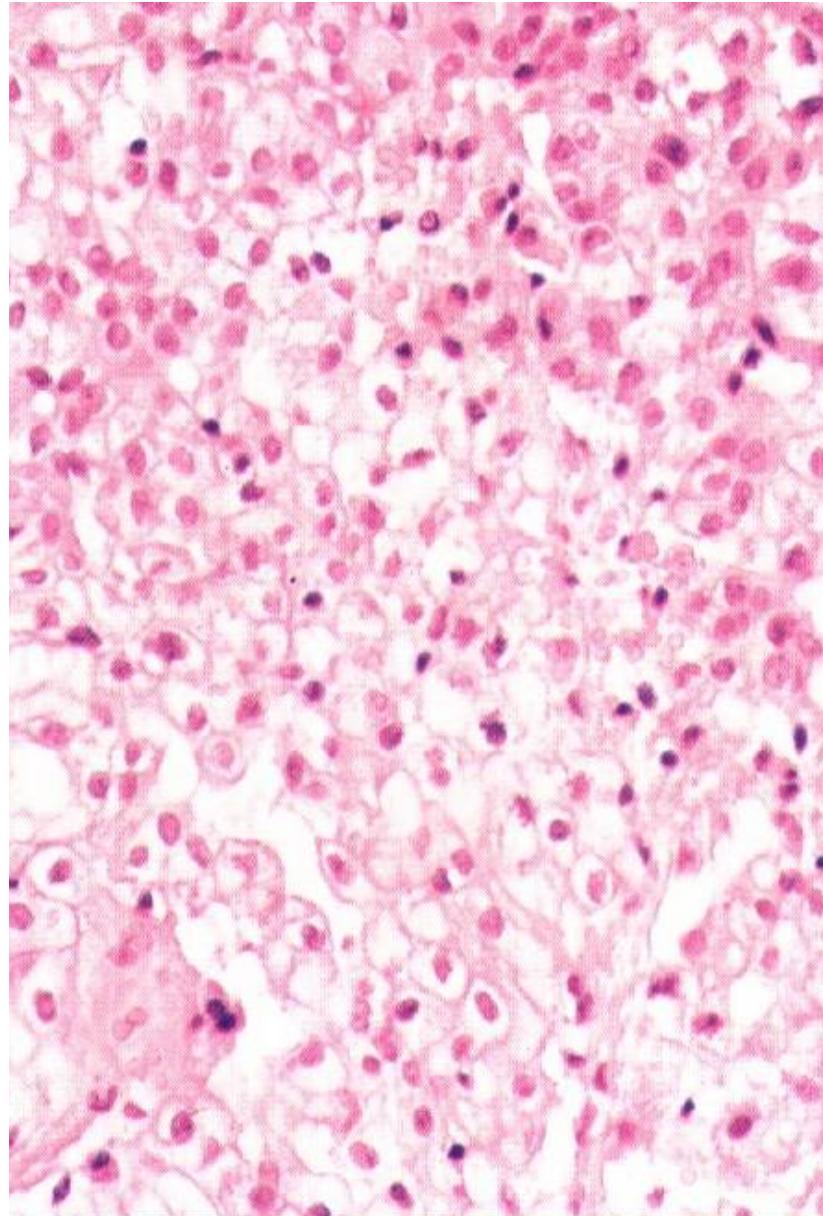
- ***Prognosis***

- Dependent upon stage and histology



# CLEAR CELL TUMOR

- Include: Clear cell carcinoma & Epimyoepithelial carcinoma
- Low grade tumor ( predominantly in minor SG) as submucosal maa in palate.
- Abundant clear cells
- Tx: Local excision with High recurrence



# SQUAMOUS CELL CARCINOMA

- Limited to major salivary glands (SM)
- Obstructive sialadenitis is predisposing factor.
- Well to moderately well-differentiated with no evidence of mucin production.
- 1.6% of salivary gland neoplasms
- 7 th -8 th decades
- M:F = 2:1
- MUST RULE OUT:
  - High-grade mucoepidermoid carcinoma
  - Metastatic SCCA to intraglandular nodes
  - Direct extension of SCCA

# POLYMORPHOUS LOW GRADE ADENOCARCINOMA

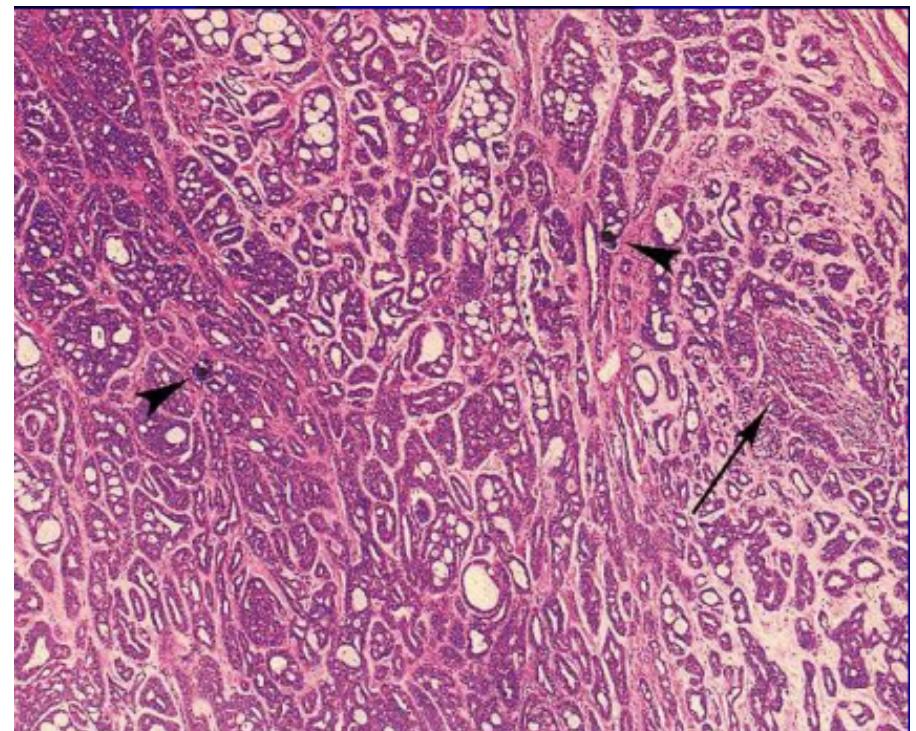
- Low grade malignancy with low risk of recurrence & metastasis.
- Origin: Reserve cells in most proximal portion of salivary duct.
- Myoepithelial differentiated cells appear in this neoplasm.
- Exclusive in minor salivary glands (palate)[second most common malignancy of MSG]
- Firm ,elevated, non-ulcerated nodular swelling
- 1-4 cm, slow growth in long duration (yrs)
- Metastasis in 10% of patients



- Painless, submucosal mass
- Morphologic diversity
- Solid, glandular, cribriform, ductular, tubular, trabecular, cystic

#### Treatment

- Complete yet conservative excision



## Fine-Needle Aspiration Biopsy

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

# TNM CLASSIFICATION & STAGING OF SGTS

<b>Tx</b>	<b>Primary tumor not assessed</b>
T0	No evidence of primary tumor
T1	Tumor 2 cm or less in greatest dimension without extra-parenchymal extension
T2	Tumor > 2 cm but not > 4 cm in greatest dimension without extra-parenchymal extension
T3	Tumor > 4 cm and/or tumor having extra-parenchymal extension.
T4a	Tumor invades skin, mandible, ear canal and/ or facial nerve
T4b	Tumor invades skull base and/or pterygoid plates and /or encase carotid artery

# TNM CLASSIFICATION & STAGING OF SGTS

NX	<b>Regional LNs can not be assessed</b>
N0	No regional LN metastasis
N1	Metastasis in single ipsilateral LN, not more than 3 cm in greatest dimension.
N2a	Metastasis in single ipsilateral LN, more than 3 cm but less than 6 cm in greatest dimension.
N2b	Metastasis in multiple ipsilateral LN, none more than 6 cm in greatest dimension.
N2c	Metastasis in bilateral or contralateral LNs, none more than 6 cm in greatest dimension.
N3	Metastasis in LN more than 6 cm in greatest dimension.

# TNM CLASSIFICATION & STAGING OF SGTS

<b>MX</b>	Distant metastasis can not be assessed
M0	No distant metastasis
M1	Distant metastasis

# Staging :

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<b>Stage I</b>	<b>T1</b>	<b>N0</b>	<b>M0</b>
Stage II	T2	N0	M0
Stage III	T3	N0	M0
	T1,T2,T3	N1	M0
Stage IVa	T4a	N0	M0
	T4a	N1	M0
	T1,T2,T3	N2	M0
	T4a	N2	M0
Stage IVb	T4b	Any N	M0
	Any T	N3	M0
Stage IVc	Any T	Any N	M1

# **SALIVARY GLAND NEOPLASIA ANOTHER CLASSIFICATION**

## **The ABCDs:**

- Architecture
- Biphasic
- Cytology
- Differential

- **Monophasic:**

1. Oncocytoma
2. Polymorphous adenocarcinoma
3. Clear cell carcinoma

- **Biphasic:**

1. Basal cell Adenoma
2. ACC
3. Epithelial-myoepithelial carcinoma

- **Triphasic:**

1. PLA
2. Acinic cell carcinoma
3. MEC

- **Tumor associated lymphoid proliferation:**

1. Warthin's Tumor
2. Acinic cell carcinoma
3. MEC
4. Lympho-epithelial carcinoma

- **High grade Transformation:**

1. Acinic cell carcinoma
  2. ACC
  3. Epithelial-Myoepithelial carcinoma
- High grade glandular:
    1. Salivary duct carcinoma
    2. Adeno-squamous carcinoma

OU

