Pathology of Head and Neck Malignancies

Dr. Asit Ranjan Mridha
MD (Pathology), A.I.I.M.S, New Delhi
Assistant Professor
School of Digestive and Liver Diseases
I.P.G.M.E. & R., Kolkata

A. Tumors of the upper respiratory tract

B. Tumors of the oral cavity

C. Salivary gland tumors

D. Tumors of thyroid and parathyroid glands

E. Tumors of the orbit

Tumors of the upper respiratory tract

A. **Nasal cavity, paranasal sinuses and Nasopharynx**
   - Primary tumors
   - Secondary tumors

B. **Larynx and Trachea**

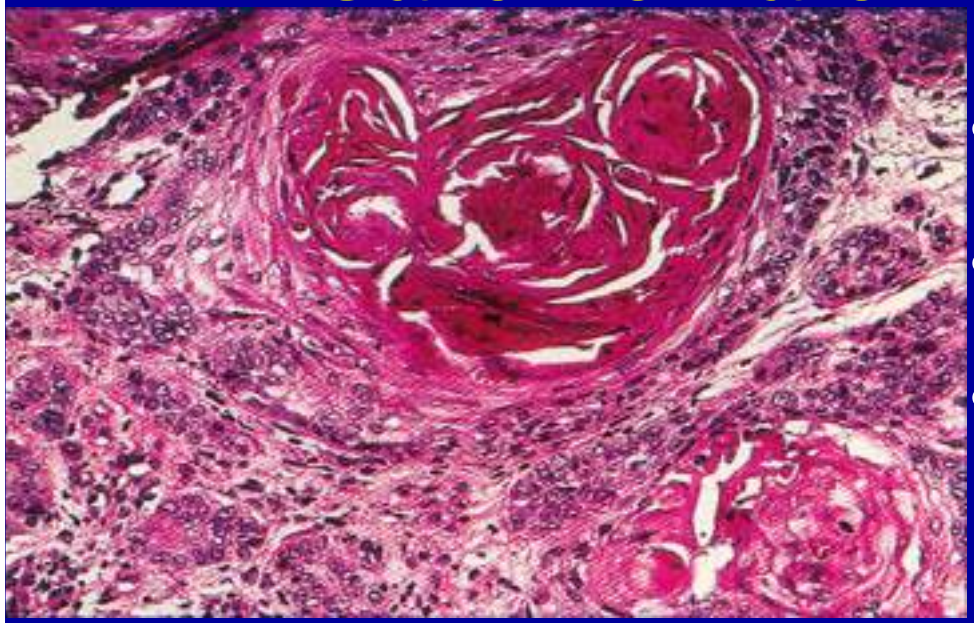
Primary tumors

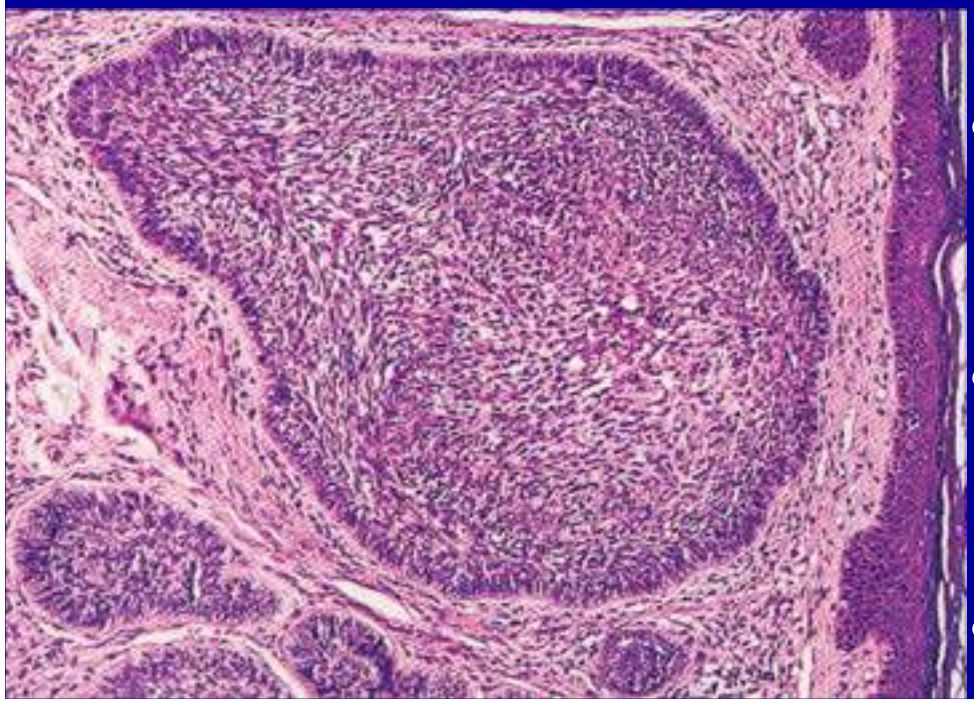
- Epithelial and neuroectodermal tumors
- Soft tissue tumors
- Hematolymphoid tumors
- Tumors of bone and cartilage
- Miscellaneous tumors

Malignant epithelial and neuroectodermal tumors

- Squamous cell carcinoma
- Adenocarcinoma
- Salivary gland tumors
- Sinonasal undifferentiated carcinoma
- Neuroectodermal tumors

Carcinoma of nasal vestibule





- Uncommon
- Age: 52-82, M>F
- Nasal vestibule or at mucocutaneous junction
- WD-SCC/basal cell carcinoma
- Treat: local excision/radiotherapy
- Prognosis: Excellent

Squamous cell carcinoma of sinonasal tract and nasopharynx

Squamous cell carcinoma

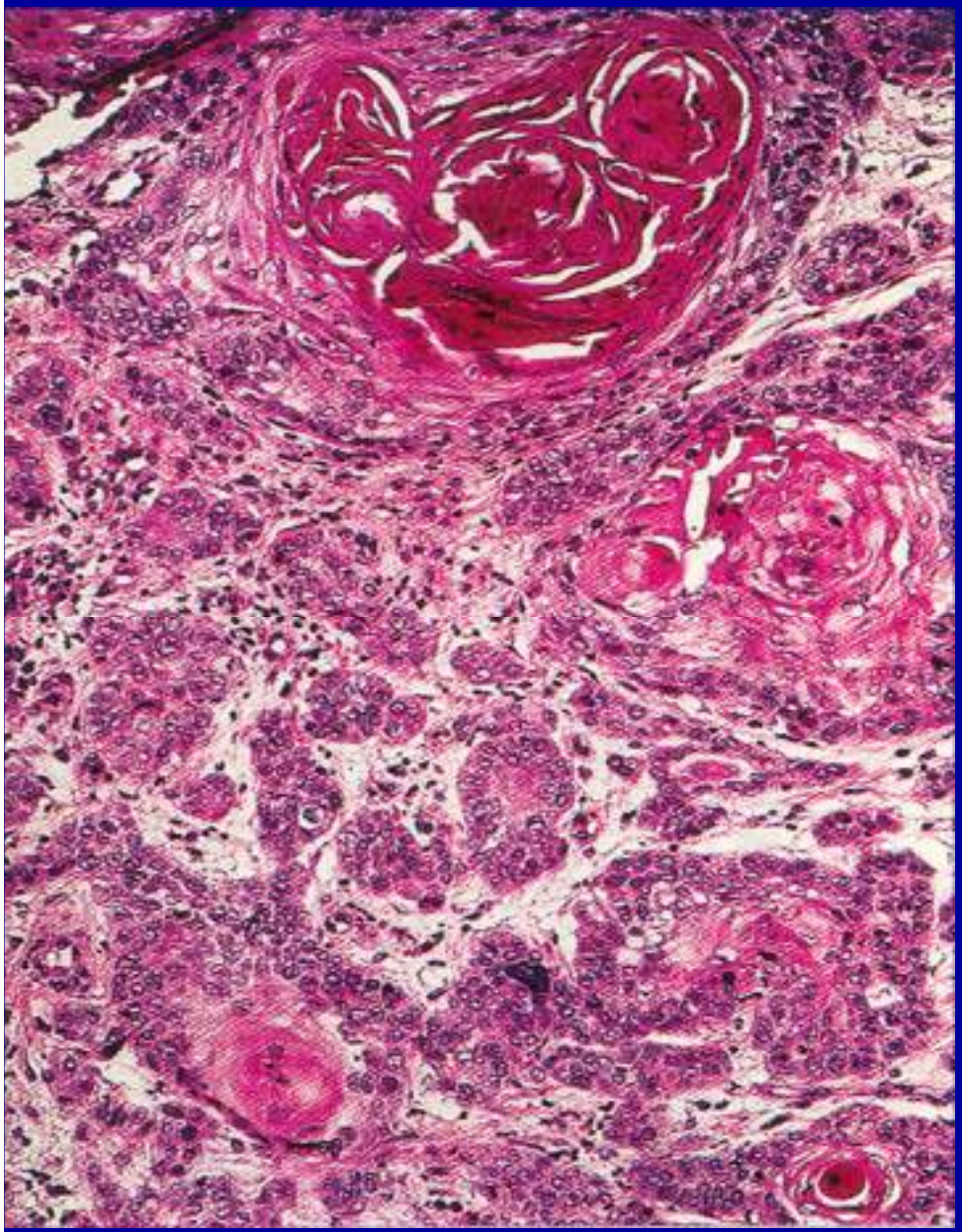
- Keratinizing
- exophytic / papillary / verrucous / spindle cell / basaloid / adenosquamous

- Non-keratinizing
  - respiratory epith, transitional, cylindrical cell

SCC Conventional type

- 3% of all head & neck cancers

  <1% of all malignancies
- M>F 6th & 7th decades (95% pts >40 yrs)
- Max antrum, nasal cavity, ethmoid, sphenoid & frontal sinuses
- Fascial asymmetry, unilateral nasal obs, epistaxis, mass lesion, pain, persistent purulent rhinorrhoea, non-healing ulcer, exophthalmos
- Diagnosis is often delayed (signs/symptoms are similar to those of chronic sinusitis)

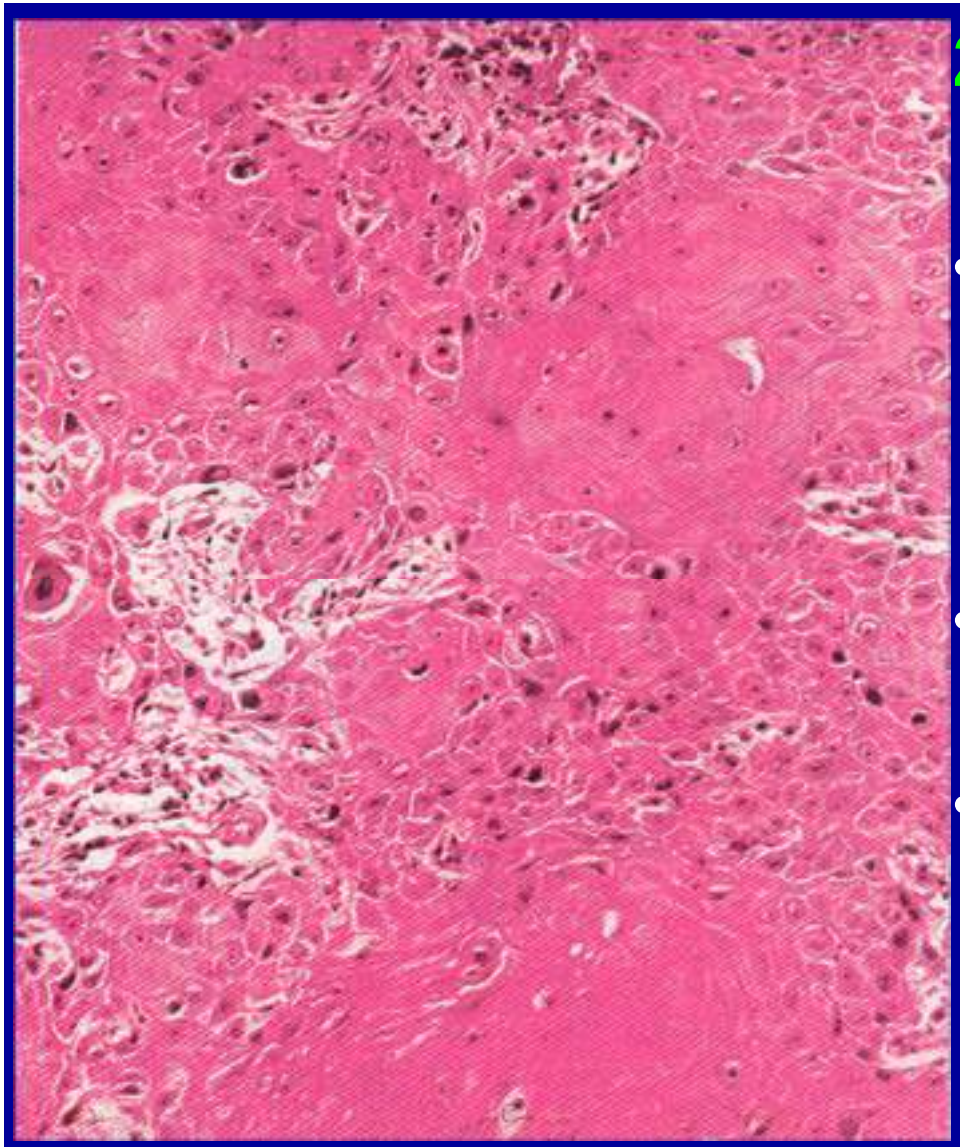


- Secondary malignancy either at another mucosal site or lung, GIT, breast

- Exophytic, papillary, fungating, inverted growth

  Well circumscribed, expansile, necrotic, fragile destructive

1. **Keratinizing**: WD, MD, PD



2. Non-keratinizing

- Treat: complete surgical resection & adjuvant RT

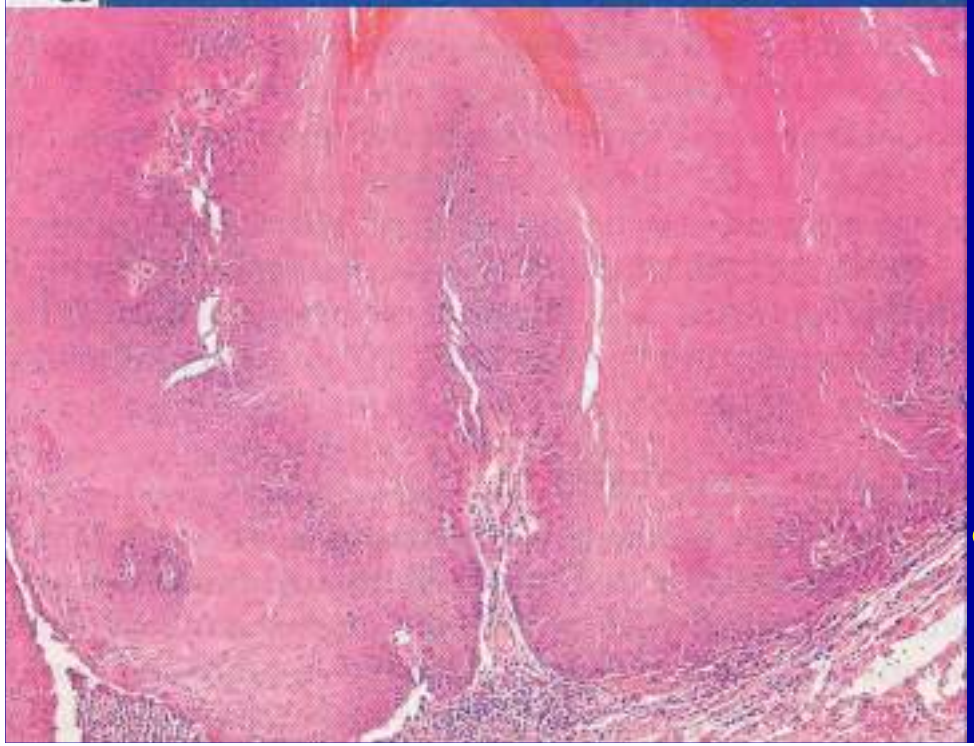
  Local recurrence: frequent

- Prognosis: poor

- Higher stage, inv > 1 anatomic sites, extension beyond nasal cavity & paranasal sinuses, LN

- Diffuse /single cell invasion associated with survival of 30-40% compared to 80-90% survival in pts with cohesive or pushing pattern

Verrucous carcinoma

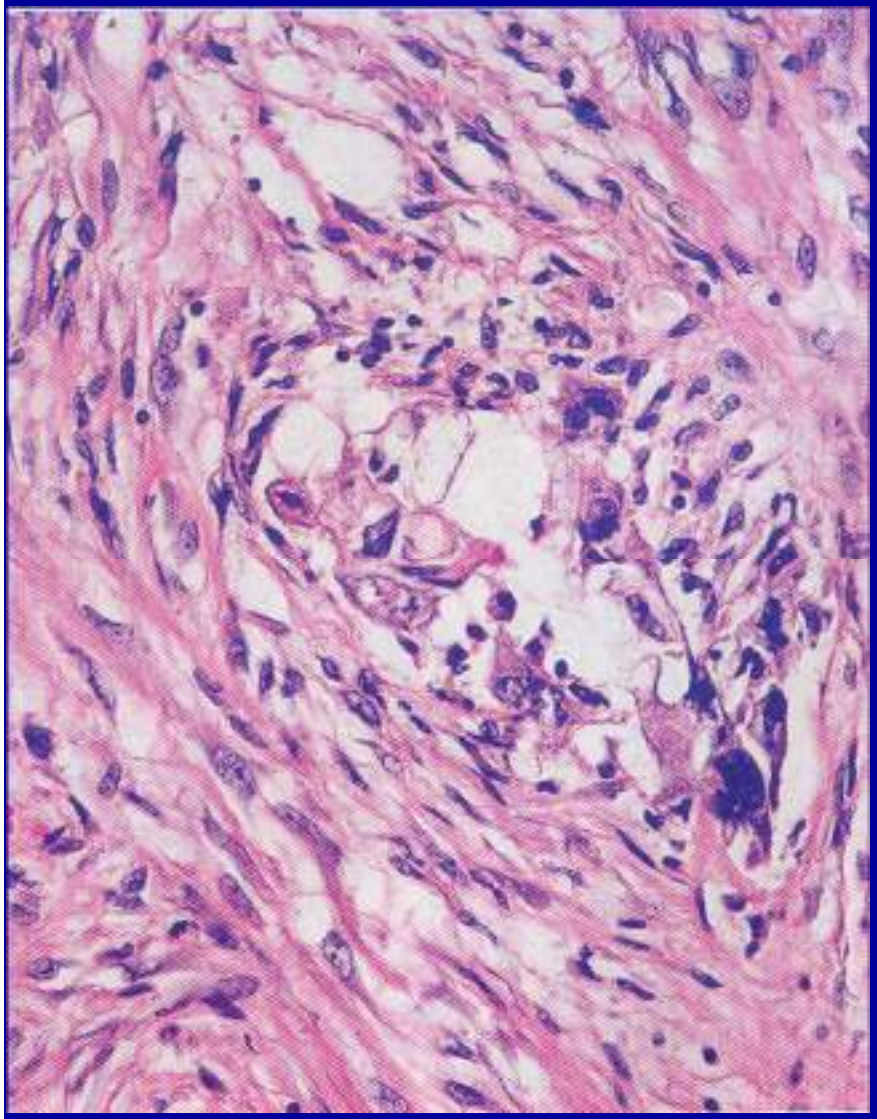


- WD locally destructive
- Oral cavity →larynx →nasal fossa →sinonasal tract →nasopharynx
- Tan/white, warty /fungating / exophytic, firm to hard

Adequate biopsy (ample eith & stromal tissue)

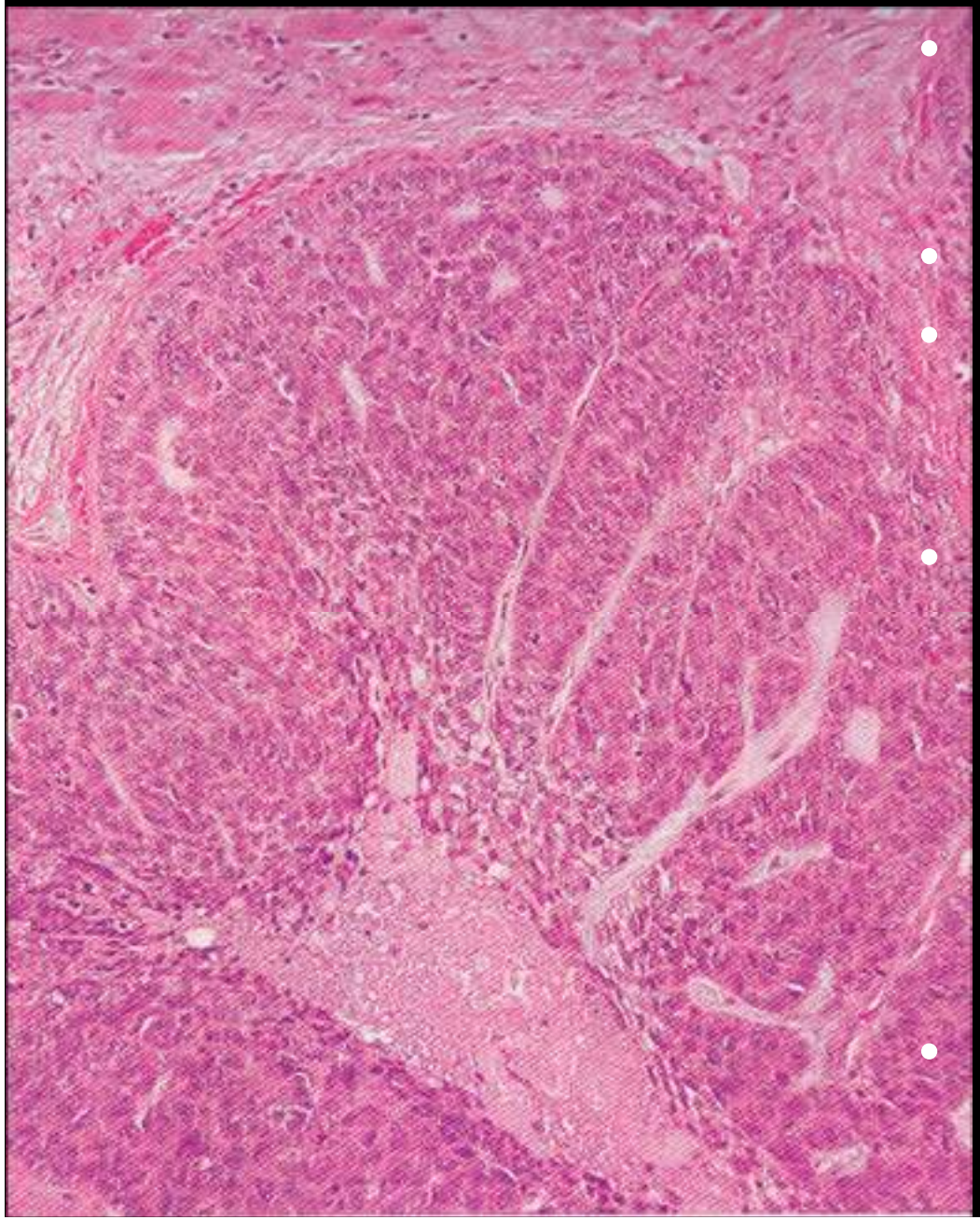
- Must be differentiated from SCC

Spindle cell squamous carcinoma



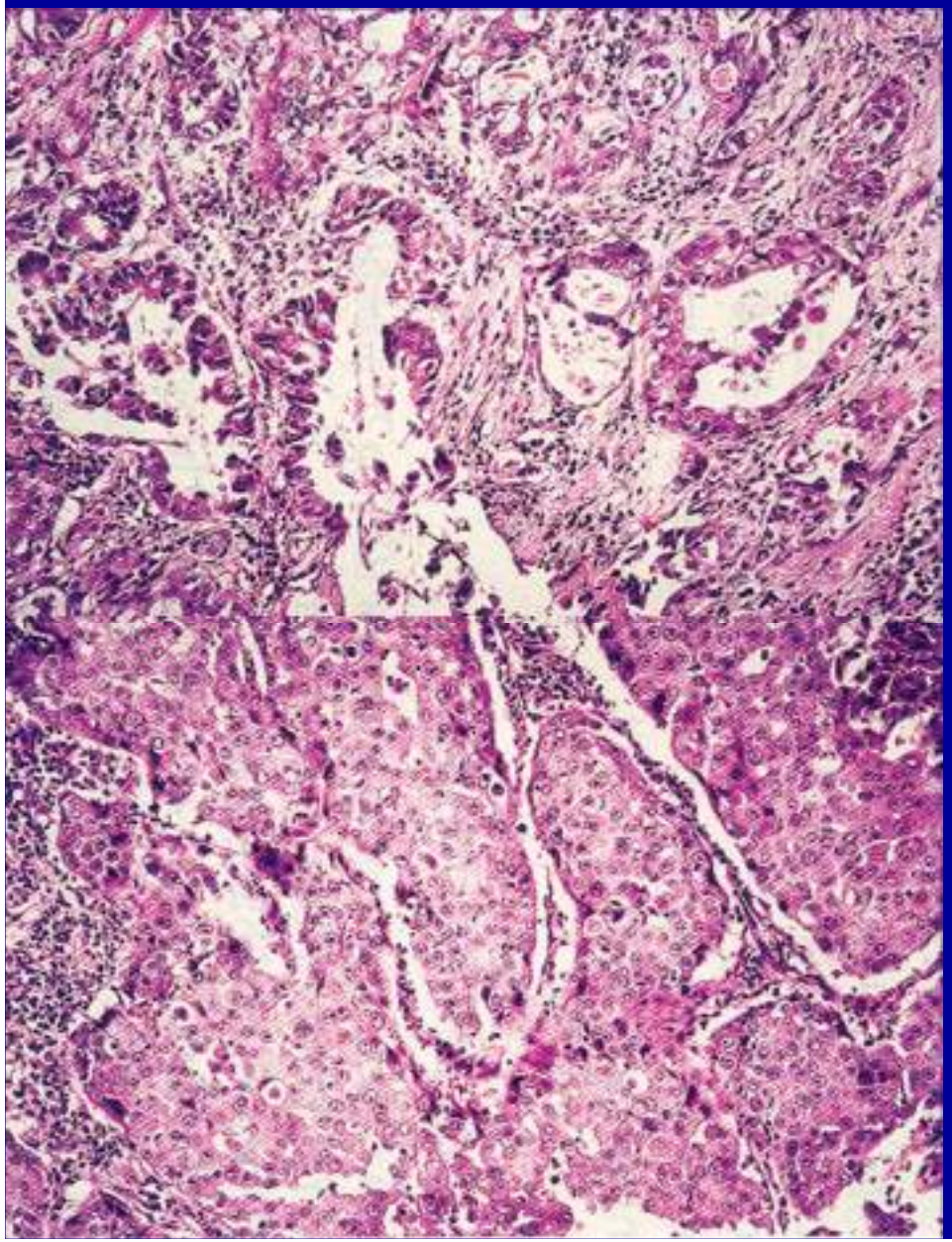
- Fungating, ulcerating, polypoidal / exophytic
- Malignant undifferentiated spindle cell proliferation in presence of differentiated squamous cell component
- CK –negative in upto 40% of cases
- Prognosis: worse

Basaloid Squamous cell carcinoma



- Pyriform sinus, supraglottic, oral cavity, tongue, tonsil, palate
- Alcohol, tobacco use
- Solid, lobular, cribriform, nest, cords, trabeculae
- Aggressive, high grade, multifocal, deeply invasive & metastatic even at initial presentation
- Early mets to LN & visceral organs
- Treat: Radical excision, neck dissection, RT & CT

Adenosquamous carcinoma



- Uncommon
- Larynx, oral cavity, sinonasal cavity
- Exophytic, submucosal, friable, edematous or granular

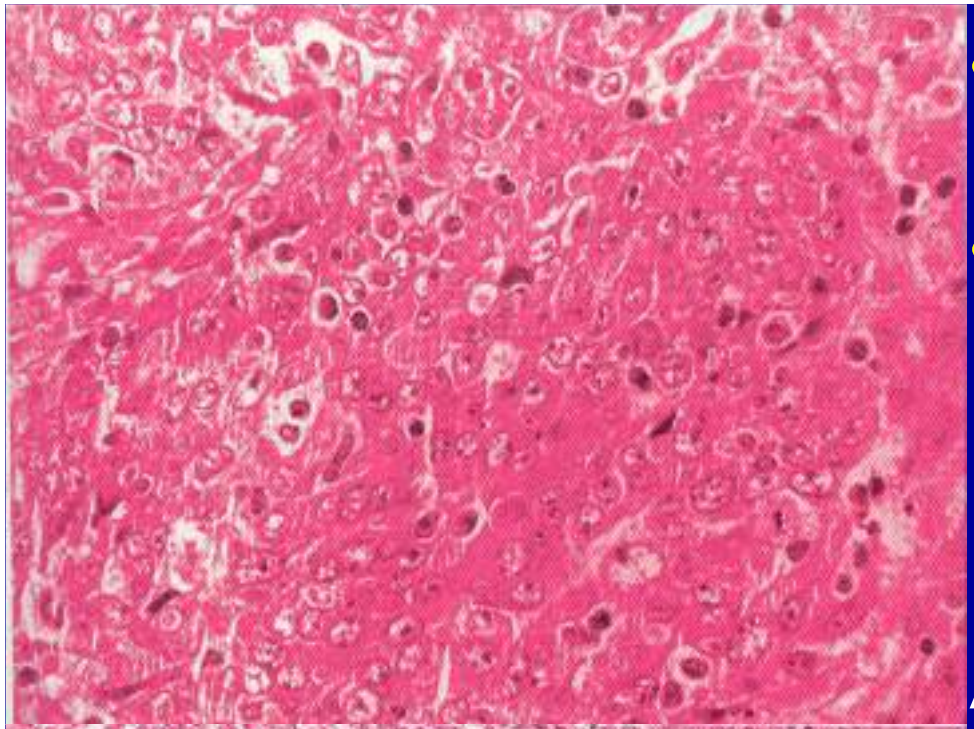
Nasopharyngeal Carcinoma

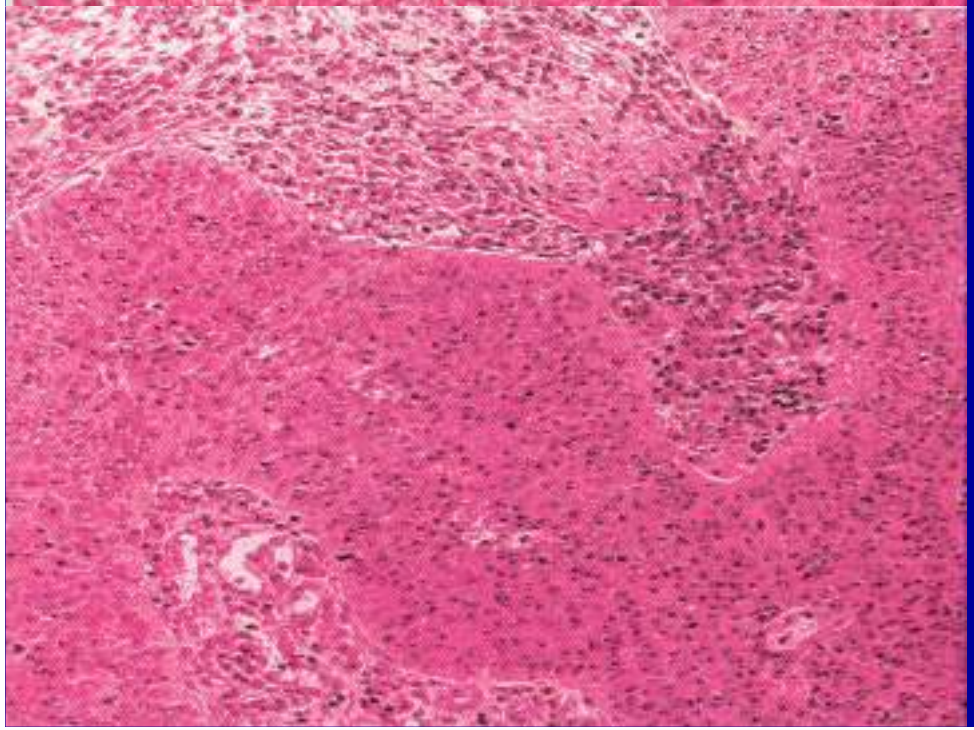
- Age range: wide, common 4^{th}-6^{th} decades
  <20% pediatric age groups
- China: 18% of all cancer
  US: 0.25%

- Nasal obstruction, discharge, epistaxis, pain, OM, otalgia, hearing loss, headache

  Asymptomatic cervical neck mass
  Cranial nerve inv 25%

- Most common site: FOR





- Genetic susceptibility:
  HLA-A2, B17, Bw46, BW58
- EBV 75-100%
  Salted fish, poor hygiene, smoke, tobacco, chemical fumes, harbal medicine

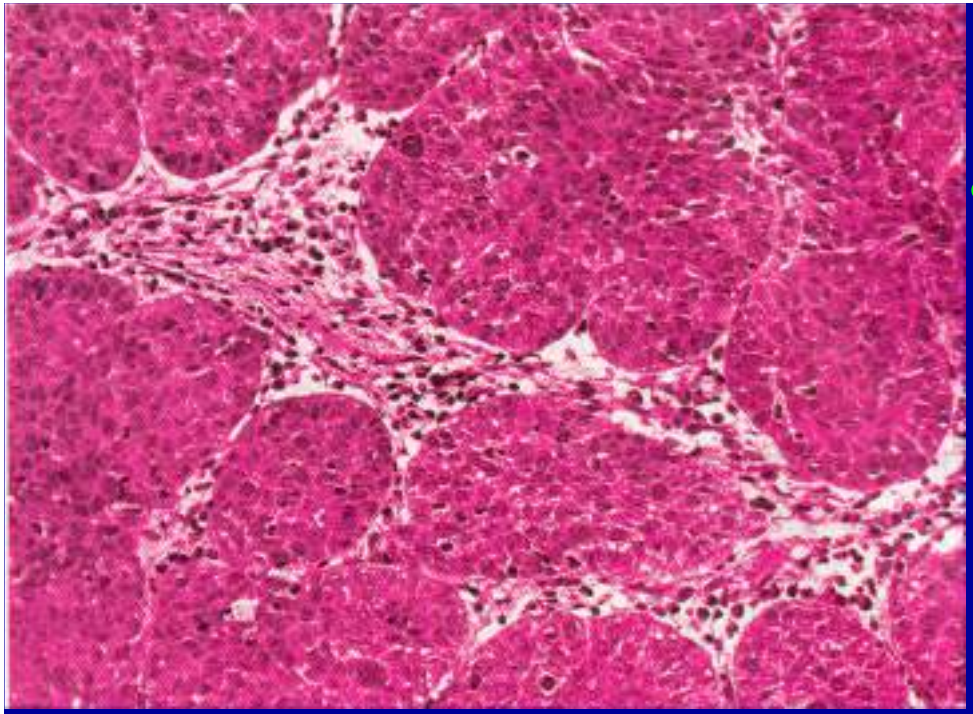
A. Keratinizing: WD, MD, PD

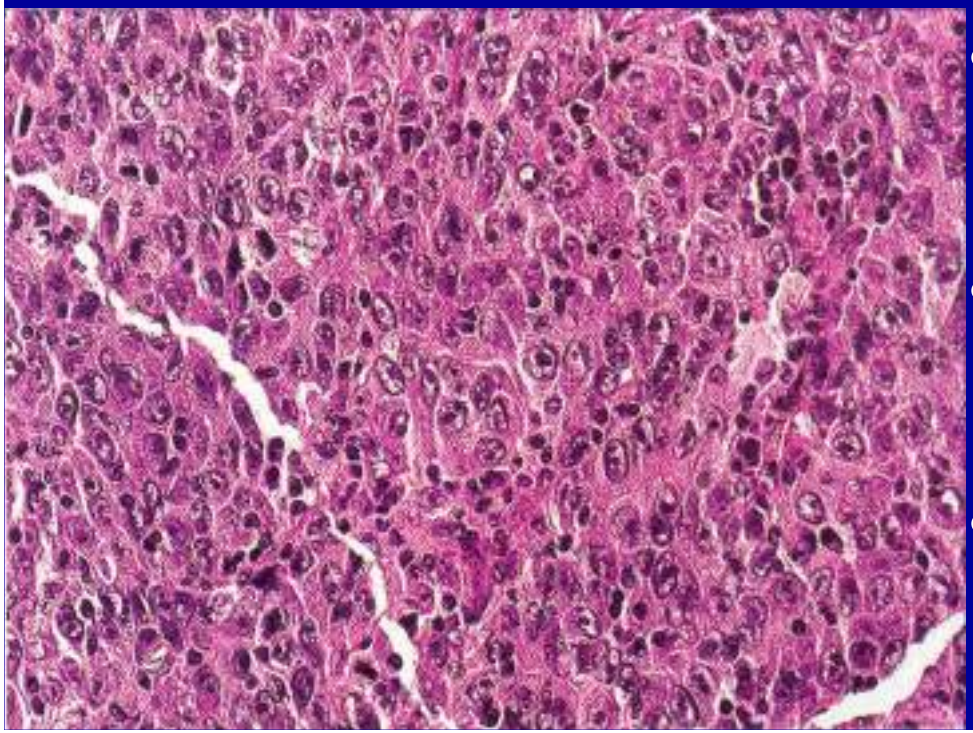
25% of all NPC

rare under 40 yrs of age

B. Non-keratinizing

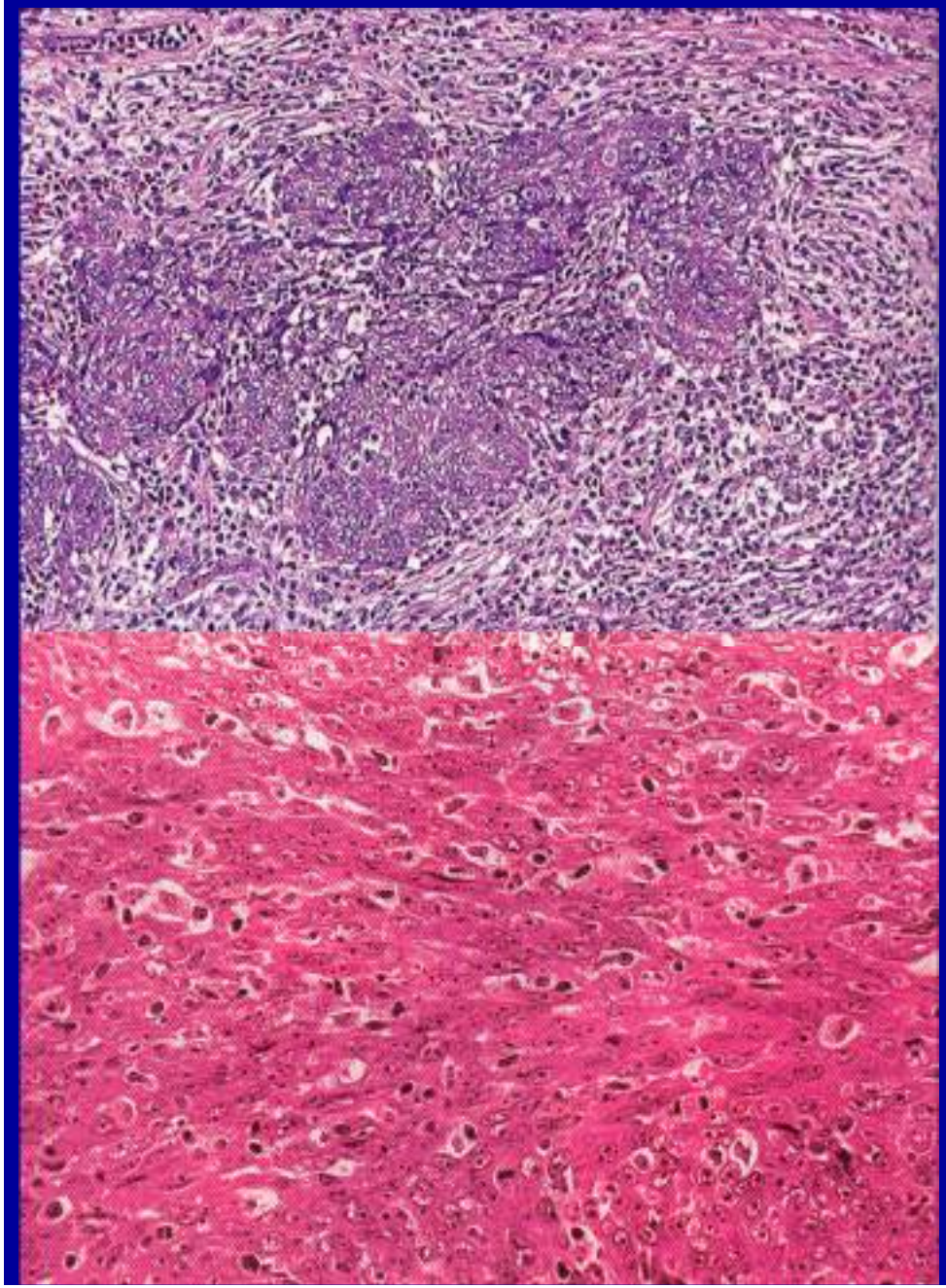
- Differentiated
- Undifferentiated





- **Non-keratinizing**
  - **differentiated** 12%
  - **Undifferentiated type** 60%
- D/D: NHL
- Treat: RT
- Prog: clinical stage, sex, age, genetic factor

Sinonasal undifferentiated carcinoma



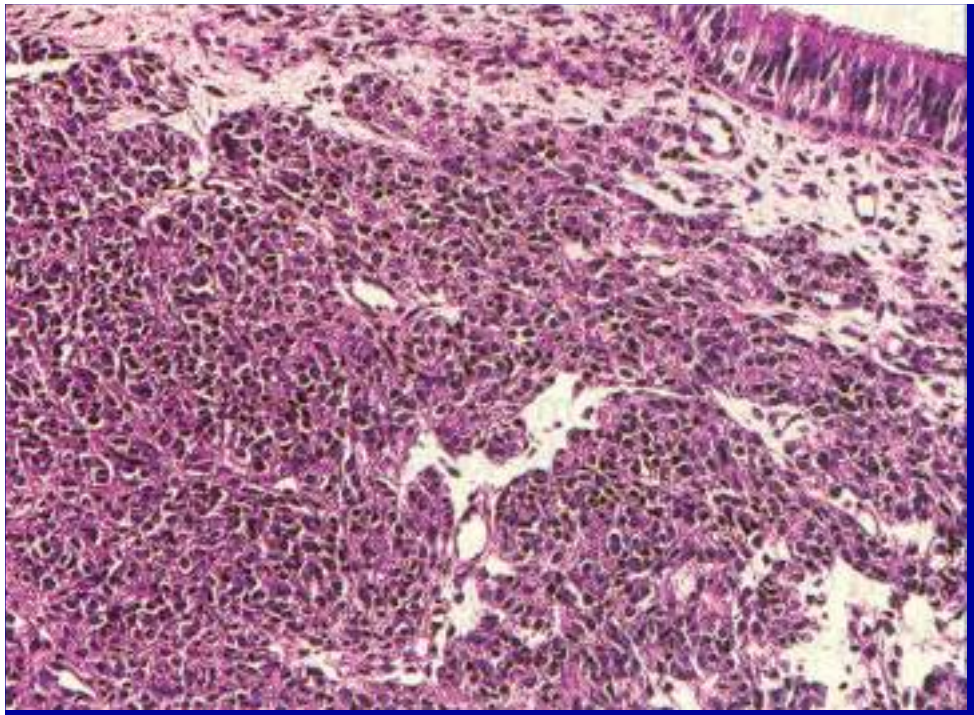
- High grade malig epith neoplasm with/without NE differentiation
- Highly aggressive
- RT, CT

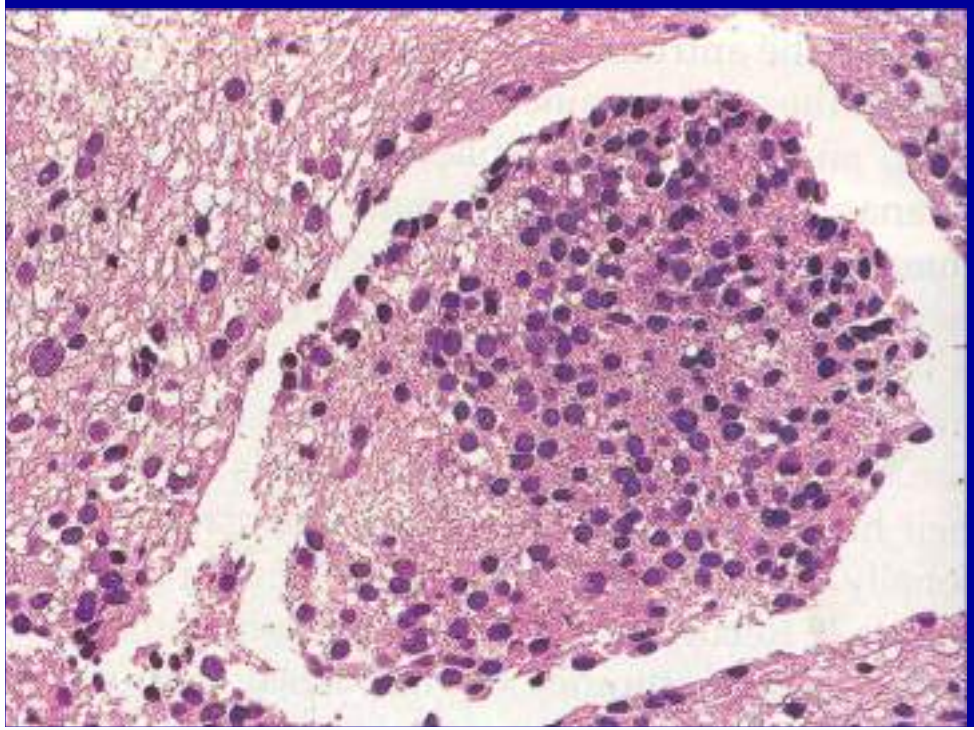
  CT→RT →radical surgery (improved survival)

Olfactory neuroblastoma

- Upper1/3rd – ½ of nasal septum, cribriform plate, superior-medial surface of superior turbinate
- Most common site: upper nasal cavity
- Uncommon (M>F)

  3 yrs- 9th decade (bimodal peak in 2nd & 6th decades)
- Nasal obstruction, epistaxis, anosmia, headache, pain, lacrimation





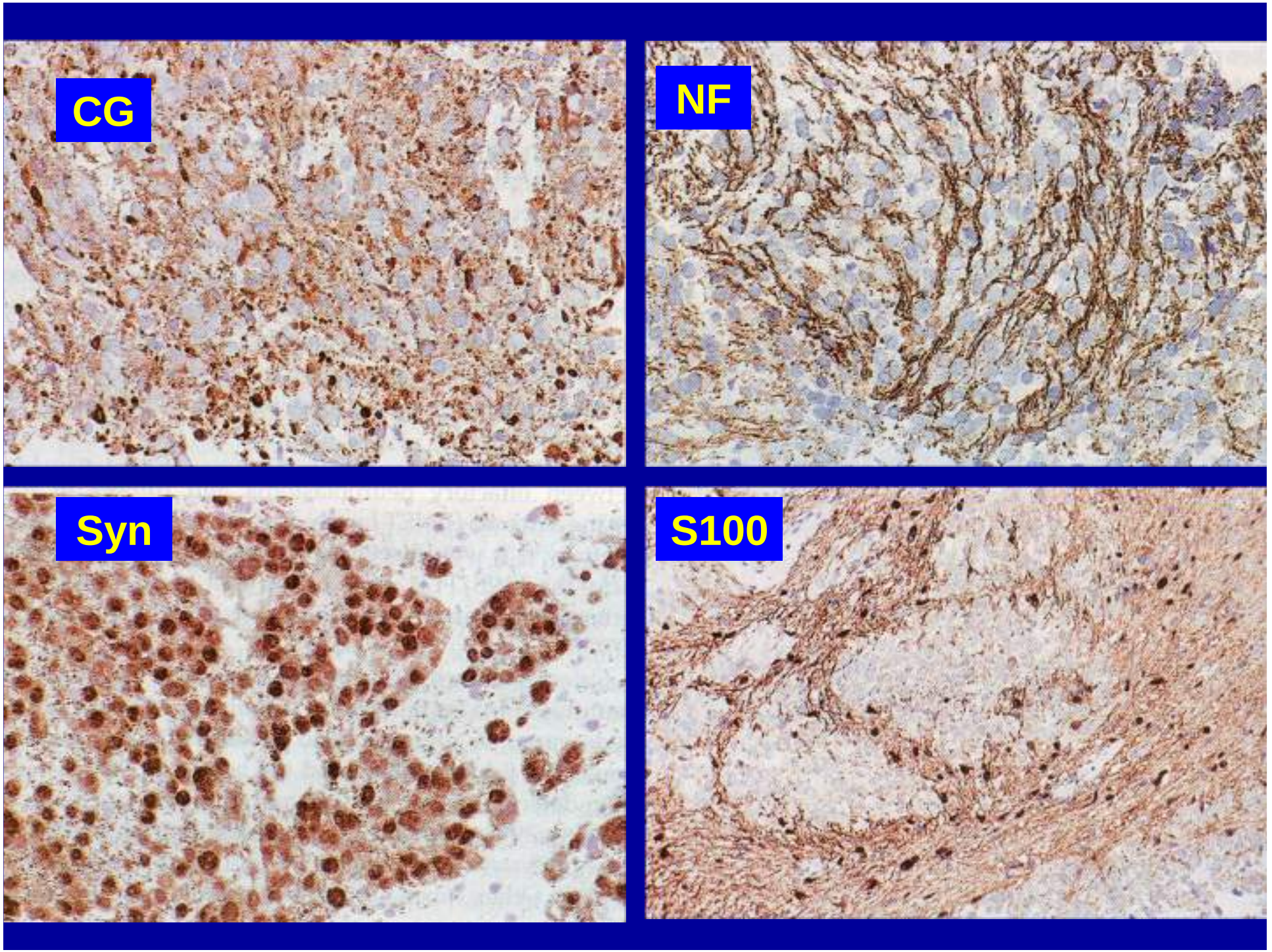
Gr I: mitosis, & necrosis absent

Gr II: mitosis+, pleo+, less NF

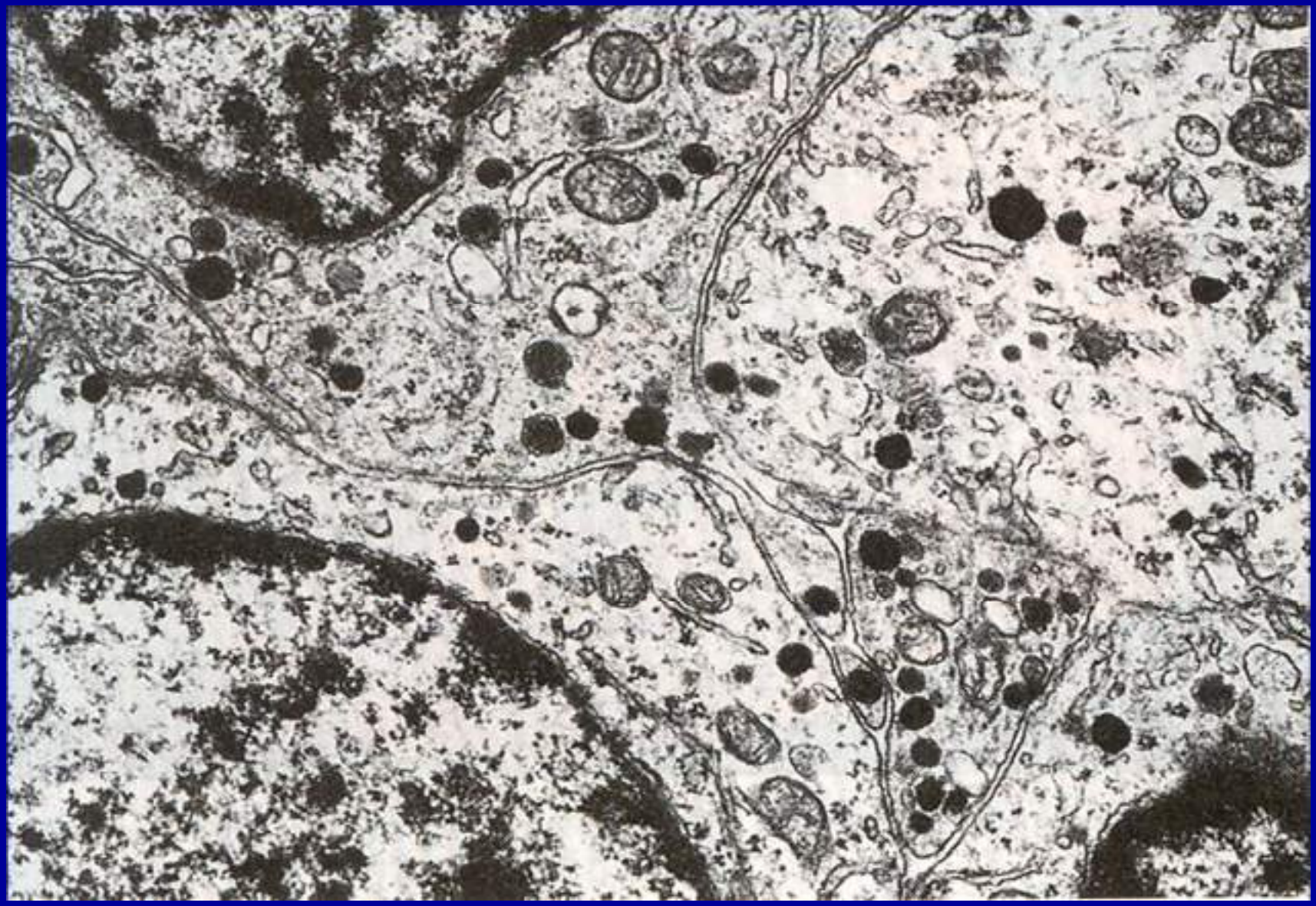
Gr III: M+, N+, pleo+, NF focally, Calcifn-

Gr IV: NF-

- Mixed ONB & carcinoma: ONB+ Adca, SCC, undifferentiated carcinoma


CG
NF
Syn
S100

EM: dense core neurosecretory granules 80-250 nm



Treat: complete surgical eradication followed by RT

5-year survival

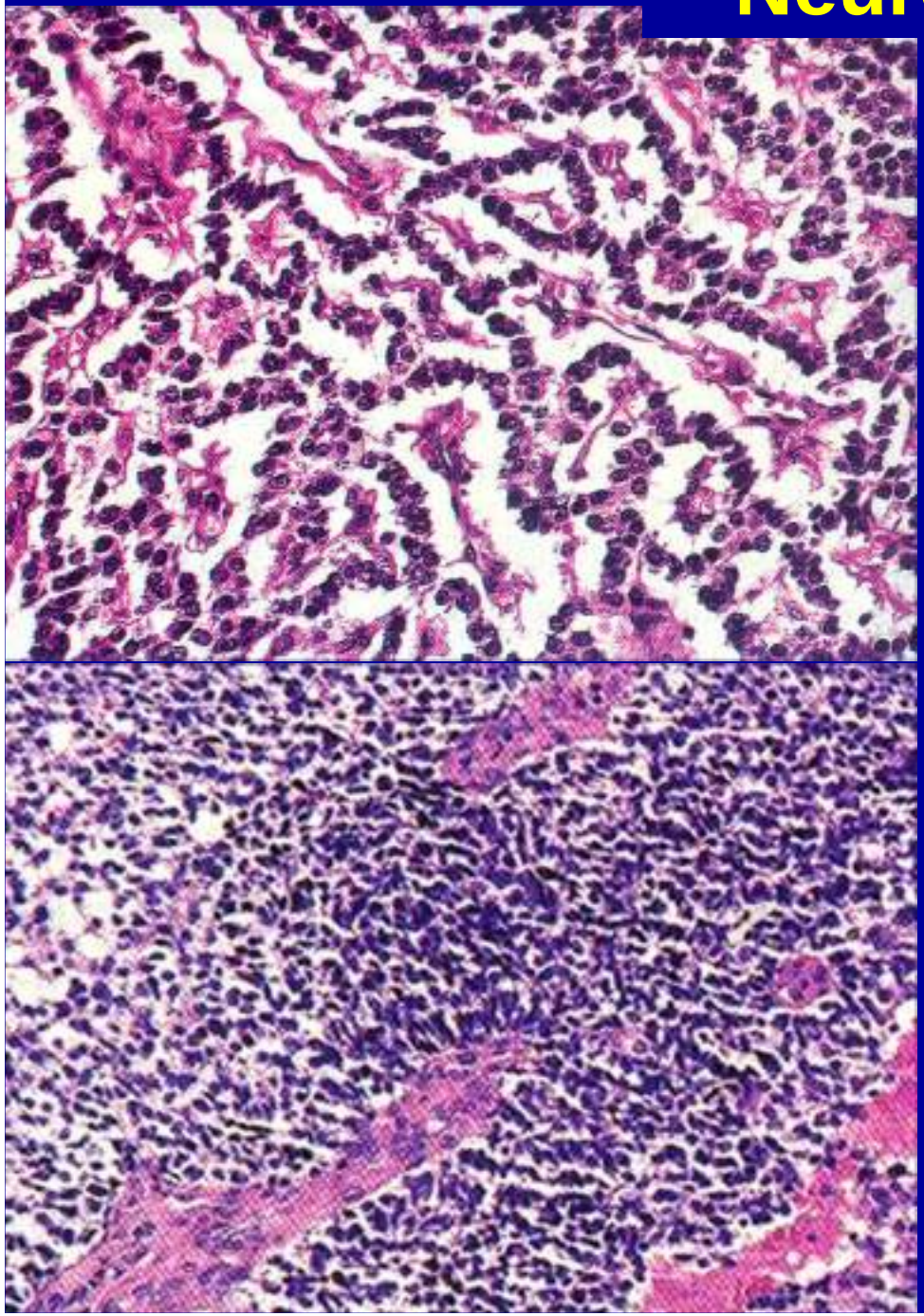
Stage A: confined to nasal cavity - 75%

Stage B: (most common) nasal cavity + one or more paranasal sinuses - 68%

Stage C: beyond sinonasal cavity - 41%

- Overall 5-, 10-, & 15-year survival rates were 78%, 71% & 68% respectively (Arch Otolaryngol 1984;110:123-126)

Neuroendocrine carcinoma



WD, MD, PD (small cell & large cell variant)

Uncommon

Upper aerodigestive tract, larynx, sinonasal tract

CK, NSE, CG, Syn, S100

Treat: CT, RT

Mucosal malignant melanoma

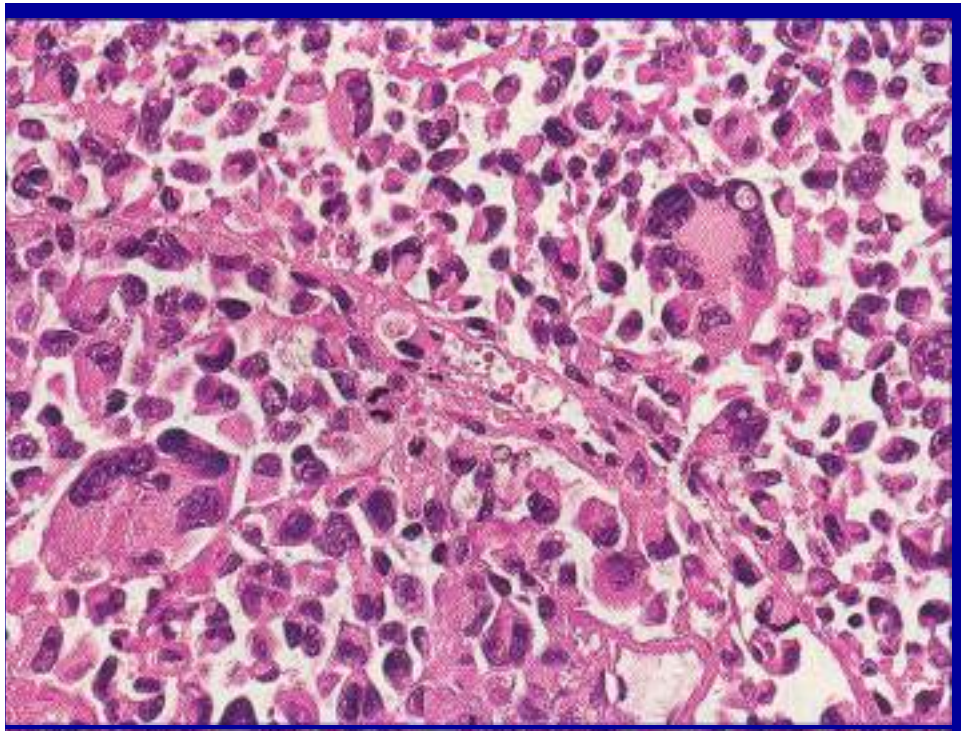
- 0.5-3% of all melanomas
- 6^{th} – 8^{th} decades
- Caucasions

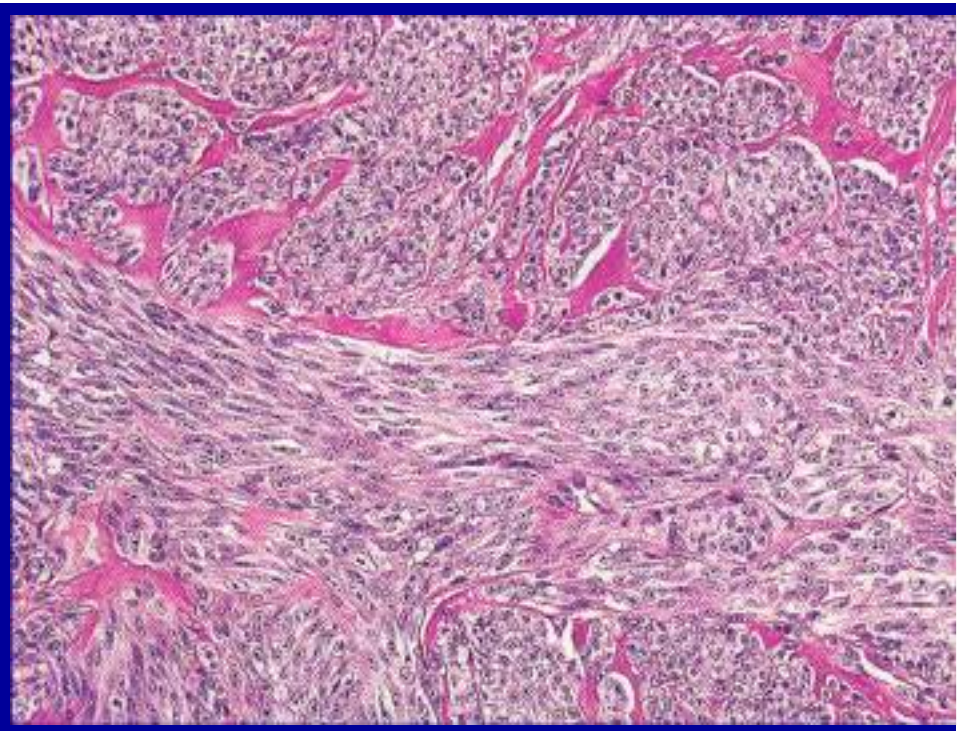
- Etiology: not known

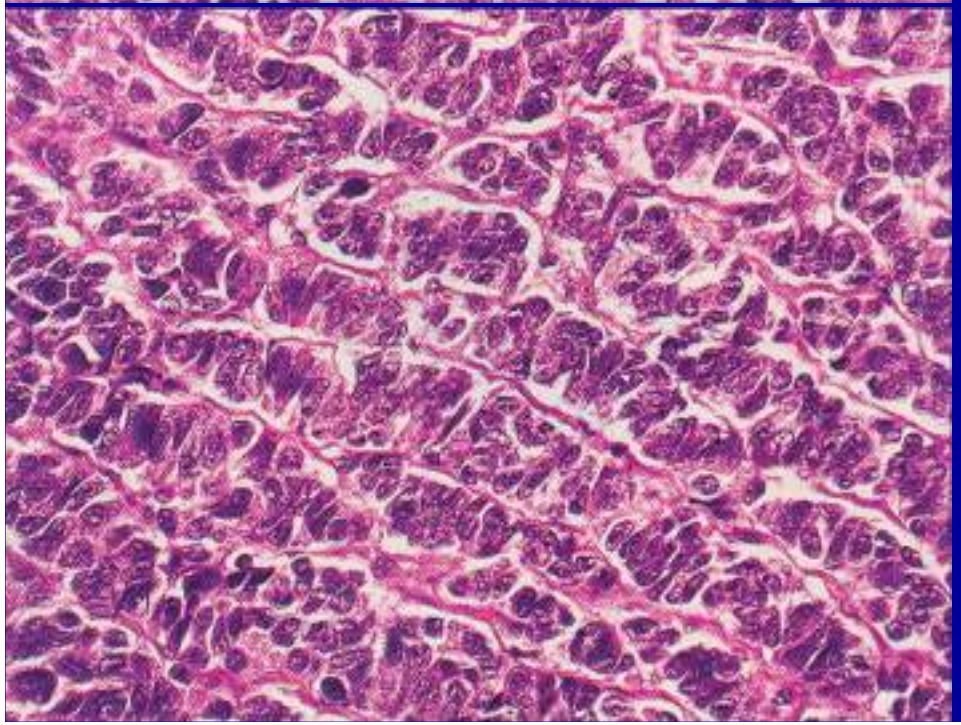
  Tobacco smoking in laryngeal MM

- Airway obstruction, epistaxis, pain, non-healing ulcer & dysphagia

- Polypoidal, sessile, brown, black, pink or white, friable

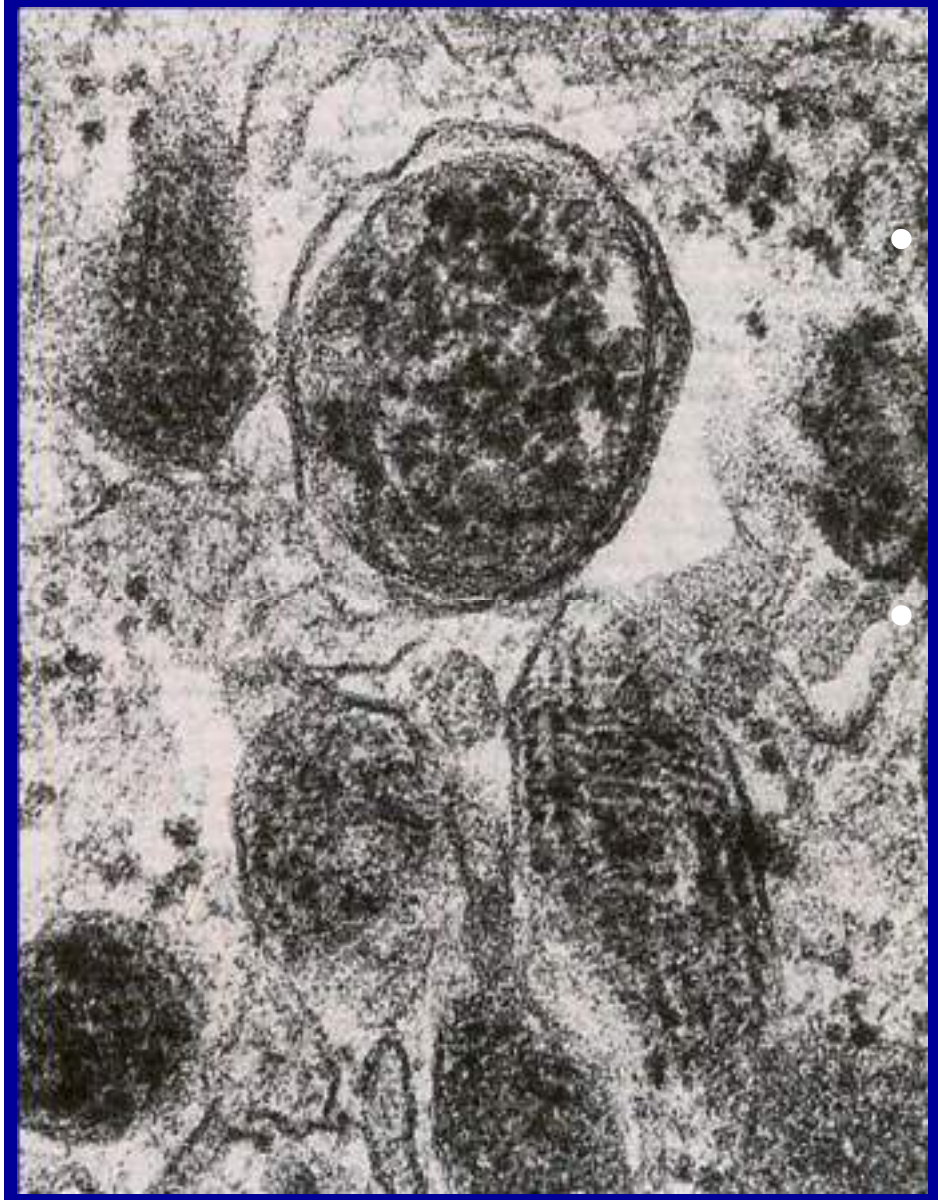






- Epithelioid
- Spindle cell
- Mixed cell type

IHC: S100, HMB-45



EM: melanosome & premelanosome

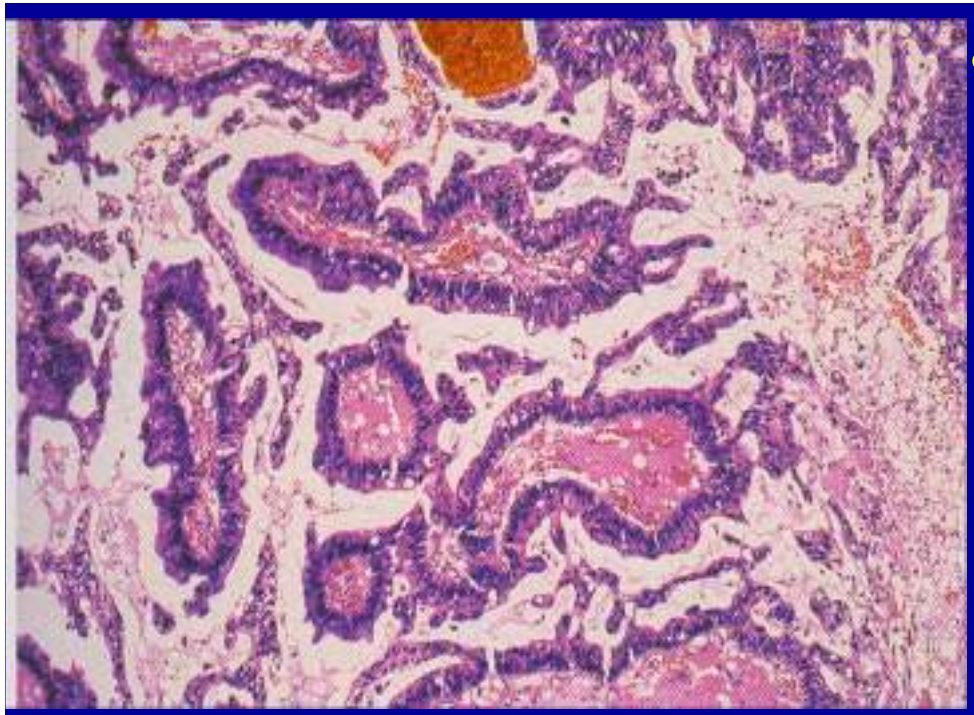
- Aggressive & highly lethal Tm
- Radical surgical excision

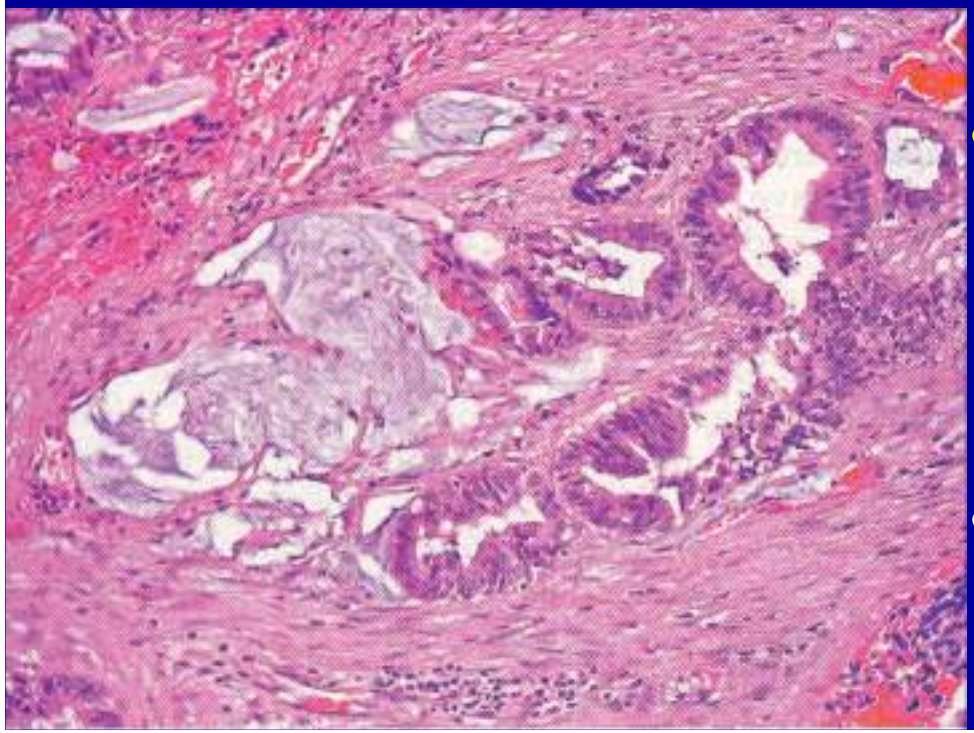
- Prog: poor
- 5-year survival <30%

- Recurrence, mets & death may occur decades after curative therapy
- Mets: lungs, LN, brain

Sinonasal adenocarcinoma

- 10-20% of all primary malignant neoplasms
- Intestinal / non-intestinal types
- M>F
- 5^{th}-7^{th} decades
- **Intestinal type** most frequently involve ethmoid sinus, may arise anywhere
- Nasal stuffiness, obstruction, epistaxis
- Woodworkers, workers in shoe & furniture industries
- **Non-intestinal**: no gender predilection, no occupational/environmental factors

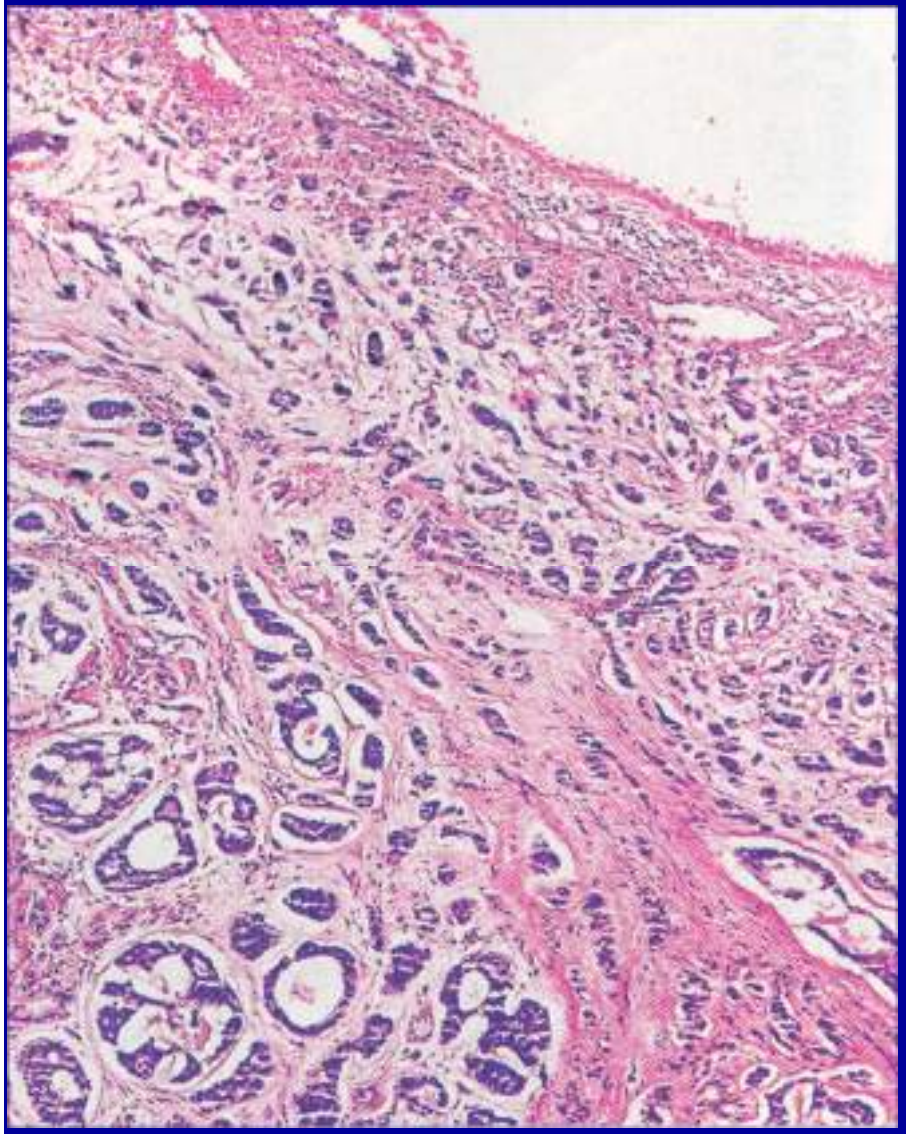




- **Intestinal/colonic types**: papillary-tubular, alveolar-mucoid, alveolar-goblet cell, signet-ring & mixed
  - Papillary-tubular:
    - Grade I: papillary, single layered pseudostratified columnar epith, mild pleo
    - Grade II: tubular >papillary

- **Non-intestinal**:
  - low/high grade
  - Papillary, clear cell & oncocytic
- Treat: complete surgical excision

Malignant salivary gland tumors



1. ACC 5% of sinonasal malignancies
2. Mucoepidermoid carcinoma
3. Acinic cell carcinoma

- Maxillary sinus-most common

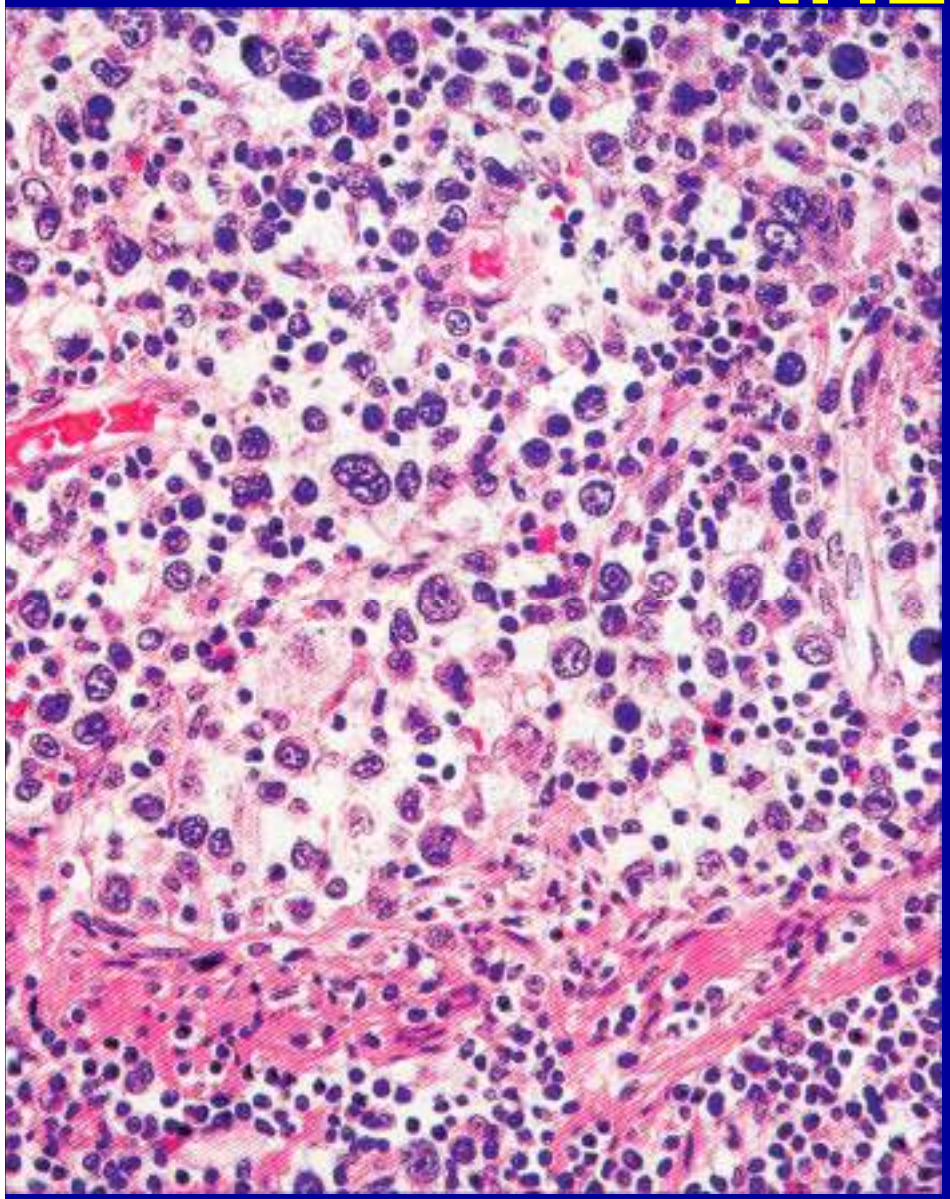
- Treat: WLE & post op RT
  Recurrence: high, related to inadequate surgical excision
- 5-yr & 20-yr survival rates are 75% & 13% respectively

10-yr survival of 75%, 43% and 15% with stage I, II, and III & IV

Non-epithelial malignant neoplasm

- **NHL**
  - Angiocentric T/NK cell lymphoma
  - B-cell lineage malignant lymphoma
  - Plasmacytoma
- **Rhabdomyosarcoma**
- **Chondrosarcoma**
- **Osteosarcoma**
- **Ewing's sarcoma**
- **Teratocarcinosarcoma**

NHL



Nasal angiocentric T/NK cell lymphoma, angiocentric immunoproliferative lesions, PTCL

1.5% of NHL in USA

6.7-8% in Asia/south America

6^{th}-8^{th} decades

Nasal cavity/paranasal sinuses

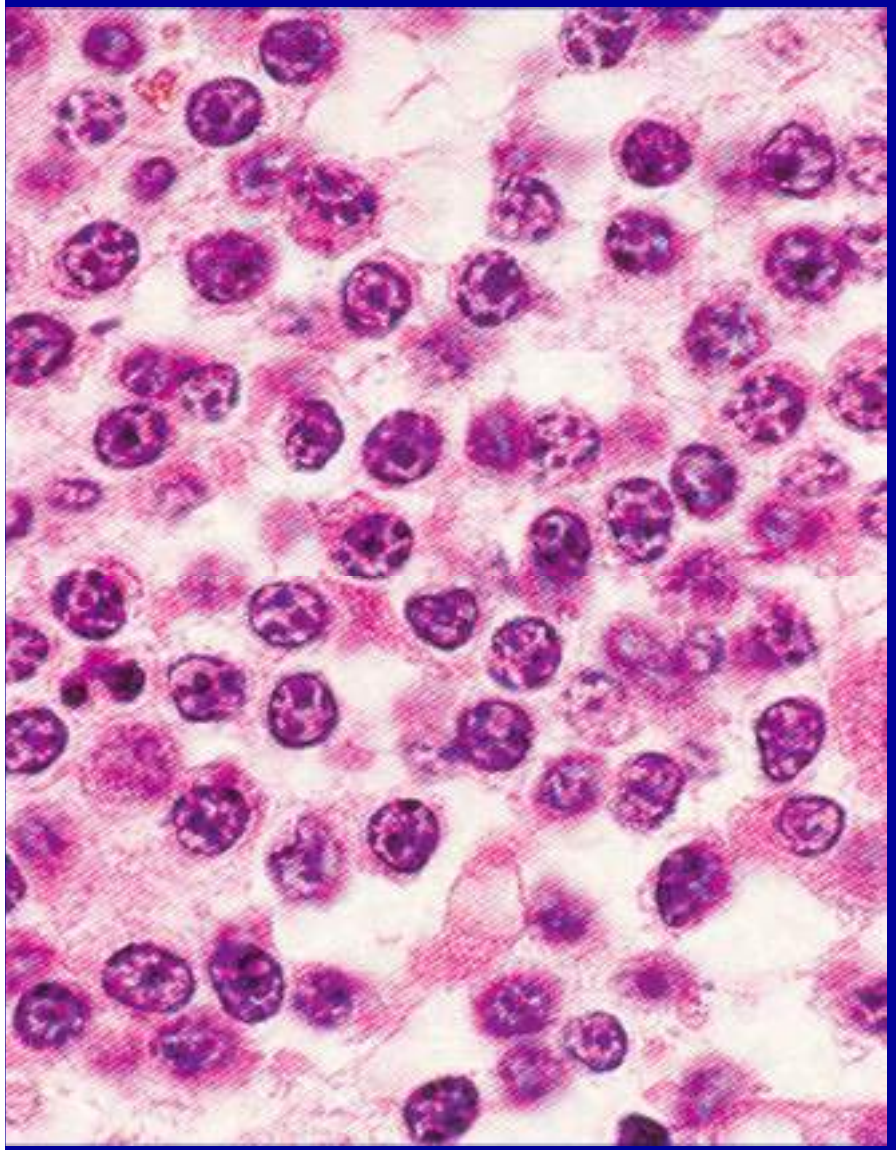
Low gr: nasal obstruction

High gr: non-healing ulcer, cranial nerve inv, facial swelling, pain, epistaxis

DLBCL: soft tissue/osseous destruction, proptosis

Angiocentric T/NK cell lymphoma: mid-facial region destruction

Extramedullary plasmacytoma



- 3-5% of all plasma cell neoplasms

  8% of EMP in head & neck

  8% primary
- M>F
- Usually 40 yrs of age
- 25% pts have M component
- Disappearance of M component may be indicative of cure
- RT or local resection followed by RT
- Median survival 7-9 yrs / after dissemination <2 yrs

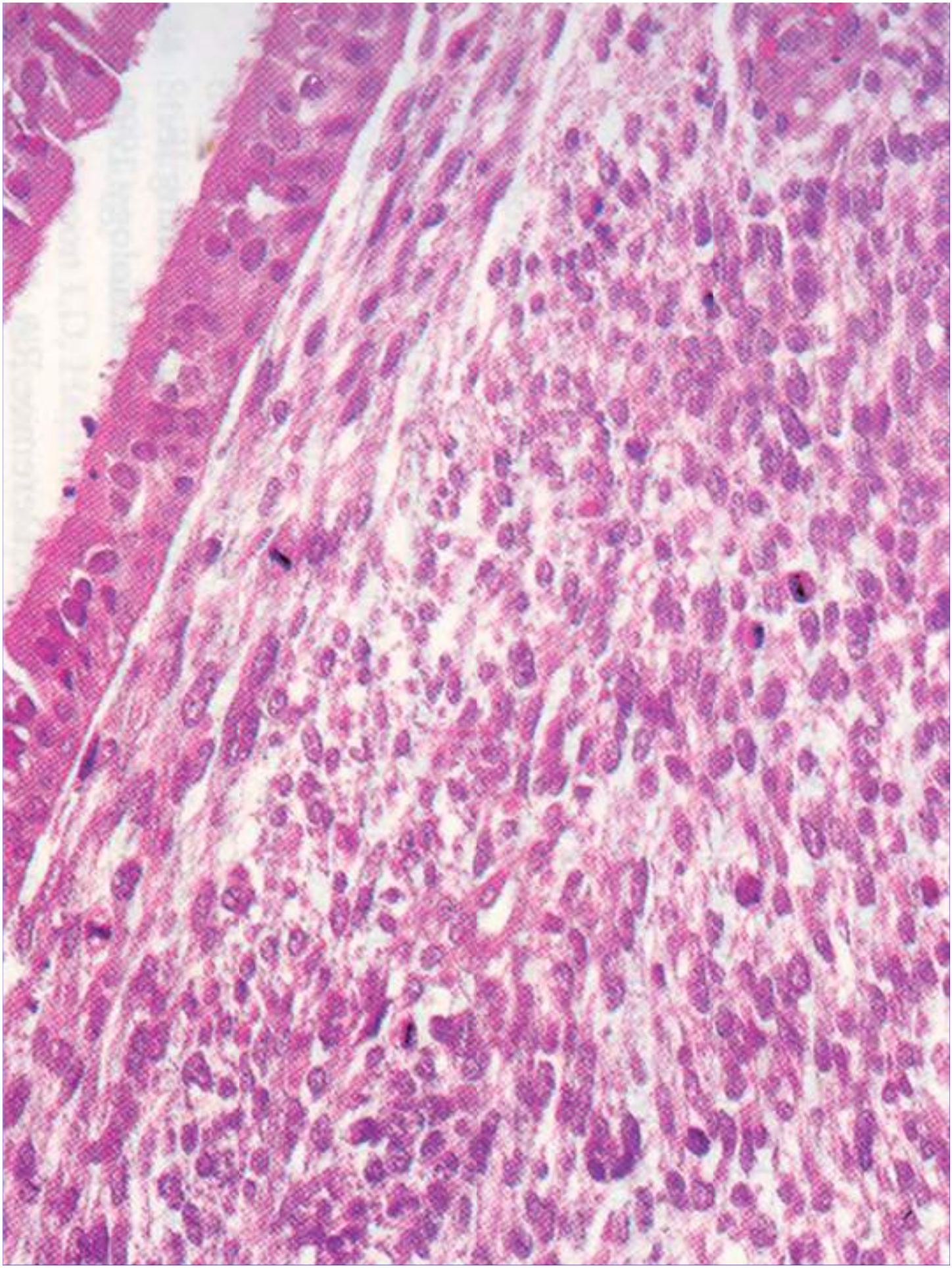
Rhabdomyosarcoma

- Primarily a disease of pediatric population
- 50% of all soft tissue sarcomas in head & neck
- In pediatric age groups up to 75%
- Most common aural malignancy

  Orbit, nasopharynx, middle ear/temporal bone, sinonasal tract
- Nodular, lobular or polypoid mass

  25% assume sarcoma botryoides
- Embryonal 80-85%, alveolar 10-15%

  Spindle cell & pleomorphic types: rare



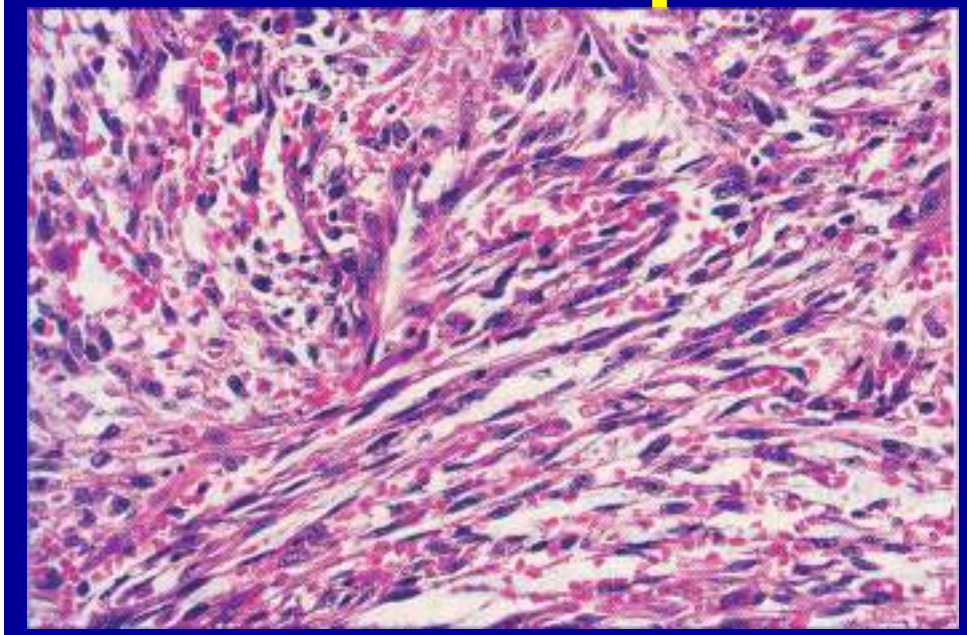
- With surgical excision 5-yr survival <20%
- With multimodality therapy (surgery+RT+CT) **5-year survival**

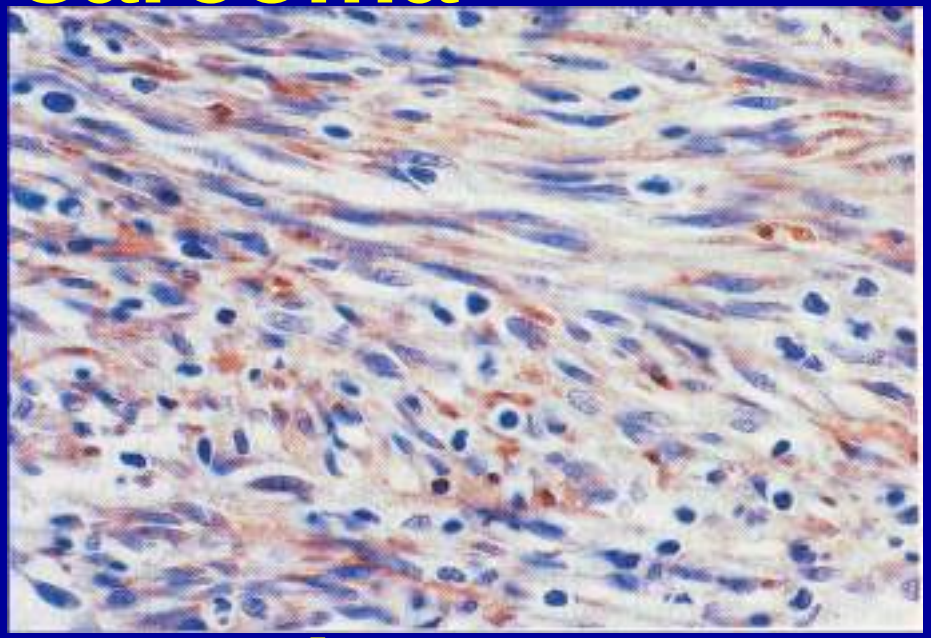
  Stage I: 83%
  Stage II: 70%
  Stage III: 52%
  Stage IV: 20%

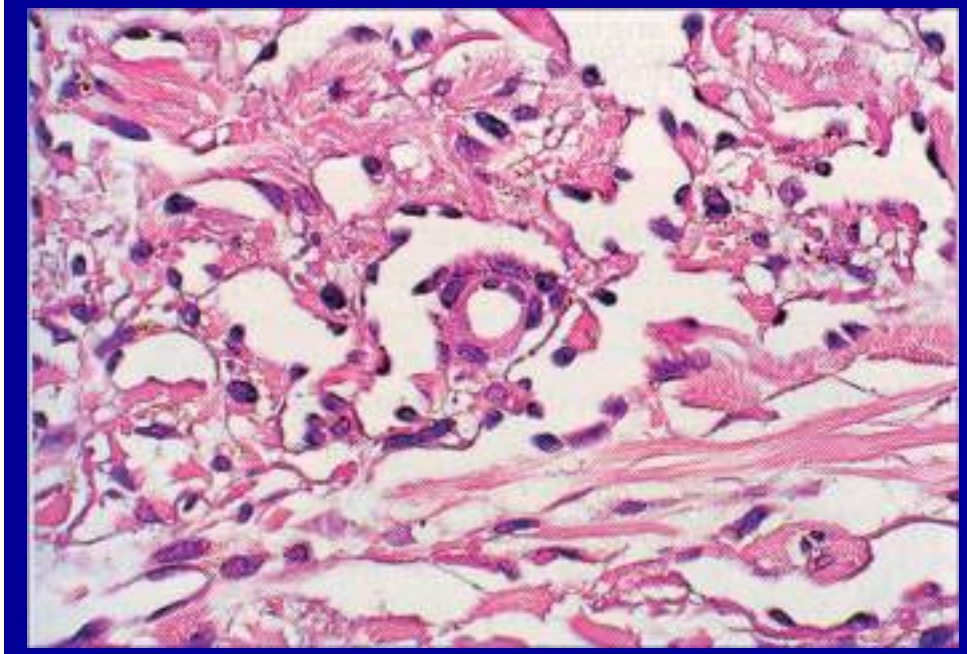
- **IRS**

1) **eye-orbit RMS** 5-yr survival 92%
2) **parameningeal** (middle ear-mastoid, external auditory canal, nasopharynx, sinonasal region, infratemporal fossa) 70%
3) **other head & neck sites** (neck, scalp, oropharyngeal region, larynx, parotid gland) 55%

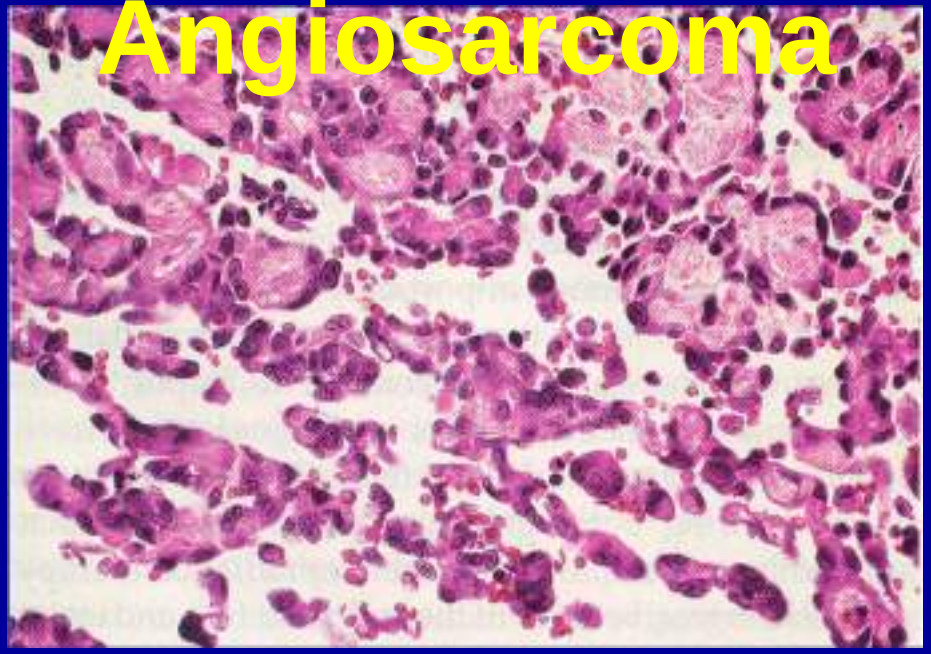
Kaposi’s sarcoma







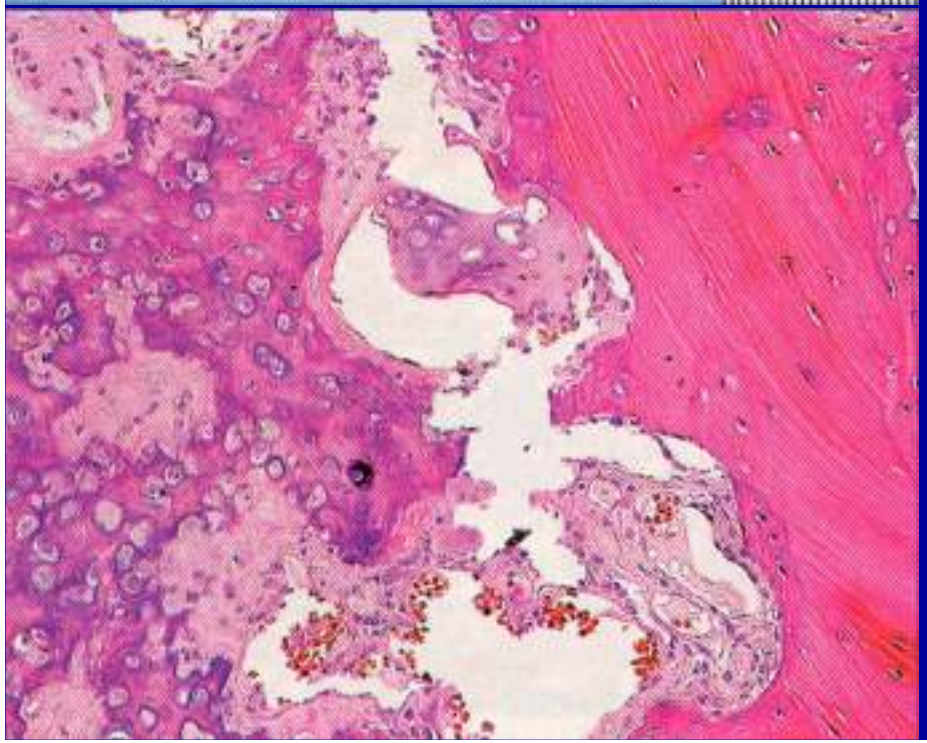
Angiosarcoma



Osteosarcoma

- 10% of OS occur in head & neck
- Most common primary malignant tumor of jaw (mandible>maxilla)
- Etiology
  - Most arise de novo
  - Radiation therapy, Paget's disease, fibrous dysplasia
- Elevated serum alkaline phosphatase

Osteosarcoma



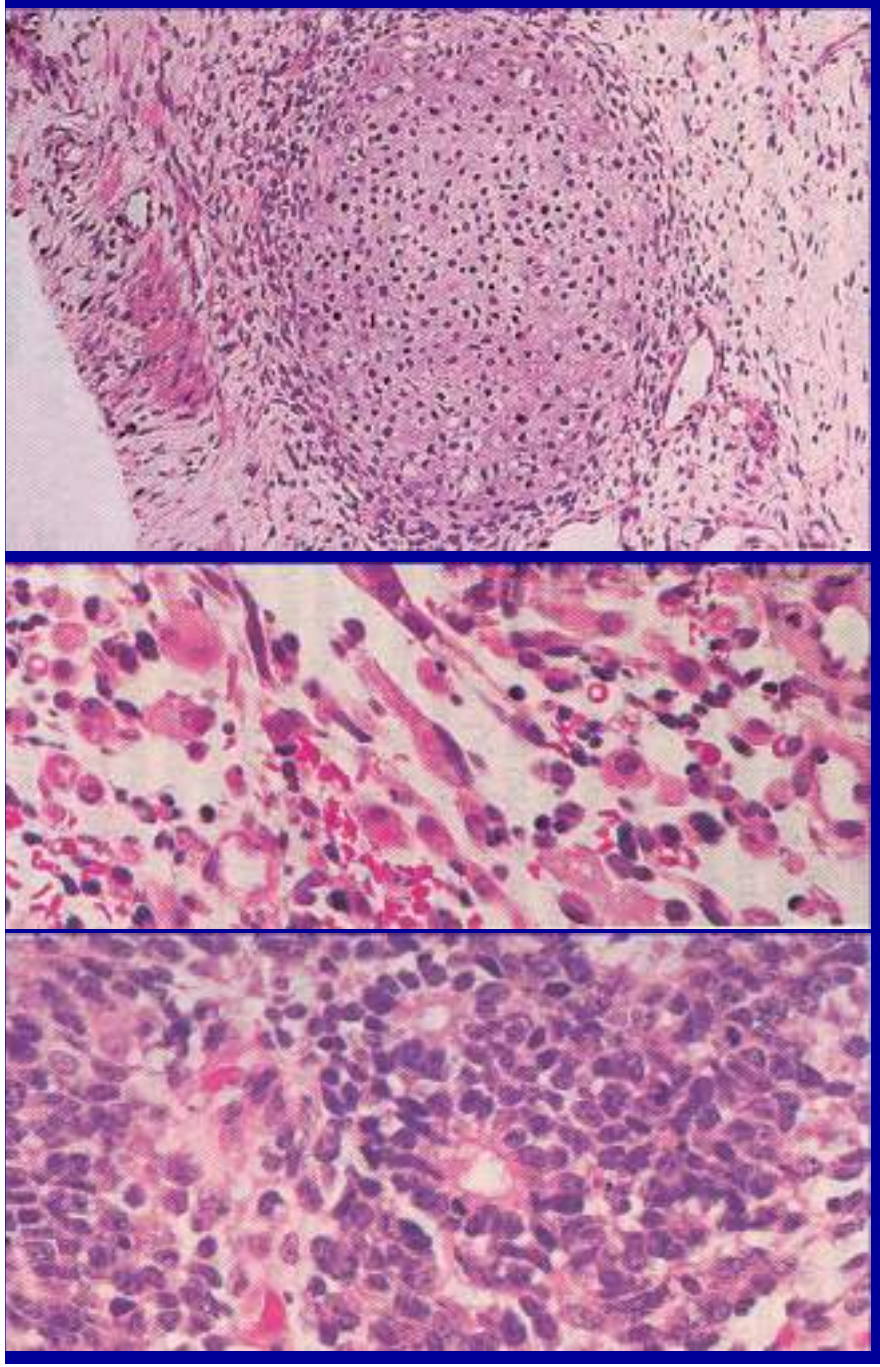
- Craniofacial OS have better prognosis than extrafacial tumor
- Overall 5-yr survival <35%
- Os arising in Paget's disease are highly malignant, 5-yr survival rates negligible
- Treat: multimodality therapy

Chondrosarcoma

- 5-12%
- 4^{th}-7^{th} decades
- 2% in pts <20 yrs of age
- Commonest site: larynx
- 5-yr survival 70%

Chordoma

- Uncommon below 40 yrs of age
- Dorsum of sella, clivus & nasopharyngeal regions
- Expansile, destructive lesion
- Treat: complete surgical excision
- 5-yr survival
- <40 years 100%, >40 years 22%



Malignant teratoma

- Unique sinonasal malignancy

  Carcinosarcoma & teratoma (primitive neuroepith)

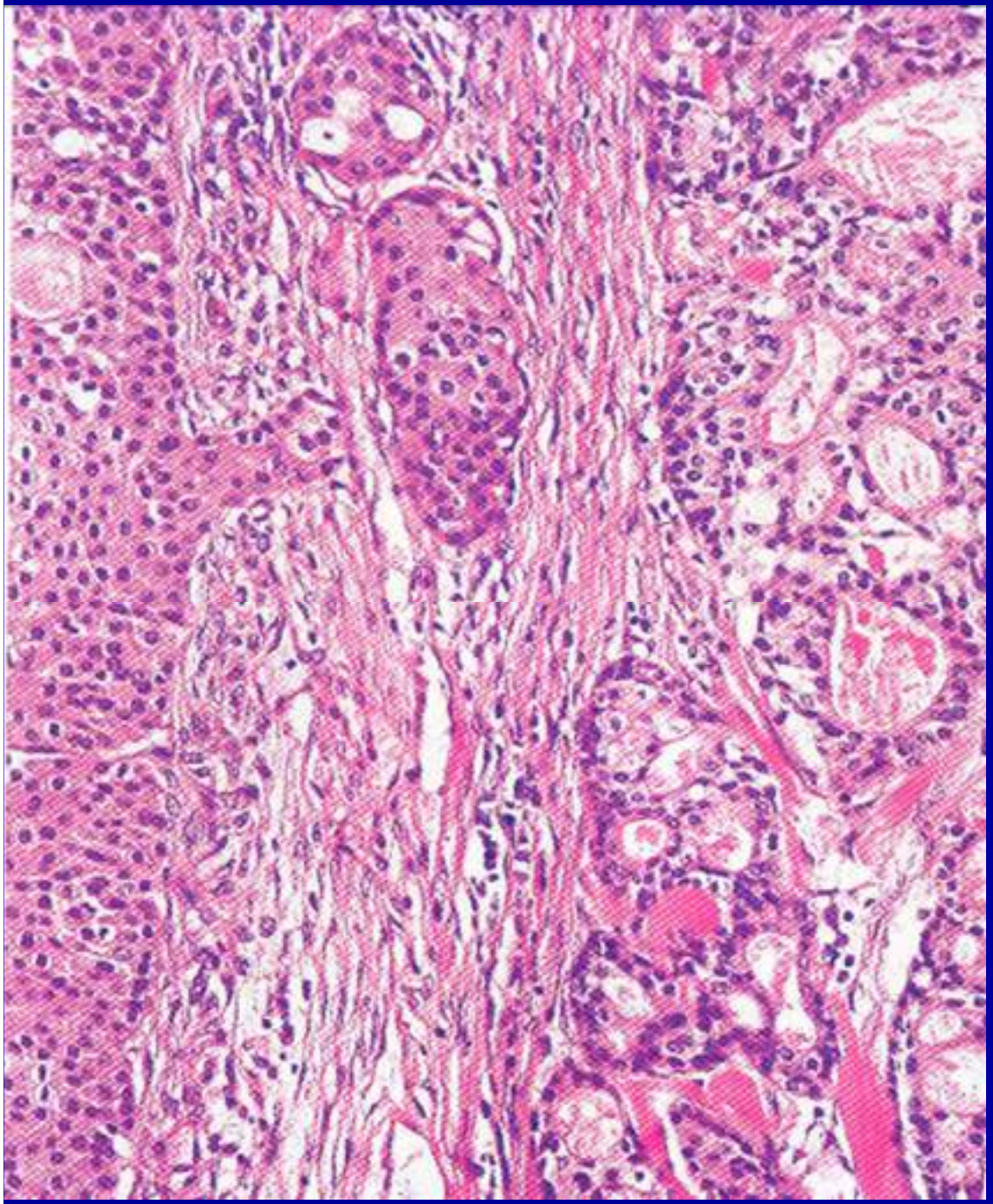
  Neuroectodermal Tm with divergent different^{n}
- Adults
- Prognosis: 60% pts not surviving beyond 3 yrs

Tumors of oral cavity

- Squamous cell carcinoma
  - Spindle cell ca
  - Adenoid squamous cell & adenosquamous
  - Basaloid squamous cell carcinoma
  - Verrucous squamous cell carcinoma
  - Papillary squamous cell carcinoma
- Odontogenic carcinomas
  - Malignant ameloblastoma
  - Primary intraosseous carcinoma
  - Malignant odontogenic epithelial tumors
  - Clear cell odontogenic carcinoma
- Odontogenic sarcomas
  - Ameloblastic fibrosarcopma
  - Ameloblastic fibrodentinosarcoma & fibroodontosarcoma
  - Odontogenic carcinosarcoma

Salivary gland tumors

- **Low grade**
  - Acinic cell carcinoma
  - PLGA
  - Basal cell Adenocarcinoma
  - Hyalinizing clear cell carcinoma
  - Epithelial-myoepithelial carcinoma (1%)
  - Carcinoma ex-pleomorphic adenoma, low grade
  - Cystadenocarcinoma
  - Adenocarcinoma, low grade
- **Intermediate grade**
  - ACC
  - Salivary duct carcinoma
  - Malignant myoepithelioma
- **High grade**
  - ME carcinoma
  - Adca, NOS, high grade
  - Squamous cell ca
  - Salivary duct ca
  - Carcinoma ex-pleomorphic adenoma, high grade
  - Oncocytic ca
  - Large cell undifferentiated carcinoma
  - Small cell ca
  - ACC



ME carcinoma

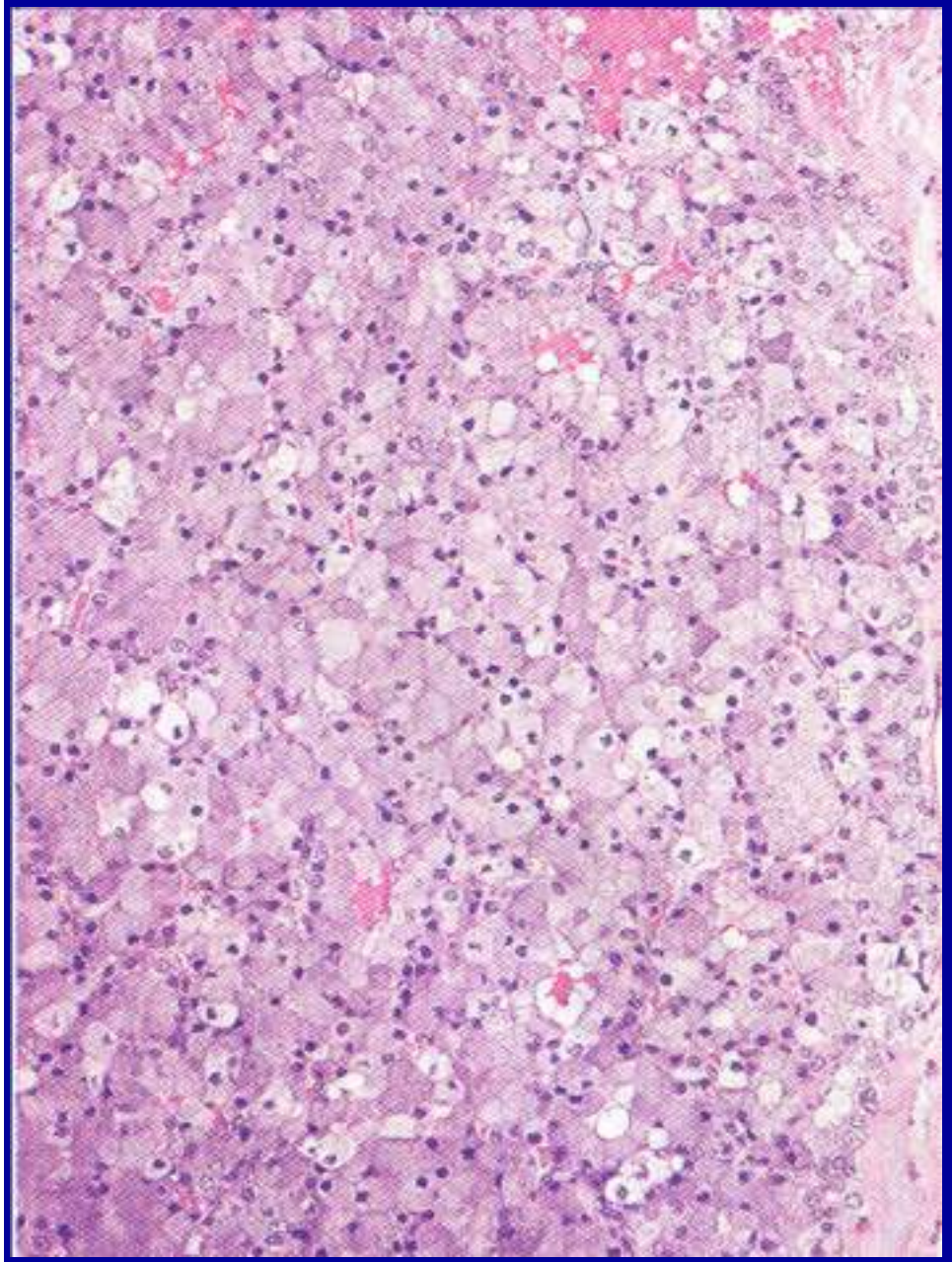
Most common malig tumor in children

Low/intermediate/high

5-yrs survival rate 98% for low grade tumor, 56% for high grade tumor

Prognosis depends on age, sex, location, vascular invasion, necrosis, mitosis, MIBI-LI, DNA ploidy

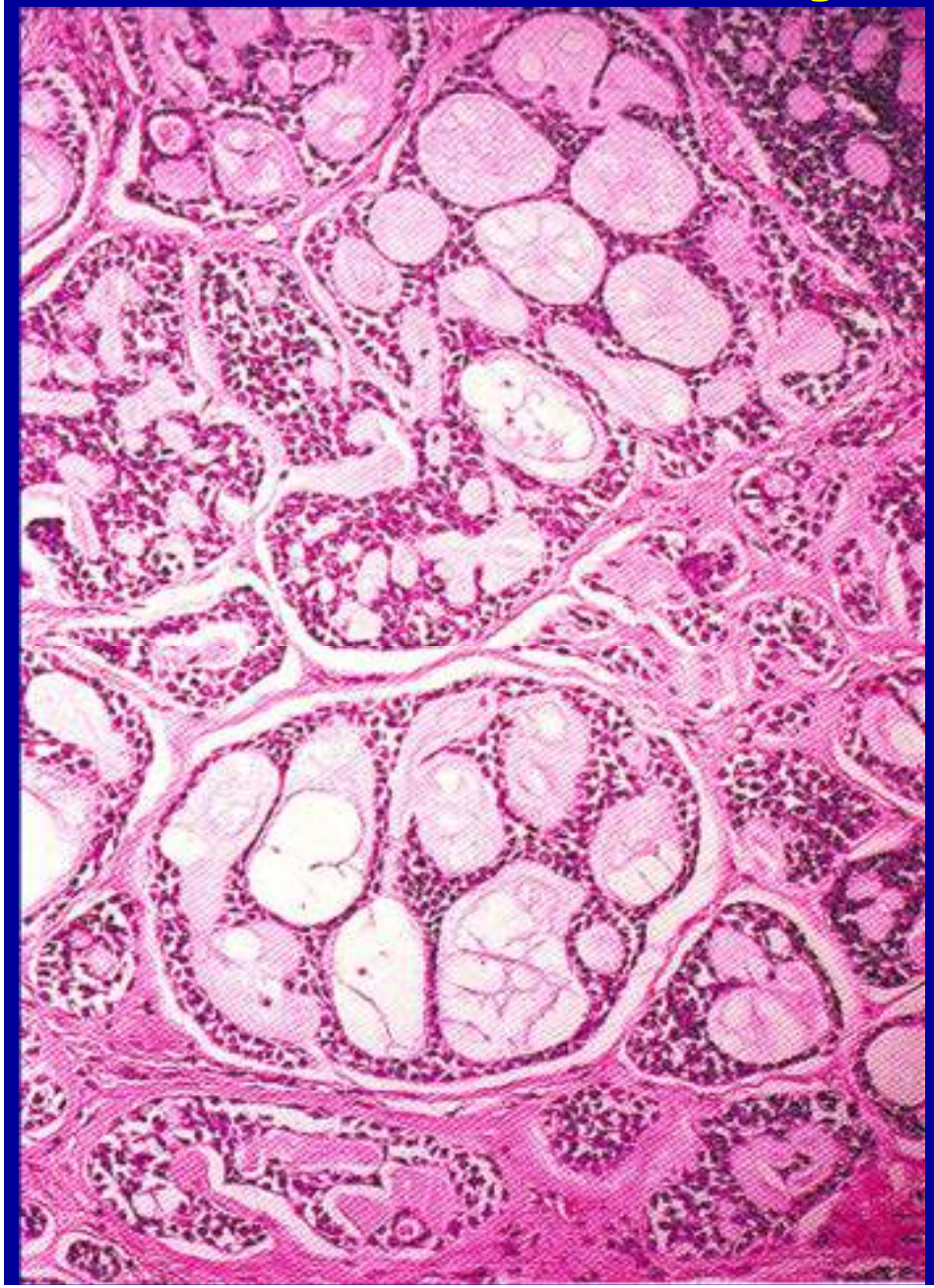
Acinic cell carcinoma



- 1-3%
- Parotid (84%), submandibular gland, buccal mucosa, upper lip and palate
- Commonest malig B/L (3%)

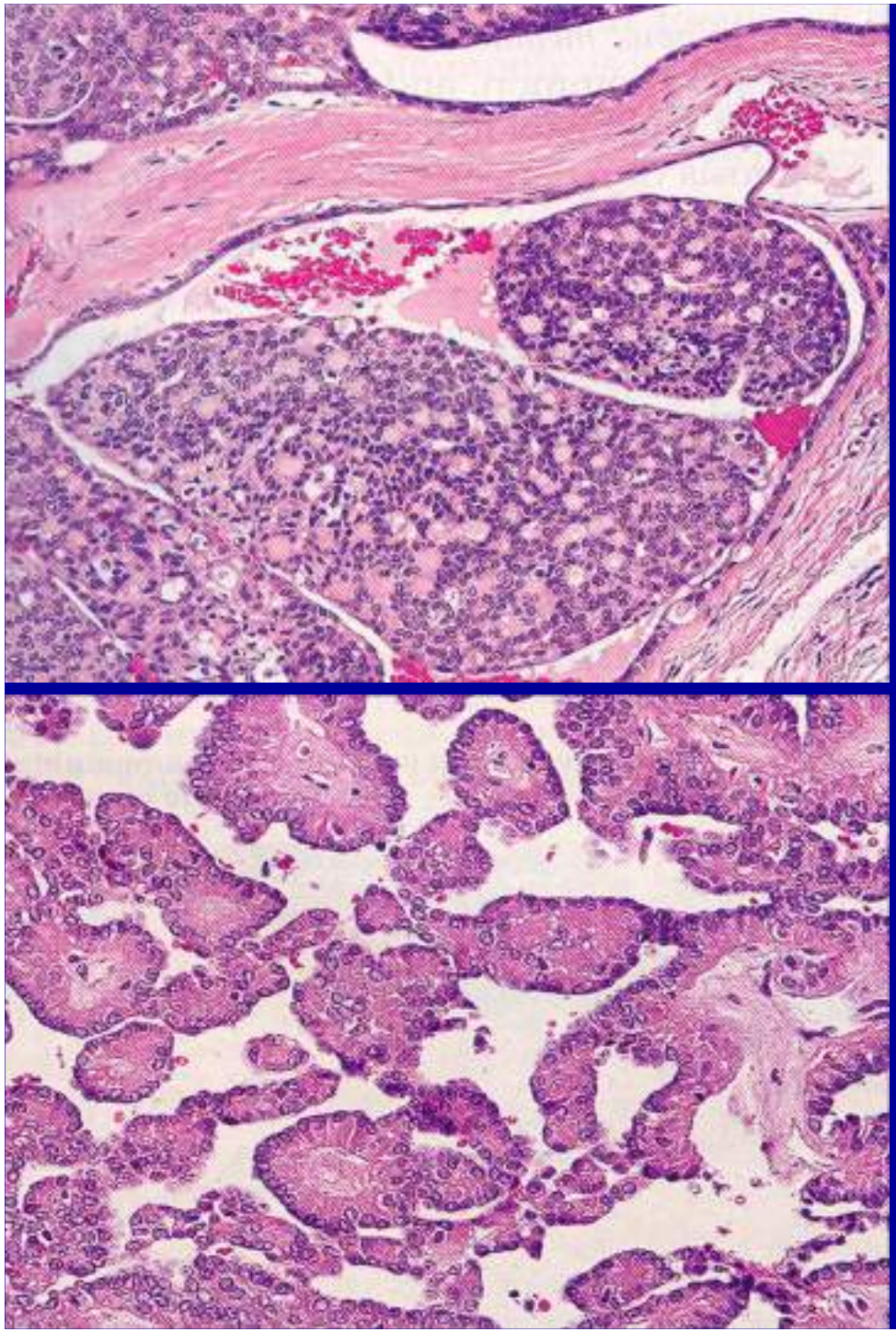
- Pain facial nerve palsy (5-10%)
- Indolent, recurrence in 44% of pts
- Overall survival 90% at 5 years, 83% at 10 yrs, 67% at 15 yrs

Adenoid cystic carcinoma



- 4^{Th}-6^{th} decades
- Parotid, SM gland, palate
- Slow growing, perineural invasion
- Prognosis: poor, multiple local recurrences & mets

  5-yr survival 60-75%
- Treat: RT



PLGA

- Adult female
- Palate most common site
- Low grade malig Tm
- Tumor with papillary component are associated with higher incidence of LN mets
- May undergo transformation to a high-grade tumor
- Treat: surgery
- Post op RT for high grade Tm

Thyroid and parathyroid malignancies

A. **Well-differentiated type**
   - Papillary carcinoma
   - Follicular carcinoma

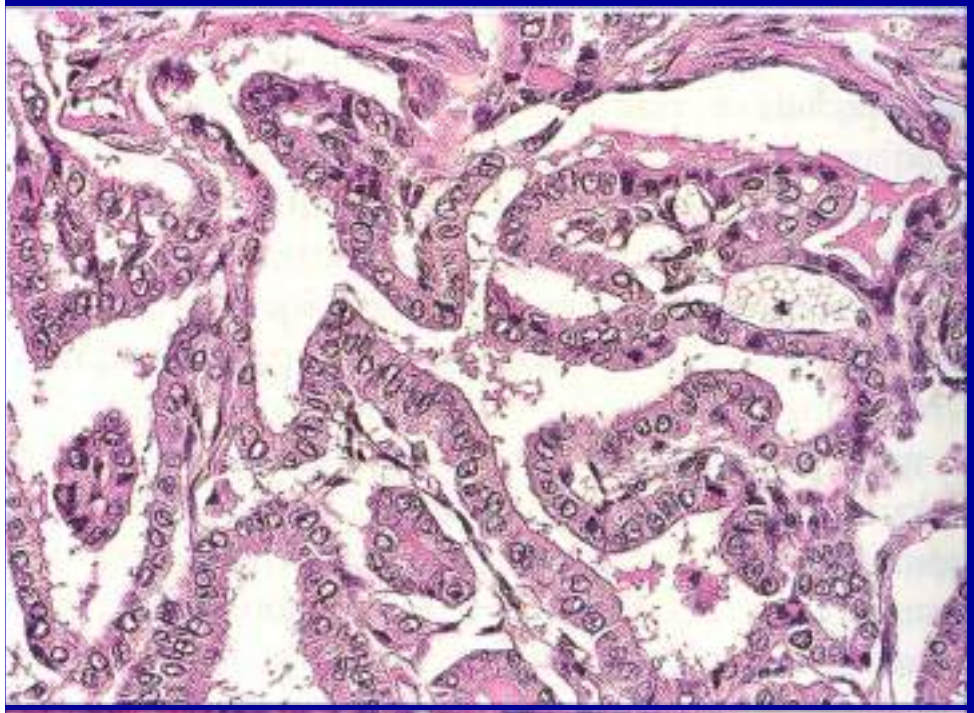
B. **Poorly differentiated carcinoma** (insular carcinoma)

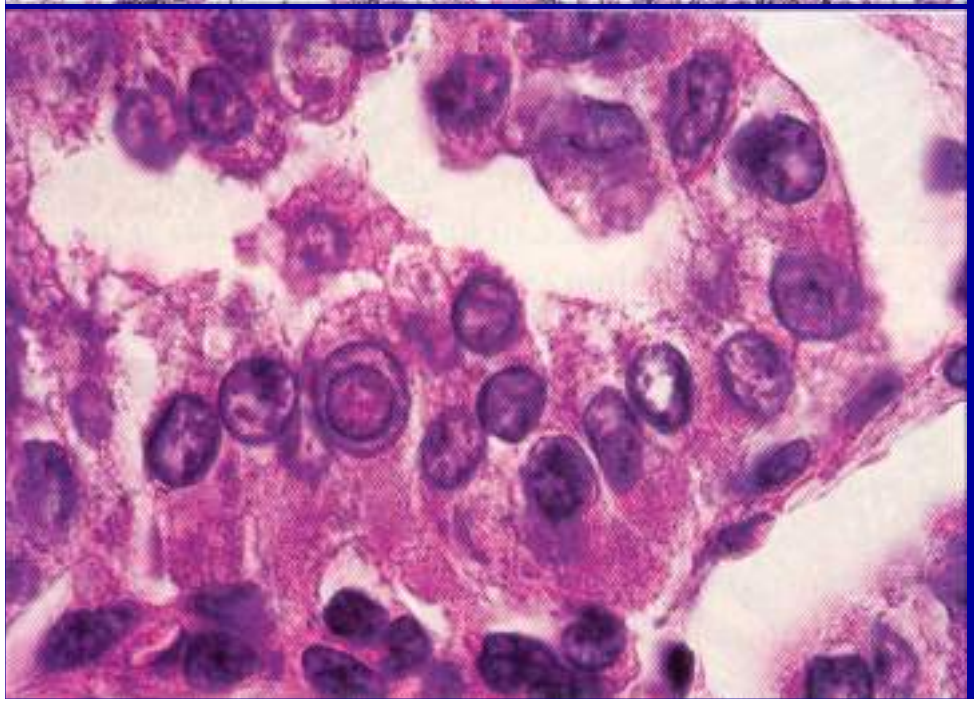
C. **Anaplastic carcinoma**

- **Medullary carcinoma**

- Other malignancies

- **Parathyroid carcinoma**

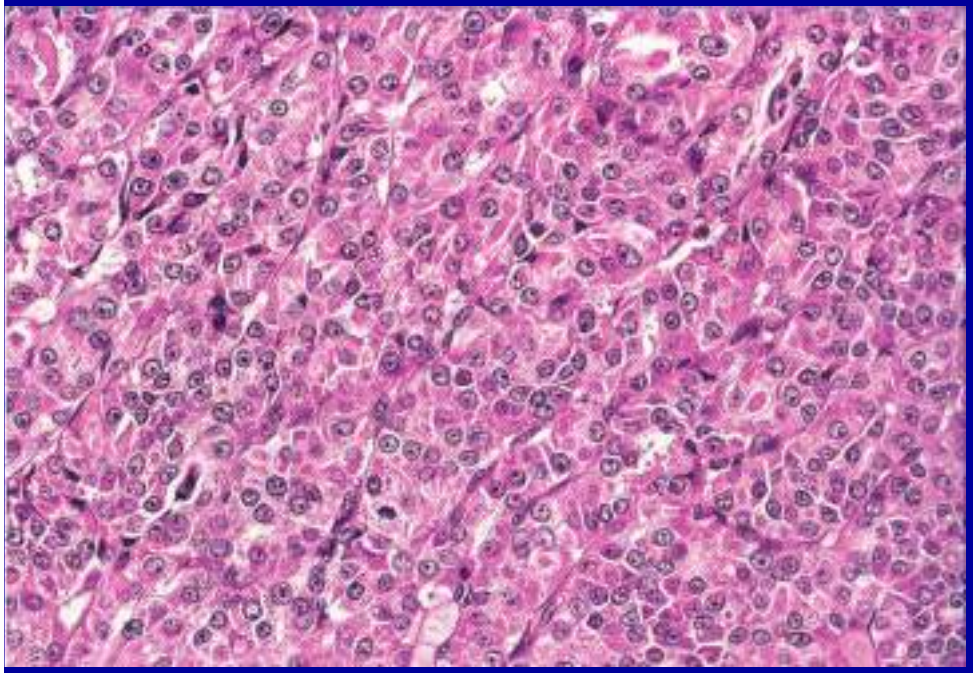


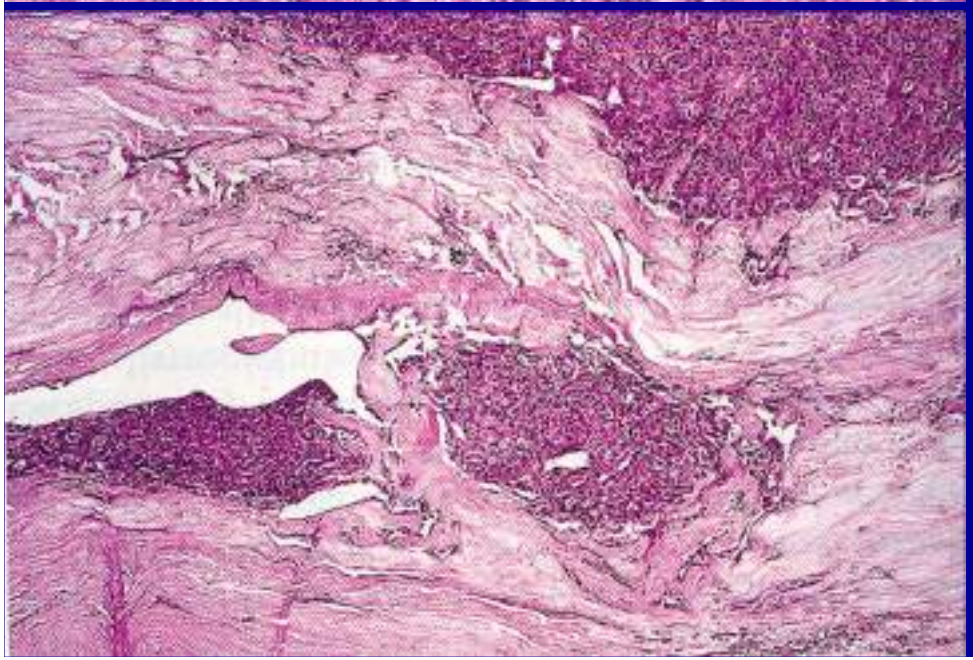


Papillary carcinoma

- Most common
- F>M
- Mean age 40 yrs
- >90 thyroid malignancies
- Irradiation, Hashimoto's thyroiditis
- RET/PTC1, RET/PTC2, RET/PTC3
- **Prognosis**: Age, sex, extrathyroidal extension, microscopic variants, irradiation, Tm size, capsule /margin, multicentricity, dist mets, DNA ploidy

Follicular carcinoma

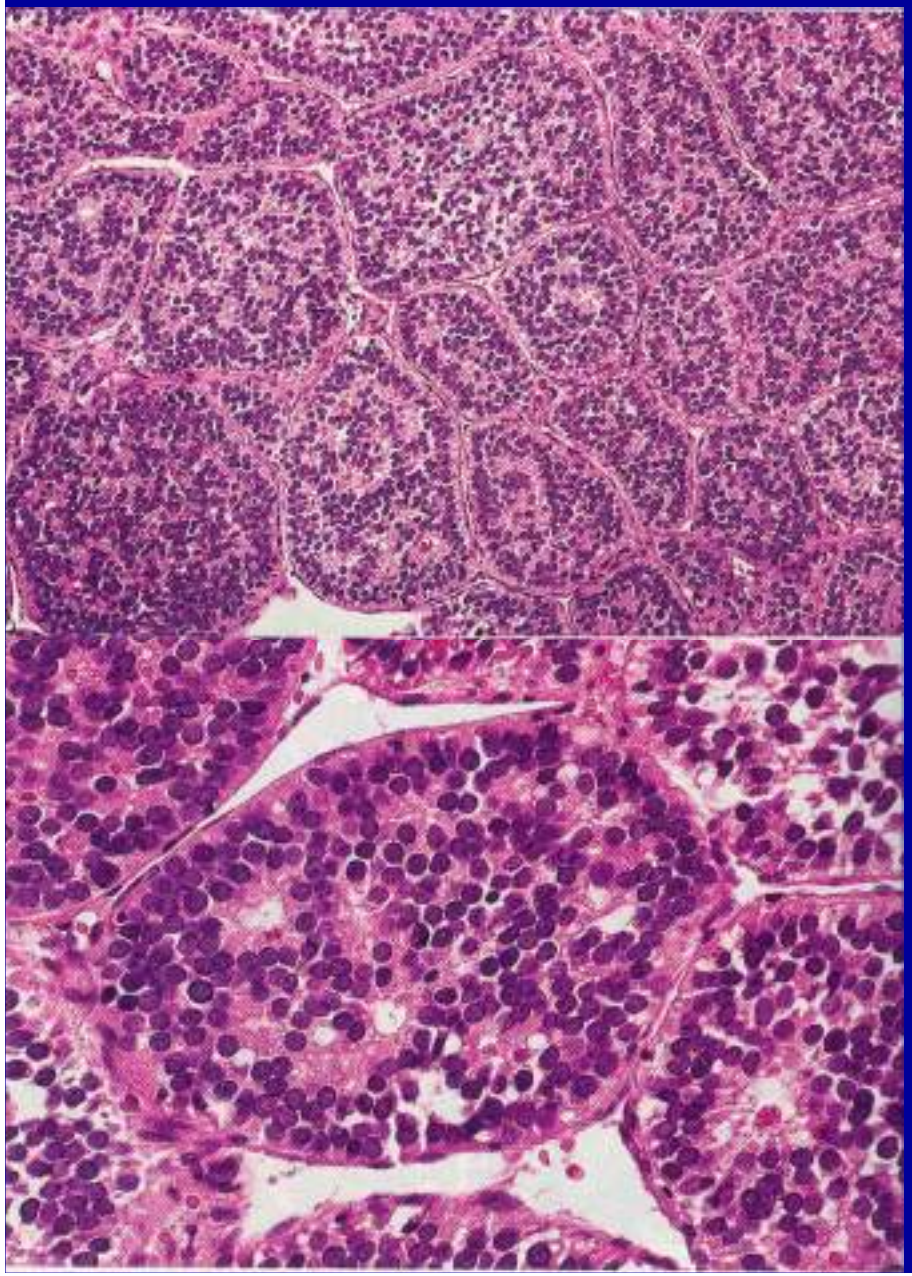




- Uncommon
- Vessels/capsule invasion
- **Encapsulated**
  - Capsular inv only
  - Limited (<4) vascular invasion
  - Extensive (≥4) vascular invasion
- **Widely invasive**

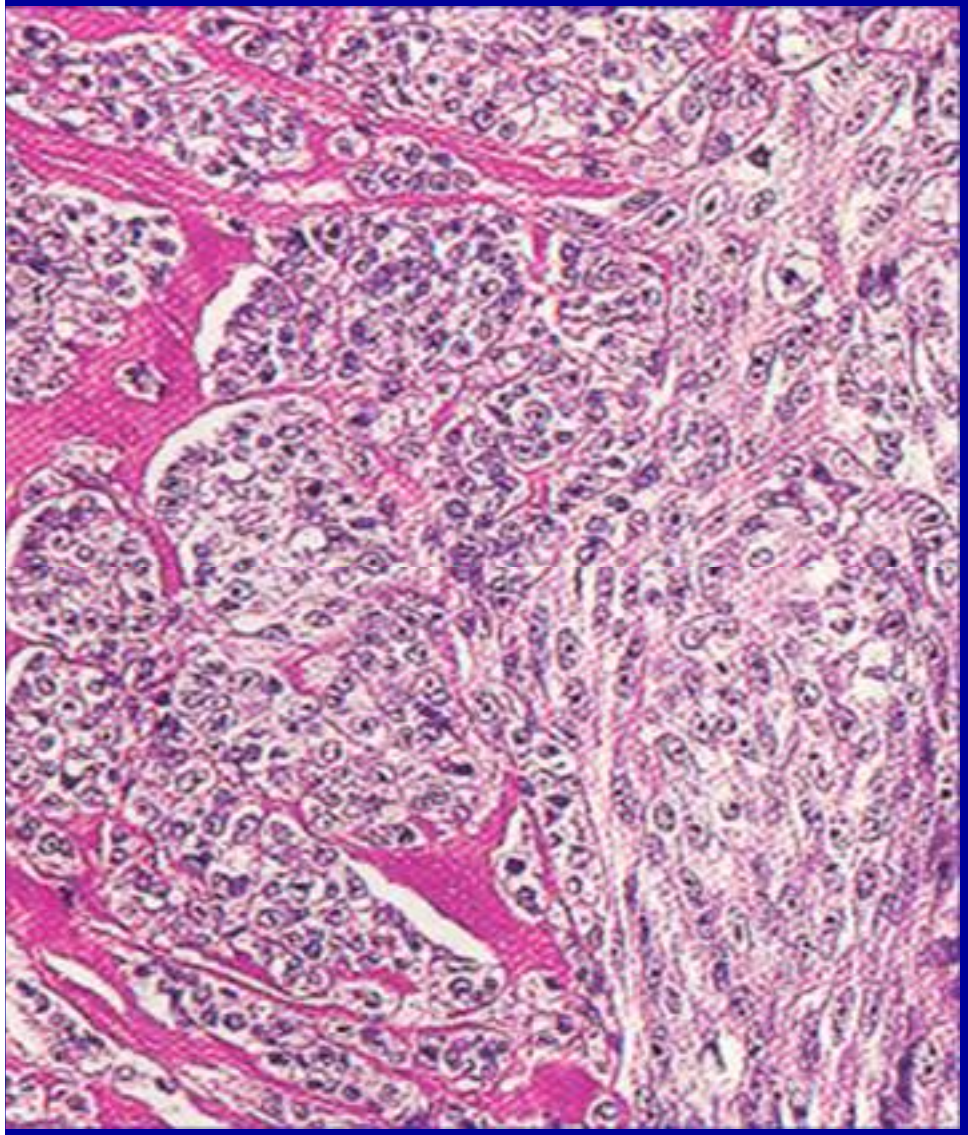
- 5-yr mortality rate 20-40%

Insular carcinoma



- Older age groups
- Grossly invasive
- Frequent LN & blood borne metastases
- Bcl2 exp >80%, p53 +ve

Anaplastic carcinoma of thyroid

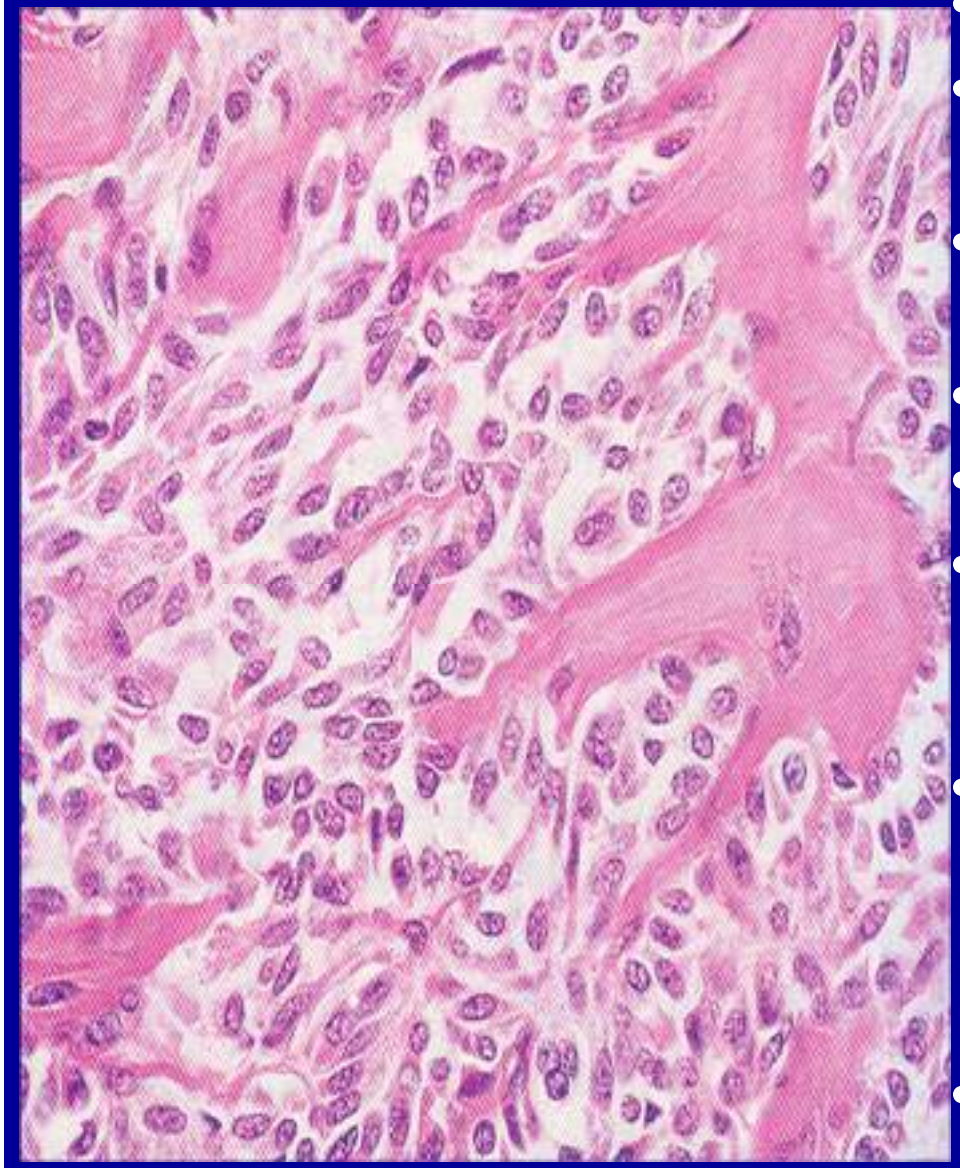


- Elderly pts
- Rapidly growing
- Hoarseness, dysphagia & dyspnoea
- Extrathyroidal extension at initial presentation
- Highly necrotic, hemorrhagic

  infiltrate, muscle, esophagus, trachea, skin & bone

  LN & distant mets common
- Mortality >95% (mean survival <6 months)

Medullary carcinoma



- C-cell origin
- Sporadic (80%)/ mean age 45 yrs/ solitary
- Familial /<35 yrs/ multiple, bilateral
- Component of MEN II
- RET (10q11.2) gene mutation
- Locally invasive, mets in cervical / mediastinal LN, lung, liver & skeletal system
- Treat: total thyroidectomy & cervical lymphadenectomy

  Responsive to radioactive iodine, RT & CT
- Local recurrence 35%
- 5-yr survival 70-80%

Orbital malignancies

- Basal cell carcinoma
- Squamous cell carcinoma
- Markel cell carcinoma
- Sebaceous adenocarcinoma / Adca of meibomian gland
- Signet ring carcinoma
- Retinoblastoma
- Malignant melanoma
- ACC
- Lymphomas
- RMS / MFH / OS / ASPS / LMS / Ewing’s / PNET

Diagnostic procedures

- FNAC: highly sensitive & specific
- Biopsy
  - H&E
  - Histochemistry
  - IHC
  - EM
- Cytogenetic studies