

Changes in AJCC Staging of Head and Neck Cancer (8th Edition)

effective January 1st, 2018

Rajeev H. Mehta, MD, FACS

ENT Surgical Consultants, Ltd

Silver Cross Hospital

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Learning Objectives

- Discuss new American Joint Committee on Cancer (AJCC) staging for human papilloma virus-positive oropharyngeal cancer (HPV+OPC)
- Compare HPV+OPC to HPV negative OPC staging
- Recognize updated staging based on tumor behavior
- Describe how staging affects treatment and prognosis

AJCC Cancer Staging Manual editions

Edition	Publication	Effective dates
1st	1977	1978-1983
2nd	1983	1984-1988
3rd	1988	1989-1992
4th	1992	1993-1997
5th	1997	1998-2002
6th	2002	2003-2009
7th	2009	2010-2017
8th	2016	2018

Changes in the AJCC/UICC

7th Edition

- Lip & Oral Cavity
- Pharynx (naso, oro, hypo)
- Larynx (supra, glottic, sub)
- Nasal Cavity & Sinuses
- Salivary Gland
- Mucosal Melanoma (new to the 7th Ed.)

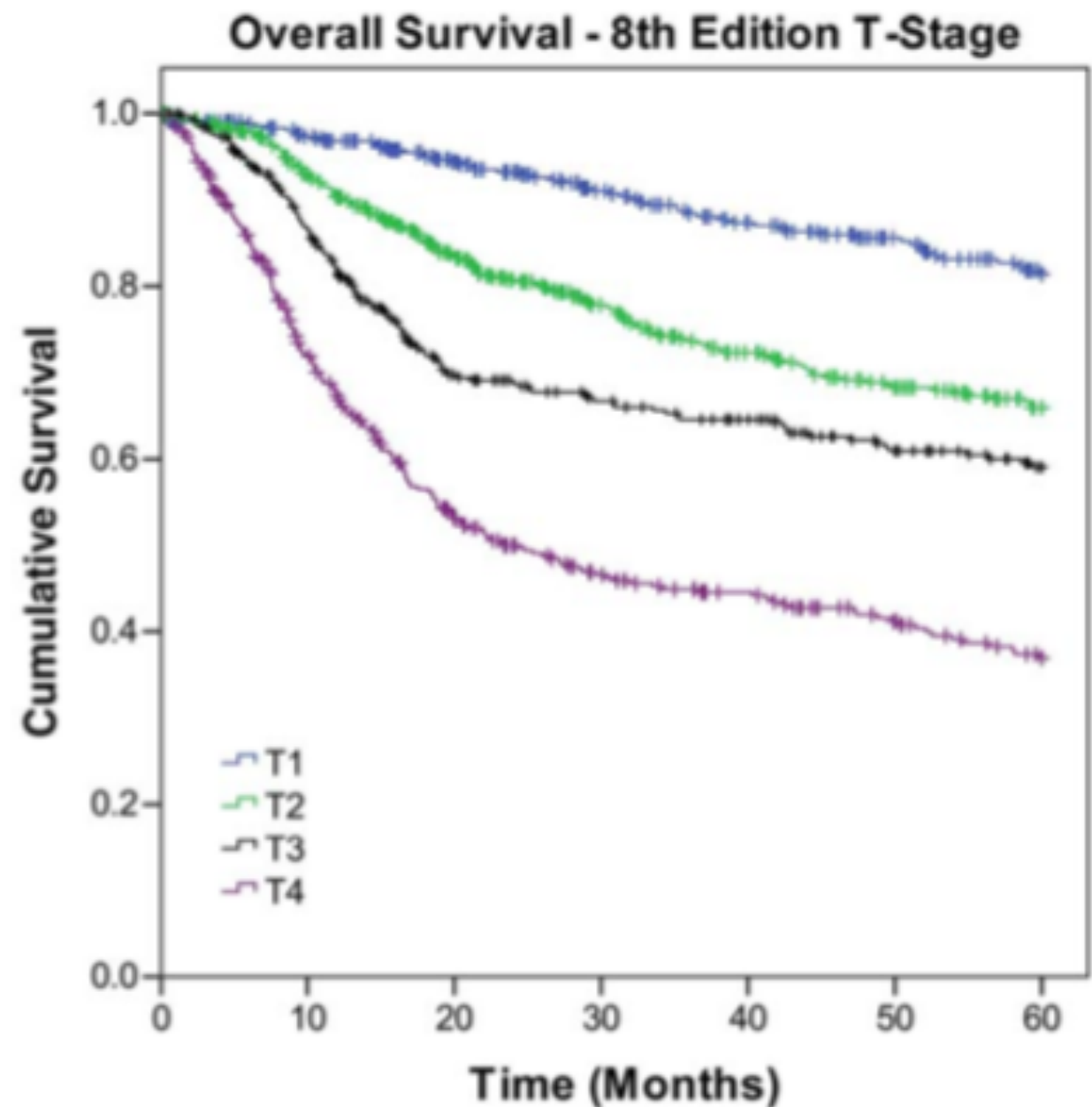
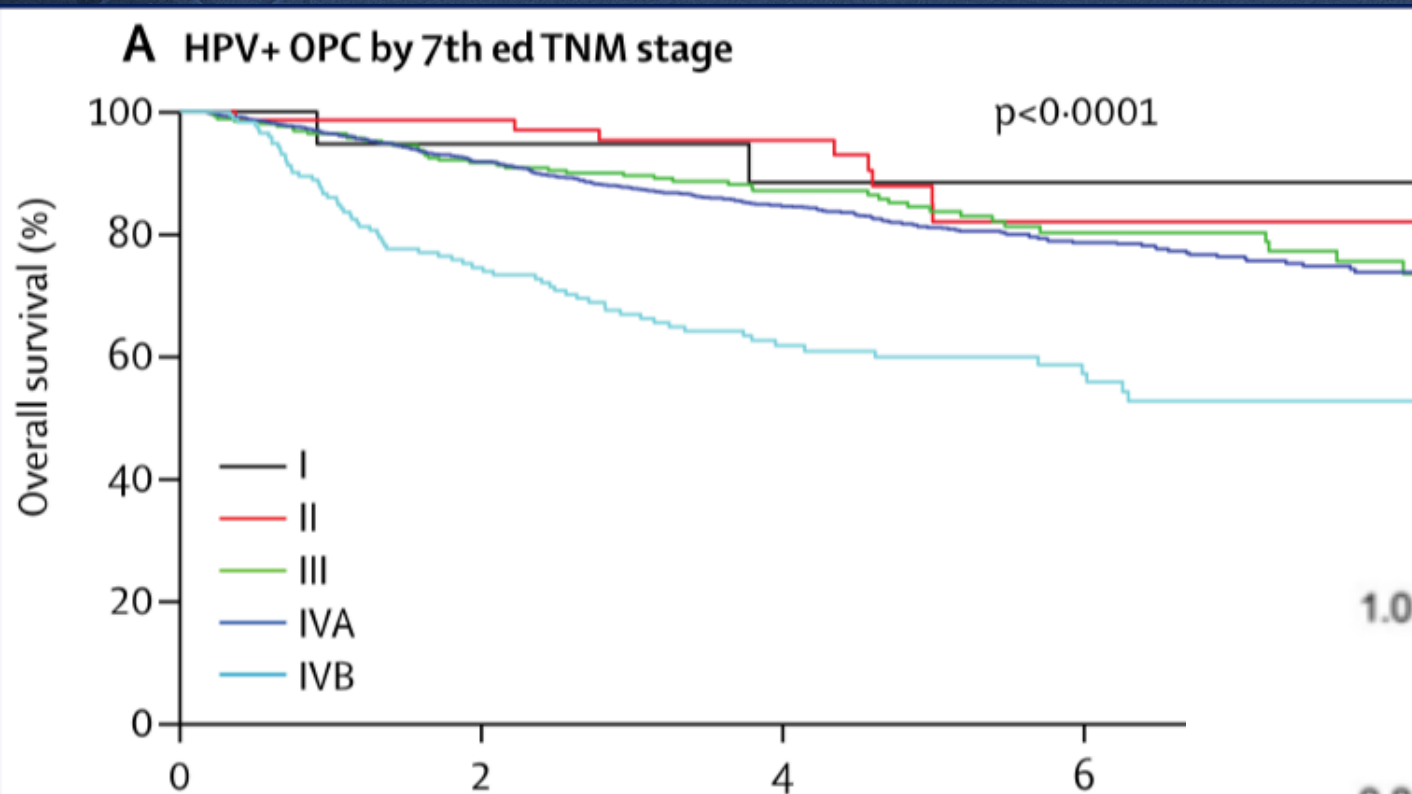
8th Edition

- Cervical Lymph Nodes & Unknown Primary
- Lip & Oral Cavity
- Salivary Gland
- Nasopharynx
- P16+ Oropharynx
- P16- Oropharynx & Hypopharynx
- Nasal Cavity & Sinuses
- Larynx
- Mucosal Melanoma of H & N
- Cutaneous SCCA of H & N

Cancer Staging: Key Principles

- Hazard consistency - staging should result in similar survival for each subgroup
- Hazard discrimination - each subgroup should have a different survival from the one above/below it
- Balance between groups - should be relatively equal numbers in each group for better statistical comparisons
- High predictive ability - Stage should give a good approximation of prognosis/survival

Cancer Staging 7th Edition vs Goal



Changes in the AJCC/UICC 8th Edition Staging

Effective January 1st 2018

-
- Pharynx move to:
 - Nasopharynx
 - p16+ Oropharynx
 - p16- Oropharynx
- New criteria for extranodal extension (ENE)
- New staging for neck disease with unknown primary
- Addition of depth of invasion in Oral Cavity T category
- New cutaneous SCCA of head and neck

Time of classification

- cTNM = Clinical Classification
 - before treatment but after full workup
- pTNM = Pathological Classification
 - after surgery used as the first definitive therapy
- ycTNM = Posttherapy Clinical Classification
 - after chemo/RT but before surgery
- ypTNM = Posttherapy Pathological Classification
 - first chemo/RT followed by surgery
- rTNM = Recurrence or Retreatment Classification
 - after recurrence or progression until treatment
- aTNM = Autopsy Classification
 - Cancers not recognized but found incidentally at autopsy

Extranodal Extension (ENE)

- ENE has profound effect on prognosis
- Inclusion of ENE in N Category
 - p16- Oropharynx and Hypopharynx
 - Unknown Primary
 - Oral Cavity
 - Larynx
 - Skin
 - Salivary Gland
 - Nasal Cavity and Sinus
 - Not for p16+ Oropharynx

Clinical Staging

Extranodal Extension (ENE)

- Strict criteria required for ENE positive diagnosis
- Clear evidence of gross ENE
 - skin/muscle invasion
 - dense tethering to adjacent structures
 - nerve invasion with dysfunction
 - supported by imaging
- Imaging alone is not sufficient
- If any doubt, assign ENE negative

Pathological Staging

Extranodal Extension (ENE)

- Clearly defined pathological ENE positive
 - tumor extends through LN capsule
 - tumor extends from LN into surrounding tissue
 - with or without desmoplasia
-
- ENEmi = microscopic = 2 or less millimeters
 - ENEma = major = more than 2 millimeters
 - If any doubt, make ENE negative

ENE for p16- OPC

- Clinical
 - Any ENE is N₃b
- Pathological
 - ENE (either minor or major) increases N by 1 step

HPV Negative OPC

Staging

- **T classification** unchanged
 - except T₀ removed; unknown primary
- **N classification** unchanged except Extra Nodal Extension (ENE)
 - N₃ divided into N_{3a} and N_{3b}
 - N_{3a} LN > 6cm without ENE
 - N_{3b} any size LN with ENE
- **M classification** unchanged
- Since ENE is now N_{3b}, more patients are stage IVb

HPV negative OPC

T classification

(To moved to unknown primary)

- Tx Primary tumor cannot be assessed
- Tis Carcinoma in situ
- T₁ ≤2cm
- T₂ tumor 2-4cm
- T₃ tumor > 4cm or extent to lingual epiglottis
- T_{4a} invades larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible
- T_{4b} invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base or encases carotid artery

HPV negative OPC

Clinical N classification

(ENE added = N_{3b})

- N_x LN cannot be assessed
- N₀ No LN mets
- N₁ Single ipsilat LN ≤ 3 cm, ENE -
- N_{2a} Single ipsilat LN 3-6cm, ENE-
- N_{2b} Multiple ipsilat LN ≤ 6 cm, ENE-
- N_{2c} Multiple bilat/contralat LN ≤ 6 cm, ENE-
- N_{3a} LN > 6 cm, ENE-
- N_{3b} any size LN, ENE positive

Also used for oral cavity, hypopharynx, larynx, unknown primary & cutaneous carcinoma of head & neck

HPV negative OPC

Pathologic N classification

(ENE added = N_{3b})

- N_x LN cannot be assessed
- N₀ No LN mets
- N₁ Single ipsilat LN ≤ 3cm ENE -
- N_{2a} Single ipsilat LN ≤ 3cm ENE+ or LN 3-6cm ENE-
- N_{2b} Multiple ipsilat LN ≤ 6cm ENE-
- N_{2c} Multiple bilat/contralat LN ≤ 6cm ENE-
- N_{3a} LN > 6cm ENE-
- N_{3b} Single ipsilat LN > 3cm ENE+, multiple ipsilat/contralat/
bilat LN any size ENE+, single contralat LN any size ENE+

Also used for oral cavity, hypopharynx, larynx, unknown
primary & cutaneous carcinoma of head & neck

HPV negative OPC Suffix

- T Suffix
 - (m) synchronous primary tumors found in single organ
- N Suffix
 - (sn) LN mets found by surgical biopsy
 - (f) LN mets found by FNA or core needle bx
 - U Mets above lower border of cricoid
 - L Mets below lower border of cricoid
- M suffix
 - cMo No distant mets
 - cMi Distant mets clinically
 - pMi Distant mets, confirmed microscopically

HPV Negative/Not Tested OPC

Stage Groups

T	N	M	Stage
Tis	No	Mo	o
T _I	No	Mo	I
T ₂	No	Mo	II
T ₃	No	Mo	III
T _{I-3}	N _I	Mo	III
T _{4a}	No-I	Mo	IVA
T _{I-4a}	N ₂	Mo	IVA
Any T	N ₃	Mo	IVB
T _{4b}	Any N	Mo	IVB
Any T	Any N	M _I	IVC

Overall Stage p16 negative OPC

T category	No	N _I	N _{2a,b,c}	N _{3a,b}
T _I	I	III	IVA	IVB
T ₂	II	III	IVA	IVB
T ₃	III	III	IVA	IVB
T _{4a}	IVA	IVA	IVA	IVB
T _{4b}	IVB	IVB	IVB	IVB

Stage IVC = M_I disease

HPV+ OPSCC

- Younger age
- Little or no tobacco exposure
- Increasing at 5% per year
- Smaller tumors with advanced nodal disease
- Less likely to have extracapsular spread relative to nodal size
- Significantly better local-regional control
- Significantly better survival after treatment

HPV Positive OPC Staging

- **T classification** unchanged
 - except Tis removed (absence of distinct basement membrane in Waldeyer's ring and indolent nature of p16+)
 - T4b removed (survival curves of T4a and T4b are the same)
- **N classification**
 - Difference between clinical & pathologic staging
 - Clinical staging - laterality and size of LN
 - Pathologic staging - number of LNs
 - ENE not included in p16+
- **M classification** unchanged
 - Stage IV reserved for M1 disease
- Overall stage: drastic change
 - Since ENE is now N3b, more patients are stage IVb

HPV Positive OPC

- Cutoff point for p16 is $>75\%$ tumor expression with at least moderate (+2/3) staining intensity
- p16 is usually localized to nuclei and cytoplasm so p16 localized only to cytoplasm is considered negative

HPV positive OPC

T classification

(To moved to unknown primary)

- T₁ ≤2cm
- T₂ tumor 2-4cm
- T₃ tumor > 4cm or extent to lingual epiglottis
- T₄ invades larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, mandible or beyond
- (T_{4a}/T_{4b} distinction only in HPV negative OPC)

HPV positive OPC Clinical N classification (Treated with Radiation)

(No ENE included)

- **N_I** = Ipsilateral LNs $\leq$ 6cm regardless of number had similar impact on survival when treated with radiation (clinical staging)
- **N₂** = Bilat/Contralat LNs $<$ 6cm had a worse outcome
- **N₃** = LNs $>$ 6cm had the worst survival

N _x	LN cannot be assessed
cN ₀	No LN mets
cN _I	Ipsilat LN $\leq$ 6cm
cN ₂	Contralat/Bilat LN $\leq$ 6cm
cN ₃	LN $>$ 6cm

When treated with radiation (clinical staging), the number of lymph nodes was not significant

HPV positive OPC Pathologic N classification (Treated with Surgery) (No ENE included)

- Neither LN size nor contralateral nodes impacted survival (unlike those treated with radiation)
- Number of LNs caused survival differences

N _x	LN cannot be assessed
pN ₀	No LN mets
pN ₁	1-4 LNs
pN ₂	5 or more LNs

The difference in behavior in N₃ neck between Clinical (radiation treatment) vs. Pathologic (surgical treatment) is unexpected

Clinical TNM Stage

P16+ OPC 8th Ed

	No	N _I	N ₂	N ₃
T ₀	I	I	II	III
T _I	I	I	II	III
T ₂	II	I	II	III
T ₃	III	II	II	III
T ₄	III	III	III	III

Pathological TNM Stage

P16+ OPC 8th Ed

	No	N _I	N ₂
T ₀	I	I	II
T _I	I	I	II
T ₂	I	I	II
T ₃	II	II	III
T ₄	II	II	III

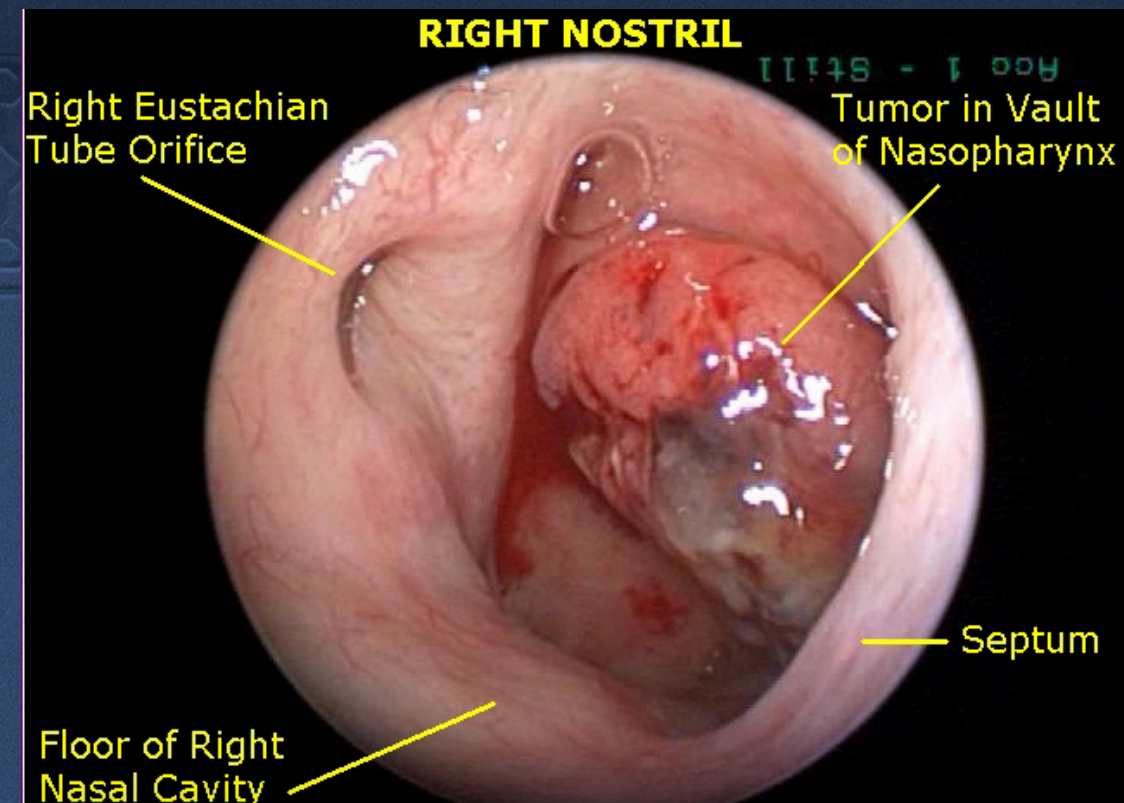
Unknown Primary

- 1. P16+ LNs --> will be staged as P16+ oropharynx (which includes To category)
- 2. EBV+ LNs --> will be staged as nasopharynx (which includes To category)
- 3. LNs that are P16 and EBV negative --> will be staged as unknown primary
- 90% of unknown primary H&N SCCA are HPV+ Oropharynx SCCA



Nasopharynx "T" Staging

- Tx Primary tumor cannot be assessed
- To No tumor but EBV+ LN
- Tis Ca in situ
- T1 tumor confined to nasopharynx or extension to oropharynx or nasal cavity without parapharyngeal (PPS) involvement
- T2 extension to PPS and/or involvement of medial or lateral pterygoid or prevertebral muscles
- T3 involves bone at skull base, cervical vertebra, pterygoids, sinuses
- T4 intracranial extension, involvement of cranial nerves, hypopharynx, orbit, parotid gland, and/or extensive soft tissue involvement beyond lateral surface of lateral pterygoid muscle

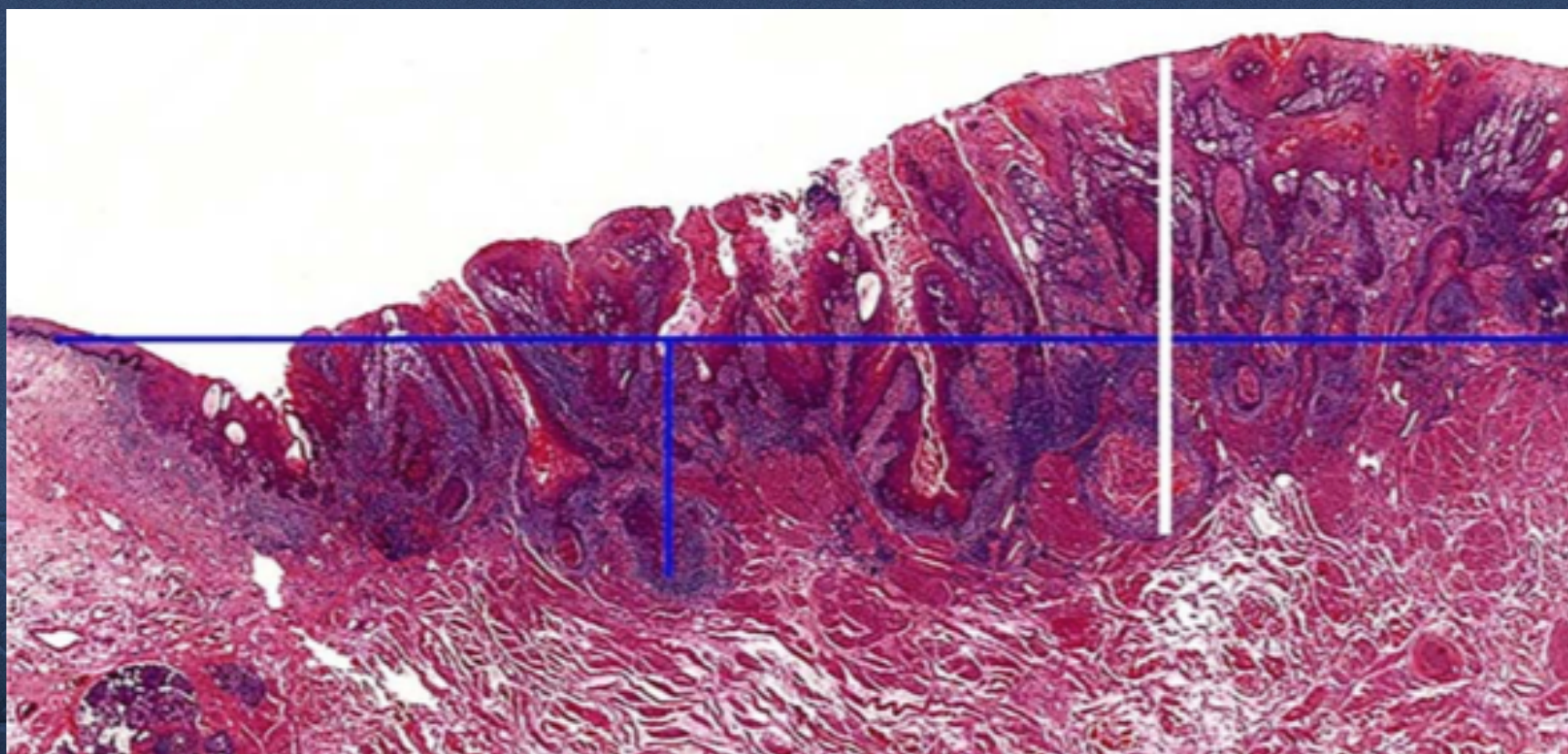
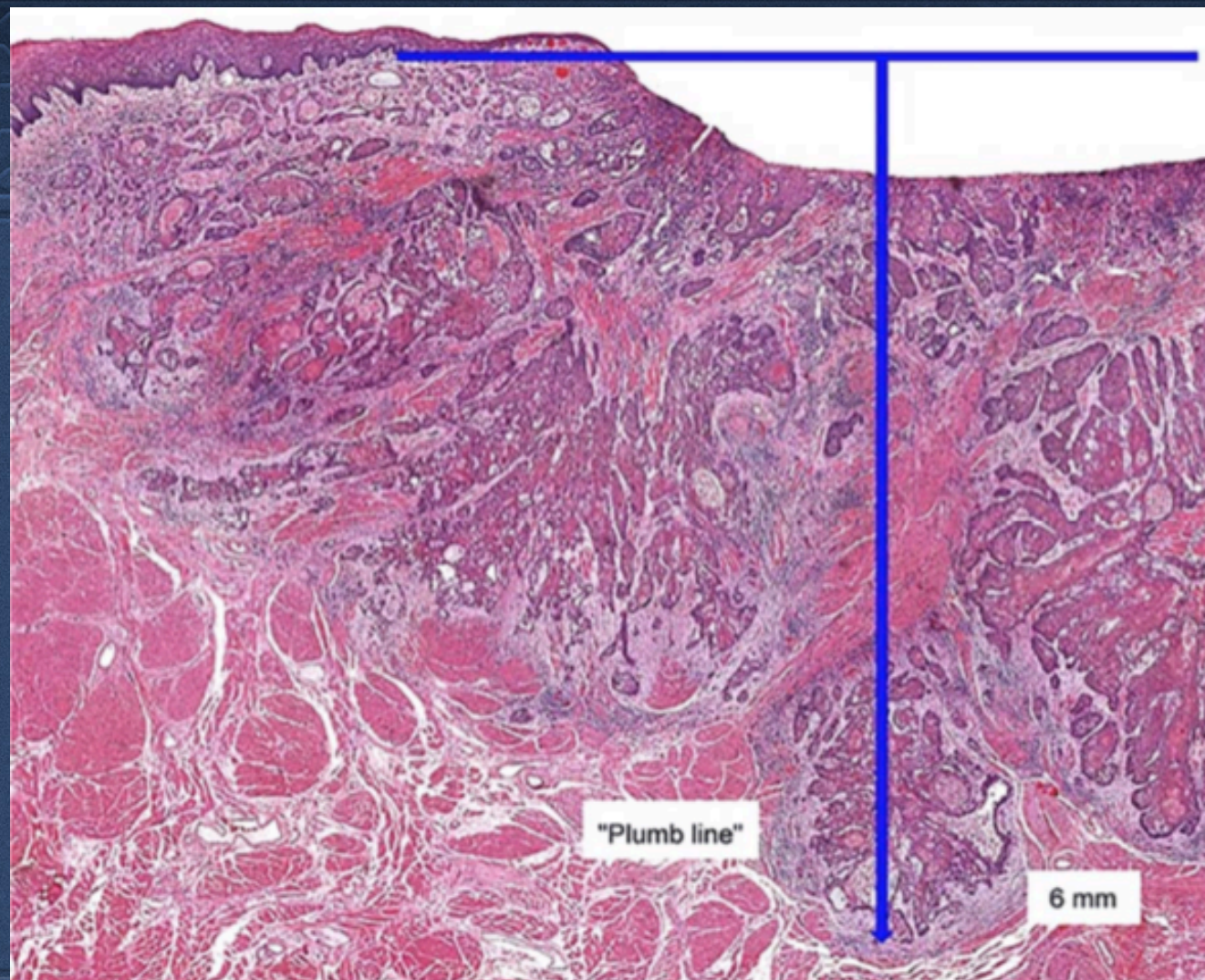


Oral Cavity "T" Staging

- T_x Primary tumor cannot be assessed
- T_{is} Ca in situ
- T₁ tumor $\leq 2\text{cm}$, $\leq 5\text{mm DOI}$
- T₂
 - tumor $\leq 2\text{cm}$, $5 < \text{DOI} \leq 10\text{mm}$
 - $2 < \text{tumor} \leq 4\text{cm}$, $\text{DOI} \leq 10\text{mm}$
- T₃
 - tumor $> 4\text{cm}$
 - any tumor with $10 < \text{DOI} \leq 20\text{mm}$
- T₄ invades masticator space, pterygoid plates, or skull base and/or encases internal carotid artery



Oral Cavity SCCA Depth of Invasion



Cutaneous Carcinoma of the Head & Neck

- Tx Primary tumor cannot be assessed
- Tis Ca in situ
- T₁ tumor ≤2cm
- T₂ 2<tumor≤4cm
- T₃ tumor>4cm or minor bone erosion
or perineural invasion or deep invasion
- T₄
 - T_{4a} gross bone invasion
 - T_{4b} skull base invasion

Deep invasion:

= beyond subQ fat

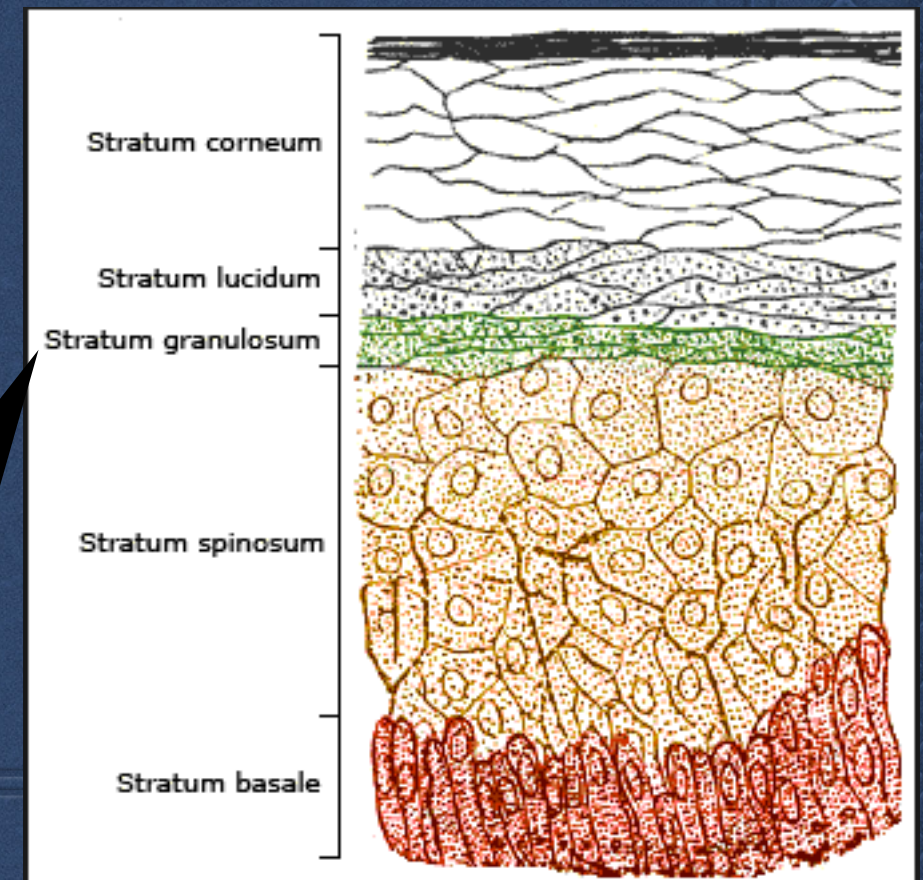
= tumor >6mm as measured from granular layer of epidermis to base of tumor

Perineural invasion:

=tumor within nerve sheath deeper than dermis

=tumor within nerve ≥0.1mm

=tumor involving named nerves



Summary

1. Pharynx move to:

- ★ p16- Oropharynx (HPV-)
 - To removed ---> moved to unknown primary
- ★ p16+ Oropharynx (HPV+)
 - Tis removed
 - T4b removed
 - Clinical staging - laterality and size of LN
 - Pathologic staging - number of LNs
 - Stage IV reserved for M1 disease
- ★ Nasopharynx (EBV+)

2. New criteria for extranodal extension (ENE)

- ★ ENE = N3b
- ★ Not for p16+ Oropharynx

3. New staging for neck disease with unknown primary

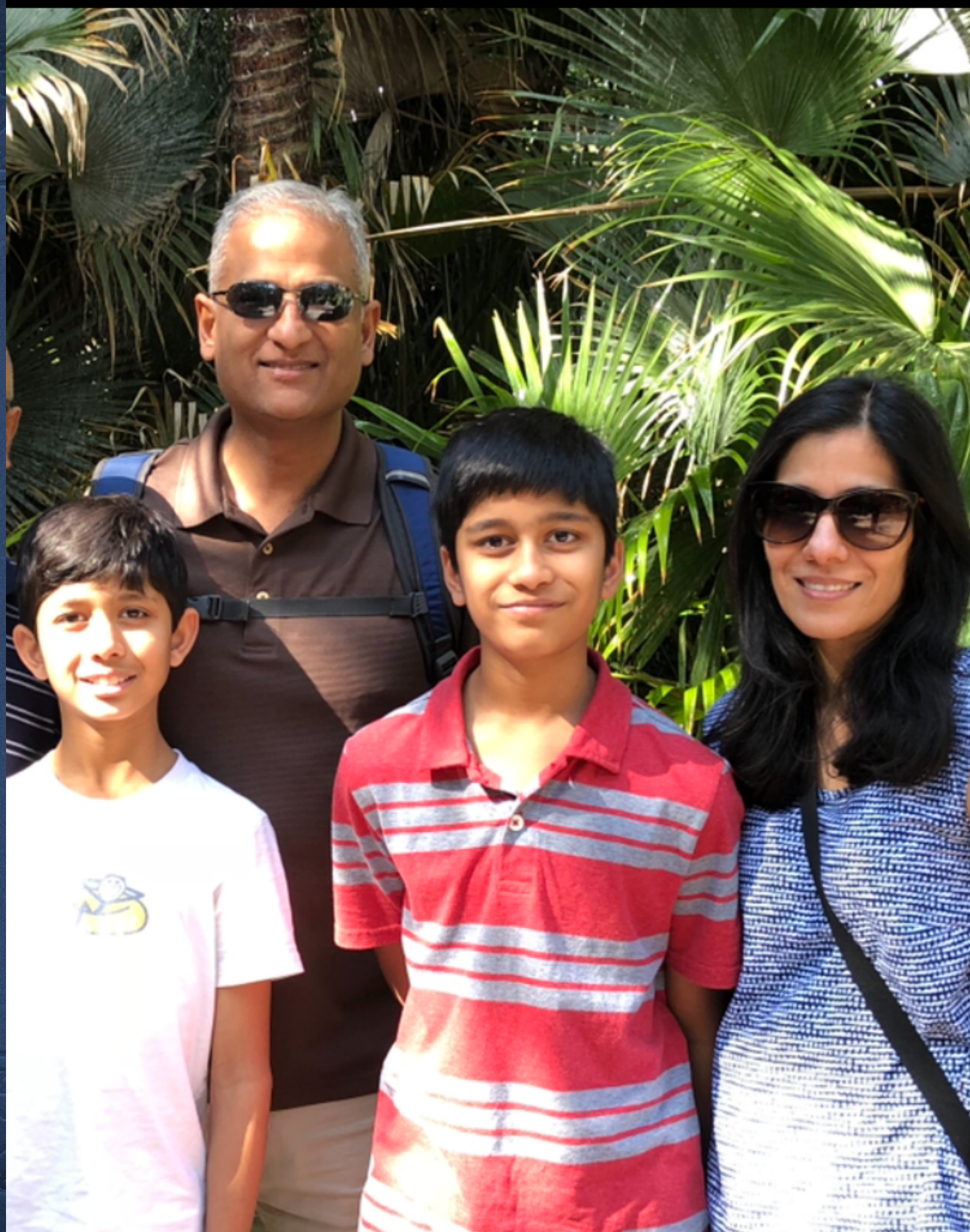
- ★ P16 negative & EBV negative

4. Oral Cavity

- ★ Addition of depth of invasion in T category

5. New cutaneous SCCA of head and neck

- ★ T3 = perineural invasion or deep invasion



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