

# Malignant neoplasms of the oropharynx – I

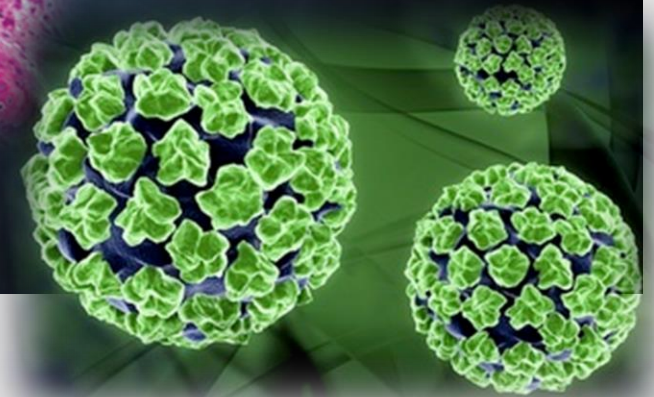
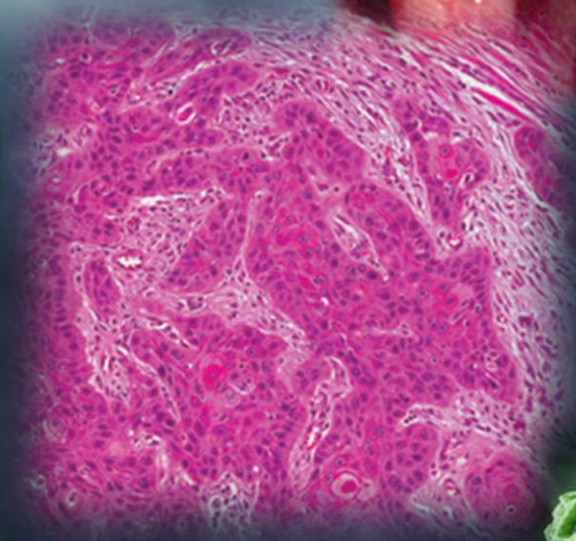
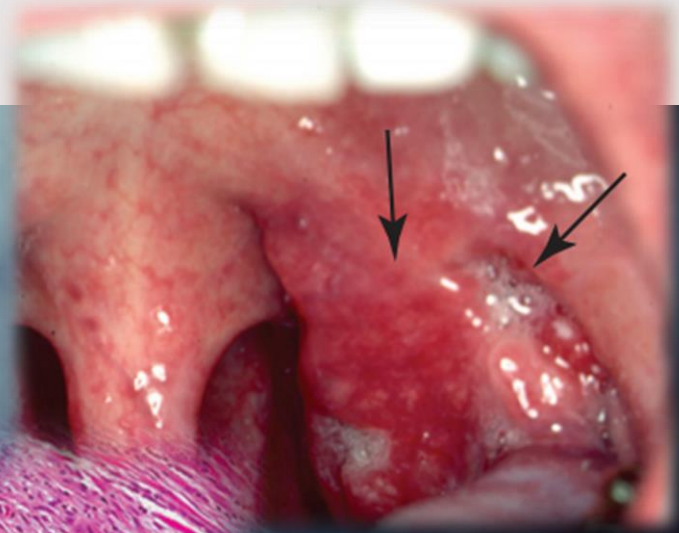
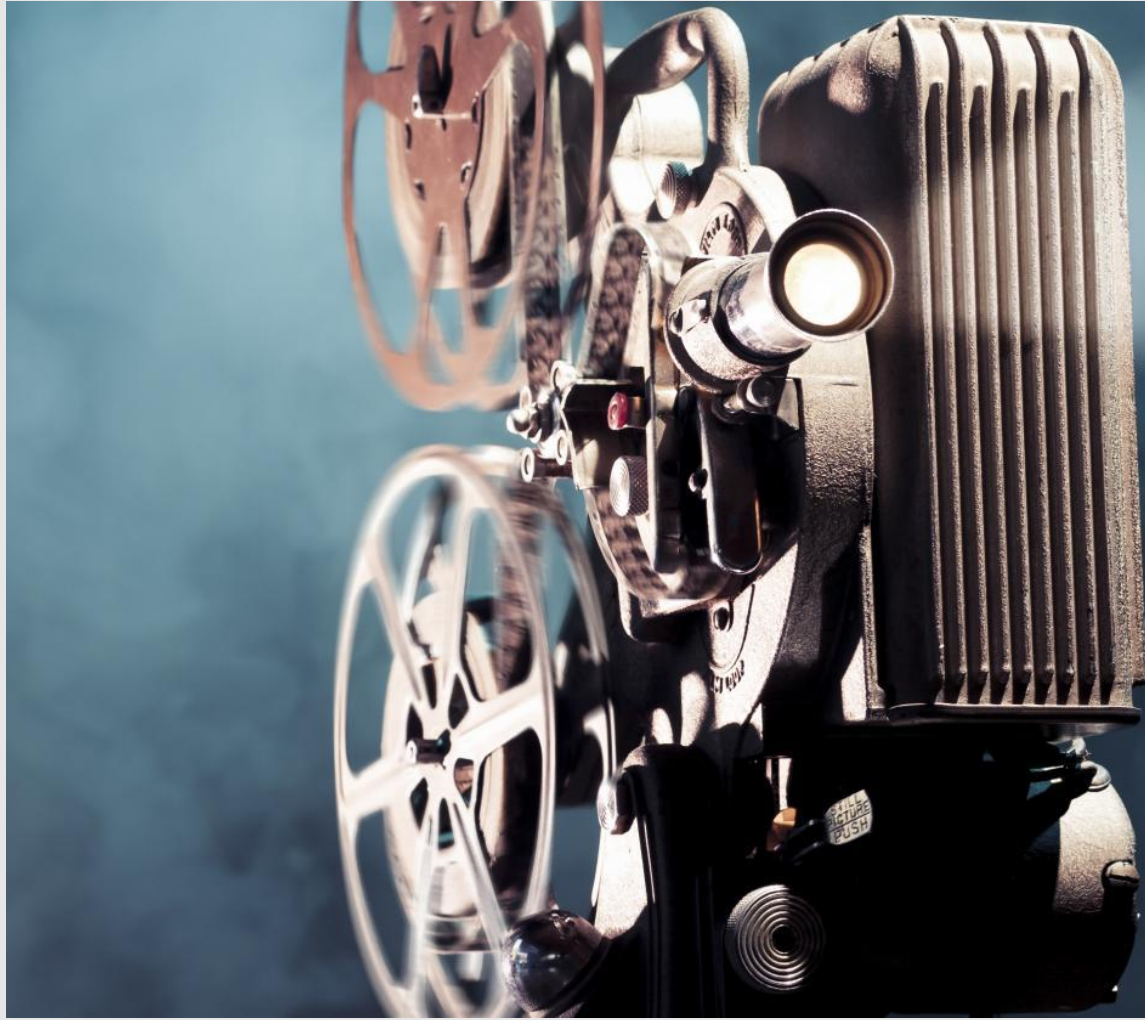
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MERITXELL TOMAS FERNANDEZ

2<sup>ND</sup> YEAR ENT RESIDENT

SON ESPASES UNIVERSITY HOSPITAL

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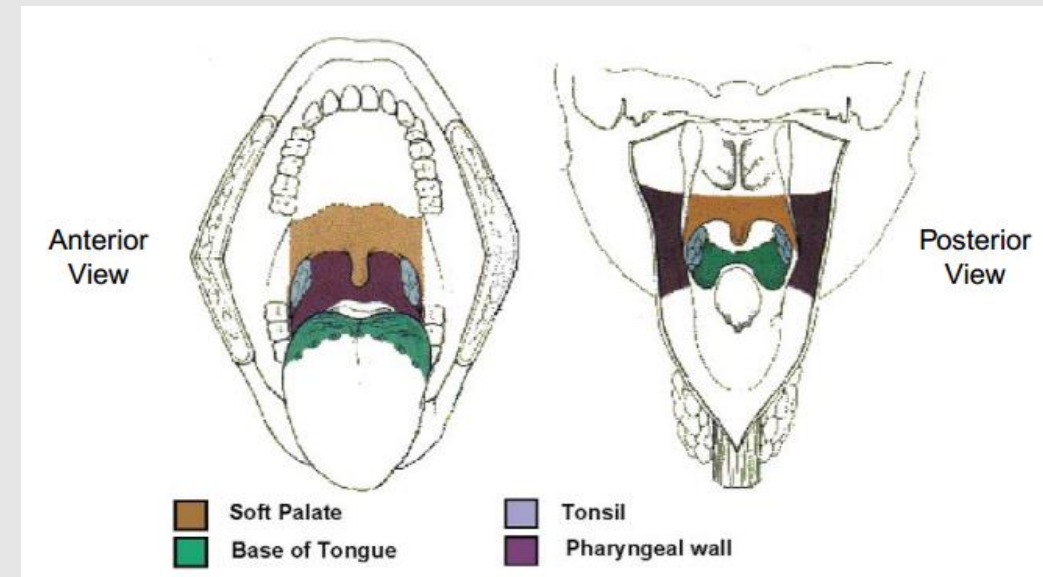
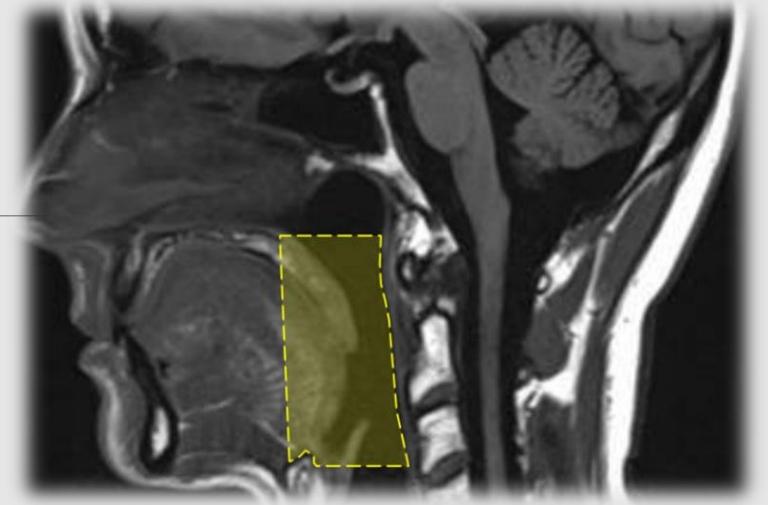
# Topics...

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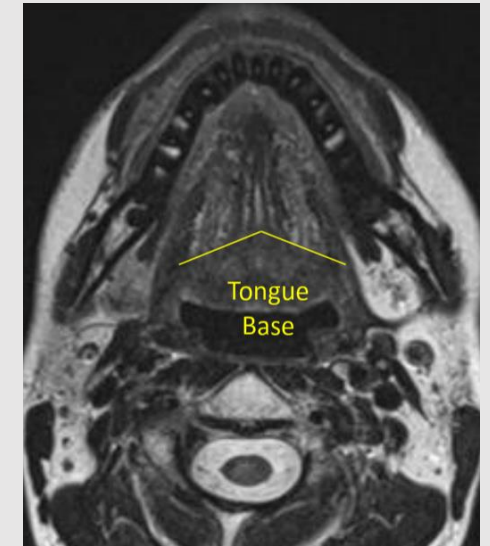
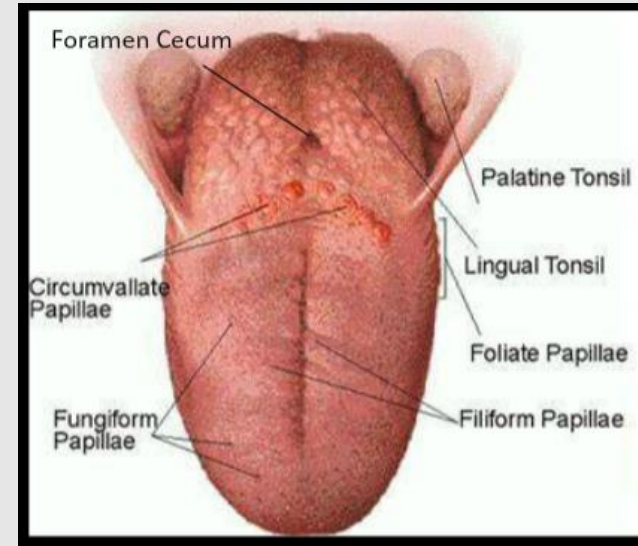
1. **Anatomy of the oropharynx**
2. **Malignant tumors of the oropharynx**

# Anatomy of the oropharynx

- It is continuous anteriorly with the oral cavity through the faucial or oropharyngeal isthmus
- The oropharyngeal borders are
  - Superiorly --- soft palate
  - Inferiorly --- Hyoid bone and vallecula
  - Ventral border --- base of the tongue
  - Laterally --- Tonsillar fossae and tonsils
  - Dorsally --- lateral and dorsal pharyngeal wall

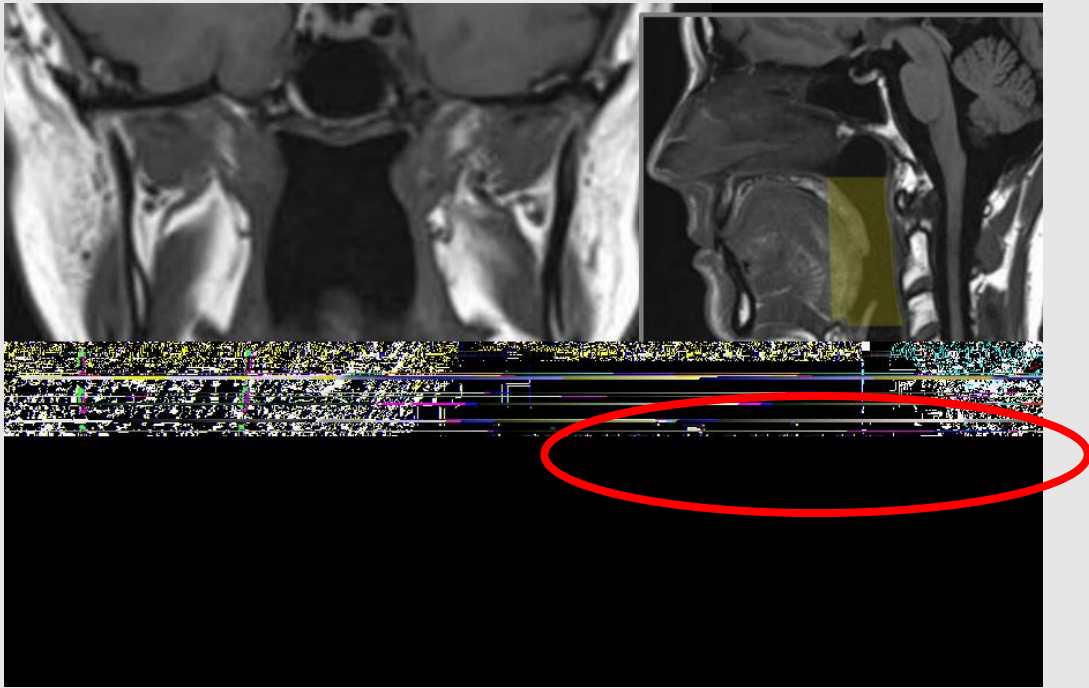






- Posterior 1/3 of the tongue
- Margins
  - Circumvalate papillae
  - Anterior tonsillar pillars (palatoglossus muscle)
  - Soft palate

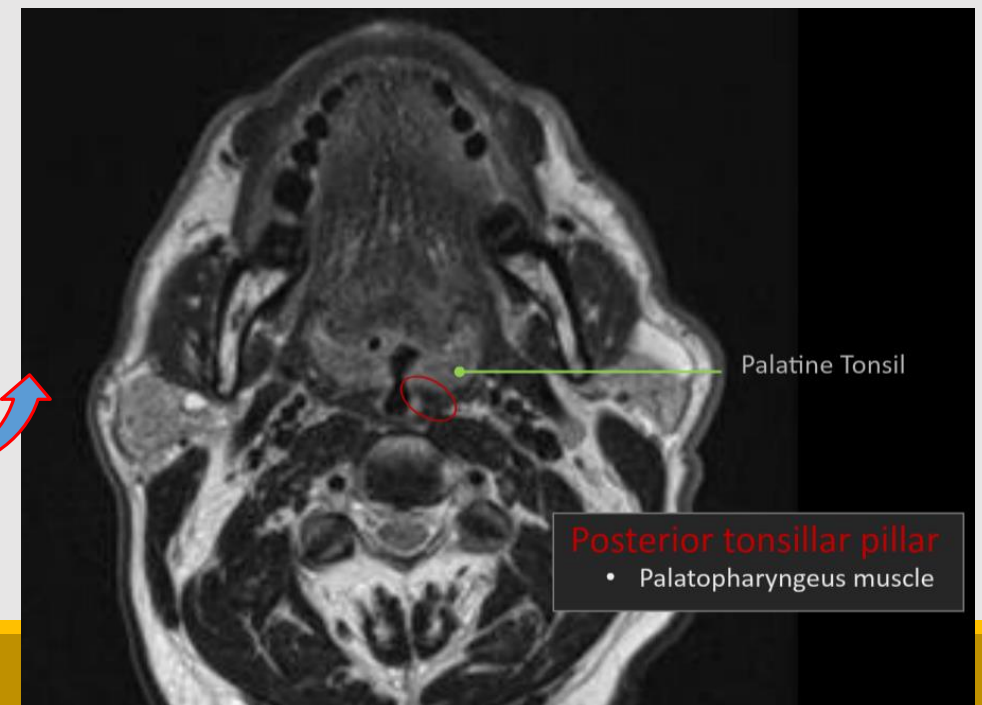
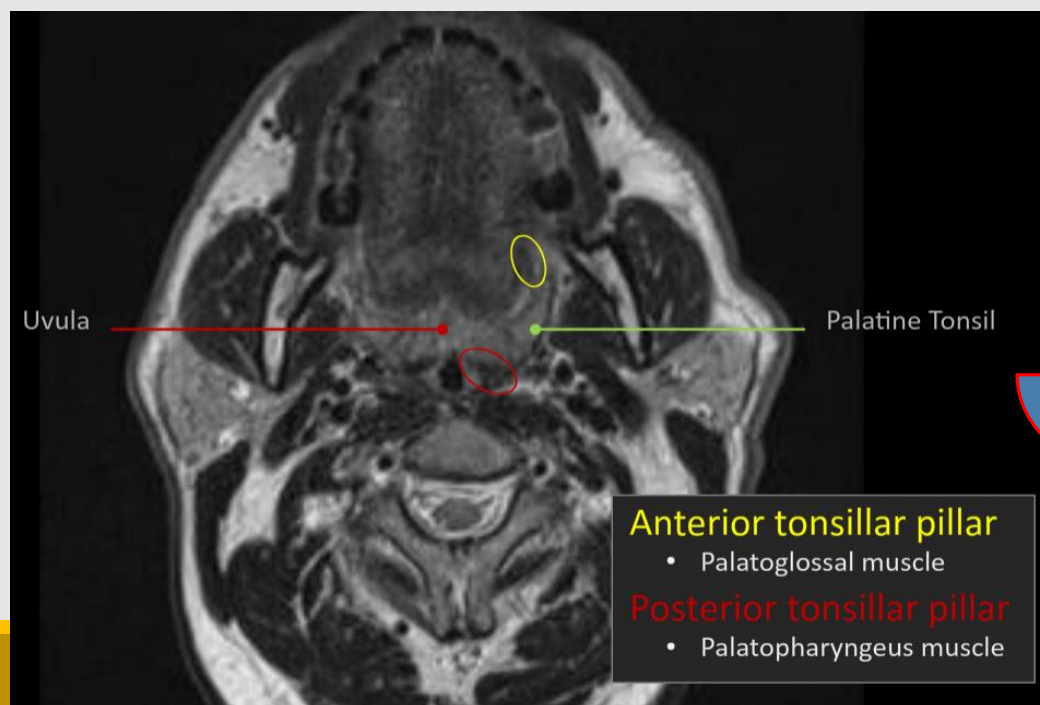
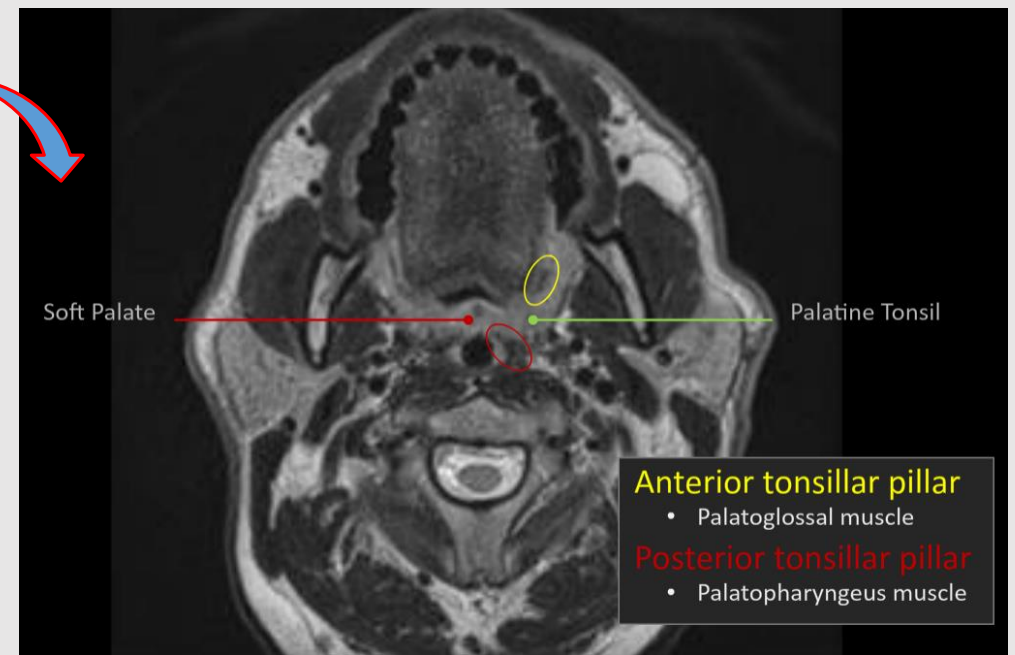
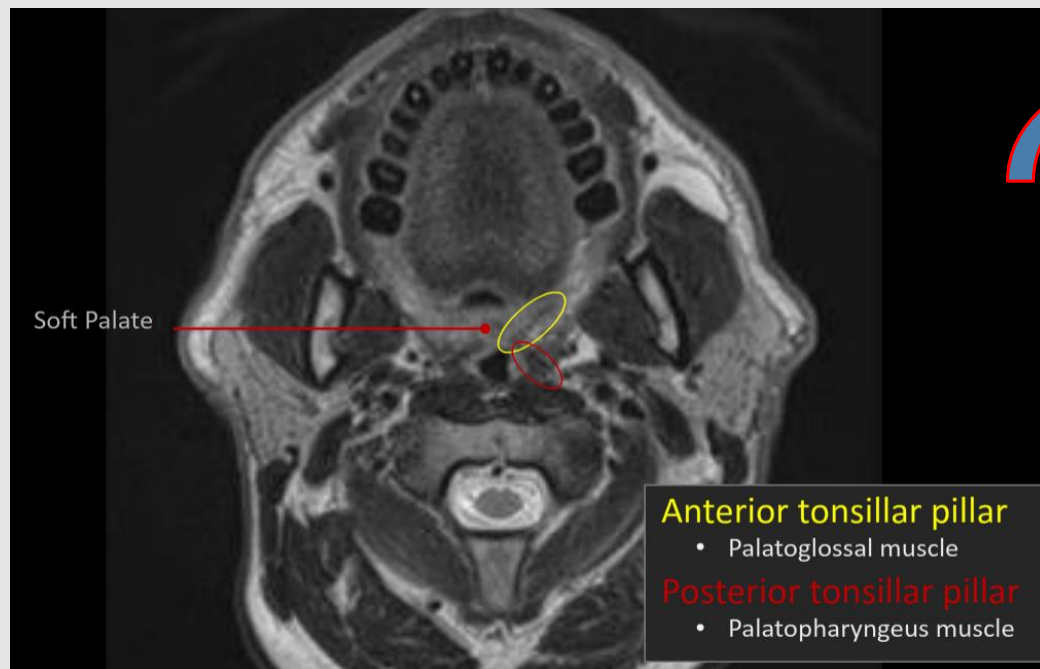




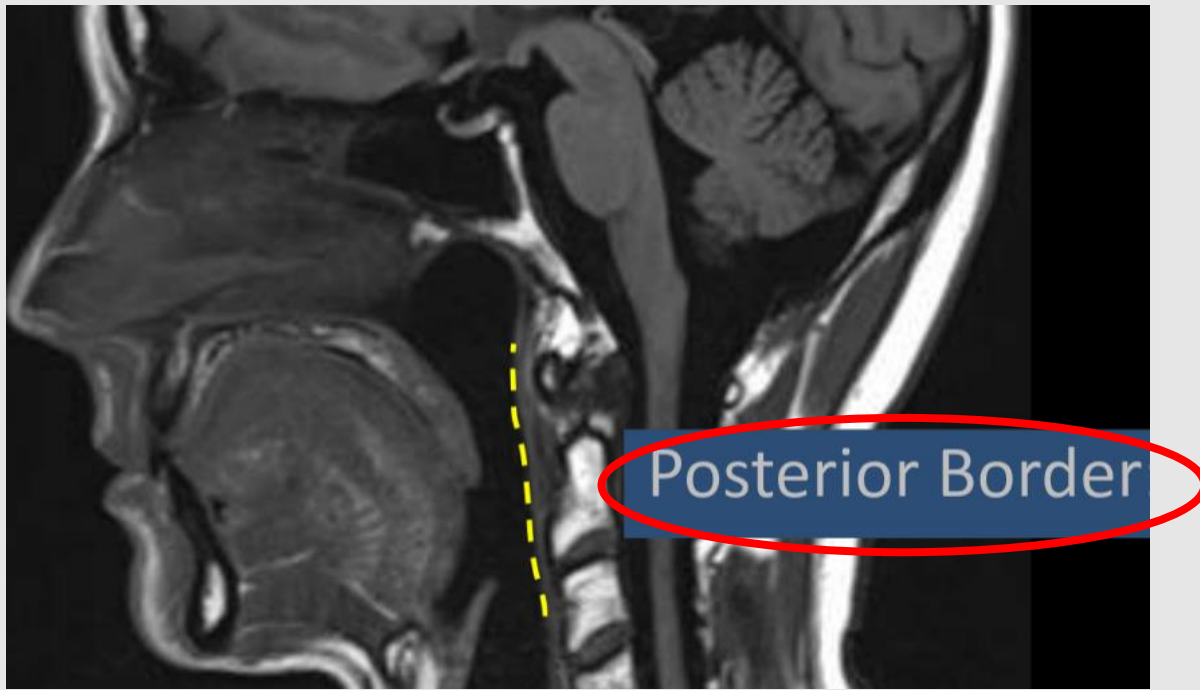
Lateral border

- Anterior tonsillar pillar: **palatoglossus muscle**
- Posterior tonsillar pillar: **palatopharyngeus muscle**
- Palatine tonsil



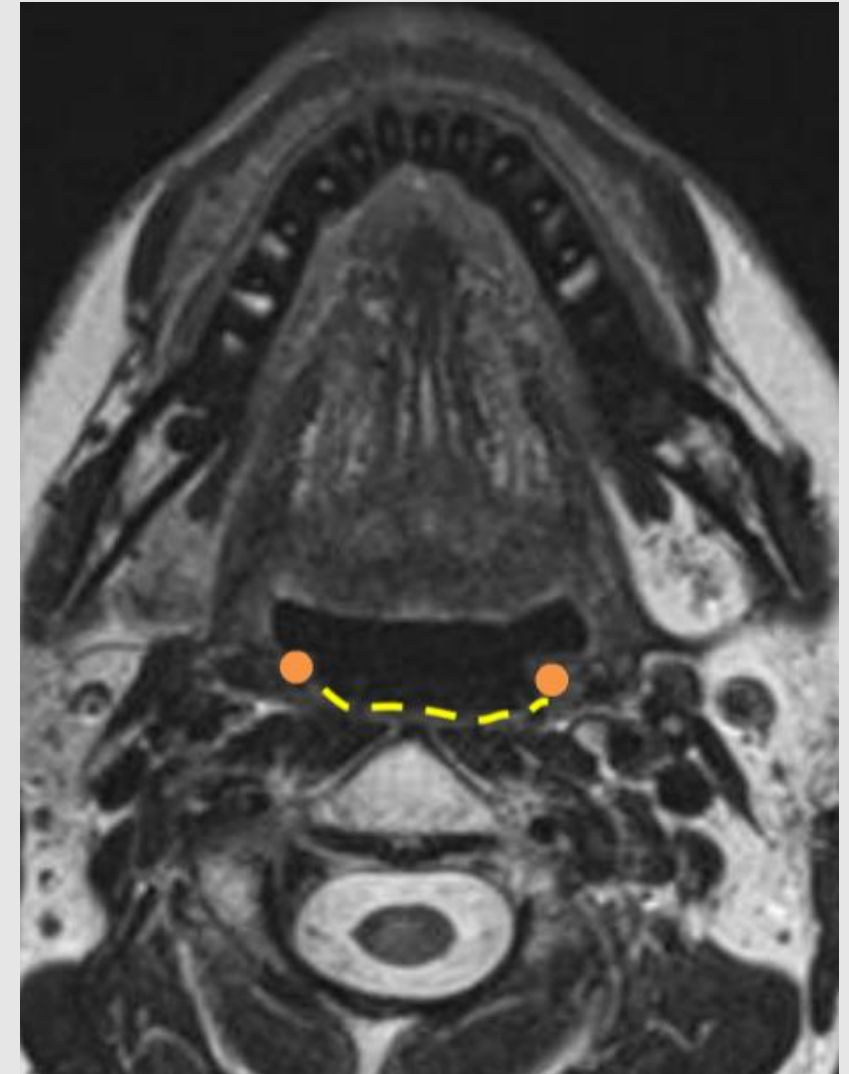




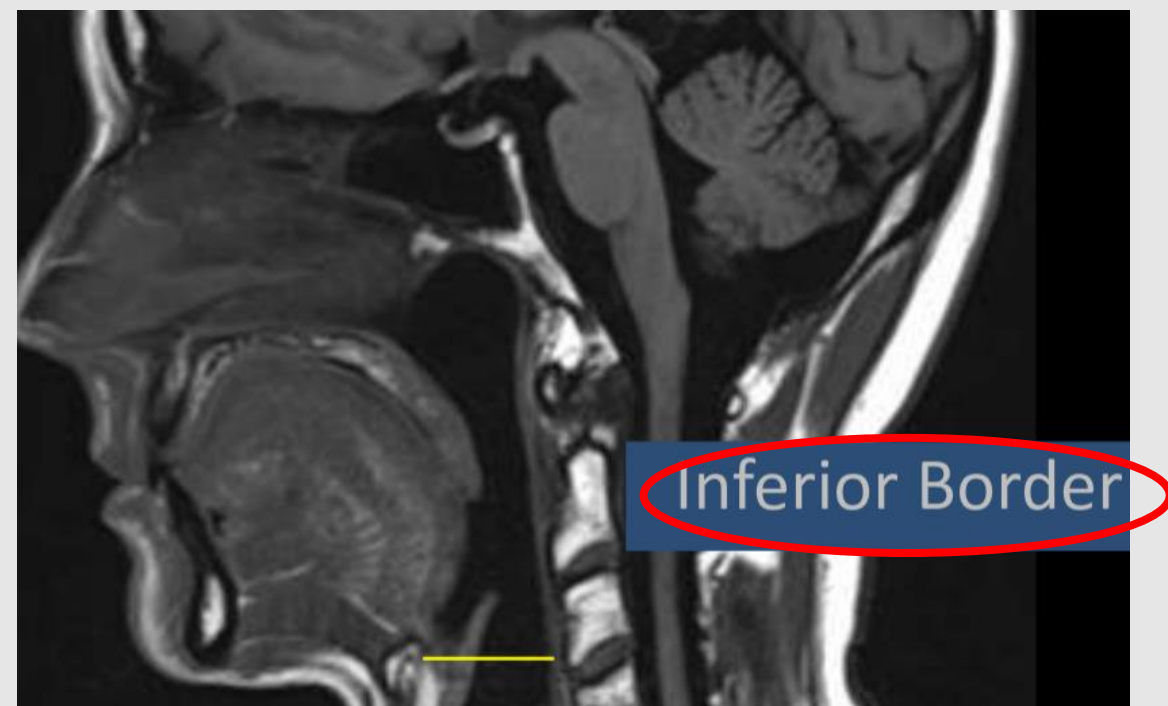
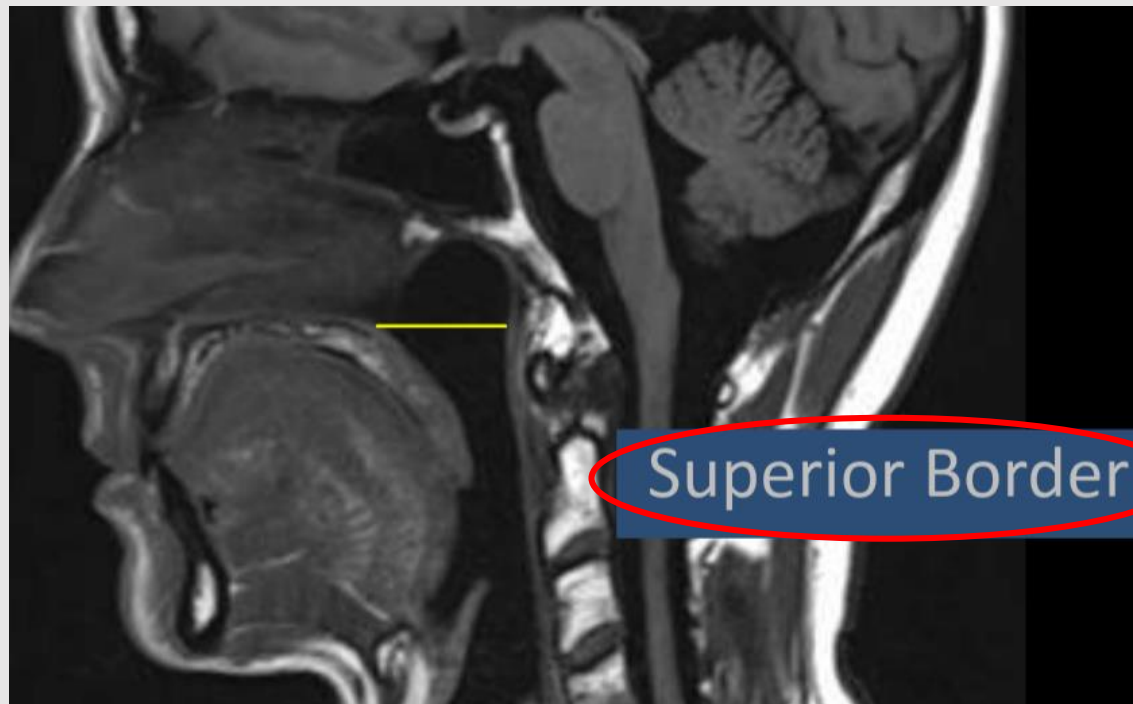


Posterior border

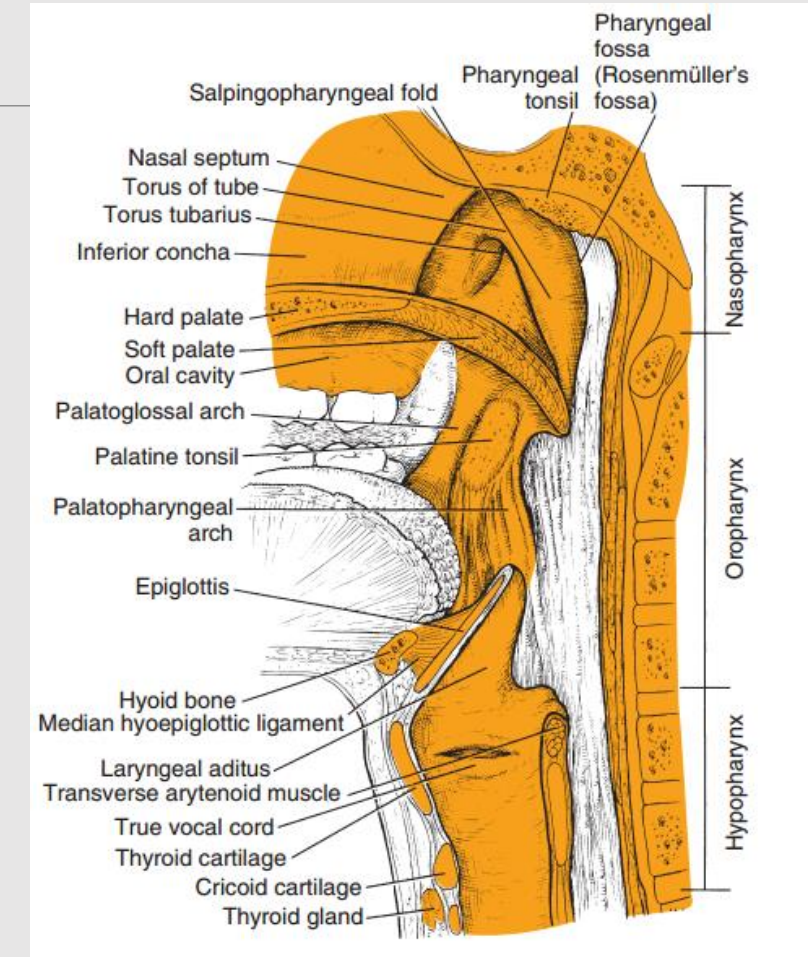
- Posterior pharyngeal wall
- Between posterior tonsillar pillars – palatopharyngeus muscles







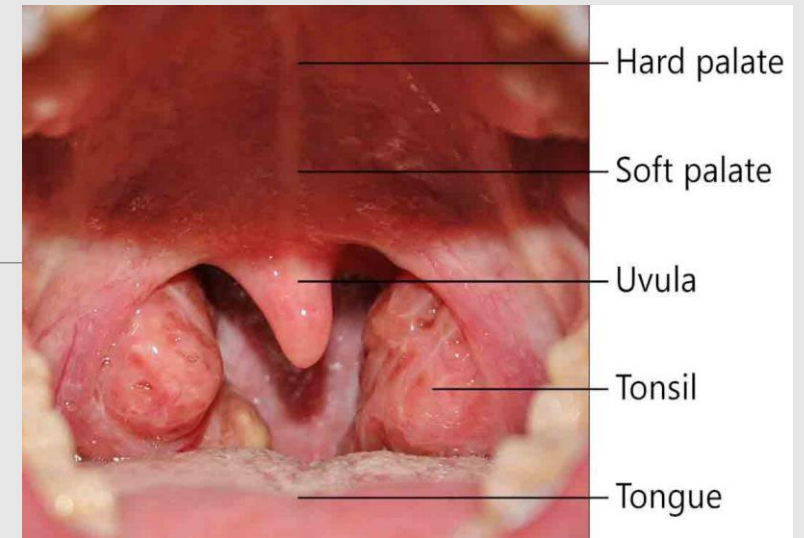
# Anatomy of the oropharynx



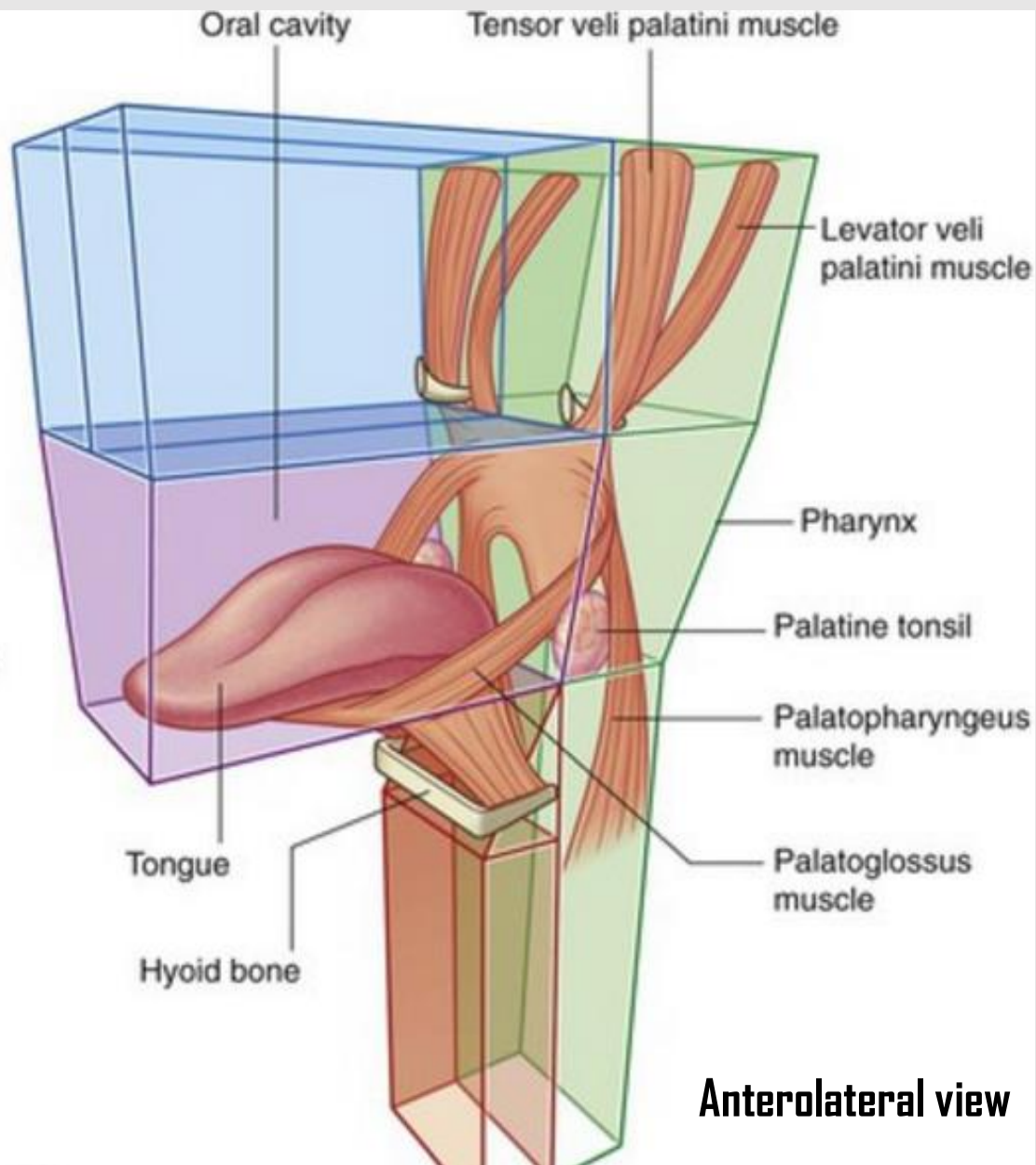
# Anatomy of the oropharynx

## SOFT PALATE

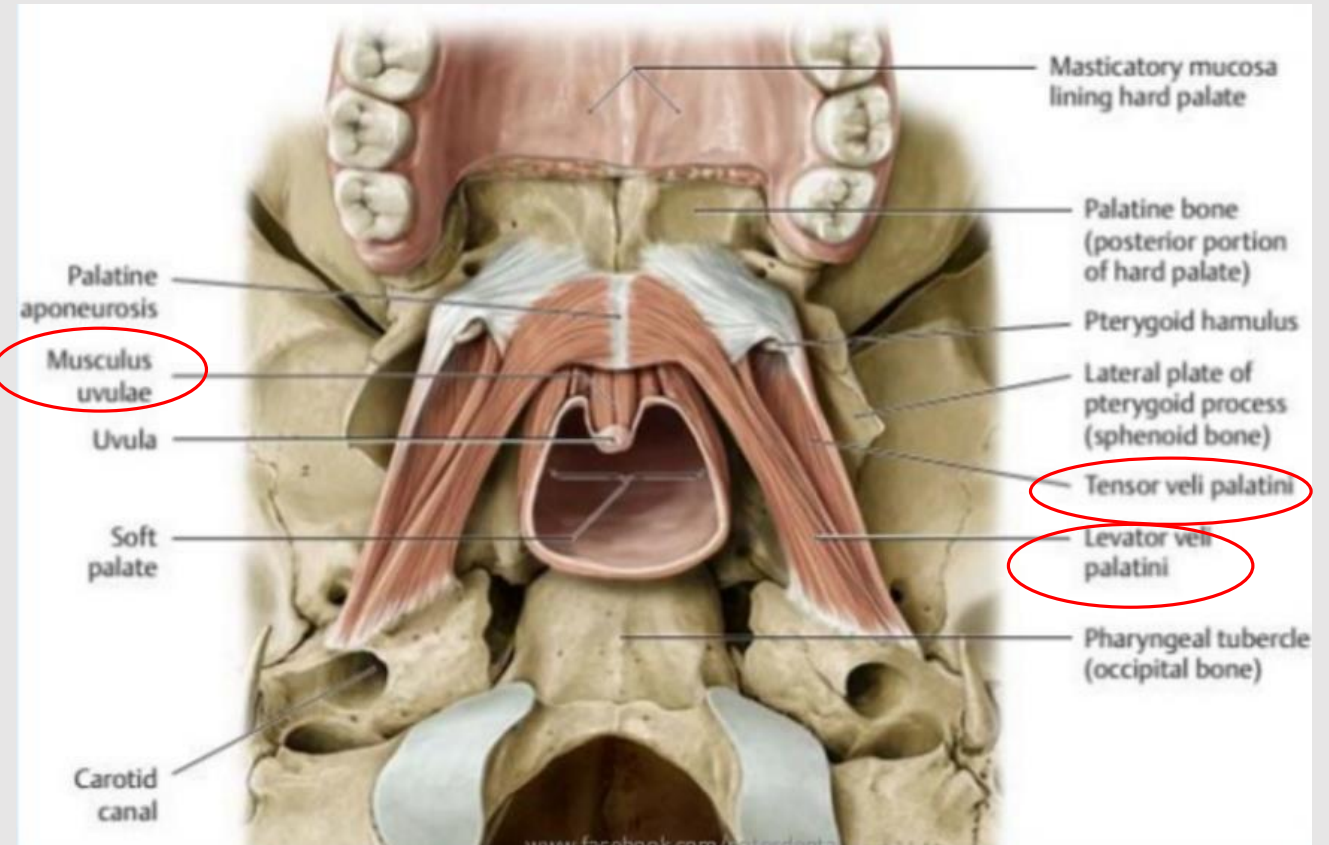
- Incompletely separates the nasopharynx and the oral cavity from the oropharynx
- It is formed by the palatopharyngeal arch and the uvula, and contains
  - Levator muscle of the palate (levator veli palatini)
  - Tensor muscle of the palate (tensor veli palatini)
  - Laterally: palatopharyngeal and constrictor muscle
  - Blood supply: ascending palatine branch of the facial artery
  - Innervation
    - Motor innervation: pharyngeal branch of the X nerve (except tensor veli palatine: mandibular nerve)
    - Sensory innervation: IX and lesser palatine nerve



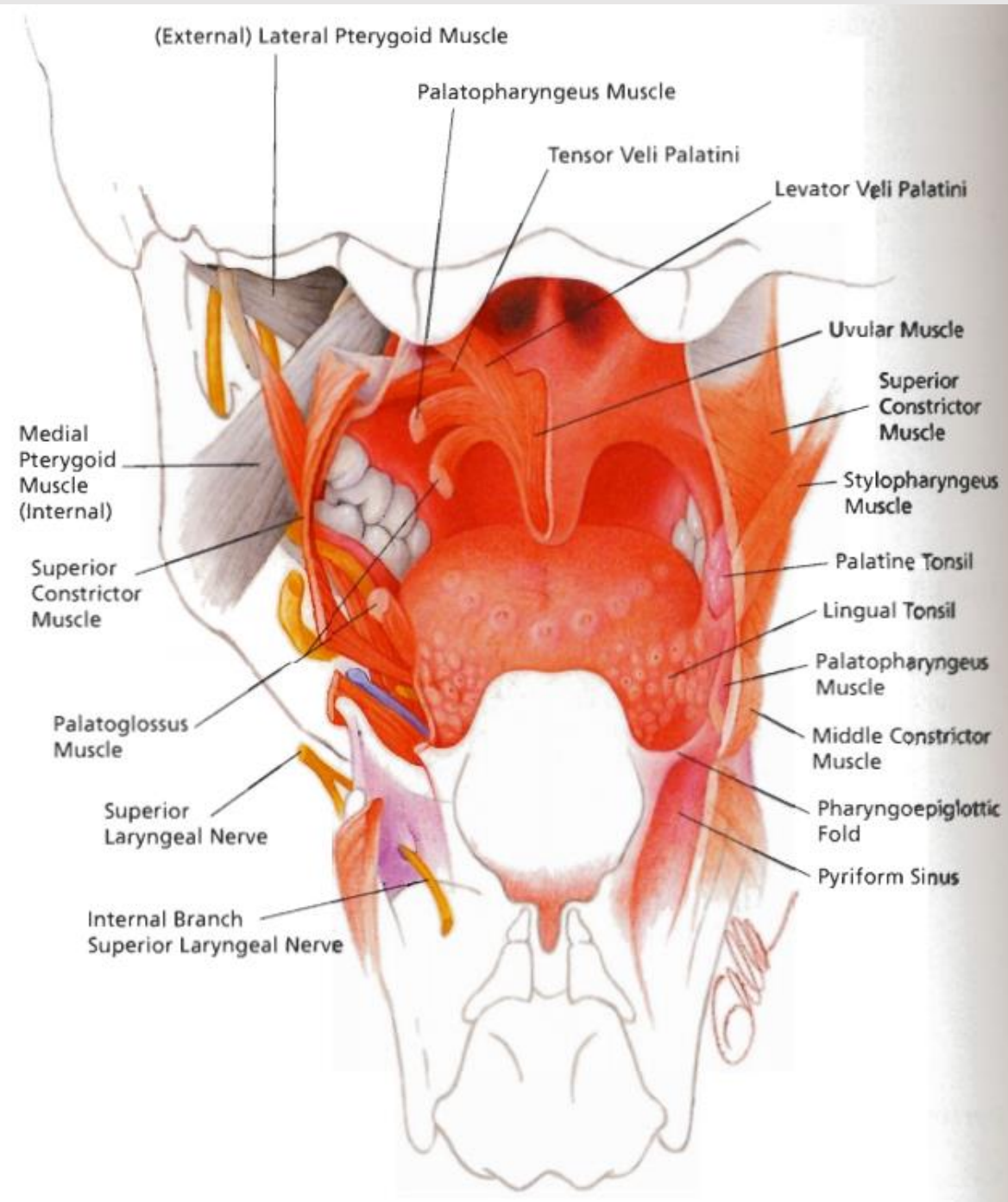




## Inferior view

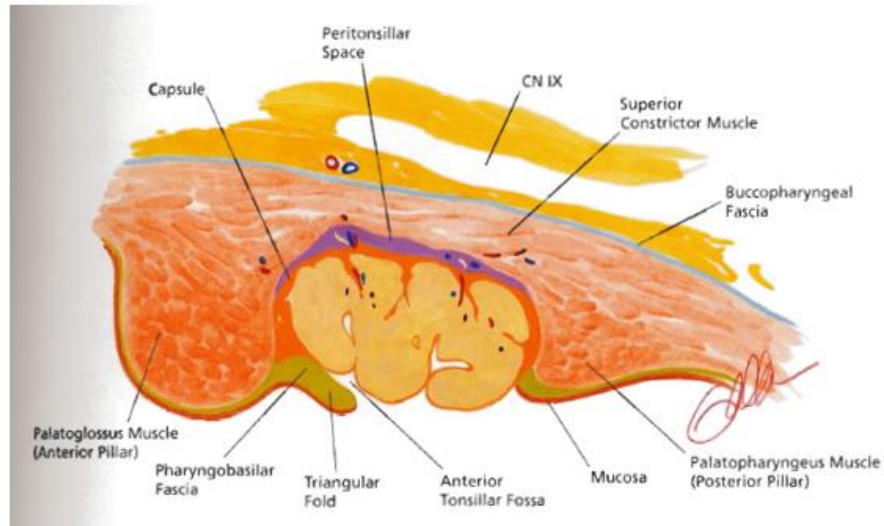






# Anatomy of the oropharynx

## TONSILLAR FOSSAE

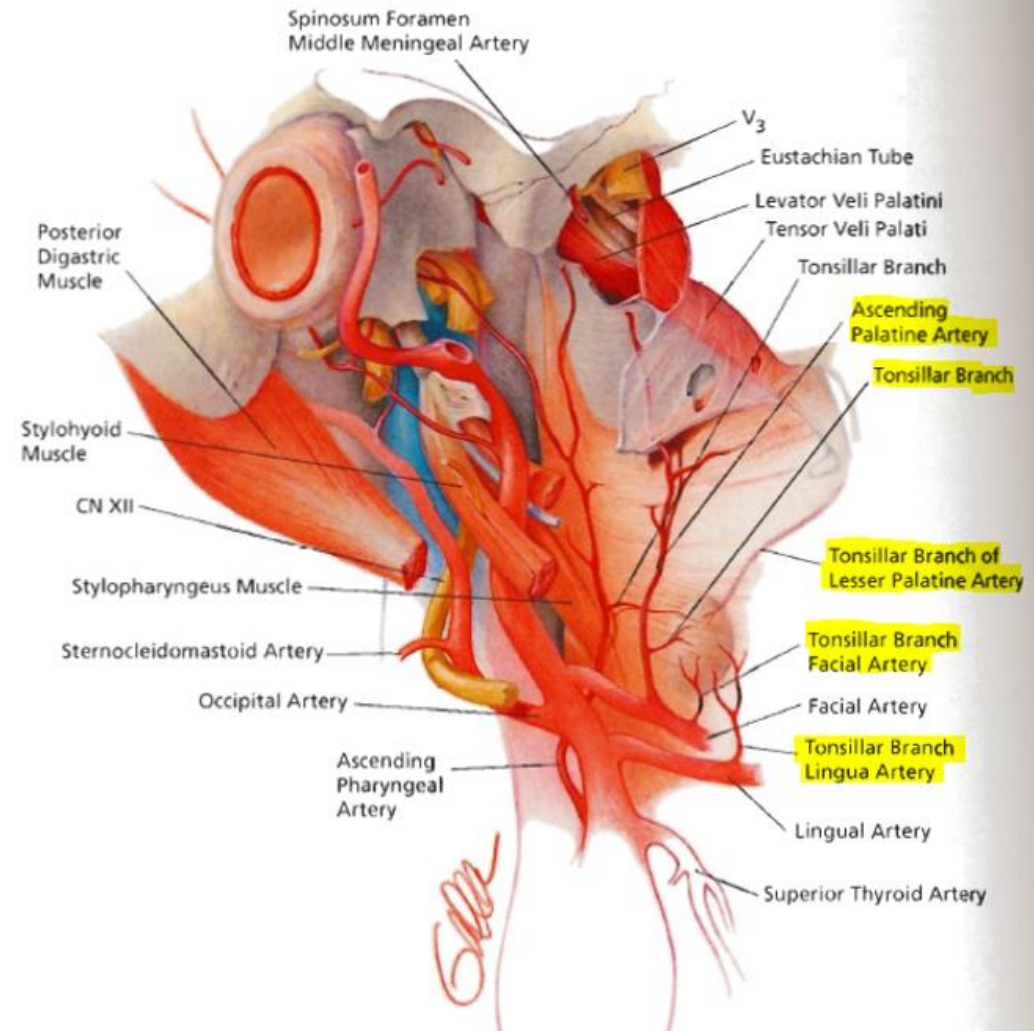


### Muscular boundaries

1. A: P-G muscle
2. P: P-P muscle
3. Lateral: superior constrictor muscle

### Tonsillar arterial supply

1. Tonsillar b. dorsal lingual artery
2. Tonsillar b. ascending pharyngeal artery (b. facial artery)
3. Tonsillar b. facial artery
4. Tonsillar b. lesser palatine artery



# Anatomy of the oropharynx

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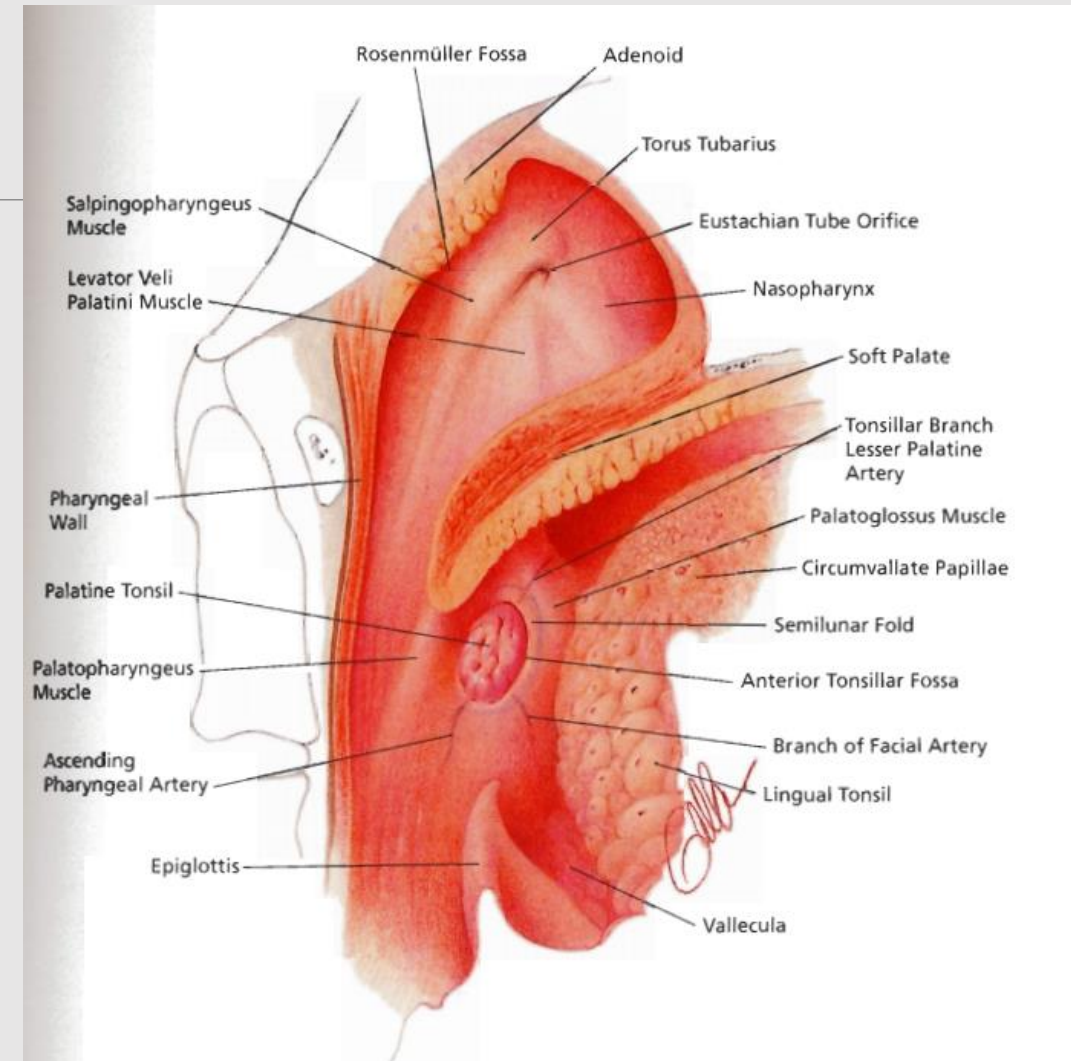
## BASE OF THE TONGUE

- Extends from the circumvallate papillae to the vallecula and to the glossopalatine sulci laterally
- Region rich in lymphatics. Lingual tonsils form part of the Waldeyer ring.
- Blood supply: lingual arteries --- dorsal lingual branch
- Motor innervation: XII nerve
- Sensory/taste innervation
  - IX nerve
  - Except for the most posteroinferior part --- internal laryngeal branch of the vagus nerve

# Anatomy of the oropharynx

## POSTERIOR OROPHARYNGEAL WALL

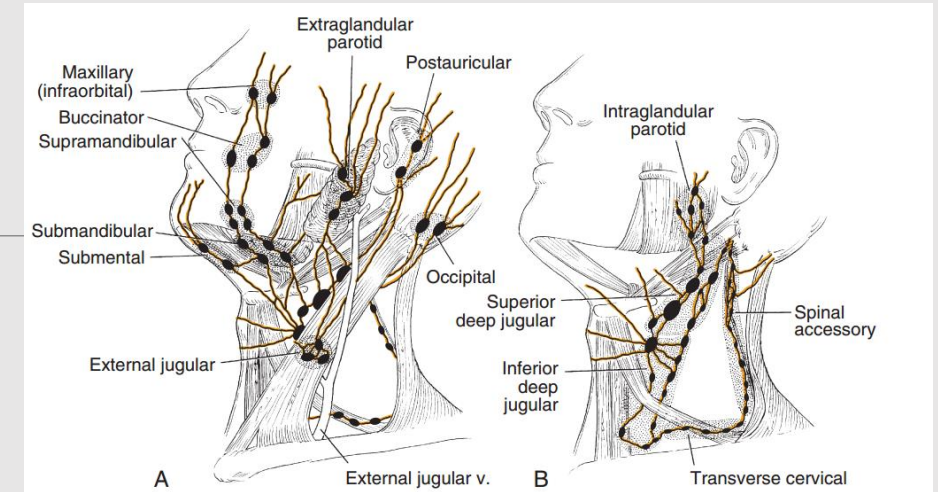
- Extends from the region of the soft palate to the epiglottis
- Borders the tonsillar fossae and the lateral aspect of the piriform sinuses laterally
- Composed of
  - Superior constrictor muscle
  - Buccopharyngeal fascia
  - Pharyngobasilar fascia





# Anatomy of the oropharynx

## LYMPHATHICS



- Lymphatic pattern of the oropharynx is complex and its knowledge is of great importance for the outcome of surgical/radiotherapy treatment of OP lesions
- Lymphatic spread from malignant lesions depends on the size and location of the primary malignancy
- **OP carcinoma is predisposed to drain to levels II, III and IV with possible further spread to other regions in extensive disease**
- Skip metastases to other nodal levels are extremely rare

# Patterns of Cervical Lymph Node Metastasis from Squamous Carcinomas of the Upper Aerodigestive Tract

Jatin P. Shah, MD, FACS, New York, New York

Retrospective review of 1081 untreated PTs whom underwent complete RND

**TABLE I**  
Distribution and Histologic Confirmation of Metastatic Disease by Site in 1,081 Patients Undergoing 1,119 Elective and Therapeutic RNDs

Primary Site	No. of Patients	No. of RNDs	Positive Nodes in Elective RNDs	Positive Nodes in Therapeutic RNDs
Oral cavity	501	516	34% (65/192)	76% (246/324)
Oropharynx	207	213	31% (15/48)	84% (138/165)
Hypopharynx	126	128	17% (4/24)	97% (101/104)
Larynx	247	262	37% (29/79)	84% (155/183)
Total	1,081	1,119	33% (113/343)	82% (640/776)

## Objective

- Study the prevalence and distribution of neck node metastasis by neck level/primary site

Oropharynx --- 213 RNDs

## Conclusions

- Levels I, II and III --- greatest risk for nodal MTX from SCC of the oral cavity--- supraomohyoid neck dissection
- Levels II, III and IV --- greatest risk for SCC of the OP, HP and larynx --- anterolateral neck dissection for II/III/IV levels

**TABLE II**  
Percentage of Metastatic Lymph Nodes Involved in Elective and Therapeutic RNDs

Level of Metastatic Lymph Nodes	Primary Site							
	Oral Cavity		Oropharynx		Hypopharynx		Larynx	
	Elective	Therapeutic	Elective	Therapeutic	Elective	Therapeutic	Elective	Therapeutic
I	58	61	7	17	0	10	14	8
II	51	57	80	85	75	78	52	68
III	26	44	60	50	75	75	55	70
IV	9	20	27	33	0	47	24	35
V	2	4	7	11	0	11	7	5

**FREQUENCY OF BILATERAL CERVICAL METASTASES  
IN OROPHARYNGEAL SQUAMOUS CELL CARCINOMA:  
A RETROSPECTIVE ANALYSIS OF 352 CASES AFTER  
BILATERAL NECK DISSECTION**

Bernhard Olzowy, MD,<sup>1</sup> Yulia Tsalemchuk,<sup>1</sup> Klaus-Juergen Schotten, MD,<sup>2</sup>  
Oliver Reichel, MD,<sup>1</sup> Ulrich Harréus, MD, PhD<sup>1</sup>

- The location of the primary malignancy in **relation to the midline** is an important consideration for guiding treatment of the neck
- Tumors of the base of the tongue, soft palate, and posterior pharyngeal wall have a higher incidence of bilateral lymphadenopathy

<b>Table 2.</b> Frequency of bilateral cervical lymph node metastases for the different localizations of the primaries ("subsites") and T classifications of all patients who received either bilateral or unilateral neck dissection.					
Subsite	Classification				All T classifications
	T1	T2	T3	T4	
Tonsillar fossa	3.3% (3/92)	10.7% (14/131)	17.6% (9/51)	8.6% (3/35)	9.4% (29/309)
Base of tongue	14.3% (4/28)	23.9% (17/71)	27.0% (10/37)	15.8% (3/19)	21.9% (34/155)
Soft palate	10.0% (1/10)	25.0% (3/12)	11.1% (1/9)	50.0% (2/4)	20.0% (7/35)
Pharyngeal wall	50.0% (1/2)	33.3% (2/6)	50.0% (2/4)	0.0% (0/4)	31.3% (5/16)
All subsites	6.8% (9/132)	16.4% (36/220)	21.8% (22/101)	12.9% (8/62)	14.6% (75/515)

*Note: Values are given in % (no. of patients with bilateral metastases/total no. of patients).*

## **FREQUENCY OF BILATERAL CERVICAL METASTASES IN OROPHARYNGEAL SQUAMOUS CELL CARCINOMA: A RETROSPECTIVE ANALYSIS OF 352 CASES AFTER BILATERAL NECK DISSECTION**

Bernhard Olzowy, MD,<sup>1</sup> Yulia Tsalemchuk,<sup>1</sup> Klaus-Juergen Schotten, MD,<sup>2</sup>  
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- The proportion of bilateral neck metastases was significantly higher for carcinomas of the base of tongue compared with carcinoma of the palatine tonsils ( $p = .004$ )
- Fewer bilateral metastases were seen for T1 tumors compared with more advanced primaries ( $p < .001$ )
- Patients with 2 or more ipsilateral neck metastases showed significantly more bilateral metastases compared with patients with fewer than 2 positive ipsilateral lymph nodes ( $p < .001$ )

### CONCLUSIONS

- **Bilateral neck dissection should be recommended for all but T1 and selected cases of T2 carcinomas of the tonsillar fossa**



# Malignant tumors of the oropharynx

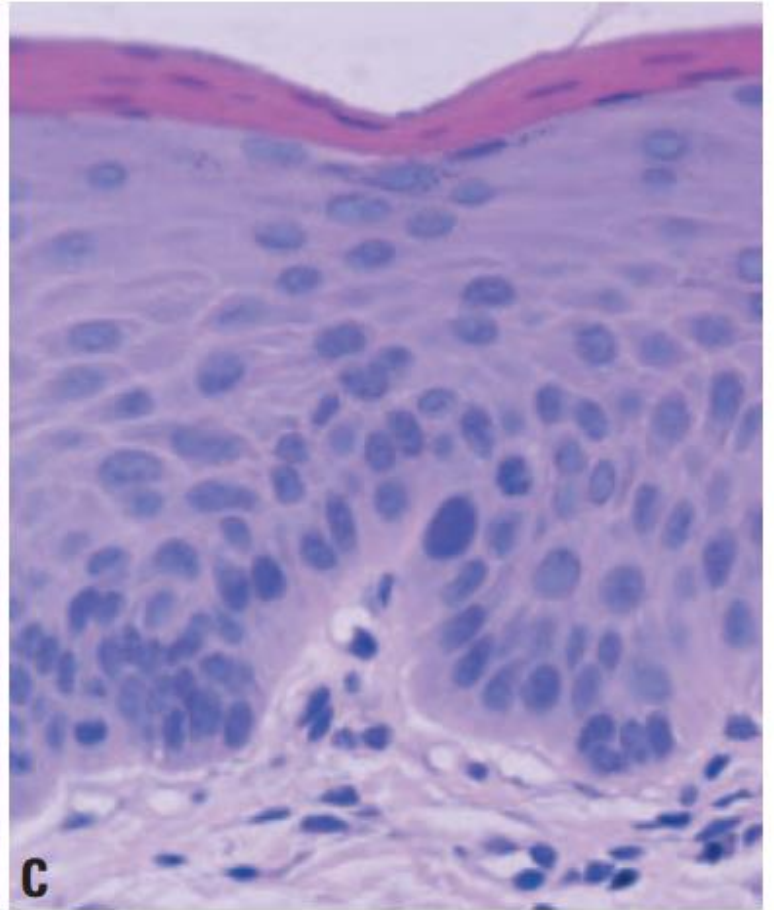
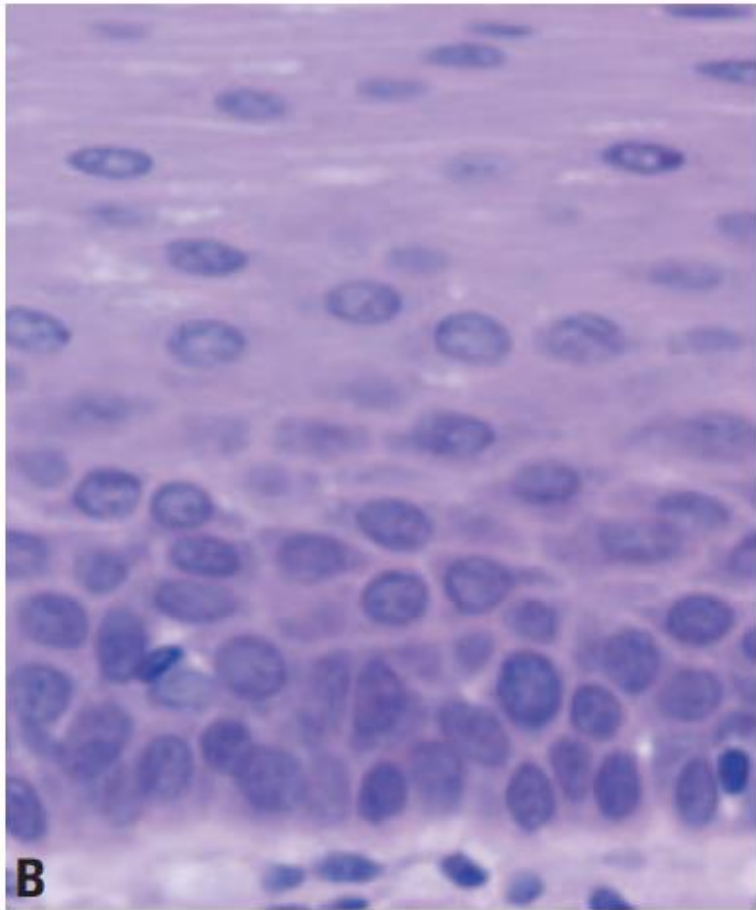
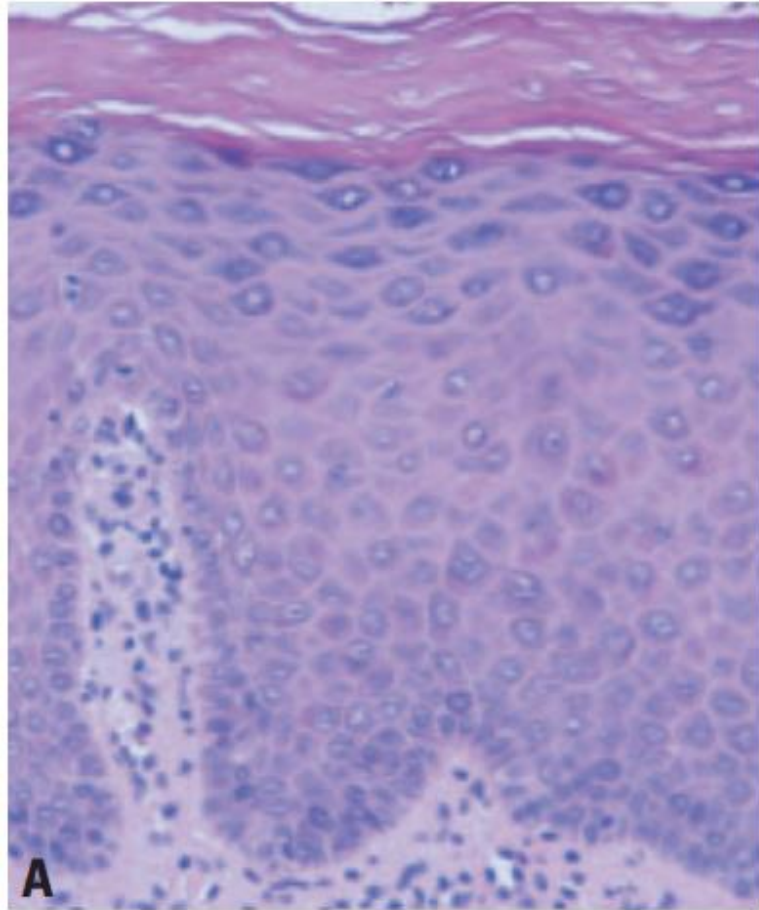
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- Epithelial precursor lesions of the oropharynx clinically present as white patches (LEUKOPLAKIA) or red patches (ERYTHROPLAKIA)
- Leukoplakia is not usually related to dysplastic cells and relates to hyperplasia
- Erythroplakia/mixed lesions is frequently related to dysplastic features --- MALIGNANCY
- Carcinoma in situ (CIS) describes malignant transformation without invasion
  - WHO: full-thickness architectural abnormality + severe cytologic atypia

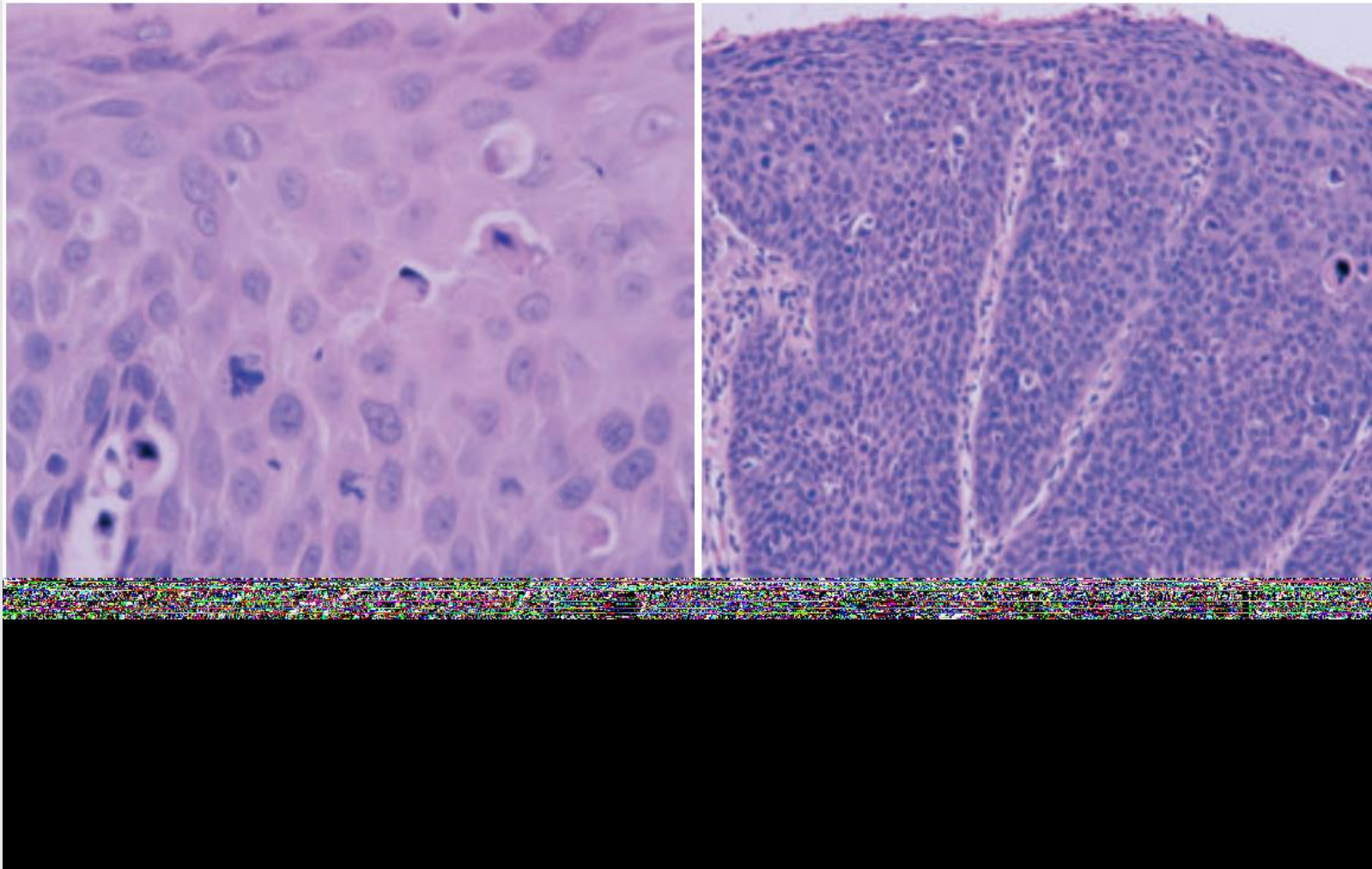
# Malignant tumors of the oropharynx

## DYSPLASIA: ARCHITECTURAL + CYTOLOGIC ATYPIA

Architecture	Cytology
Irregular epithelial stratification	Abnormal variation in nuclear size (anisonucleosis)
Loss of polarity of basal cells	Abnormal variation in nuclear shape (nuclear pleomorphism)
Drop-shaped rete ridges	Abnormal variation in cell size (anisocytosis)
Increased number of mitotic figures	Abnormal variation in cell shape (cellular pleomorphism)
Abnormally superficial mitoses	Increased nuclear-cytoplasmic ratio
Premature keratinization in single cells (dyskeratosis)	Increased nuclear size
Keratin pearls within rete pegs	Atypical mitotic figures
	Increased number and size of nucleoli



**Fig. 4.14** **A** Acanthosis. Hyperplastic epithelium with thickened stratum spinosum. **B** Basal cell hyperplasia. Increase in progenitor compartment without dysplasia. **C** Mild dysplasia. Basal cell hyperplasia with relatively mild cytological change confined to lower third of epithelium.



**C** - Severe dysplasia into upper third of epithelium with prominent cytological change including abnormal mitoses

**D**- Carcinoma in-situ. Abnormal cells seen throughout the full thickness of epithelium



# Malignant tumors of the oropharynx

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- SCC (squamous cell carcinoma) is the most common malignancy --- > 90% of all malignant OP tumors
- The WHO (World Health Organization) classification of tumors outlines the presently known malignancies

## Epithelial Tumors

Squamous cell carcinoma

Verrucous carcinoma

Basaloid squamous cell carcinoma

Papillary squamous cell carcinoma

Spindle cell carcinoma

Acantholytic squamous cell carcinoma

Adenosquamous cell carcinoma

Carcinoma cuniculatum

Lymphoepithelial carcinoma

## Salivary Gland Tumors

Acinic cell carcinoma

Mucoepidermoid carcinoma

Adenoid cystic carcinoma

Polymorphous low-grade adenocarcinoma

Basal cell adenocarcinoma

Epithelial-myoepithelial carcinoma

Clear cell carcinoma not otherwise specified

Cystadenocarcinoma

Mucinous adenocarcinoma

Oncocytic carcinoma

Salivary duct carcinoma

Myoepithelial carcinoma

Carcinoma ex pleomorphic adenoma

## Soft Tissue Tumor

Kaposi sarcoma

## Hematolymphoid Tumors

Diffuse large B-cell lymphoma

Mantle cell lymphoma

Follicular lymphoma

Extranodal marginal zone B-cell MALT type lymphoma

Burkitt lymphoma

T-cell lymphoma

Extramedullary plasmacytoma

Langerhans cell histiocytosis

Extramedullary myeloid sarcoma

Follicular dendritic cell sarcoma/tumor

Mucosal malignant melanoma

Secondary tumors

# Malignant tumors of the oropharynx

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## SQUAMOUS CELL CARCINOMA (SCC)

- Invasive epithelial neoplasm with varying degrees of squamous differentiation and a propensity to EARLY and EXTENSIVE LYMPH NODE METASTASES, occurring predominantly **in alcohol and tobacco using adults in the 5<sup>th</sup> and 6<sup>th</sup> decades of life**
- Epidemiology
  - > 90% of malignant neoplasms of the oral cavity/OP are SCC
  - Males >>> females
  - Significant increases in incidence in younger subjects (particularly males) have been reported from many western countries in western decades --- HPV +

## SQUAMOUS CELL CARCINOMA (SCC)

### ➤ Etiology

#### ➤ Tobacco smoking and alcohol

- Dominant risk factors and strongly synergistic
- For the highest consumption levels, RR from 70 to 100 have been reported

#### ➤ Tobacco chewing

- Major cause of oral/OP SCC in the Indian subcontinent, parts of South-East Asia, China and Taiwan
- In India, about 50% of OP cancers in males and 90% in females are caused by chewing tobacco

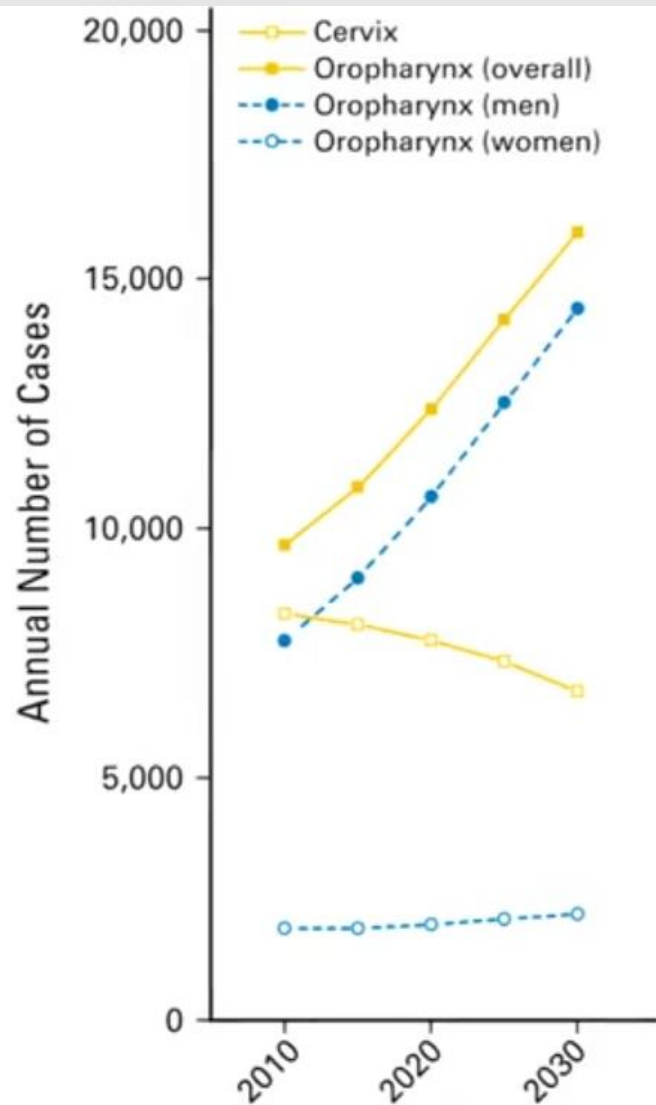
#### ➤ Human papillomavirus infection

- Related to the oncogenic genotypes –HPV 16 (most common), 18, 31 and 33
  - Studies suggest that up to 40% of OP cancer cases may be due to HPV infection

HPV – OPSCC

HPV + OPSCC

2011 publication --- WORLD WIDE EPIDEMIC



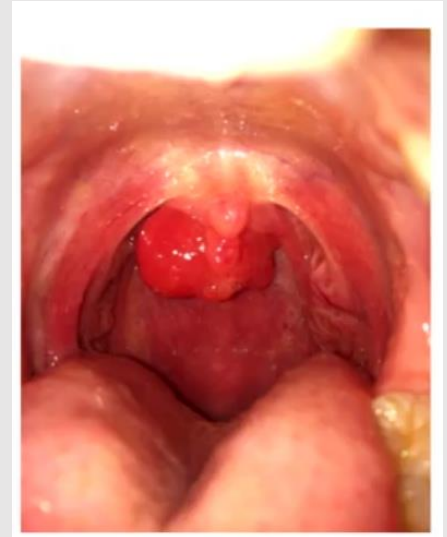
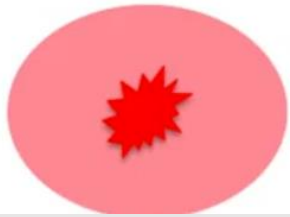
**HPV-Infection is now the Leading Cause of Oropharyngeal Cancer**

Nation	1985	2004
USA <sup>1</sup>	40%	80%
UK <sup>2</sup>	22%	67%
Australia <sup>3</sup>	19%	60%
Sweden <sup>4</sup>	29%	93%



**TABLE 97-3. Traditional vs. HPV-Associated Oropharyngeal SCC: Demographics, Clinical Presentation, and Prognosis**

Variables	Traditional Oropharyngeal SCC	HPV-Associated Oropharyngeal SCC
Demographics	≥60 yr, M:F = 3:2	40-60 yr, M:F = 3:1
Risk profile	Tobacco, alcohol	Reduced/no addiction habit Epidemiologic sexual history correlation
Molecular biology	p16 inactivation	p16 overexpression
Pathology	Keratinizing SCC, well to moderate to poorly differentiated	Nonkeratinizing SCC, poorly differentiated
Clinical presentation	Less bulky nodes	Small/unknown primary with bulky, cystic, or multiple nodes
Prognosis	Guarded, 5-year survivals ~40% to 60%	Good, 5-year survivals ~80% to 90%
Prognostic variables	T, N, and AJCC stage, margin, ECS, smoking	T stage, margins, three or more nodes
Local recurrence	Higher	Infrequent
Distant metastasis	~20%	~5% to 6% (surgical ± adjuvant therapy), ~7% to 12% (nonsurgical therapy)



# Malignant tumors of the oropharynx

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## LYMPHOEPITHELIAL CARCINOMA

- Poorly differentiated SCC or undifferentiated carcinoma, accompanied by a prominent reactive lymphoplasmacytic infiltrate
- Morphological features are indistinguishable from those from nasopharyngeal nonkeratinizing carcinoma with a rich lymphoplasmacytic infiltrate
- Epidemiology
  - Accounts for 0.8-2% of all oral or OP cancers

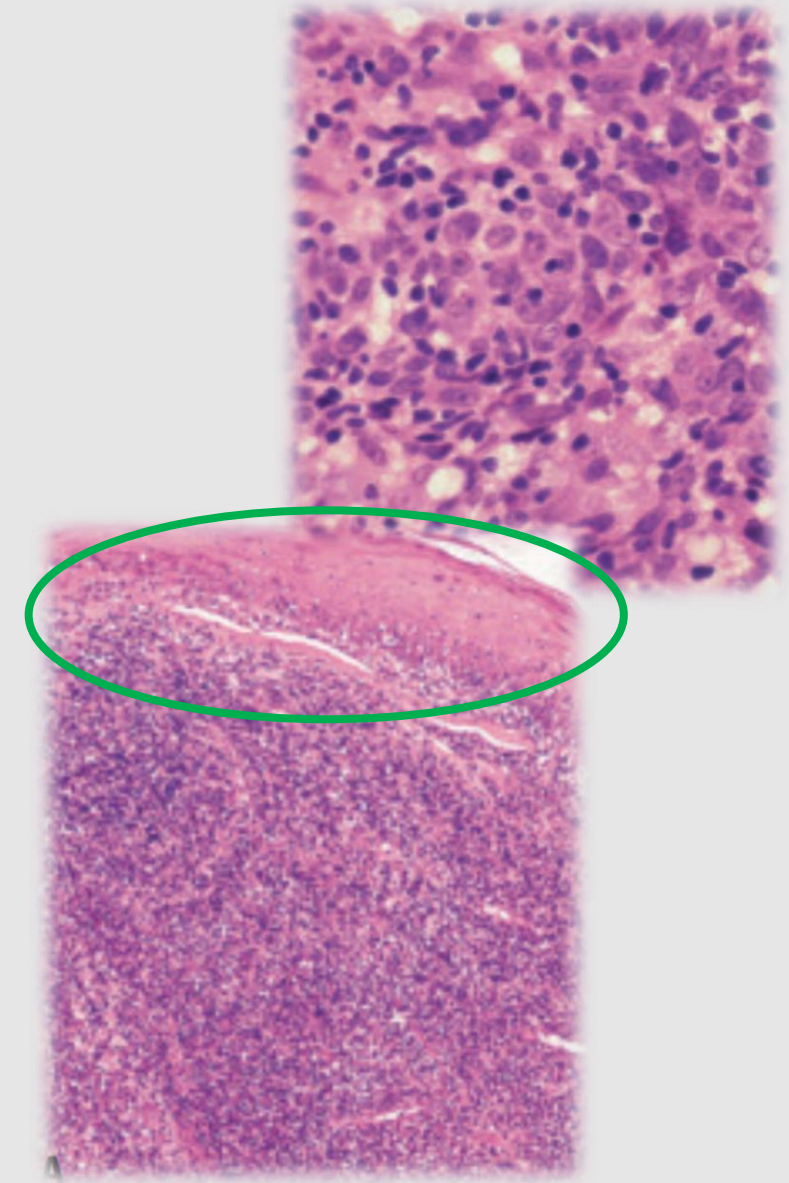
# LYMPHOEPITHELIAL CARCINOMA

## ➤ Etiology

- EBV has been tested in only a limited number of cases
  - EBV encoded RNA (EBER) + by in-situ hybridization in oral/OP LEC (chinese patients)

## ➤ Histopathology

- LEC of the oral cavity/OP shows morphologic features indistinguishable from its NP and sinonasal counterpart
- The surface epithelium is often intact + syncytial sheets/cluster of carcinoma cells (prominent nucleoli/ill-defined borders) + rich lymphoplasmacytic infiltrate



# Lymphoepithelial-like Carcinoma of the Oropharynx

## *A Morphologic Variant of HPV-related Head and Neck Carcinoma*

*Aatur D. Singhi, MD, PhD,\* Edward B. Stelow, MD,†  
Stacey E. Mills, MD,† and William H. Westra, MD\**

- HPV-HNSCC represents an important subgroup of H&N characterized by distinct epidemiologic, clinical and a **relative constant microscopic appearance**
- Those cancers that deviate from the morphologic prototype, an association with HPV may not be recognized and tumor classification not achieved
- STUDY ---identify 22 HPV-HNSCC with well-developed lymphoepithelial features ( EVB-induced undifferentiated carcinoma of NP)
  - P16 + by IHC (100%)
  - HPV 16 + by in-situ hybridization (86%)
  - EVB – by in-situ hybridization (100%)
- Conclusions
  - For carcinomas of the H&N with lymphoepithelial features, EBV-driven process can not be assumed
  - Describe an HPV-HNSCC microscopically indistinguishable from EVB related carcinoma
  - For lymphoepithelial carcinomas presenting as cervical lymph node metastases, **testing for HPV and EBV should be mandatory**



# LYMPHOEPITHELIAL CARCINOMA

## ➤ Clinical features

- Intra-oral mass, which can be ulcerated
- A proportion of PTs present with neck mass due to regional lymph node involvement

## ➤ Location and metastatic spread

- >90% of all oral and OP LEC occur in the tonsil and tongue base
- High propensity for regional cervical lymph node involvement (>70% of the cases at presentation)
- Distant metastases tend to occur in the liver and lung

## ➤ Prognosis and predictive factors

- Radiosensitive tumor
- Local control can be achieved in a high % of cases, even in the presence of lymph node metastases

# Malignant tumors of the oropharynx

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## SALIVARY GLAND TUMORS

### Salivary Gland Tumors

Acinic cell carcinoma  
Mucoepidermoid carcinoma  
Adenoid cystic carcinoma  
Polymorphous low-grade adenocarcinoma  
Basal cell adenocarcinoma  
Epithelial-myoepithelial carcinoma  
Clear cell carcinoma not otherwise specified  
Cystadenocarcinoma  
Mucinous adenocarcinoma  
Oncocytic carcinoma  
Salivary duct carcinoma  
Myoepithelial carcinoma  
Carcinoma ex pleomorphic adenoma

- 9%-23% of salivary gland tumors are found in the oral cavity/oropharynx
  - ≈ 50% are malignant
- Most common OP sites are the soft palate, tonsillar fossae and base of the tongue
- Among malignant salivary gland tumors **adenoid cystic carcinoma** and **mucoepidermoid carcinoma** are the most common

# Malignant tumors of the oropharynx

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## KAPOSI SARCOMA

- Locally aggressive, growing neoplasm that can present cutaneously, but it can also present as a mucosal lesion
  - Can also affect lymph nodes and visceral organs
  - Rarely metastasizes
  - Associated with human herpesvirus 8 (HHV-8)
- Presents as...
  - Indolent variant in elderly men in the Mediterranean/Eastern Europe
  - Endemic disease in equatorial Africa
  - Immunosuppressed PTs



## KAPOSI SARCOMA

- The palate (hard and soft) are the commonest sites of involvement for KS of the H&N
- KS clinically present as...
  - Reddish blue or brown nodules or plaques with possible ulceration
  - The AIDS-related form of KS is the most aggressive form
- Patients might be treated with surgery, radiation and chemotherapy, depending on the epidemiology of the disease
- The incidence and course of the disease has improved with antiretroviral therapy in HIV-PTs





THE NEW ENGLAND JOURNAL of MEDICINE

## IMAGES IN CLINICAL MEDICINE

Chana A. Sacks, M.D., *Editor*

A 33-YEAR-OLD MAN PRESENTED TO THE EMERGENCY DEPARTMENT WITH FATIGUE AND WITH LESIONS IN the oral cavity and on the skin. Physical examination revealed multiple, firm, nontender, violaceous plaques of the palate and gums. He had similar lesions on his face, chest wall, and legs. Laboratory studies revealed leukopenia (white-cell count, 2900 per cubic millimeter; normal range, 4000 to 11,000) and a CD4 count of 76 cells per cubic millimeter (normal range, 430 to 1276). A diagnosis of human immunodeficiency virus infection was made. Biopsies of the skin and oral lesions revealed spindle-cell neoplasm, which was positive for CD34 and human herpesvirus 8 on immunohistochemical testing — findings that are consistent with Kaposi's sarcoma. Antiretroviral therapy (ART) and chemotherapy were both initiated. Kaposi's sarcoma, a cancer that indicates the presence of an immunodeficient state, is caused by human herpesvirus 8. Cutaneous lesions may occur alone or with visceral lesions of the oral cavity, gastrointestinal tract, and respiratory system. The presence of extensive oral Kaposi's sarcoma, as seen in this patient, is associated with a poor prognosis. After several months of treatment, the tumors in this patient diminished in size. Several months after the completion of chemotherapy, the patient is continuing to take ART, with an increased CD4 count and no progression of the oral and skin lesions.

# Malignant tumors of the oropharynx

## HEMATOLYMPHOID TUMORS

- On the basis of complex lymphatic tissue in the OP, lymphoid malignancies often occur in this area
- **Non-Hodgkin lymphoma**
  - Palatine tonsils, palate and base of the tongue as most common sites
  - Clinical symptoms can be fullness of throat, dysphagia, snoring or pain
  - Systemic symptoms are rare
  - Lesions present as exophytic masses, submucosal swelling and sometimes ulceration
- **Non-Hodgkin lymphoma**
  - Most are B-cell lymphomas (>> diffuse large B-cell lymphoma)

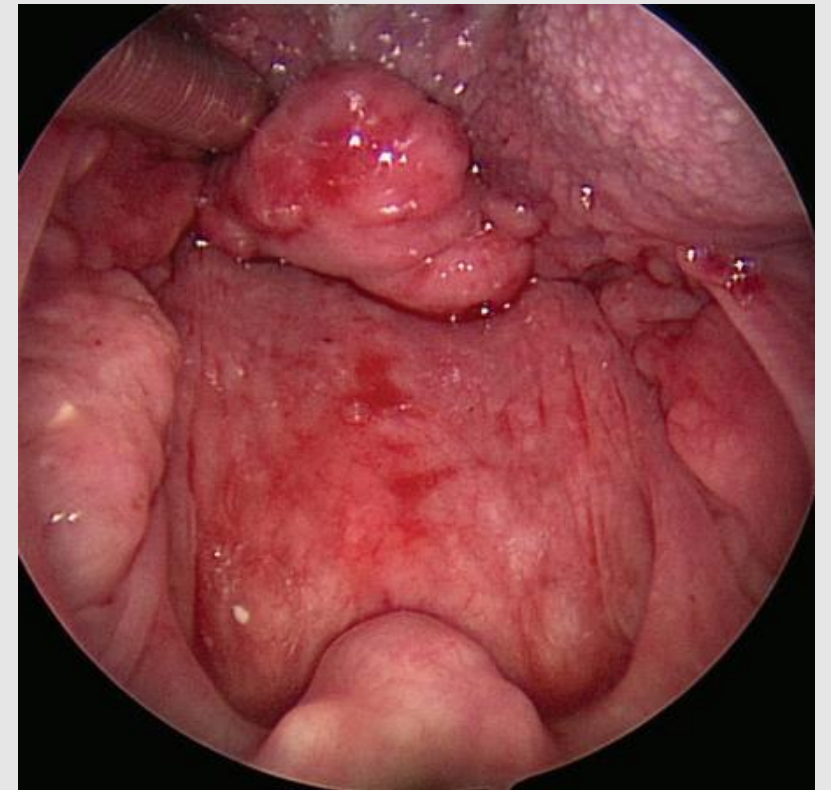


Non-Hodgkin lymphoma

# Malignant tumors of the oropharynx

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- Treatment is based on radiotherapy , with or without chemotherapy.
- 5-year survival rate for localized disease has been to from 50% to 80%
- **Solitary extramedullary plasmacytoma** is a rare hematologic malignancy
  - 80% of these tumors arise in the mucosa of the upper aero digestive tract
  - Radiotherapy is the treatment of choice
  - Surgery is considered inadequate and chemotherapy has no role in the treatment
  - Local control rate after RT is 80% to 100%



Base of the tongue plasmacytoma

# Malignant tumors of the oropharynx

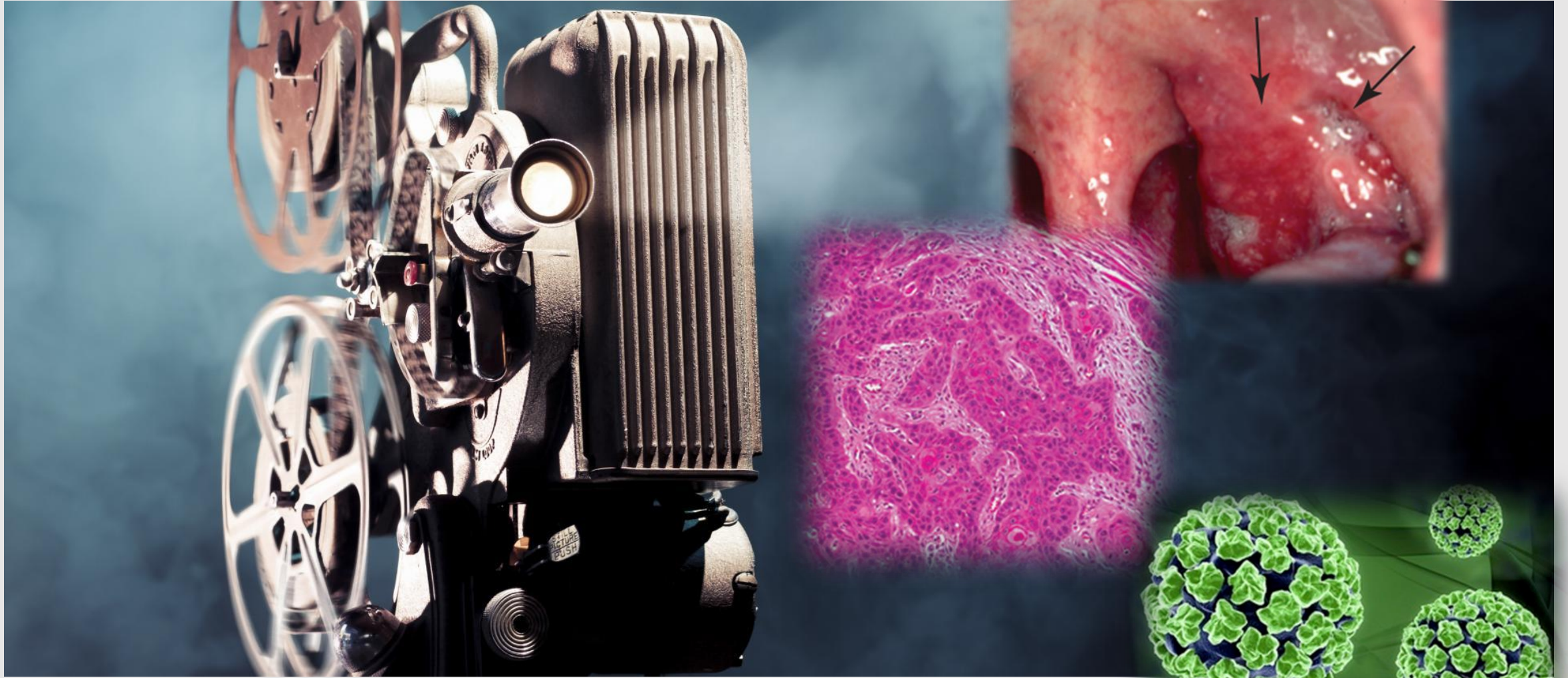
## MUCOSAL MALIGNANT MELANOMA

- Only 1.3% of all melanomas are mucosal melanomas
  - 55.4% are mucosal MM of the H&N
- Malignant transformed melanocytes at the epithelial-connective tissue interface with migration into the epithelium and connective tissue
- No known etiologic factors exist
- Presentation
  - Lesions can present as black, gray or reddish; they are rarely amelanotic
  - Ulcerations and bone infiltration are common
  - Oral bleeding, dysphagia and sensations of pain can occur
  - Usually diagnosed in an advanced stage



STANDARD OF CARE: AGGRESSIVE SURGICAL RESECTION





To be continued...