

Role of pathology in otorhinolaryngology (head and neck pathology)

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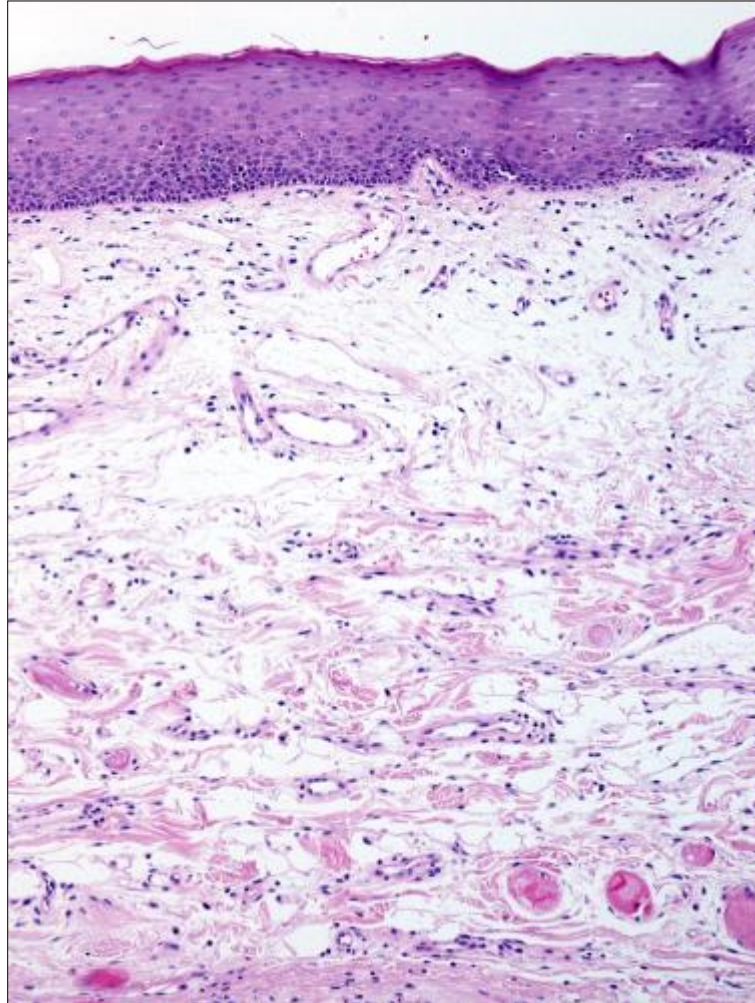
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Types of tissues in head and neck

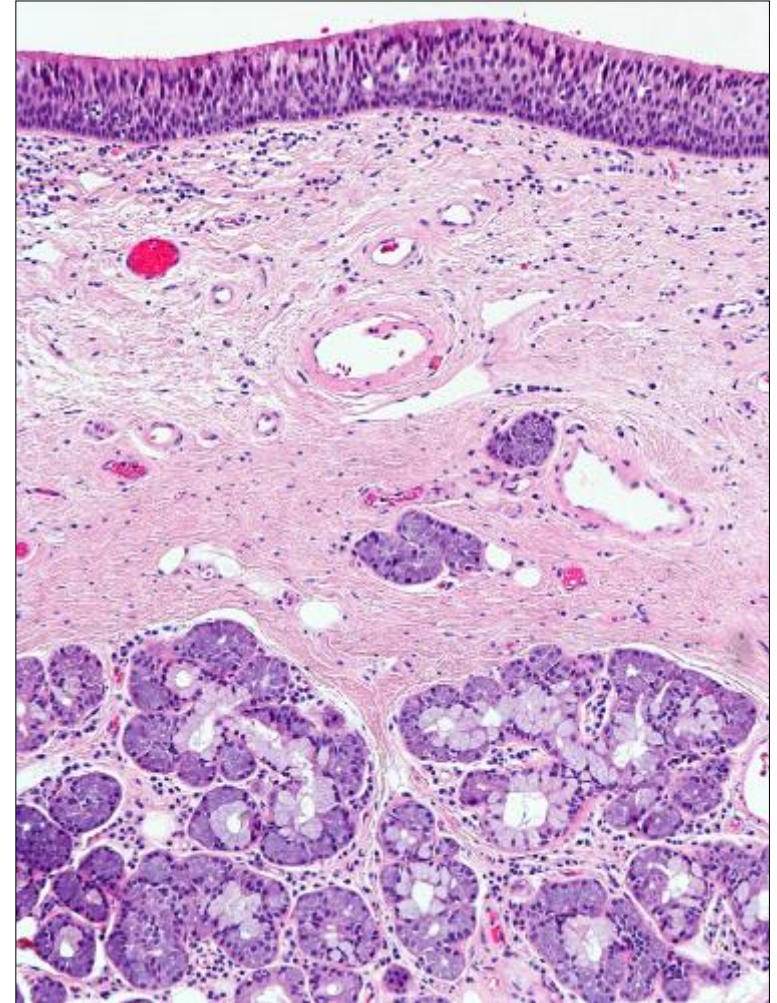
1. Mucosal membrane
2. Skin
3. Salivary glands
4. Waldeyer's ring
5. Lymph nodes
6. Soft tissue and bone
7. Endocrine glands

Normal mucosa

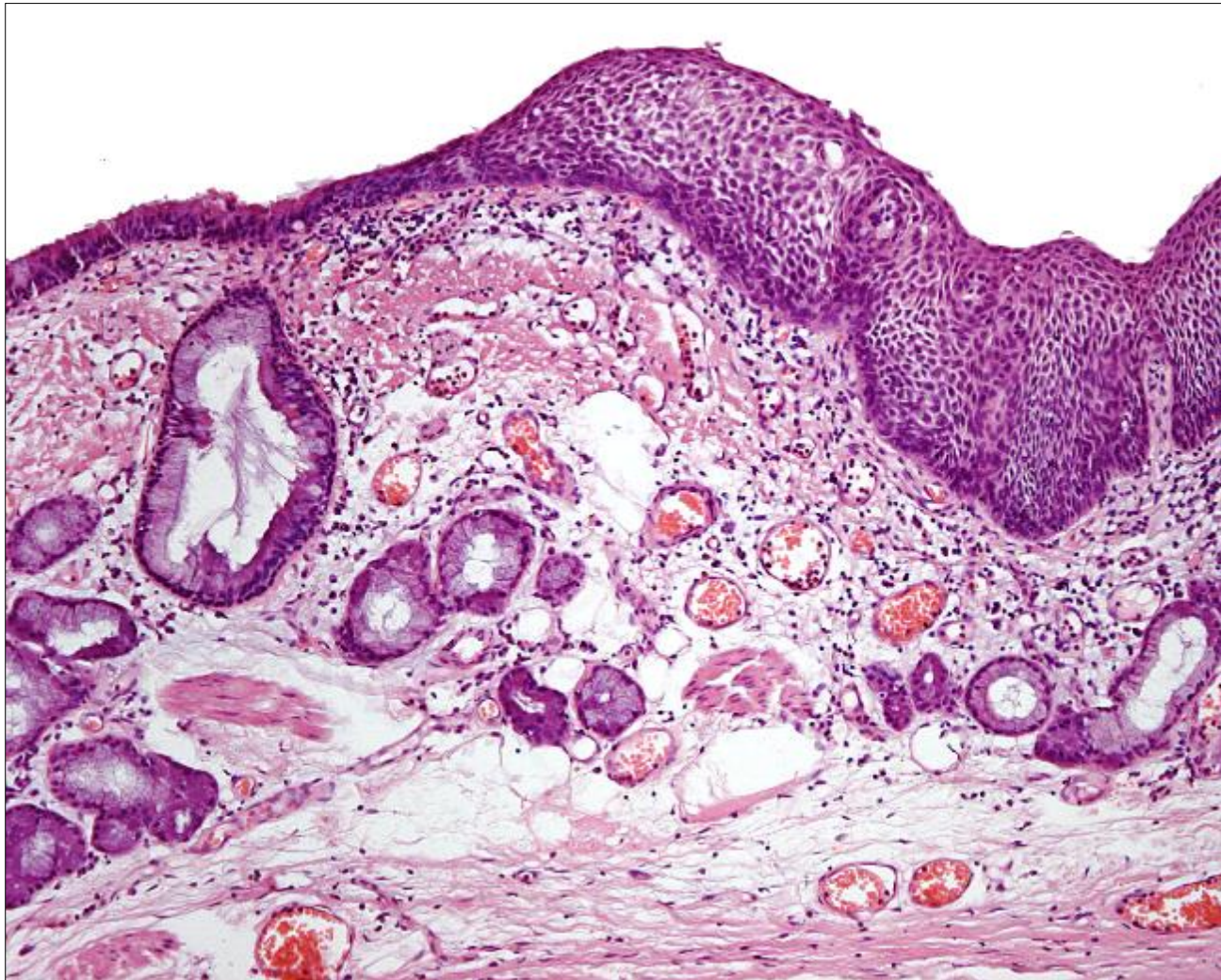
oral cavity



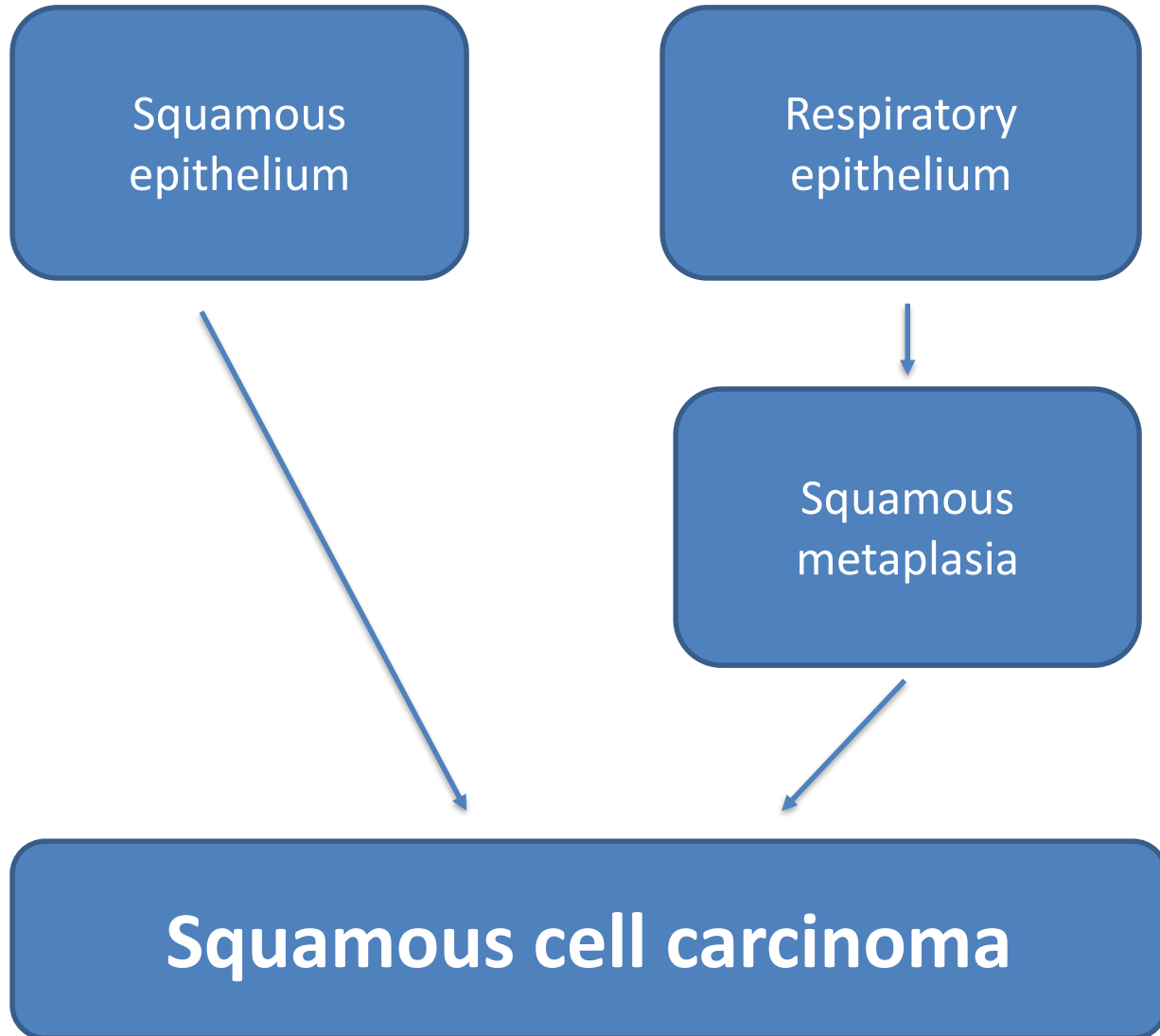
larynx



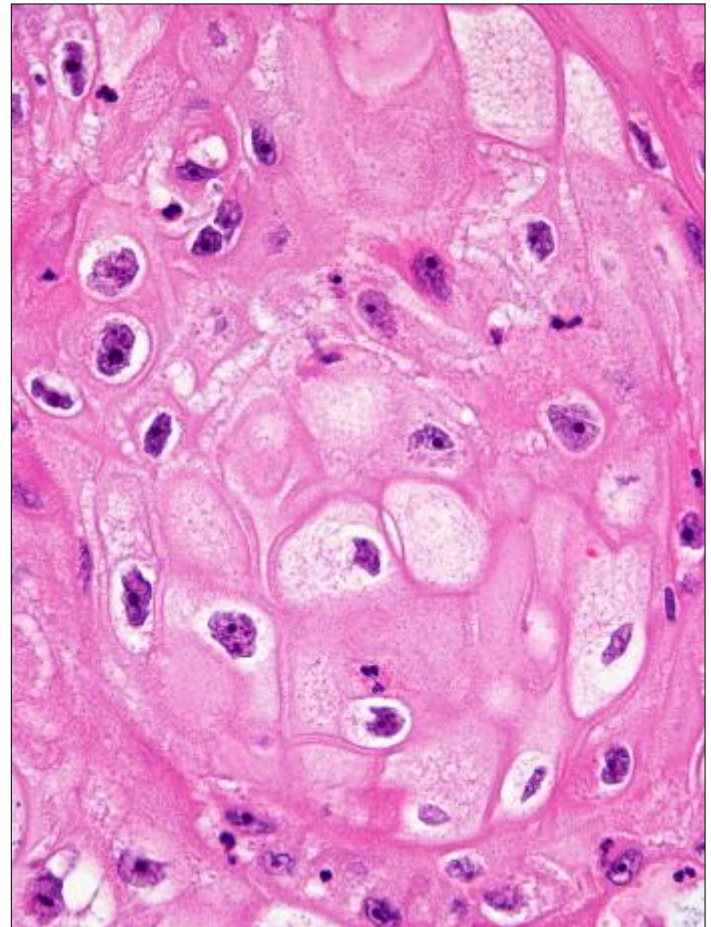
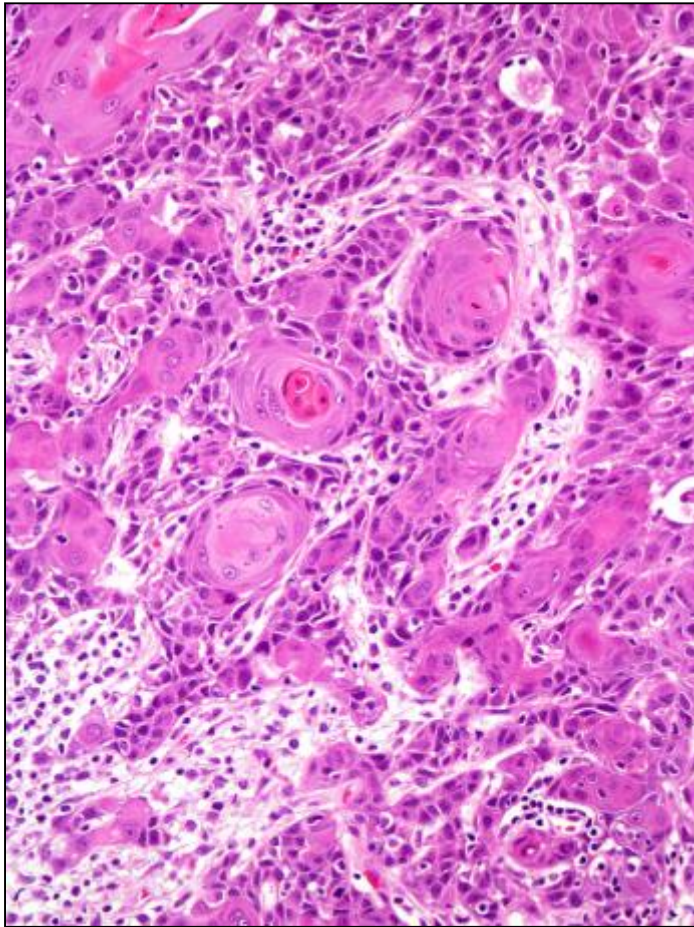
Squamous metaplasia



Mucosal membranes of the head and neck



Squamous cell carcinoma: keratinization and/or desmosomes



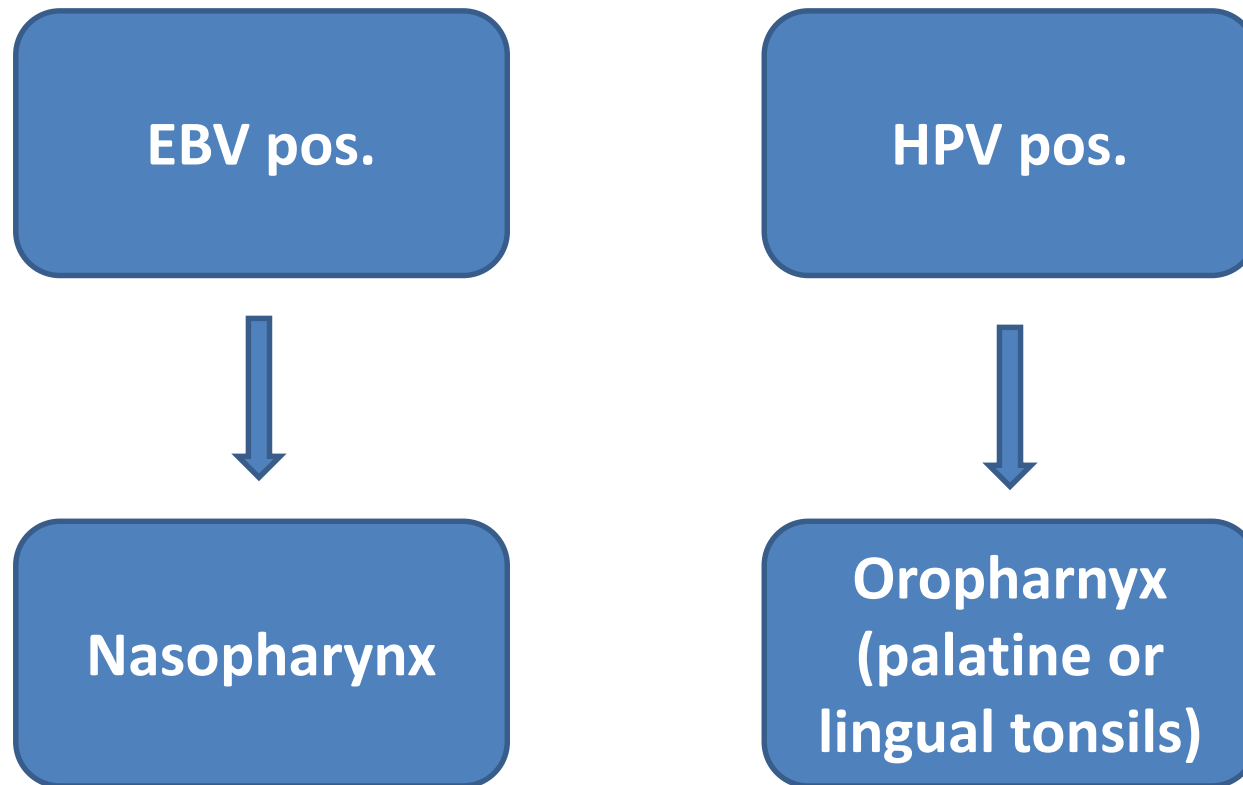
Squamous cell carcinoma

- Oral cavity
- Pharynx
- Larynx
- Nasal cavity
- Paranasal sinuses
- Salivary glands
- Skin
- Esophagus
- Anal and genital region
- Uterine cervix
- Lungs

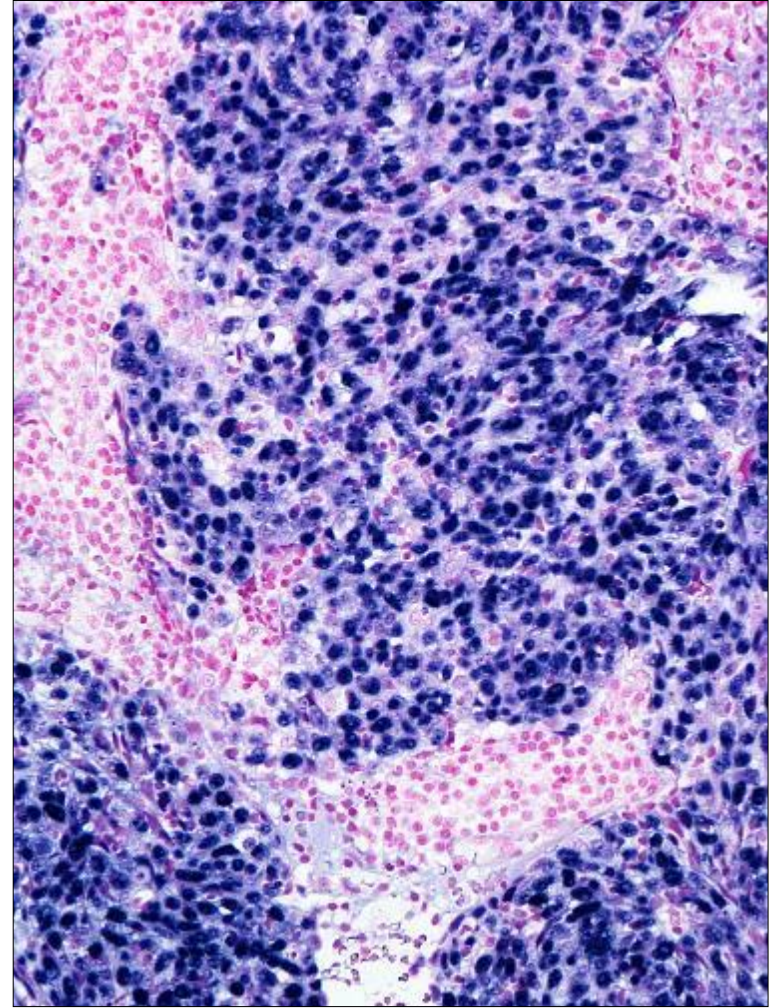
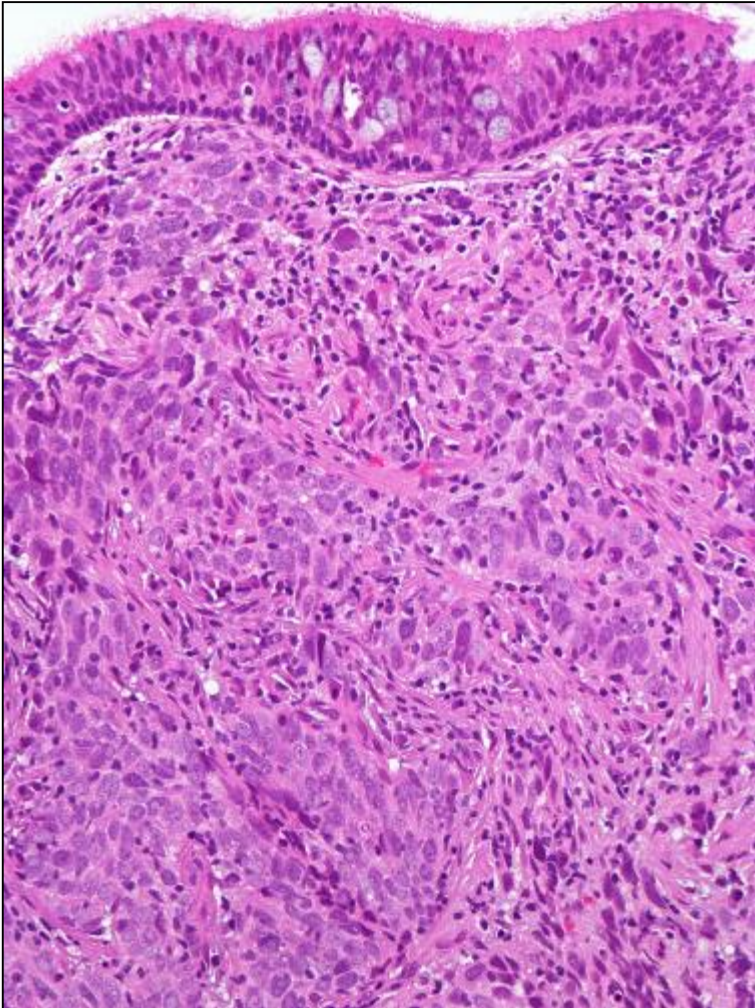
Etiology of squamous cell carcinoma of the head and neck

- Smoking
- Alcohol
- HPV (oropharynx, paranasal sinuses)
- EBV (nasopharynx)
- Other: reflux (GORD)
- Unknown in some patients

Practical implication: nodal metastasis of unknown primary

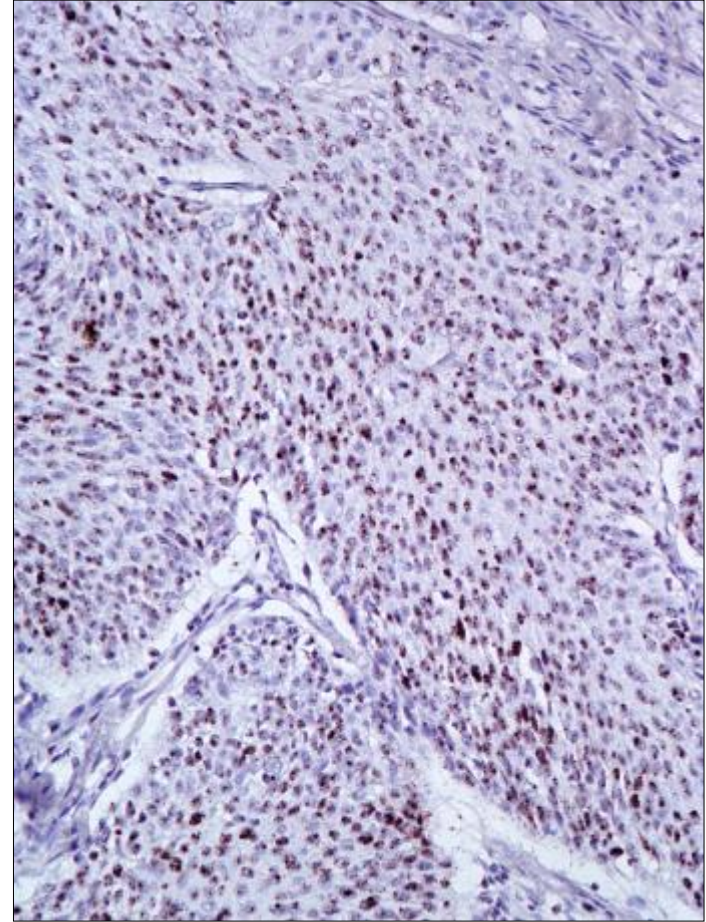
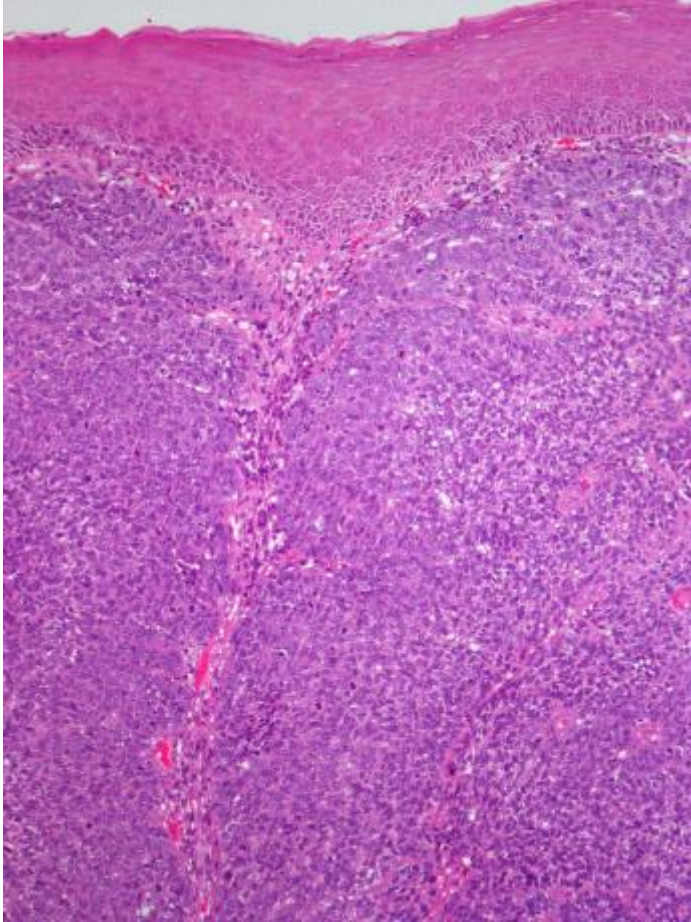


Nasopharyngeal carcinoma



Epstein-Barr virus

Oropharyngeal carcinoma



HPV

Precancerosis

Definition: Mucosal epithelium with morphological changes, caused by accumulation of genetic changes, associated with an increased risk of progression to squamous cell carcinoma

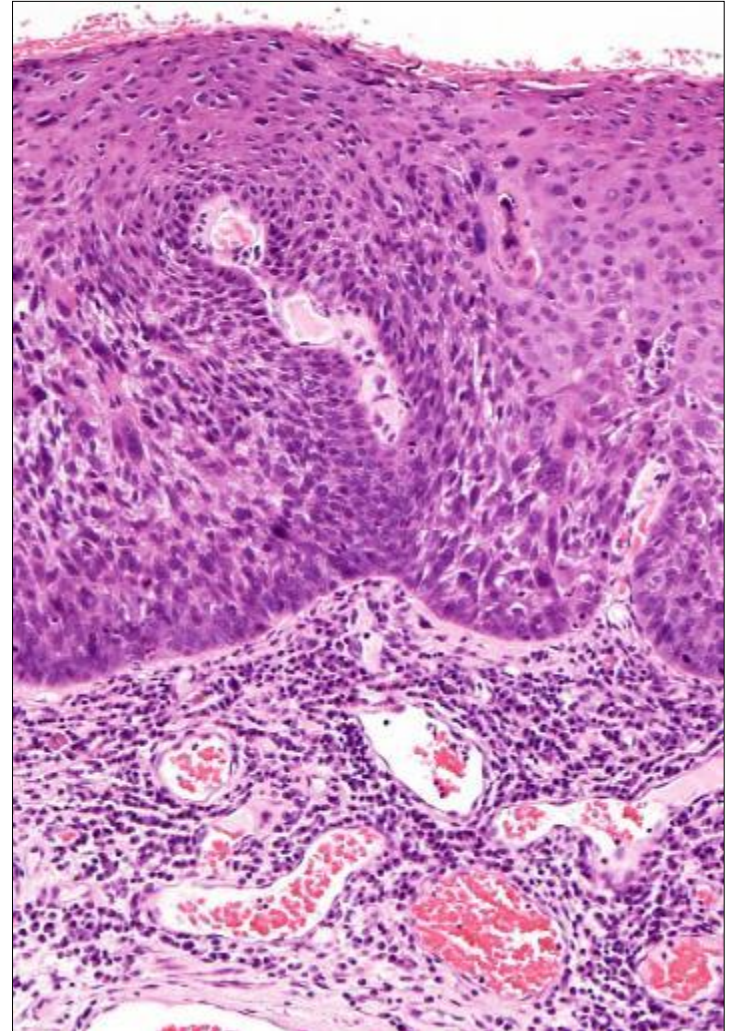
Synonyms: dysplasia, squamous intraepithelial neoplasia (SIN), squamous intraepithelial lesions (SILs)

Precancerosis

- Terminology: Ljubljana classification, WHO classification, others
- Etiology: alcohol, tobacco, HPV ?
- Clinical features not specific
- It can regress, progress to carcinoma, recur
- Field cancerization

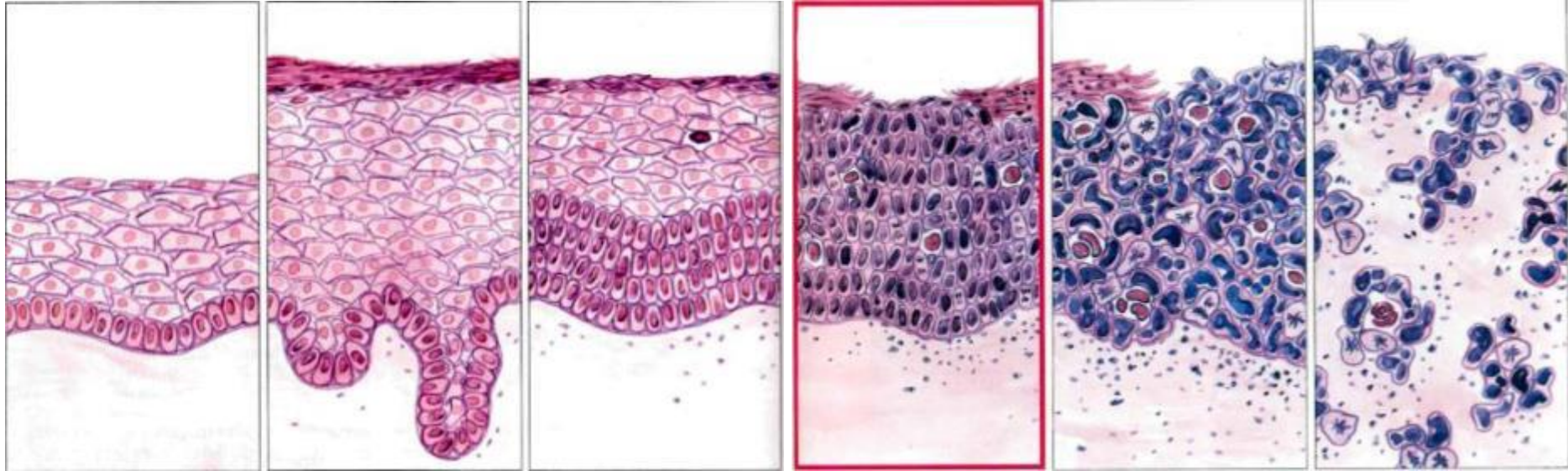
Grading precancerosis

- nuclear and cell polymorphism (variation in size and shape)
- cellular atypia
- nuclear/cytoplasmic ratio increased
- nucleoli increased in number and size
- increased mitoses
- molecular marker ???



Squamous intraepithelial lesions (dysplasia)

1. **Low grade:** progression to carcinoma in 2% of patients
2. **High grade:** progression to carcinoma in 13% of patients
3. **Carcinoma in situ:** cytologically carcinoma, but does not extend beyond the basement membrane and cannot metastasize



Normal

Hyperplasia

Dysplasia

Ca in situ

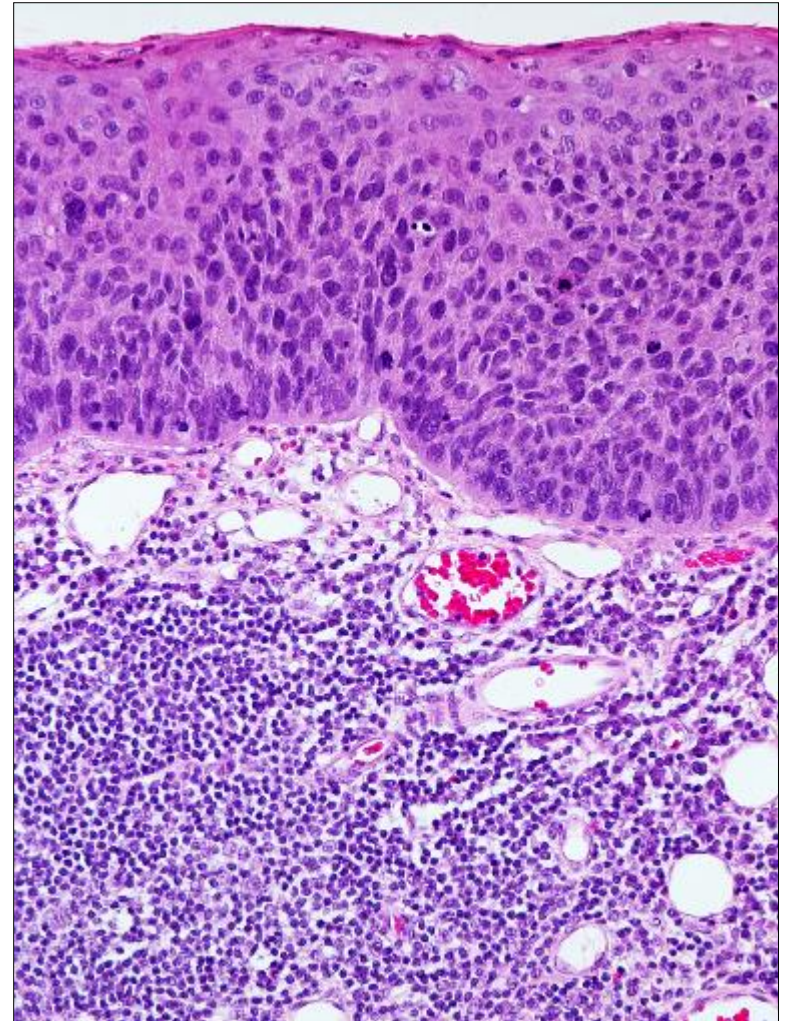
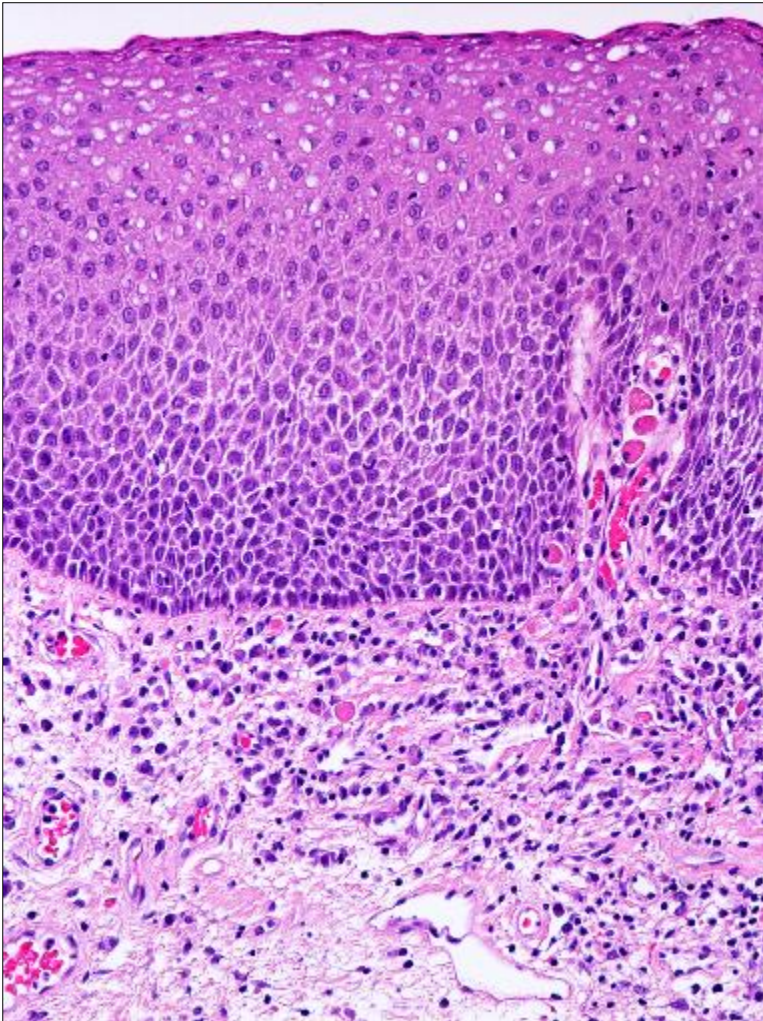
Invasive ca

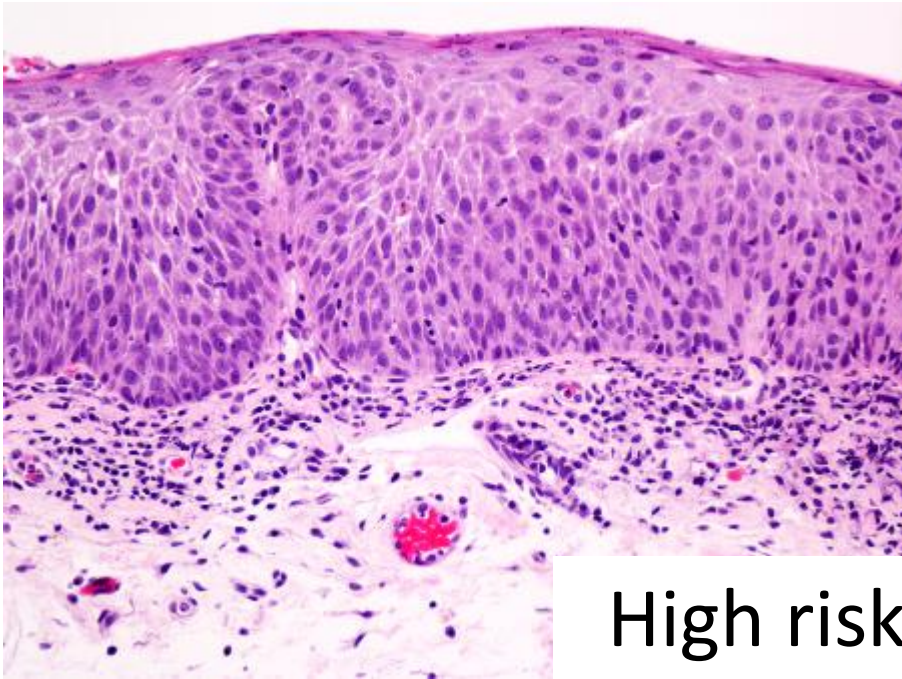
Kambič V and Gale N. Epithelial hyperplastic lesions of the larynx. Elsevier 1995

Dysplasia

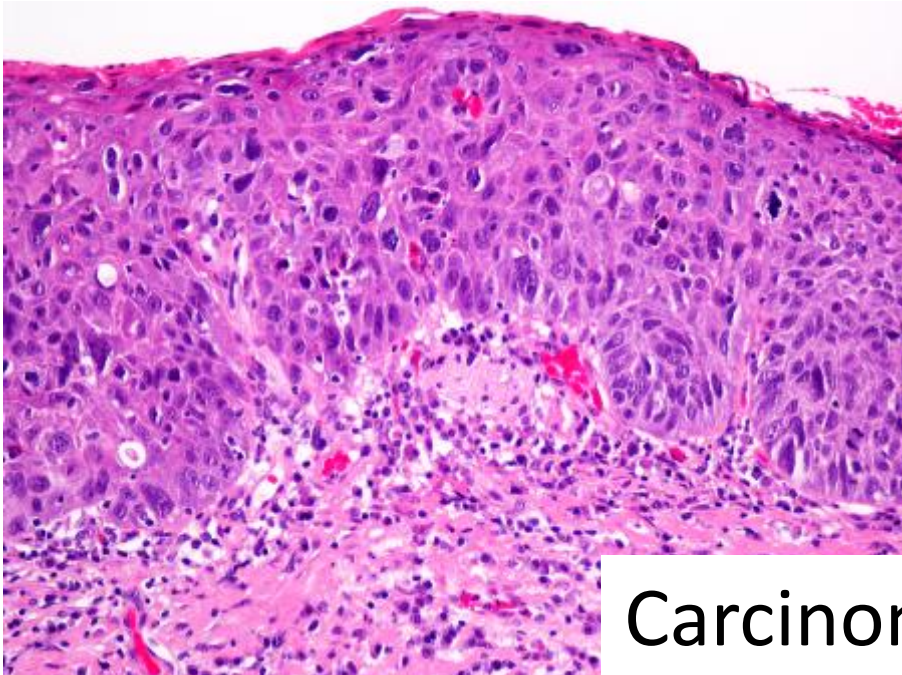
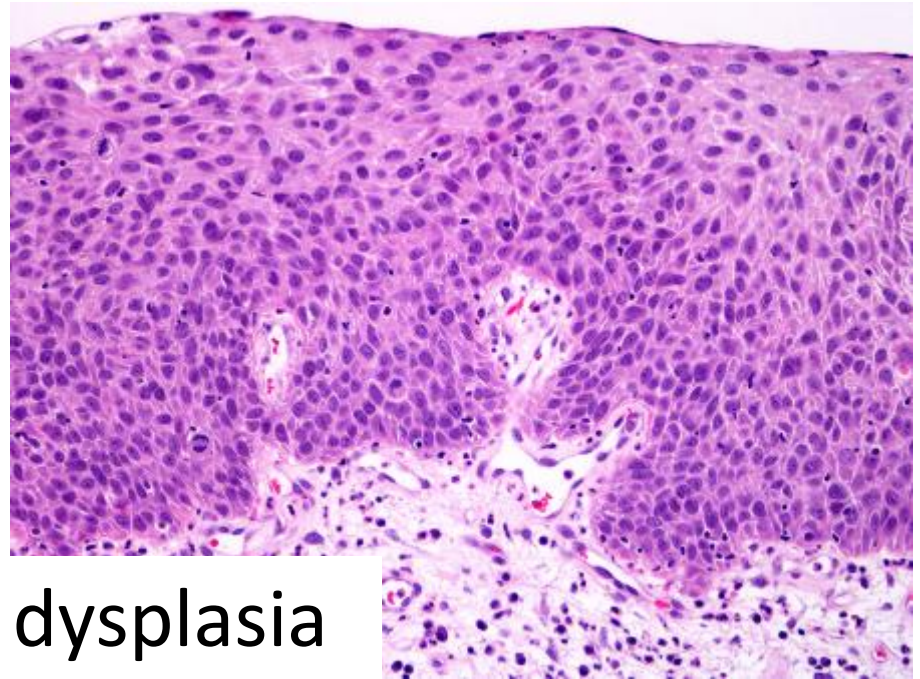
low grade

high grade

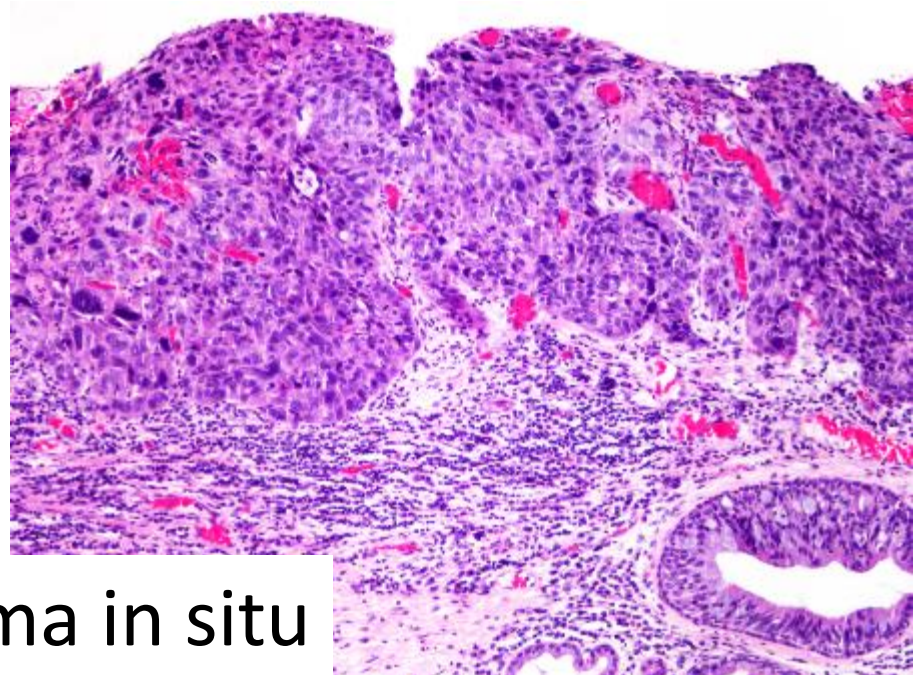




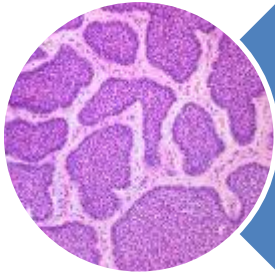
High risk dysplasia



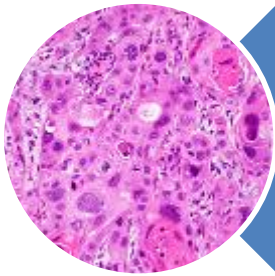
Carcinoma in situ



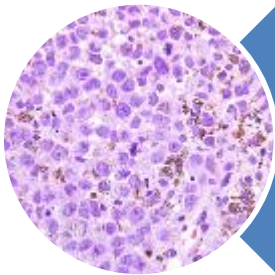
Skin



Basal cell carcinoma



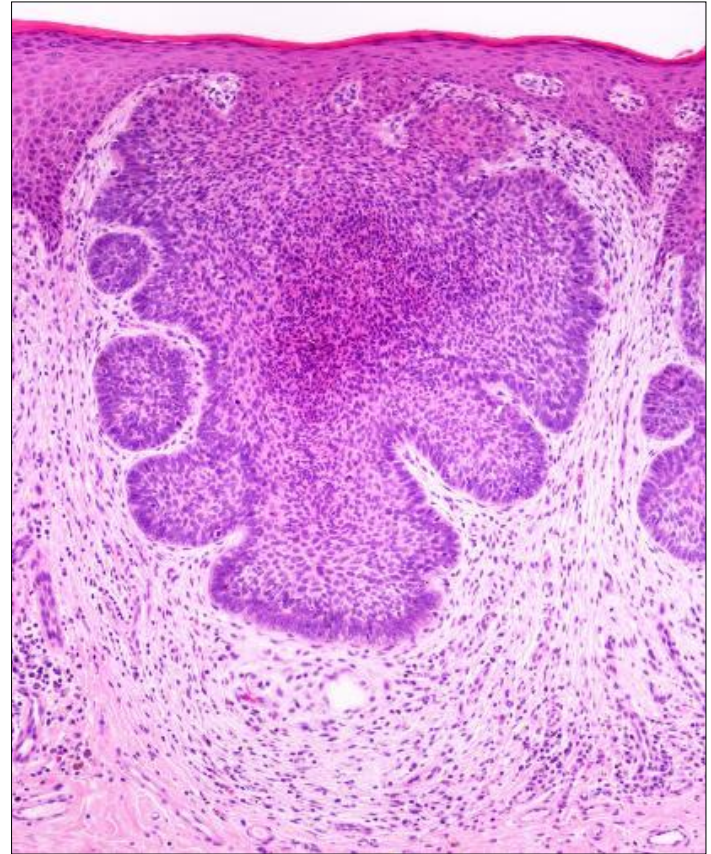
Squamous cell carcinoma



Melanoma

Basal cell carcinoma

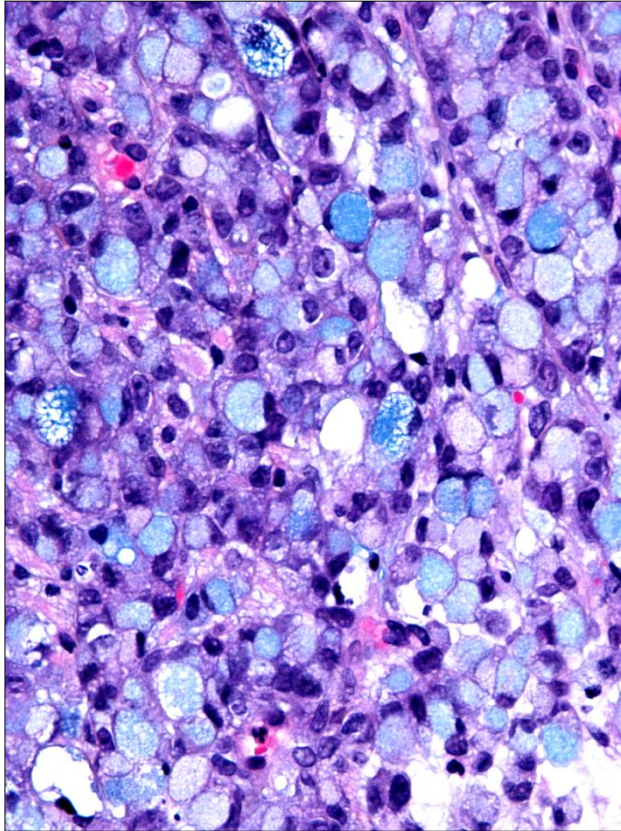
- most frequent cancer in humans
- sun exposed skin
- slow growth, **tissue destruction**
- metastases only exceptionally
- Th: excision (margins free of tumor)



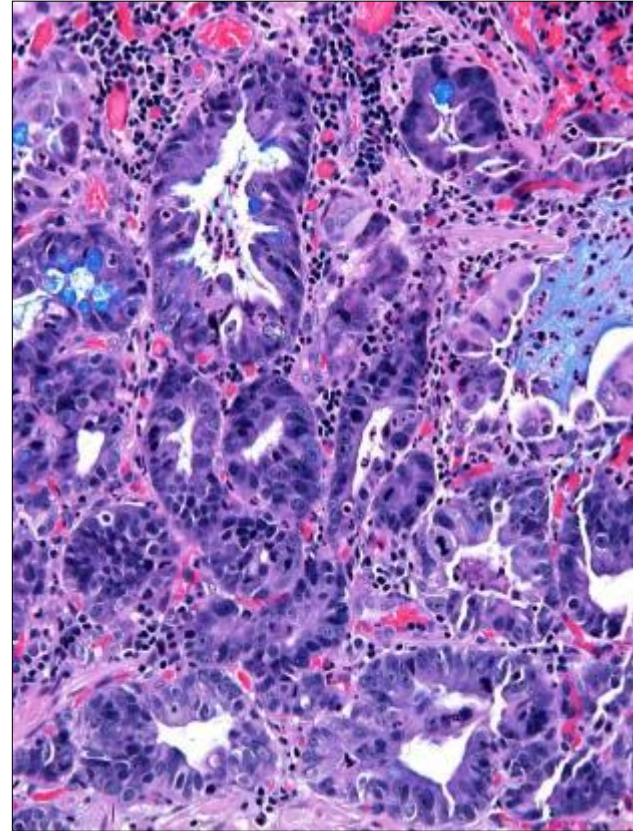
Salivary gland tumors

Adenocarcinoma: features of glandular differentiation

Mucin production (intra. or extracellular)



Gland structure formation (tubuli, acini, villi)



Salivary gland tumors

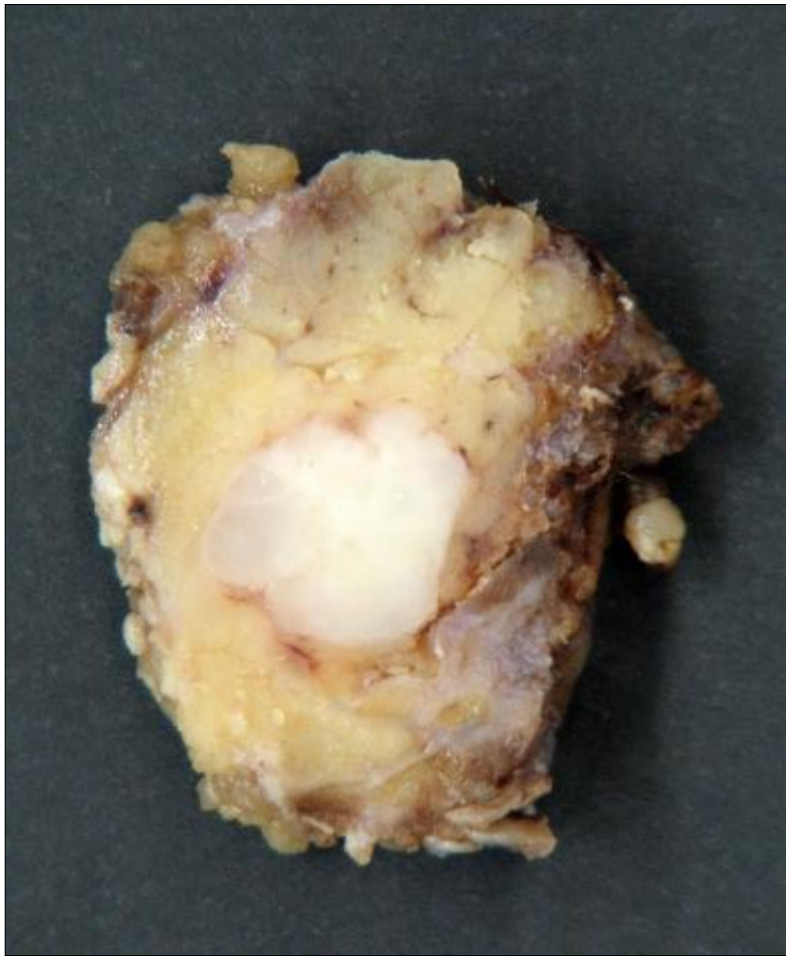
- benign

- Pleomorphic adenoma
- Whartin's tumor

- malignant

- Adenoid cystic ca
- Mucoepidermoid ca
- Epithelial-myoepithelial ca
- Myoepithelial ca
- Salivary duct ca
- Polymorphous adenoca
- Basal cell adenoca
- Secretory carcinoma
- Lymphomas

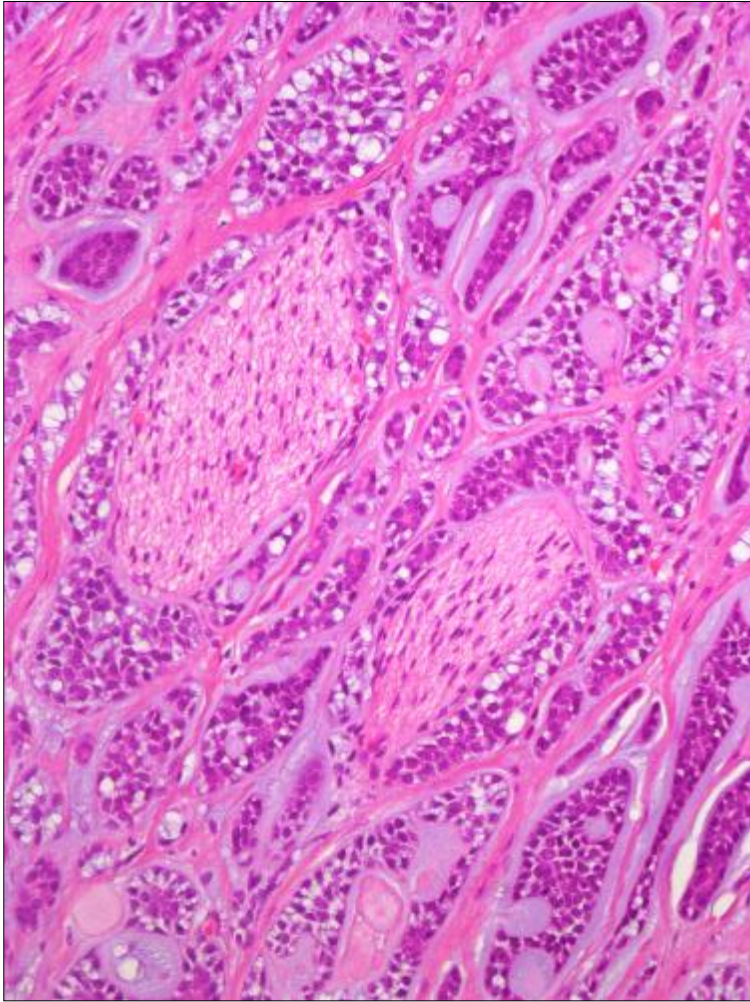
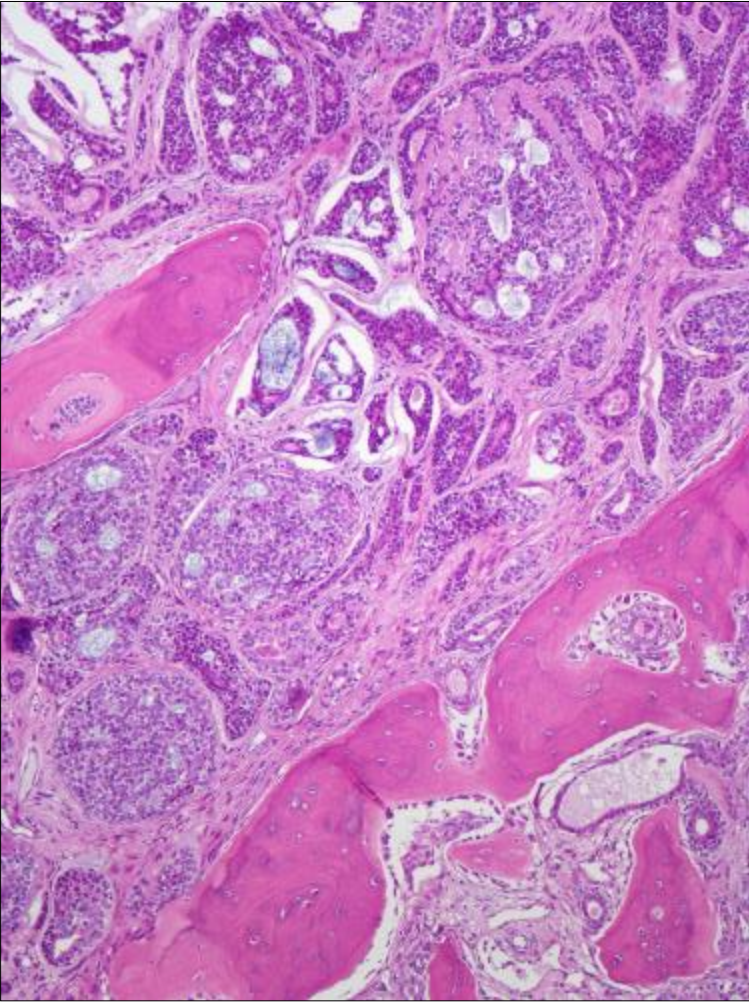
Pleomorphic
adenoma



Salivary duct
carcinoma



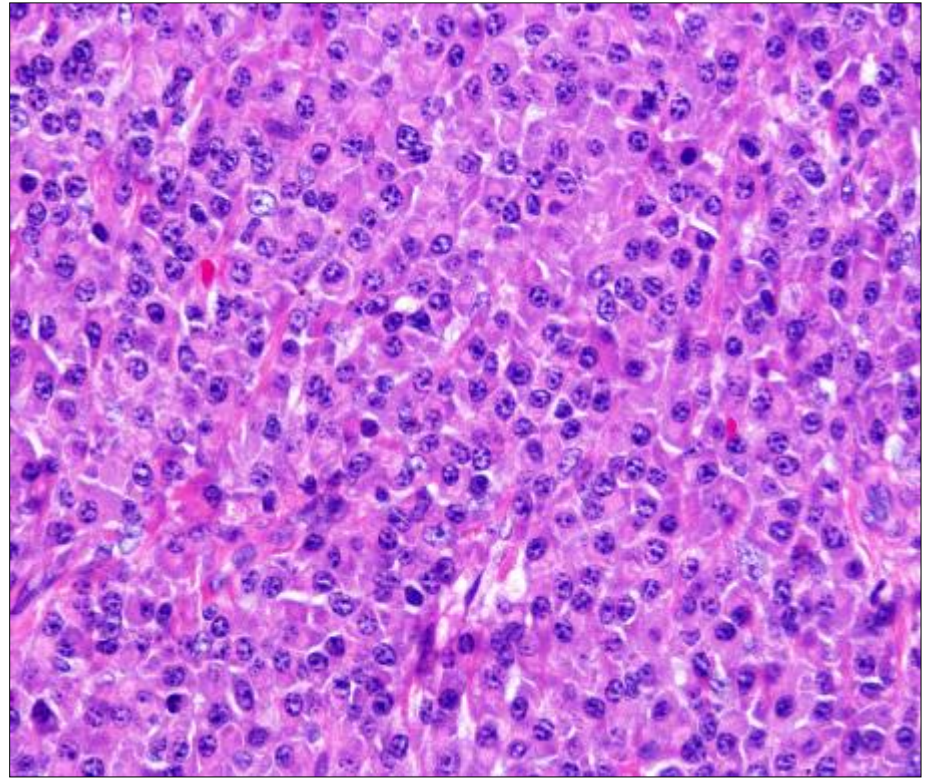
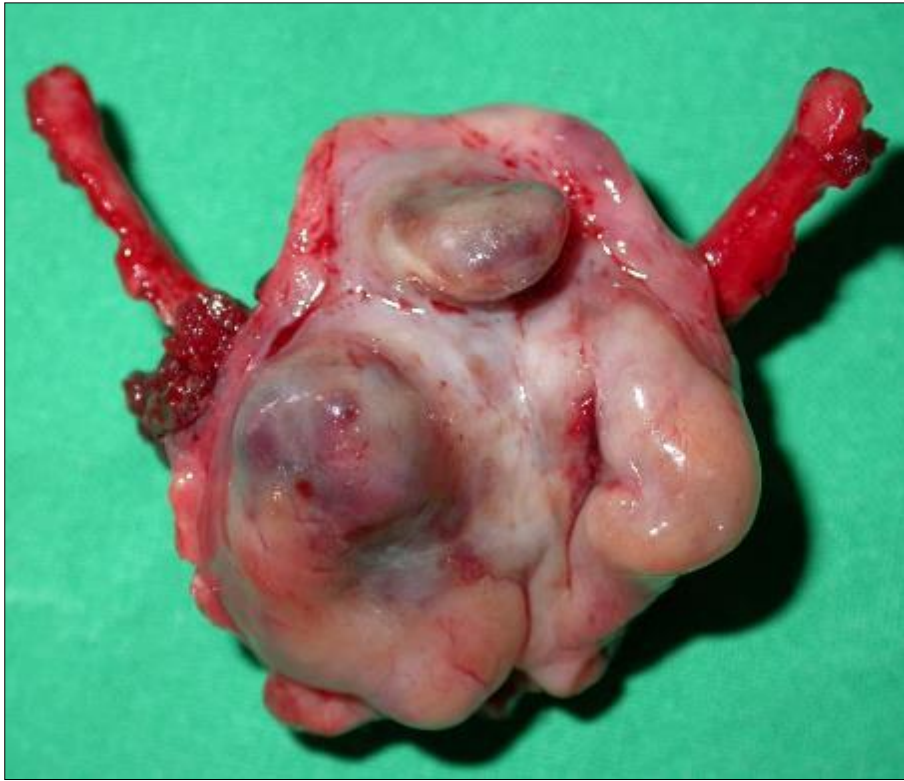
Adenoid-cystic carcinoma: perineural invasion



Lymphomas

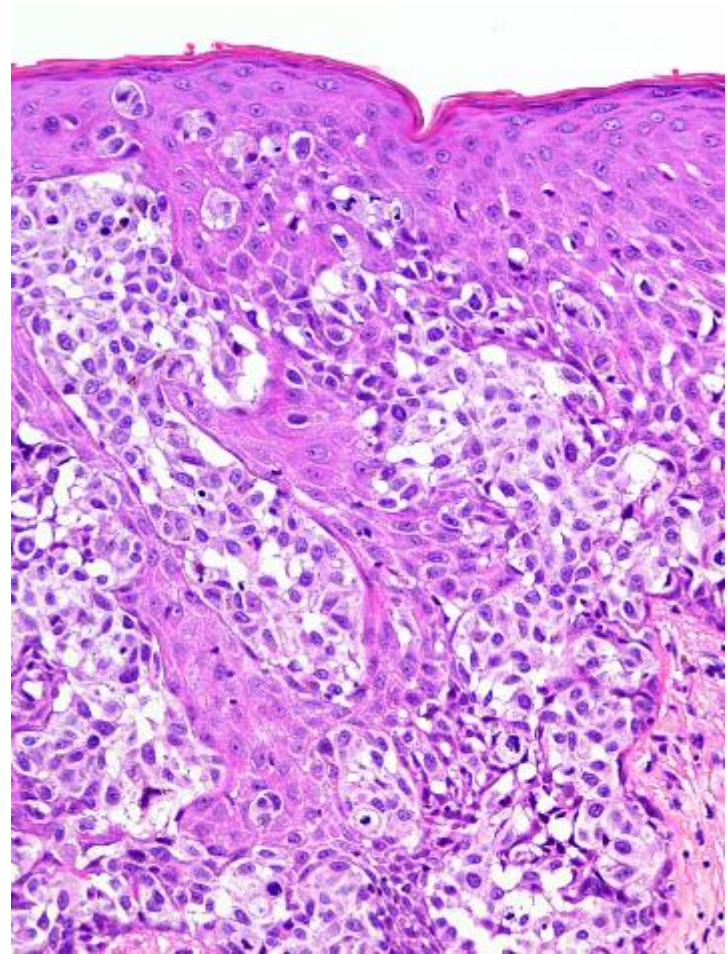
- Hodgkin, non-Hodgkin lymphomas, lymphatic leukemias, plasmacytoma
- Lymph nodes
- Waldeyer's ring (tonsils)
- Mucosa-associated lymphoid tissues (MALT):
acquired MALT (salivary glands)

Supraglottic laryngectomy: extramedullary plasmacytoma

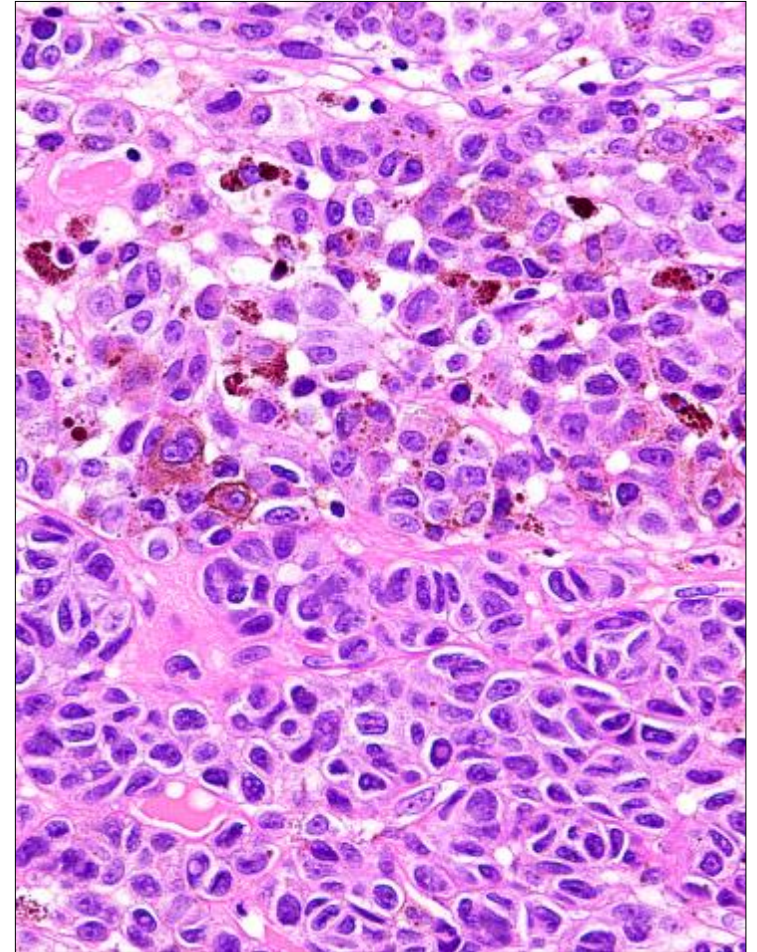


Melanoma

- Skin
- Mucosa (nasal, oral)
- Aggressive, poor prognosis
- Late diagnosis in mucosal melanomas



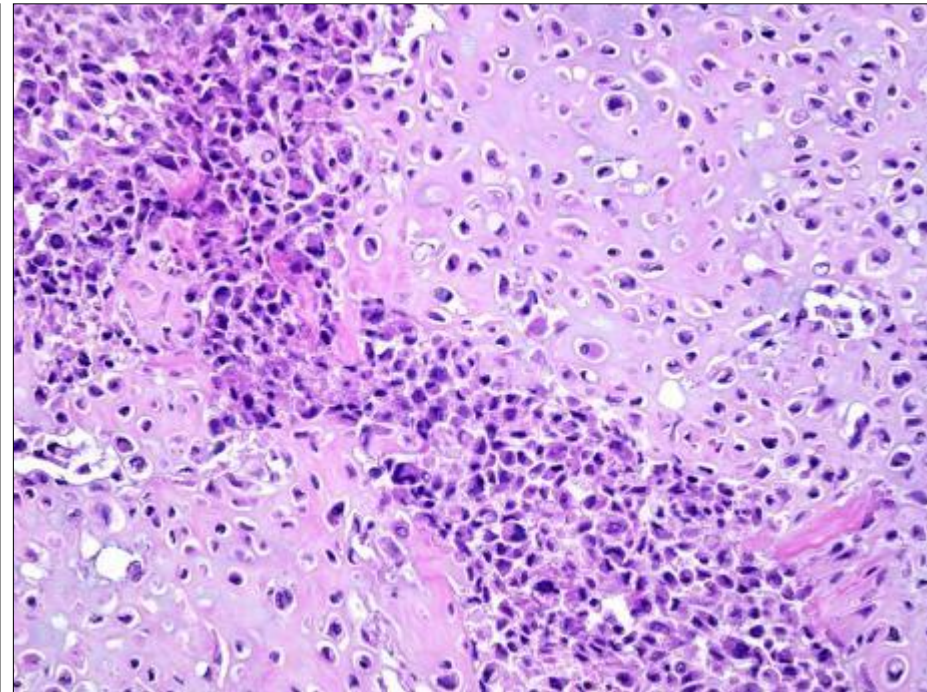
Melanoma of the hard palate and maxilla



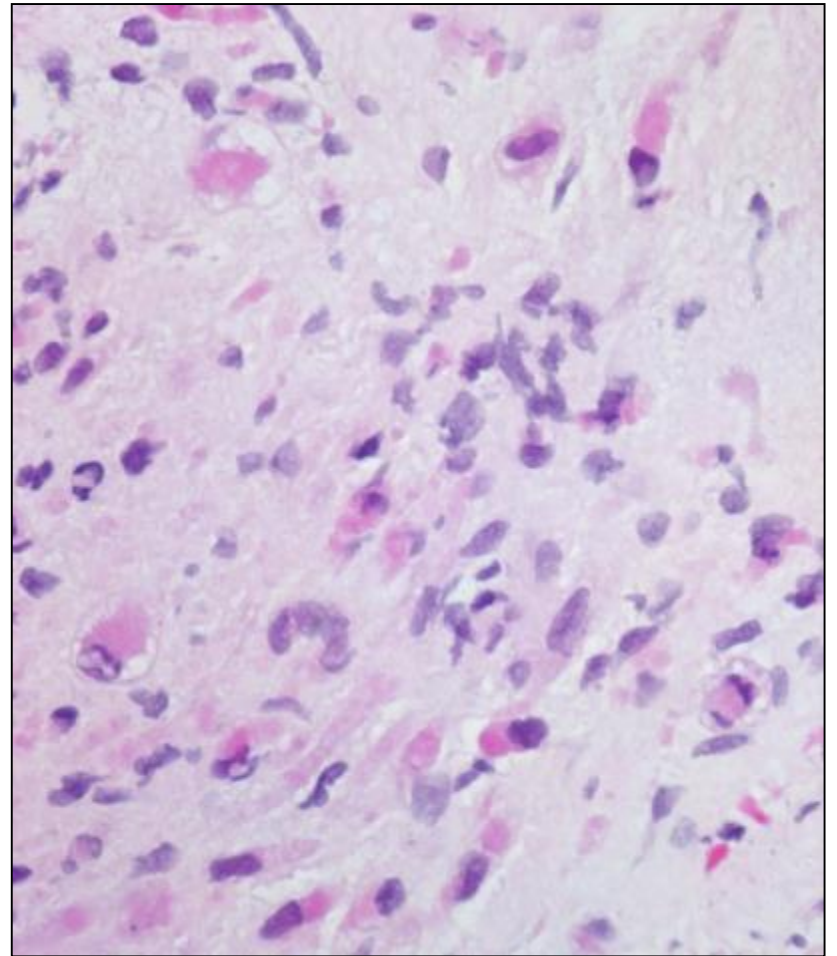
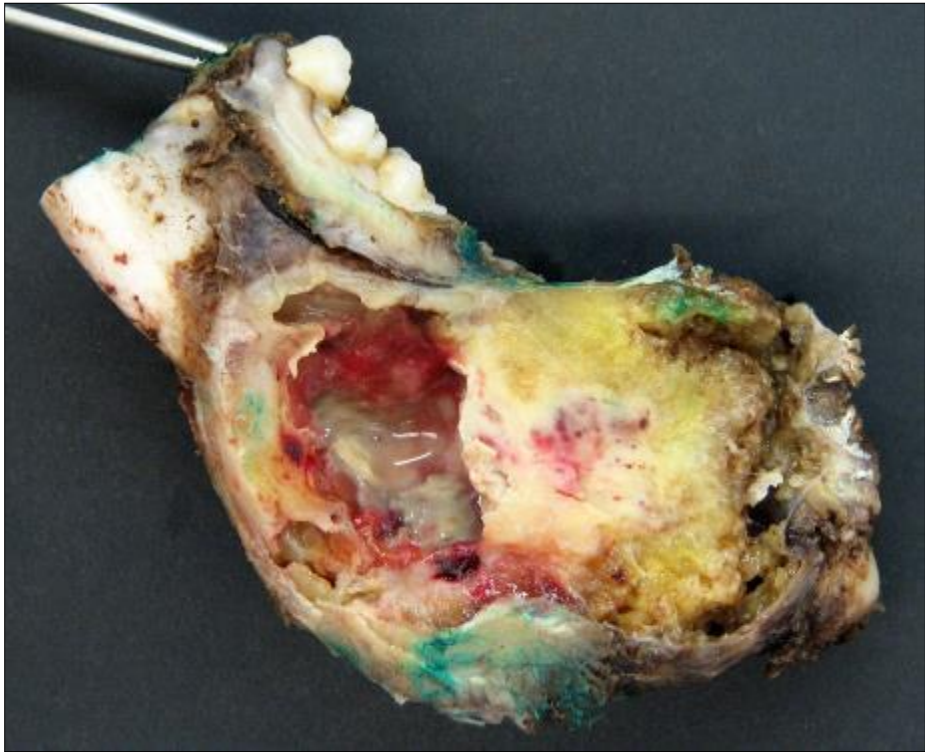
Tumors of the soft tissue and bone

- **Benign:** lipoma, hemangioma, schwannoma, fibroma, leiomyoma, chondroma
- **Malignant (sarcoma):** liposarcoma, chondrosarcoma, leiomyosarcoma, myxoid fibrosarcoma, MPNST
- **Benign:** osteoma, osteoblastoma, osteoid-osteoma, giant cell tumor
- **Malignant:** osteosarcoma, Ewing sarcoma, PNET, lymphoma, plasmacytoma

Chondrosarcoma of the larynx



Rhabdomyosarcoma of the jaw



Role of HPV in tumors of the head and neck

HPV-positive squamous cell carcinoma of the oropharynx

- palatine tonsils
- lingual tonsil (base of the tongue)

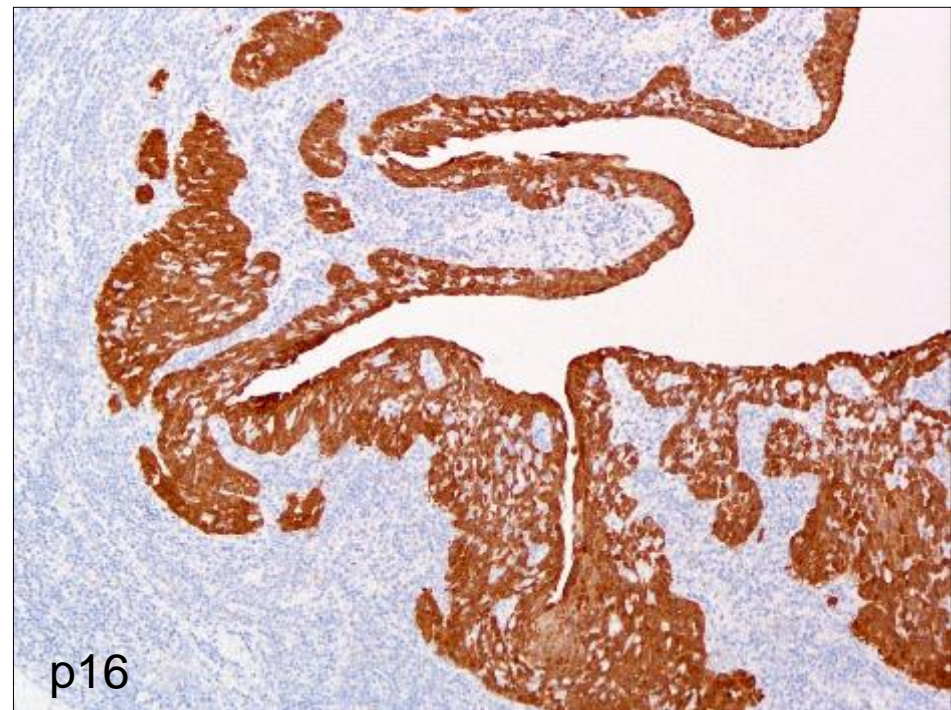
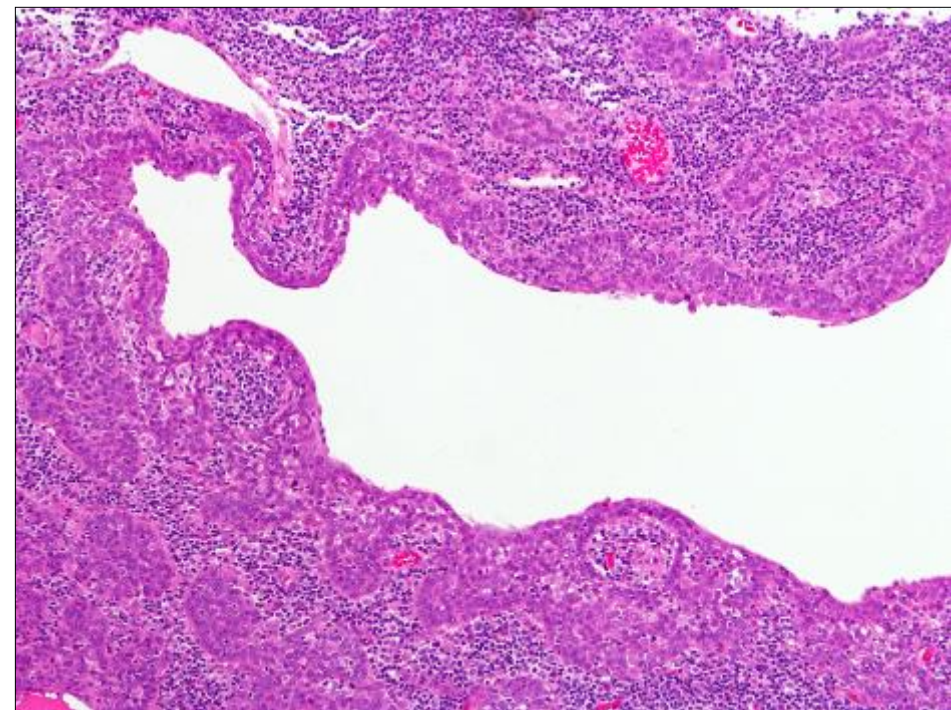
| Characteristics | HPV-positive SCC | HPV-negative SCC |
|-----------------------------------|--|---------------------------|
| Median age | 50-56 years | 60-70 years |
| Risk factors | Sexual behaviour | Smoking and alcohol abuse |
| Lymph node metastases | Frequently cystic | Uncommonly cystic |
| Postulated origin | Reticulated epithelium of invaginated crypts | Surface epithelium |
| Dysplasia | Rare | Often present |
| Morphology | Commonly non-keratinizing | Conventional SCC |
| Grading | Not applicable | Applicable |
| p16 immunohistochemistry | Positive | Negative |
| Overall survival (3 years) | 82% | 57% |

El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ, eds. WHO Classification of Head and Neck Tumours. 4th ed. IARC: Lyon; 2017

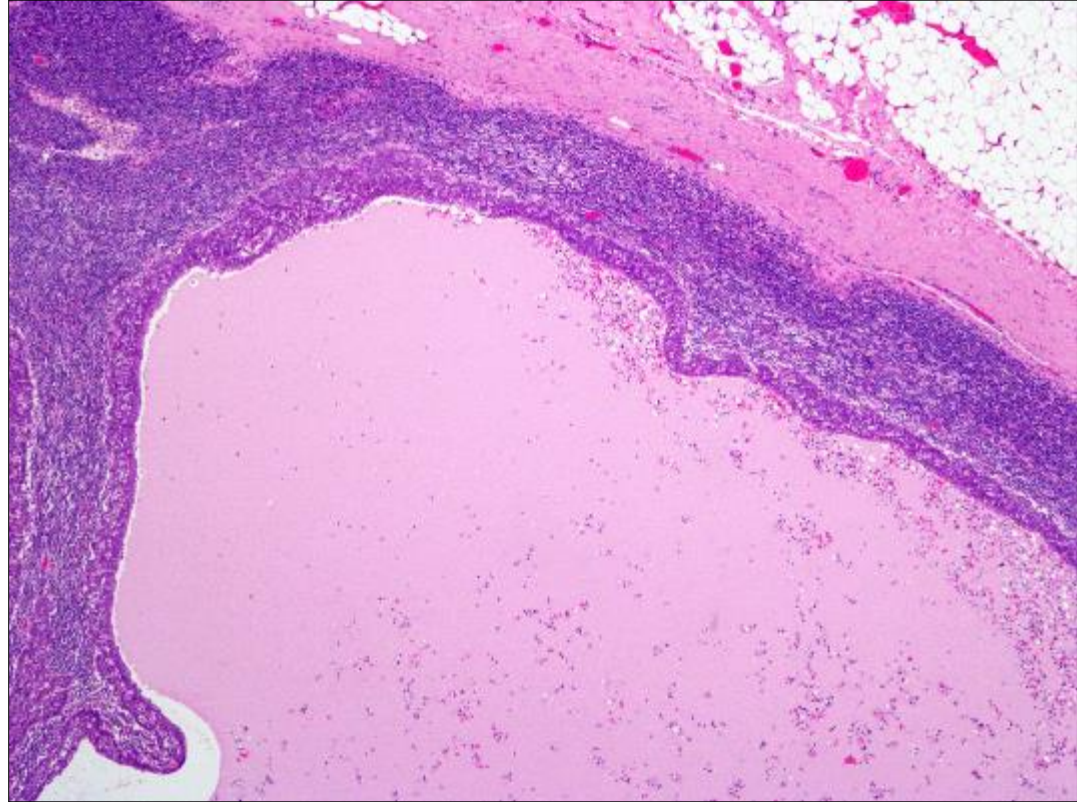
HPV-pos. SCC of the oropharynx

- HPV16 (85%), 18, 31, 33, 35, 39, 45, 51, 52, 56, 59, 68, 69, 73,
- 35-80 % in US to 13-20 % in some European countries
- at a younger age
- weaker association with tobacco and alcohol abuse
- associated with sexual behavior
- palatine or lingual tonsils, non-keratinizing morphology
- early metastases to regional lymph nodes
- enhanced sensitivity to irradiation treatment
- better overall survival: 82% for HPV+ vs 57% for HPV neg

Ang KK, Harris J, Wheeler R et al. HPV and survival of patients with oropharyngeal cancer. N Engl J Med 2010; 363: 24-35

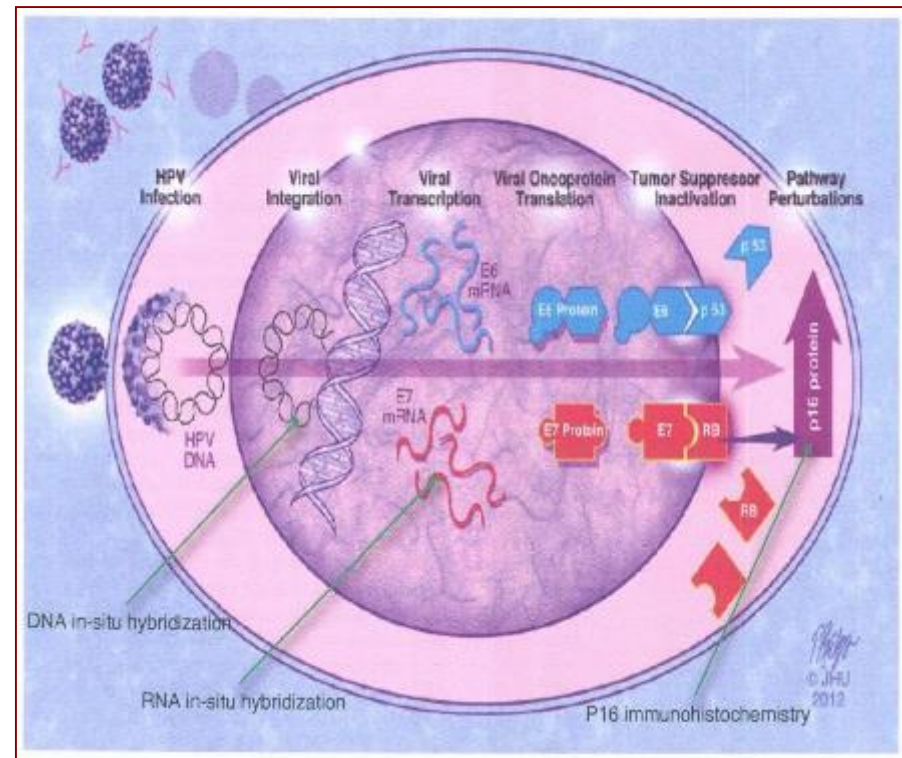


Cystic lymph node metastases



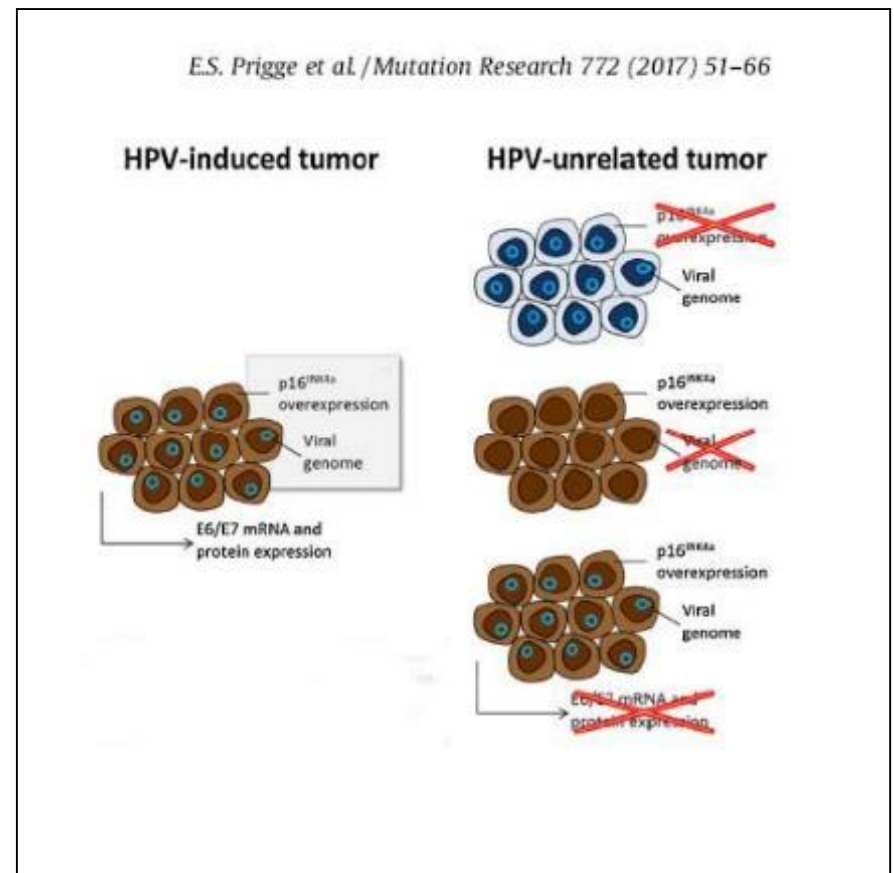
Pathogenesis of HPV-related carcinoma

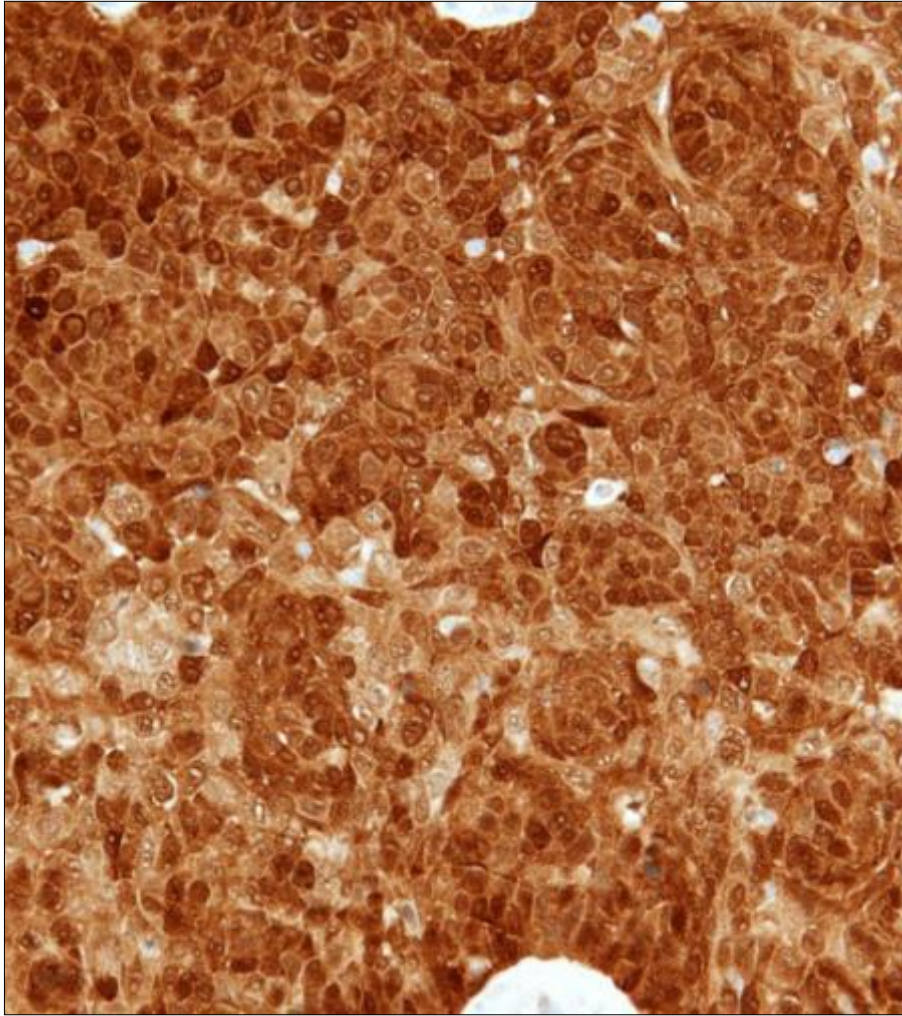
- HPV integration into the host genom
- Expression of viral mRNA
- Translation of viral oncoproteins
- Disruption of tumor suppressor pathways
- E6 and E7 – inhibition of p53 and Rb
- overexpression of p16



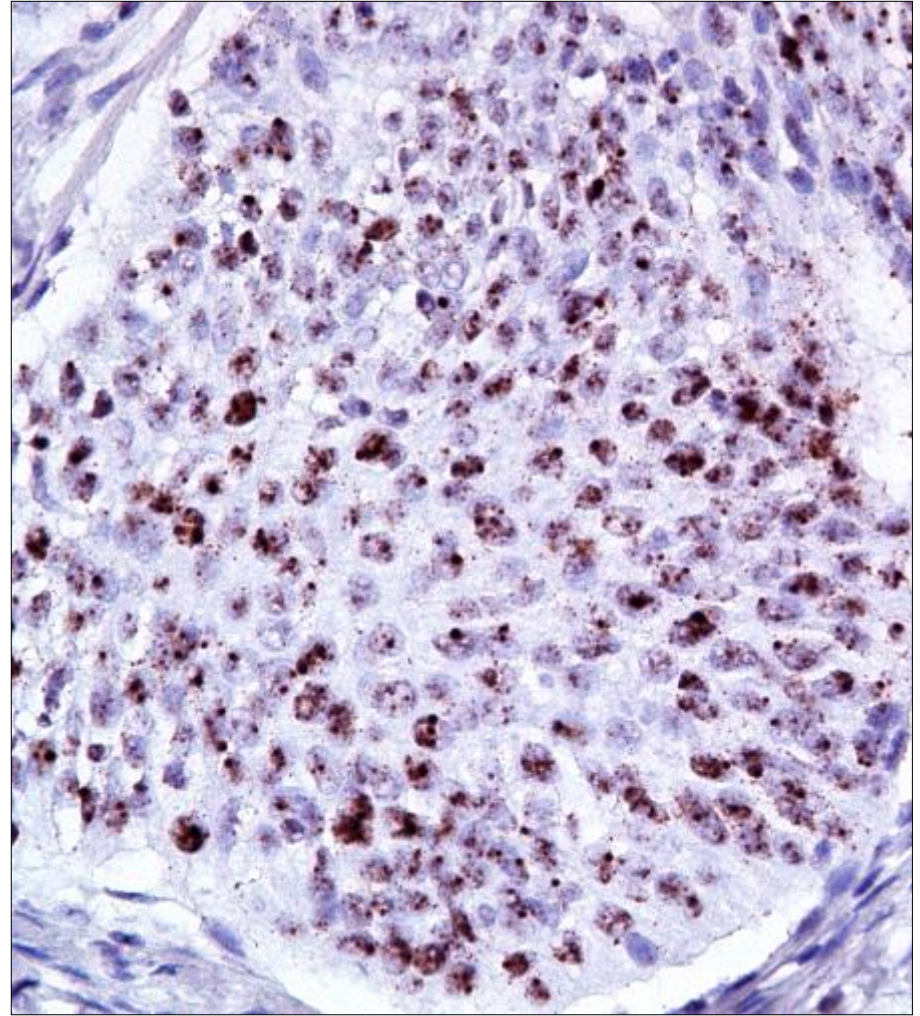
Diagnosis of HPV-related carcinoma

p16^{INK4}
overexpression
+
expression of high risk HPV
E6/E7 mRNA





p16



In situ hybridization E6/E7 high risk HPV

HPV and carcinoma of the sinonasal tract

- 2nd most common location of head & neck
- HPV in 20-30 % of sinonasal tumours
- HPV 16, 18, 31, 33
- non-keratinizing sinonasal SCC (41%)
- keratinizing sinonasal SCC (5%)
- new entity: HPV-related multiphenotypic sinonasal carcinoma
- other tumor types (papillary, basaloid, adenosquamous carcinoma, neuroendocrine carcinoma)

Prognostic significance of HPV
positivity in sinonasal carcinoma ???

A trend towards an improved survival for HPV-pos. sinonasal tumours

Alos L, Moyano S, Nadal A et al. HPV are identified in a subgroup of sinonasal squamous cell carcinomas with favorable outcome. *Cancer* 2009; 115:2701-9

Bishop JA, Guo TW, Smith DF et al. HPV-related carcinomas of the sinonasal tract. *Am J Surg Pathol* 2013; 37:185-92

Laco J, Sieglová K, Vošmiková H et al. The presence of high-risk HPV E6/E7 mRNA transcripts in a subset of sinonasal carcinomas is evidence of involvement of HPV in its etiopathogenesis. *Virchows Arch* 2015; 467:405-15

Prevalence of HPV in oral and laryngeal SCC: <4%

J Cancer Res Clin Oncol
DOI 10.1007/s00432-017-2481-8

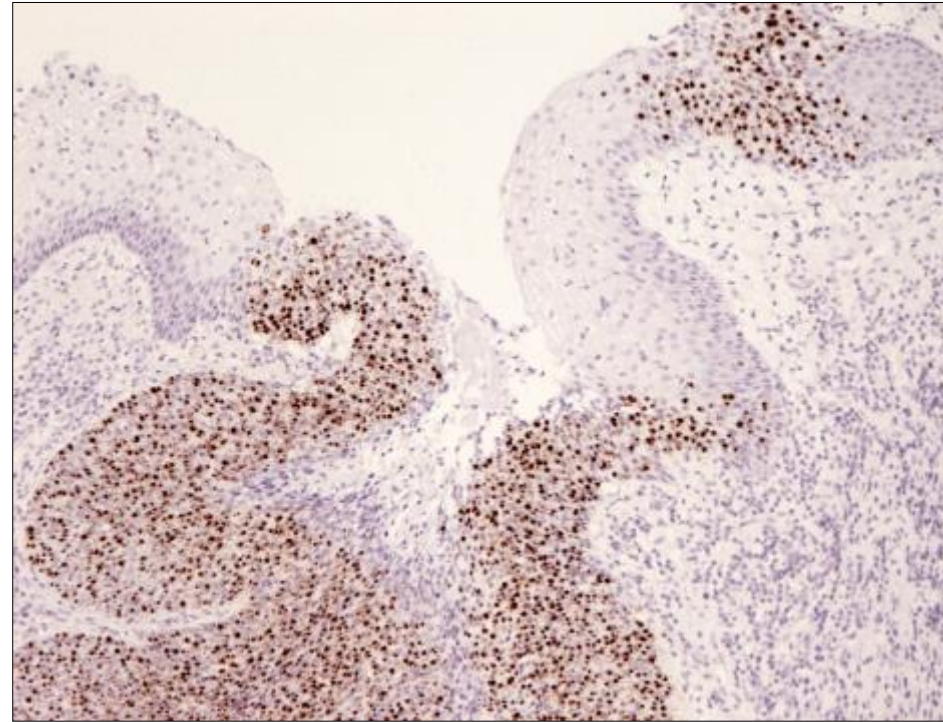
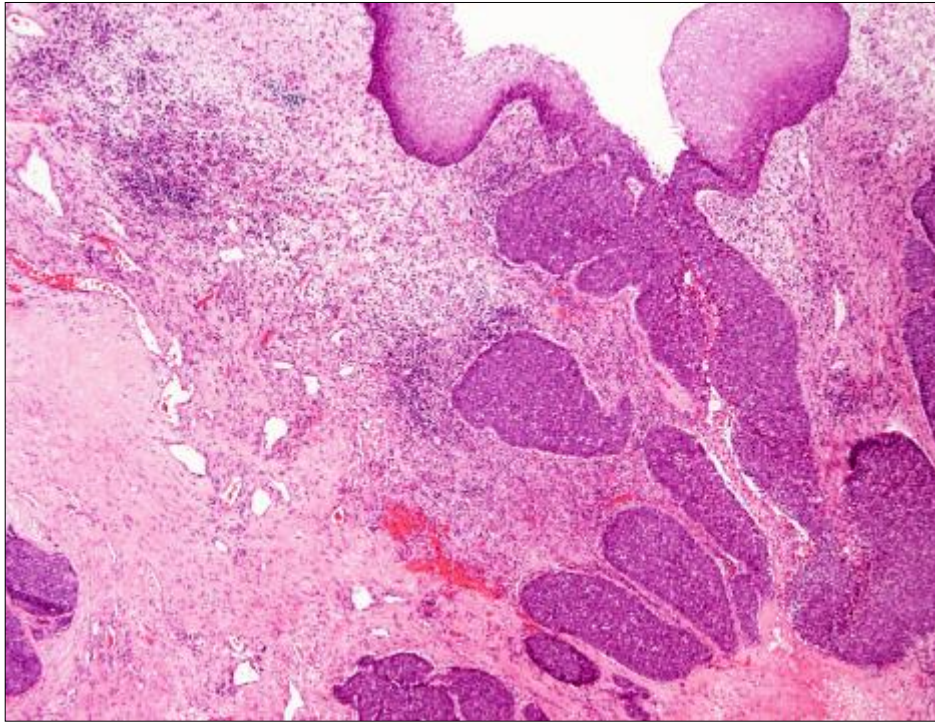
ORIGINAL ARTICLE – CLINICAL ONCOLOGY

Prognostic implications of human papillomavirus status for patients with non-oro-pharyngeal head and neck squamous cell carcinomas

Huaising C. Ko¹ · Paul M. Harari¹ · Ryan M. Sacotte² · Shuai Chen³ ·
Aaron M. Wieland⁴ · Menggang Yu³ · Andrew M. Baschnagel¹ · Justine Y. Bruce⁵ ·
Randall J. Kimple¹ · Matthew E. Witek¹

Overall survival was significantly higher for patients with HPV-pos. versus HPV-neg. non-oro-pharyngeal SCC.

HPV in the larynx



In situ hybridization E6/E7 high risk HPV