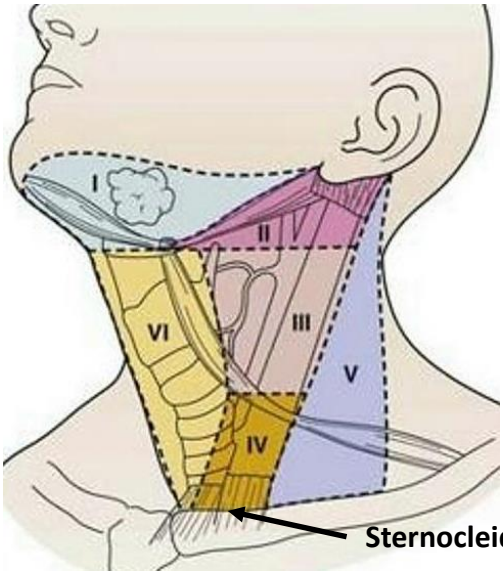
Prepared by Dr. Kurt Schaberg

Neck Lesions

Neck Lymph Node Levels



Level	Name	Source of Metastases
I	Submental & Submandibular	Oral and nasal cavities. *(Also includes submandibular gland)*
II	Upper Jugular	Many sites: oral & nasal cavities, pharynx, & parotid
III	Mid Jugular	Many sites: oral & nasal cavities, & pharynx
IV	Lower Jugular	Hypopharynx, cervical esophagus, and larynx
V	Posterior Triangle	Nasopharynx, oropharynx, and scalp
VI	Anterior (Central) Compartment	Thyroid and larynx

Sternocleidomastoid ("*SCM*")—an important regional landmark

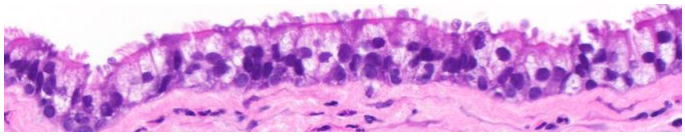
Developmental Lesions

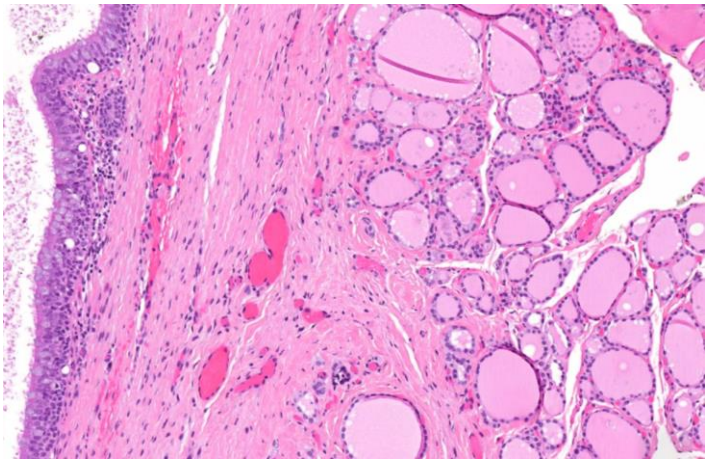
Thyroglossal Duct Cyst

Persistence of the thyroglossal duct.
Midline, often attached to hyoid bone.
Presents as painless mass (if infected→ painful)

Usually lined by **respiratory epithelium** (sometimes squamous). *May* have **thyroid in tissue in cyst wall**.

Treatment is resection (Sistrunk procedure)





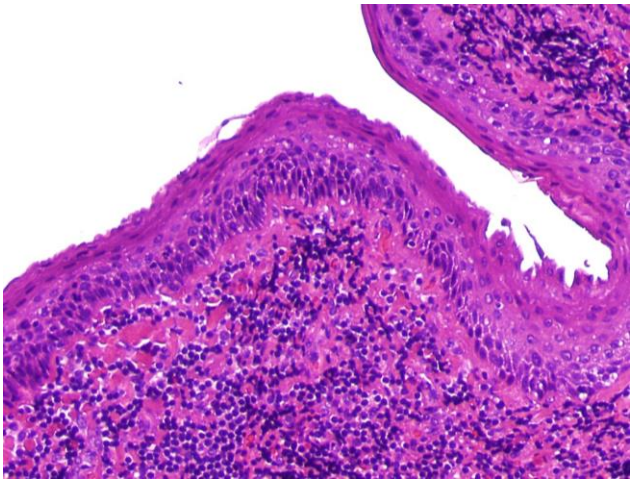
Branchial Cleft Cyst

Congenital **malformations of branchial apparatus**.
Can come to attention at any age, but often **young adults**
Found in **lateral** neck. Often near anterior SCM.
Usually non-tender masses (If inflamed→ painful)

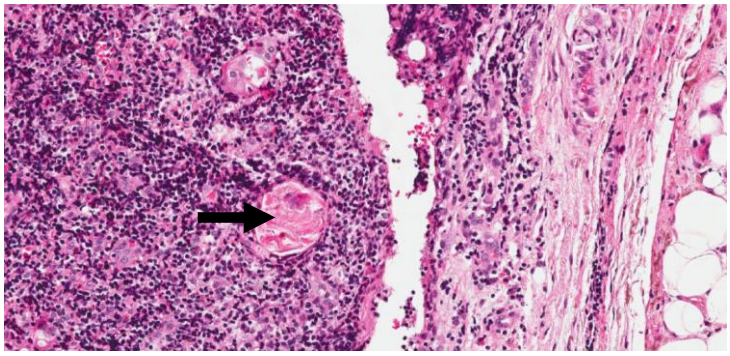
Usually lined by **bland squamous epithelium** (rarely glandular lining). The wall often has abundant **lymphoid tissue**, often with germinal centers.

Can also have Branchial Cleft Sinuses and Fistulas.

Must exclude SCC metastasis, especially if >50yrs old!



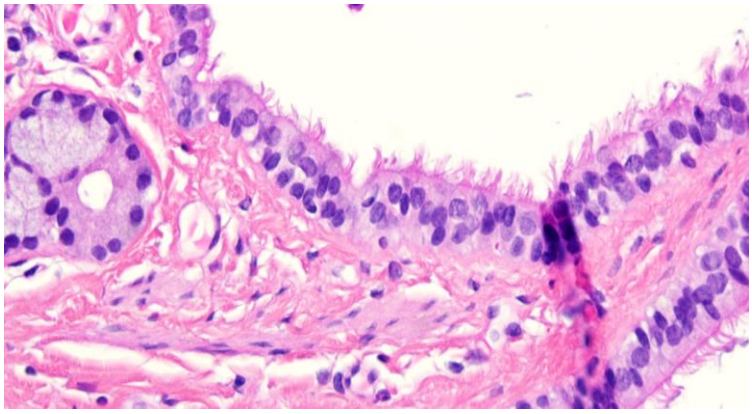
Thymic Cyst



Wall contains thymic tissue (often easiest to see is Hassall's corpuscles→)
Lined by cuboidal, columnar, or squamous epithelium.

Usually kids. Usually anterior cervical triangle.
May see associated parathyroid.

Bronchogenic Cyst

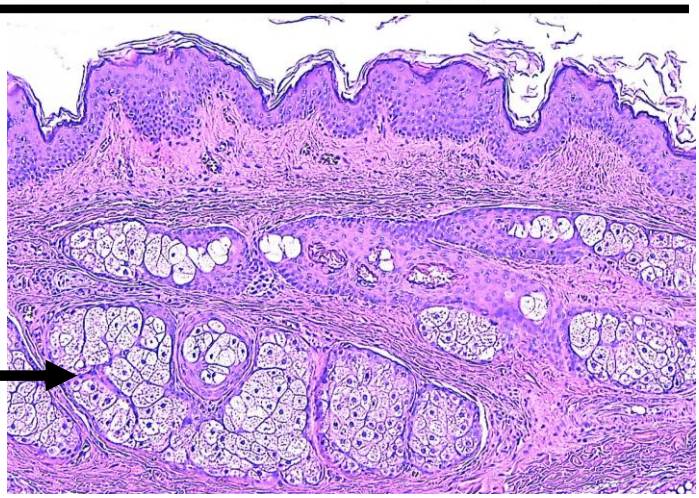


Lined by **respiratory-type epithelium**

Cyst wall contains **mucoserous glands**, **cartilage**, **smooth muscle**, and scant lymphoid tissue.

Usually kids. Midline, near sternum.
May compress nearby structures.

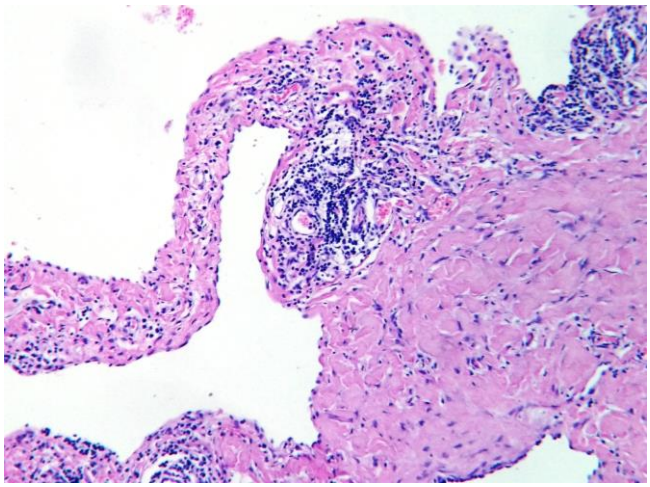
Cutaneous Cysts



Epidermal inclusion Cyst—Unilocular cyst lined by **squamous epithelium with a granular layer**. Lumen contains abundant laminated keratin. May rupture→ acute/granulomatous inflammation. Very common in **adults**.

Dermoid Cyst—Histologically same as above, but **associated adnexal structures** like hair follicles and sebaceous glands. **Usually face of children** along embryonic closure lines

Lymphangioma



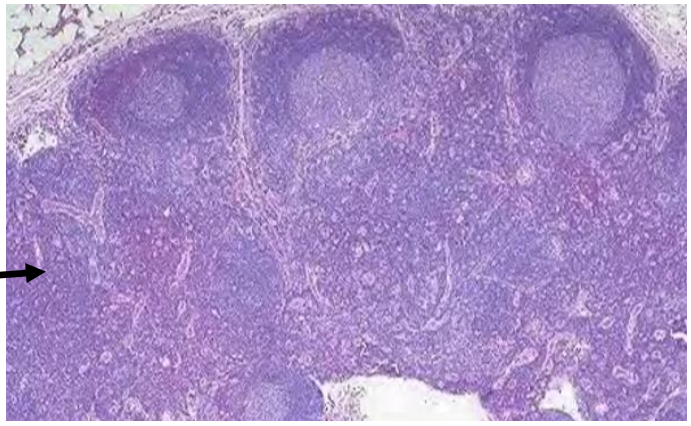
Benign vascular lesion, but may recur.
Localized collections of dilated lymphatics.
Variably thick walls. Often have **lymphoid aggregates**.
Lined by **flattened endothelium**.
Can have some smooth muscle or fibrous tissue.
Lumina empty or with proteinaceous lymphatic fluid.

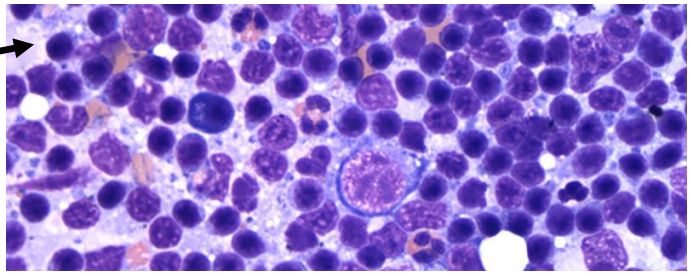
IHC: (+) D2-40, PROX1, CD31; (±)CD34.

Usually **Kids/infants**. Variable locations, but most often posterior head/neck. Can be associated with Turner's syndrome ("cystic hygroma")

Infectious Lesions

Reactive Lymphoid Hyperplasia





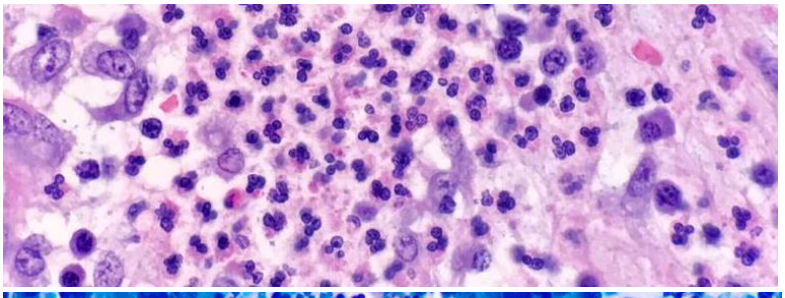
Proliferation/collection of lymphoid cells in response to nearby inflammation/infection.

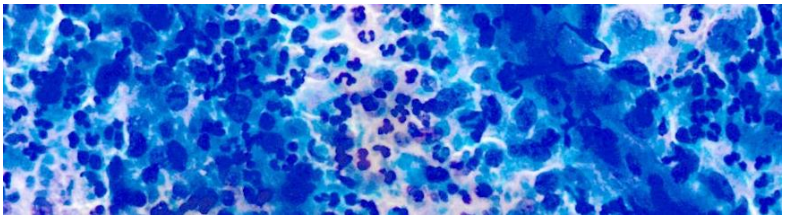
Common causes in head/neck: Upper respiratory tract infections, Dental infections

Intact lymph node architecture
Separated follicles with "Open" sinuses
Polarized germinal centers/mantle zones
Prominent mitotic figures.
Heterogeneous cell population.

On FNA: Often very cellular aspirate.
Mixture of small and large lymphocytes (range of maturation) with a **predominance of small lymphocytes**.
Frequently plasma cells and **tingible macrophages**
Consider sending for Flow Cytometry

Abscess





Large collections of Neutrophils (some of which may be degenerating)

Necrosis and fibrin ("*Fibrinopurulent debris*")

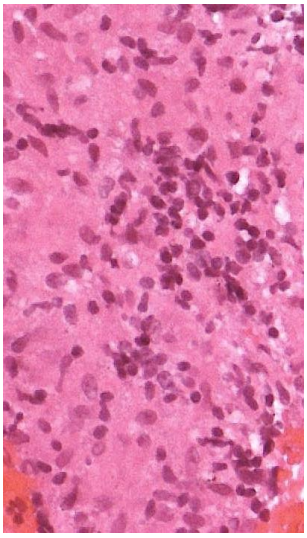
Macrophages, bacteria, foreign material, granulation tissue, and chronic inflammation.

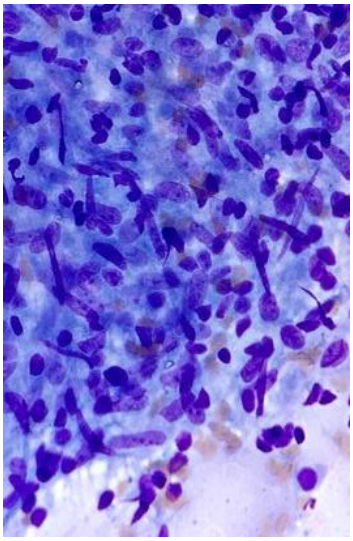
Send for ***culture*** if doing an FNA.

Often bacterial, sometimes actinomyces.

Often associated with **poor dentition.**

Granulomas





Well-formed collections of histiocytes and multinucleated cells.

May have central "caseating" necrosis.

Main DDX:
Sarcoidosis (usually non-necrotizing, Dx of exclusion)
Mycobacterium tuberculosis (usually necrotizing)
Bartonella henselae ("Cat Scratch," suppurative)
Fungal infections (rare)

Get Bug Stains!

Mycobacterial Spindle Cell Pseudotumor

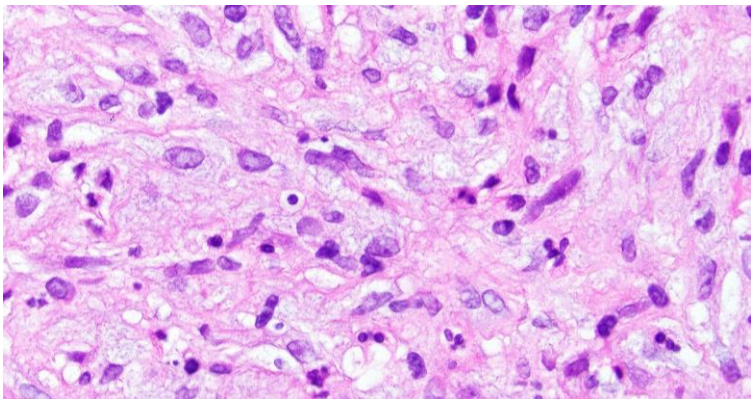
Pseudoneoplastic spindle cell proliferation
Almost exclusively in setting of **HIV**
Presents as firm mass

Cellular proliferation of storiform spindled cells. Effacement of lymph node architecture.

Special stains (FITE, AFB) highlight organisms.
Usually caused by ***M. avium-intracellulare***.

IHC: **(+) CD68,** vimentin. (±)S100, desmin, SMA.
(-) CD31, CD34

Treatment: **Treat infection**

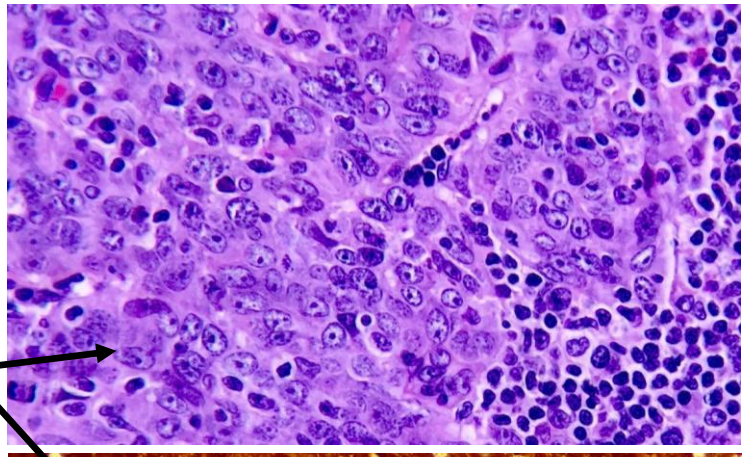


Neoplasms

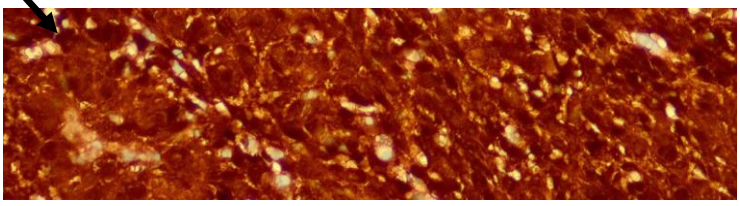
Metastatic Carcinoma

Usually from a head and neck primary.
Most often Squamous cell carcinoma.
Most often **level II**. Often cystic (central necrosis).

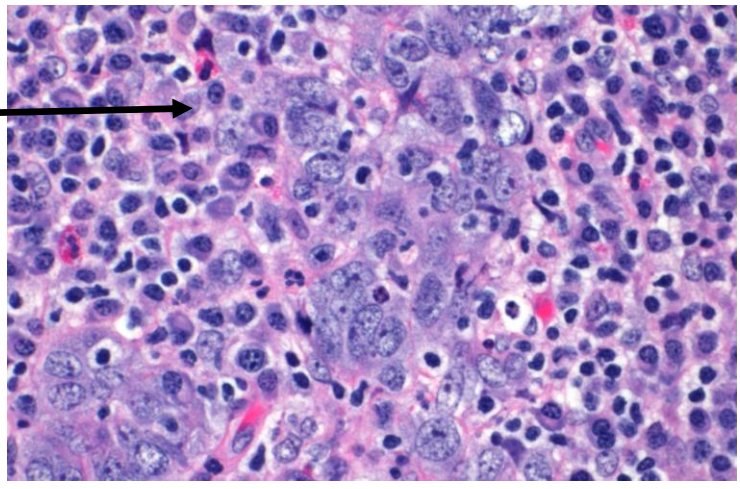
Most common site of ***occult*** primary:
Oropharynx and Nasopharynx (viral-associated)



Squamous cell carcinoma, HPV-positive
Variable appearance, but often **high N:C ratio**
Often non-keratinizing
"Block-positive" P16 (Strong, diffuse ≥70% nucleus and cytoplasm) or HPV ISH/PCR positive



Squamous cell carcinoma, HPV-negative
Often keratinizing, "conventional" appearance
P16 negative or patchy, HPV ISH/PCR negative



Nasopharyngeal carcinoma
Variety of appearances, squamous differentiation
Mediated by EBV→ EBER positive

Less common sites of origin:
Thyroid (especially PTC), hypopharynx, larynx.

Common diagnostic work-up: FNA of mass→
Panendoscopy/imaging to identify site of origin.

HPV Testing in the Head and Neck

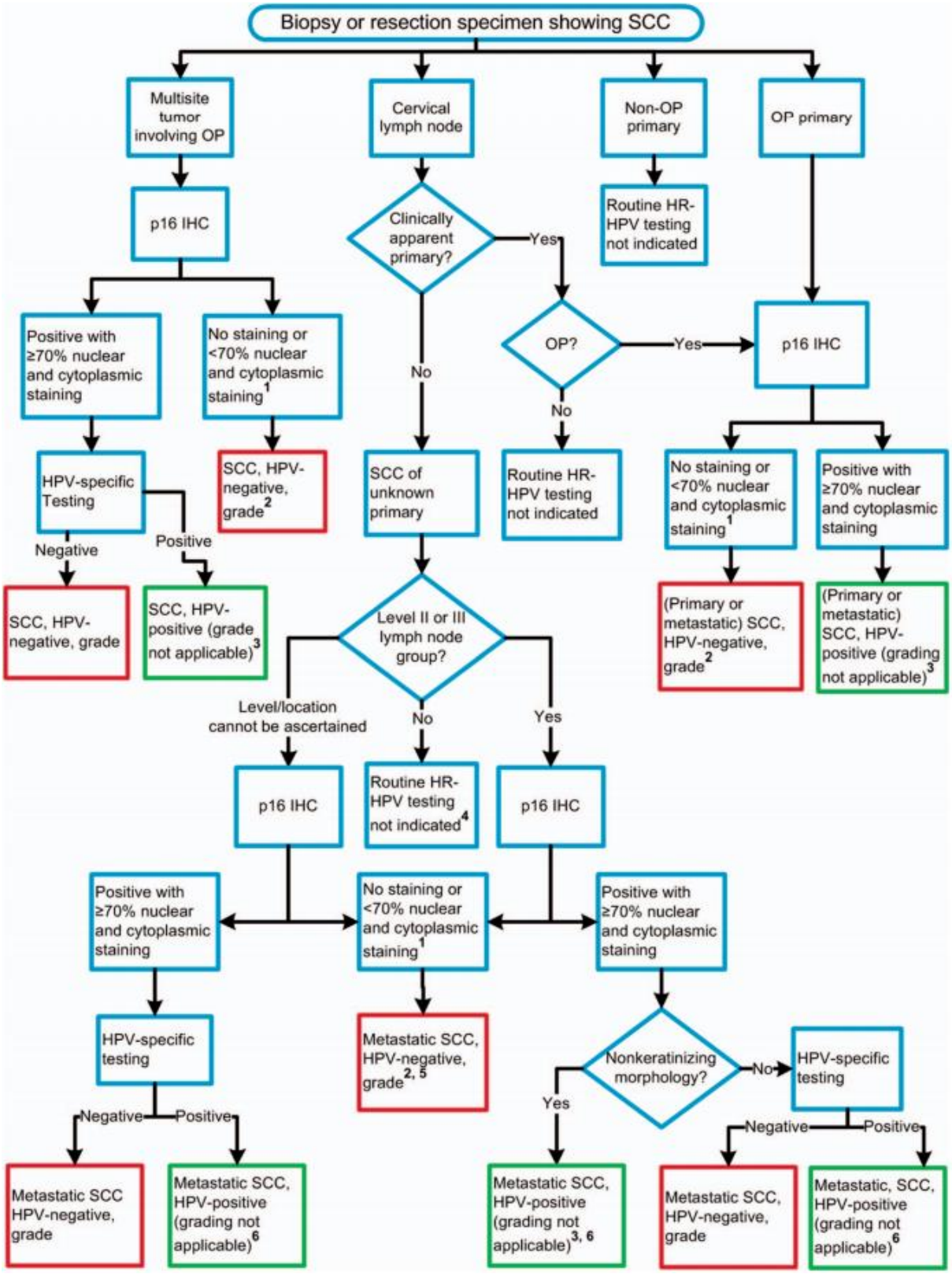


Figure 1. *High-risk human papillomavirus (HR-HPV) testing in head and neck squamous cell carcinomas (SCCs). Abbreviations: IHC, immunohistochemistry; OP, oropharyngeal. [1]Consider HR-HPV–specific testing for equivocal p16 results (50%–70% nuclear and cytoplasmic staining). [2]May also be reported as p16 negative with a comment specifying that the tumor is very likely HPV negative. [3]May also be reported as p16 positive with a comment specifying that the tumor is very likely HPV positive. [4]HR-HPV may be indicated in patients where the clinical suspicion for an HPV-positive SCC is high. [5]Consider Epstein-Barr encoding region (EBER) in situ hybridization for Epstein-Barr virus for the rare metastatic nonkeratinizing squamous cell carcinoma that is HR-HPV negative. [6]Include comment, "Likely oropharyngeal primary."*

HPV-Testing *(continued)*

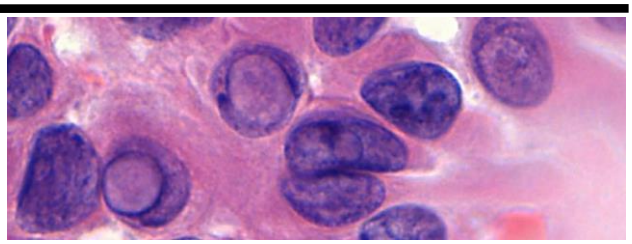
In many instances, P16 is an adequate ***surrogate* marker for High-risk (HR) HPV infection.**

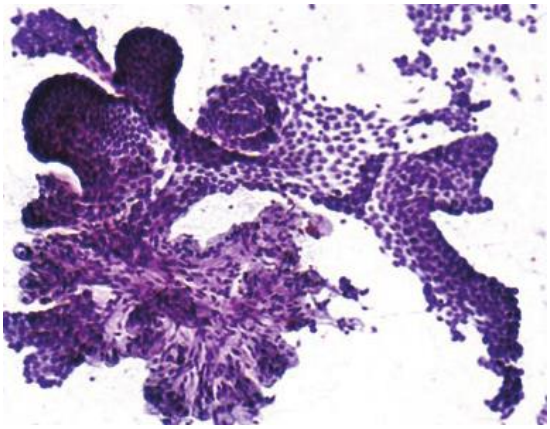
Tissue specimens (***non***-cytology) from metastatic SCC of unknown origin in an upper cervical lymph node should first undergo P16 IHC→ positive with ≥70% nuclear and cytoplasmic staining with classic non-keratinizing morphology→ "Metastatic SCC, HPV-positive"

Otherwise, should do HR-HPV testing with either in situ hybridization (ISH) or PCR.

Cytology Specimens: No current widely-accepted P16 staining cutoff, so HR-HPV testing is recommended.

Papillary Thyroid Carcinoma





Frequently metastasizes to cervical lymph nodes.

Lymph nodes can be **very cystic**, sometimes yielding scant epithelium→ if you're just getting cyst fluid only, but are concerned for PTC, try sending cyst fluid for **thyroglobulin** levels→ if elevated, these findings suggest metastatic thyroid carcinoma (esp. PTC).

If get epithelium, look for classic PTC features:
Intranuclear pseudoinclusions
Papillary structures with/without fibrovascular cores
Powdery, pale chromatin. Nuclear grooves.
Squamoid cytoplasm. "Bubble gum" colloid

Other Neoplasms to Consider

Many salivary gland, thyroid, hematolymphoid, and soft tissue tumors can also present as "neck masses," so it's best to often keep a broad differential.

Please refer to the respective guides for additional information.

Thyroid tumors:
Medullary thyroid carcinoma
Anaplastic thyroid carcinoma

Common systemic metastases:
Melanoma
Lung carcinoma
Breast carcinoma

Salivary gland tumors:
Pleomorphic adenoma
Warthin's Tumor
Adenoid cystic carcinoma
Mucoepidermoid carcinoma
Salivary duct carcinoma

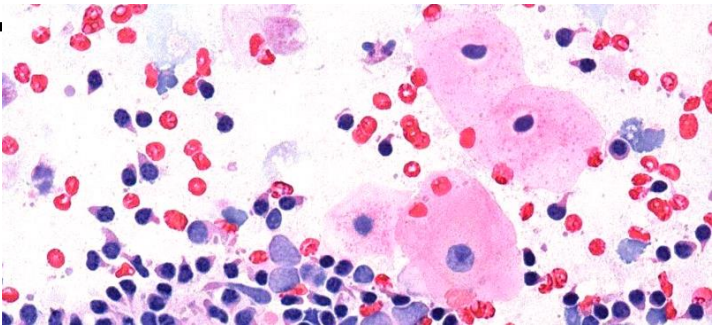
Soft tissue tumors:
Lipoma (and variants)
Schwannoma
Fibromatosis
Nodular fasciitis
Paraganglioma
Elastofibroma
Nuchal-type fibroma
Perineurioma
Synovial sarcoma
Chordoma
Liposarcoma
Rhabdomyosarcoma

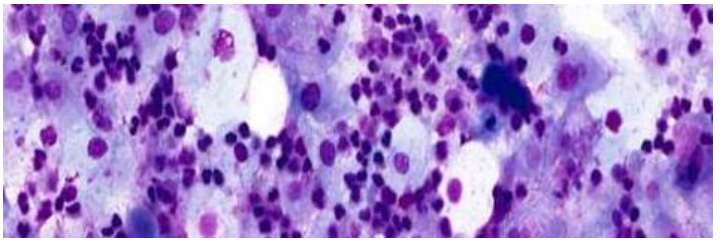
Lymphoma

Squamous Cyst Cytology

It can be hard to sample the cyst wall leading to a false negative

"Bland Squamous Cyst"



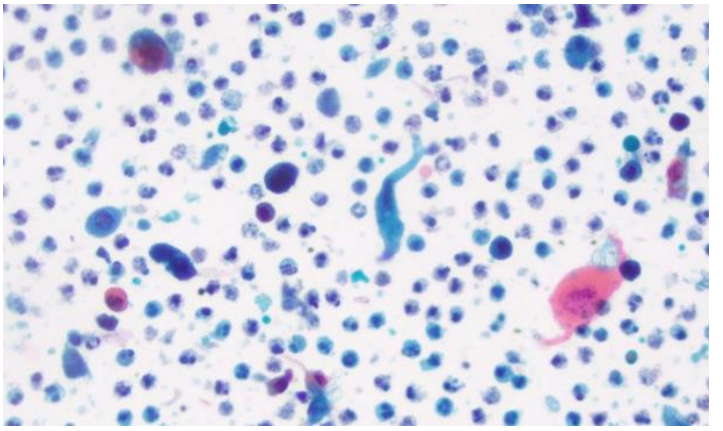


Cytologically bland squamous cells
Round to oval nuclei. Normochromatic.
Often abundant "dense" keratinizing cytoplasm

Often associated inflammatory cells (if ruptured)
May see debris and macrophages from cyst lumen

Main DDX:
Branchial cleft cyst (if in lateral neck, near SCM)
Epidermal Inclusion cyst (if very superficial)
Lymphoepithelial cyst (parotid, patients with HIV)
Thyroglossal duct cyst (respiratory epithelium, midline)

"Squamous Cyst with Atypia"

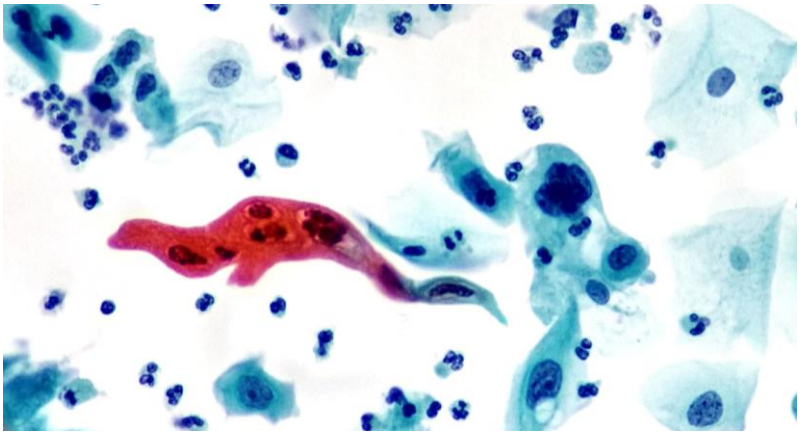


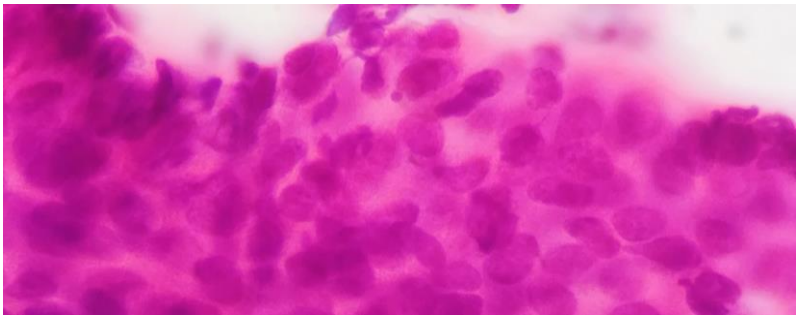
Worrisome, but not definitive cytologic atypia (that seem more than one would like for benign, but not "enough" for malignant).

My threshold often depends on the clinical scenario (i.e., Higher in younger patients with no primary; Lower in older patients with a known primary)

Main DDX:
Degenerative/reactive squamous cyst
Well-differentiated SCC metastasis

Squamous Cell Carcinoma





Hyperchromatic, pleomorphic nuclei
Often background of cystic necrotic debris
May see mitoses

***If keratinizing*→ large, polygonal cells with abundant dense cytoplasm** and irregular cytoplasmic extensions.

***If non-keratinizing*→ think HPV-mediated**!→ often more cohesive, uniform, higher N:C ratio, open chromatin

Often **cystic** with **central necrosis**.

Also consider Mucoepidermoid carcinoma→ Look for goblet cells!

Try to get a cell block to test for HPV if the primary is unknown!