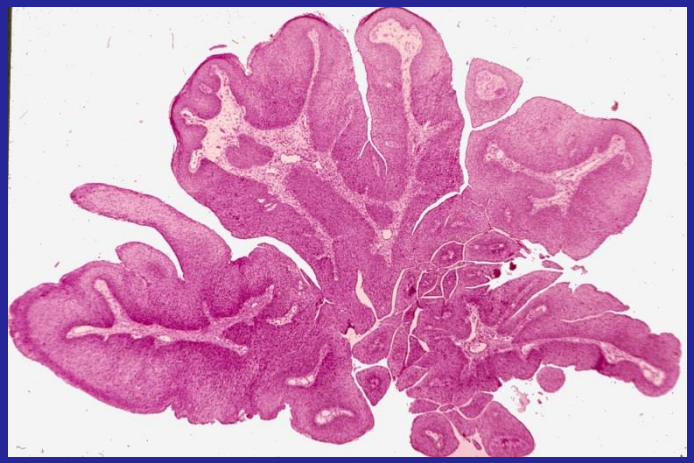
Oral lesions, oral neoplasms, preneoplastic lesions

Attila Zalatnai

Benign tumors

Papilloma



HPV 6/11

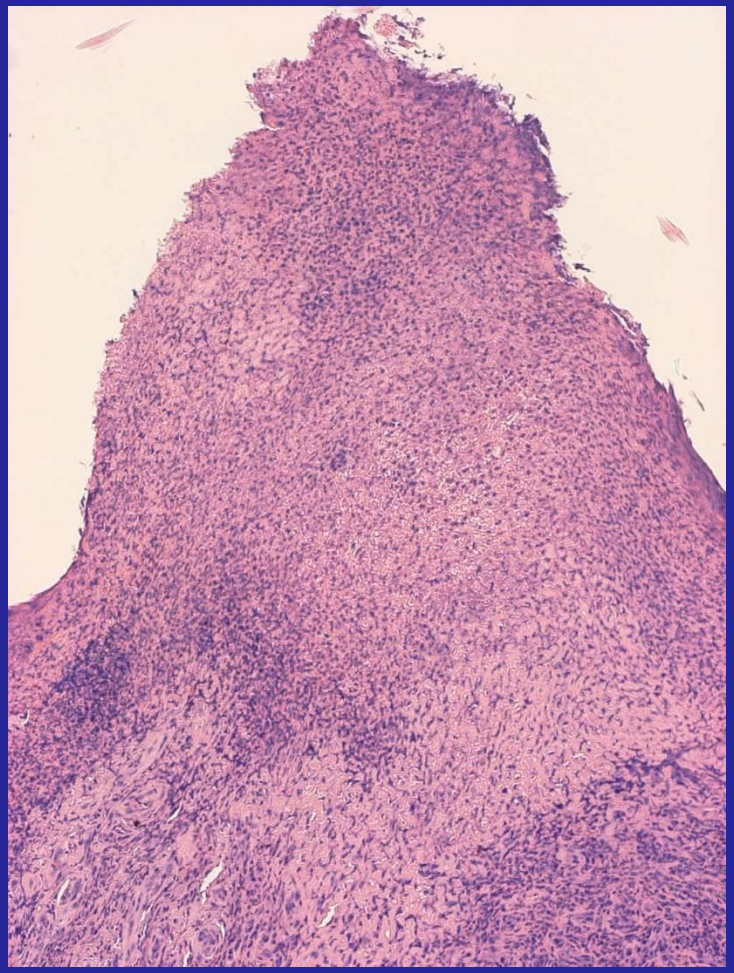
More prevalent in women

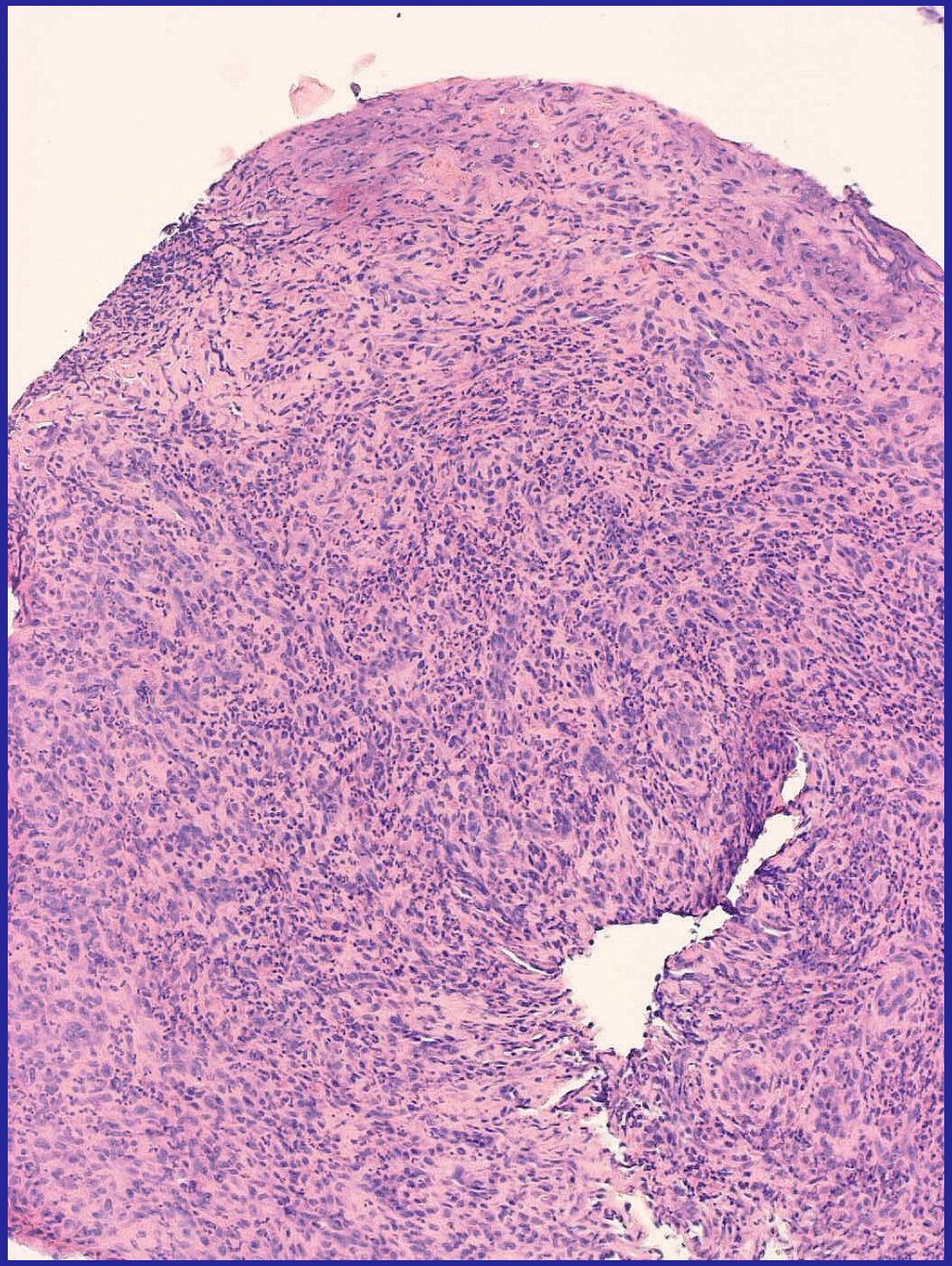
No malignant risk

Fibroma

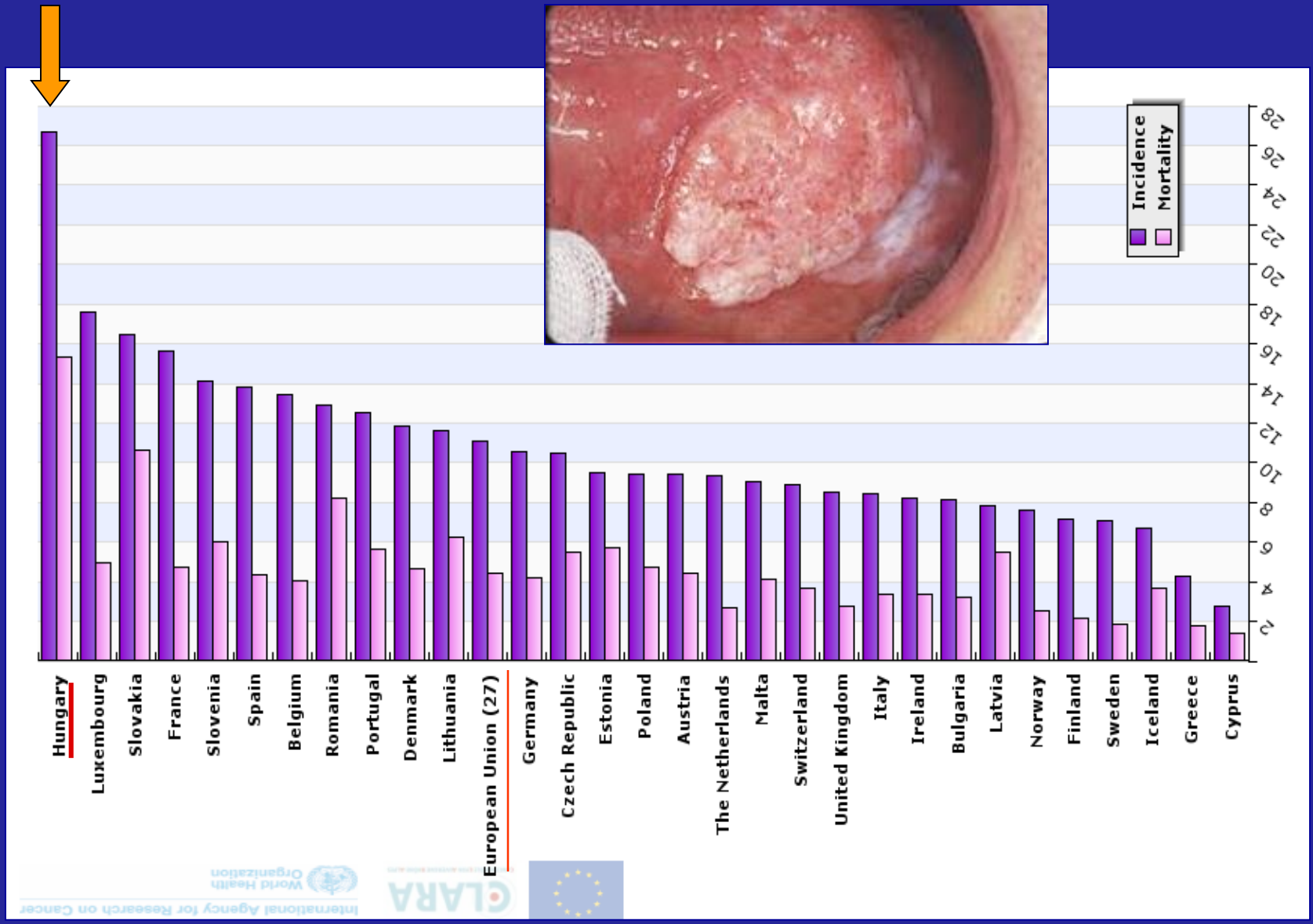
Most frequent

Hemangioma ⇆ Pyogenic granuloma

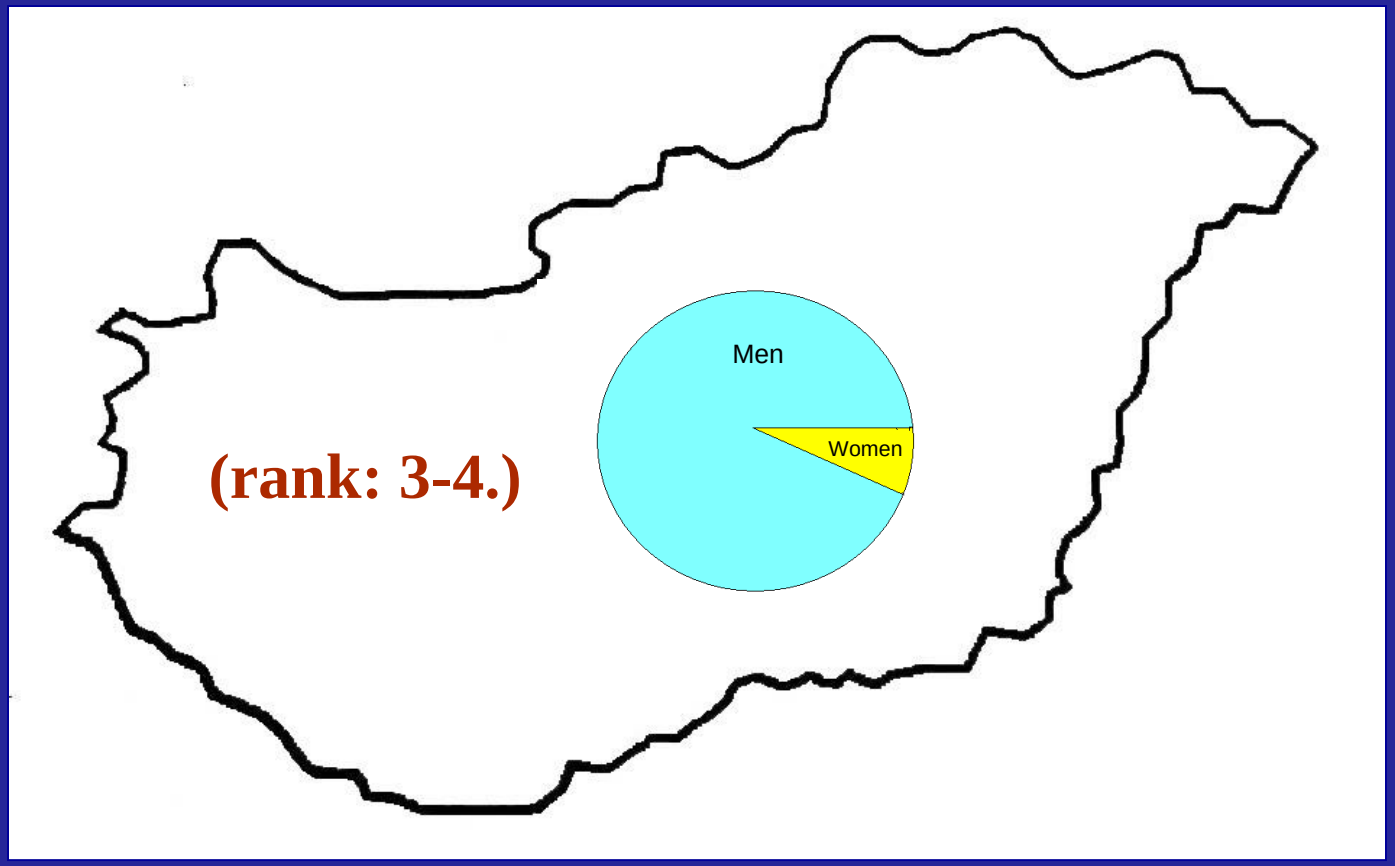




Carcinoma



(European Cancer Observatory, 2008.)

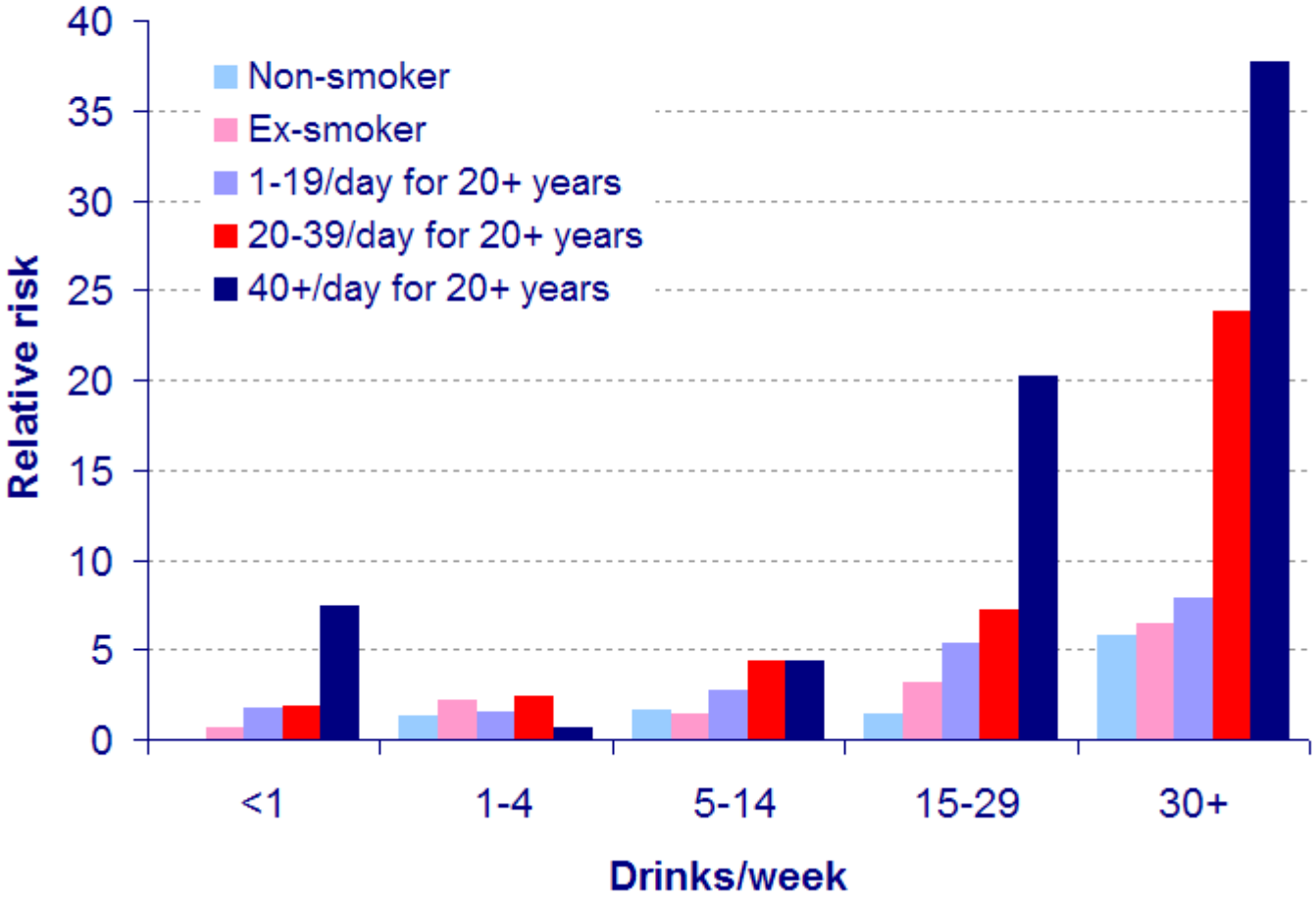


…+ rapid increase!

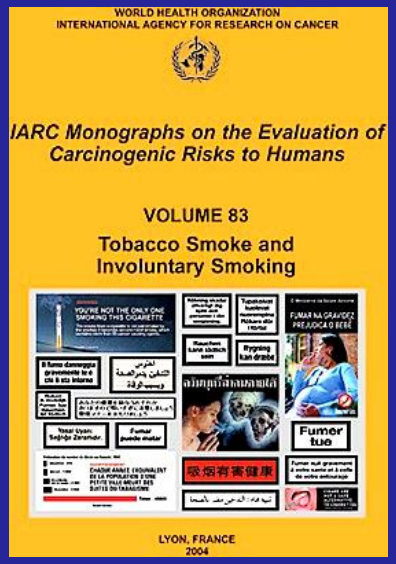
5 year survival: 35 %

more frequent under 40

Relative risk of oropharyngeal cancer in males by alcohol/tobacco consumption using US measures



(alcohol: a good solvent for absorption of carcinogens + adducts)



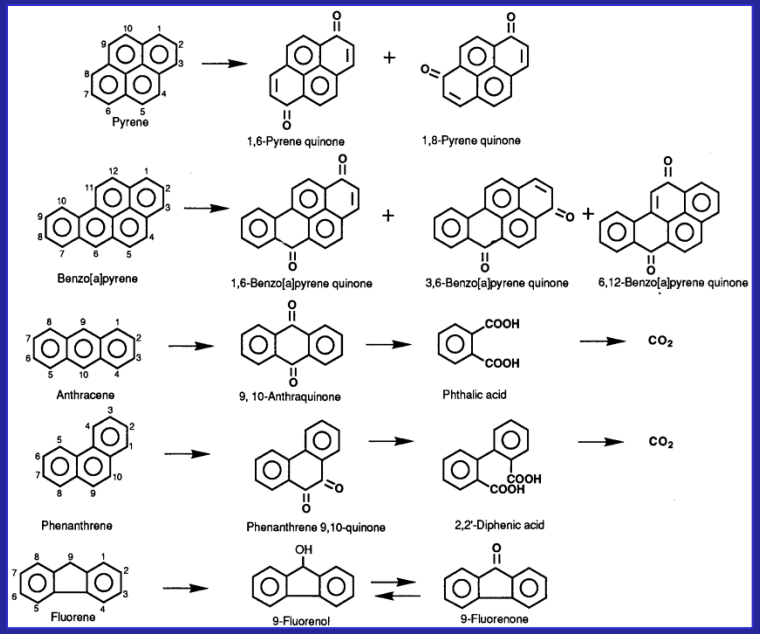
Cigarette smoke:

Category 1 (carcinogenic to humans)

***sufficient evidence* of carcinogenicity in humans**

Over 4700 chemicals

(60 carcinogens, >20 promoters)



Tar

Polyclic aromatic hydrocarbons (PAH)

Benz(a)pyrene

Dimethyl-benzanthracene

Benzo(b,j)fluorantrene

5-methylchrysene

3-methylcholantrene

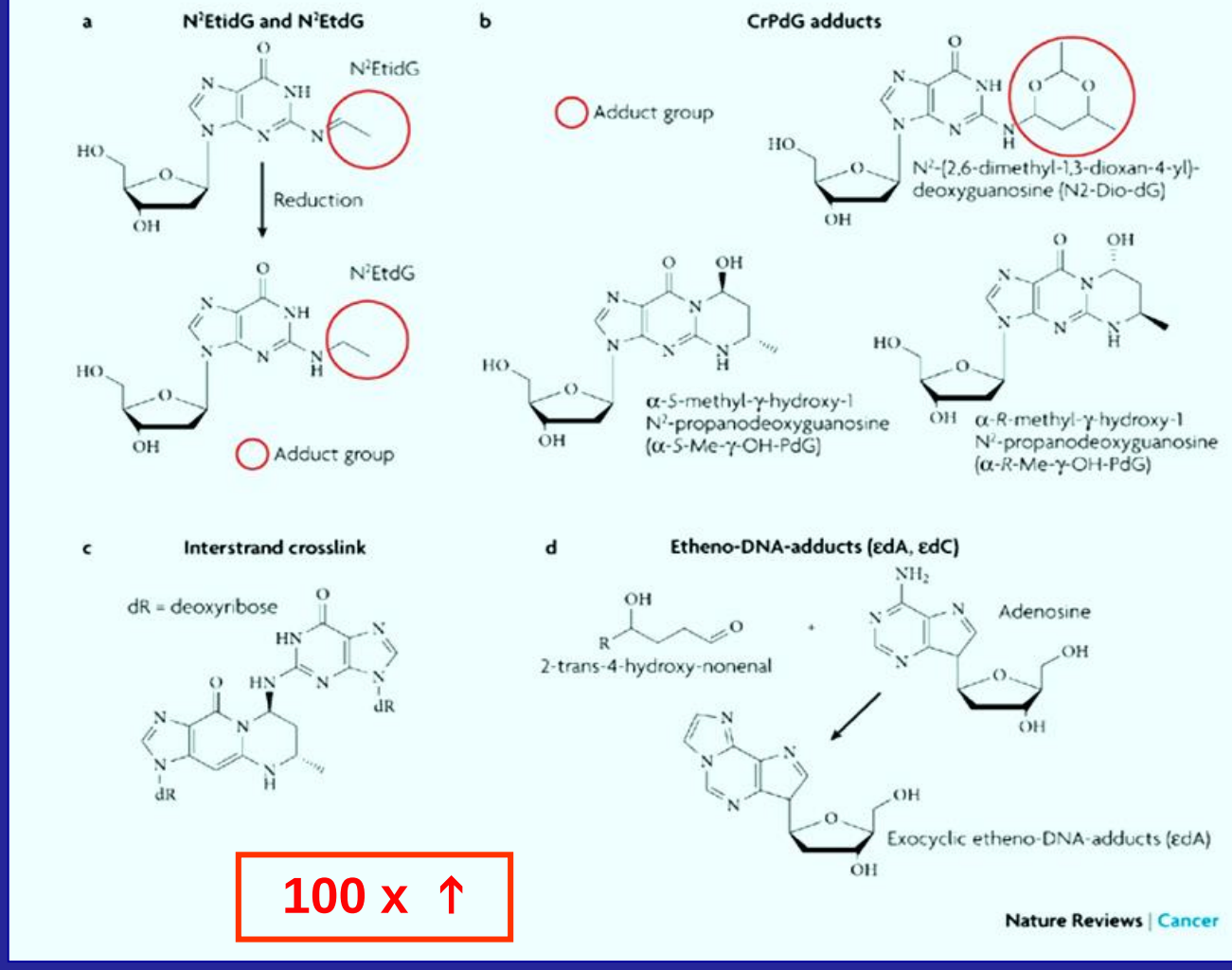
NNK (nicotine-derived nitrosamine keton)

Nitrosamines (DEN, DMN…)

Aromatic amines

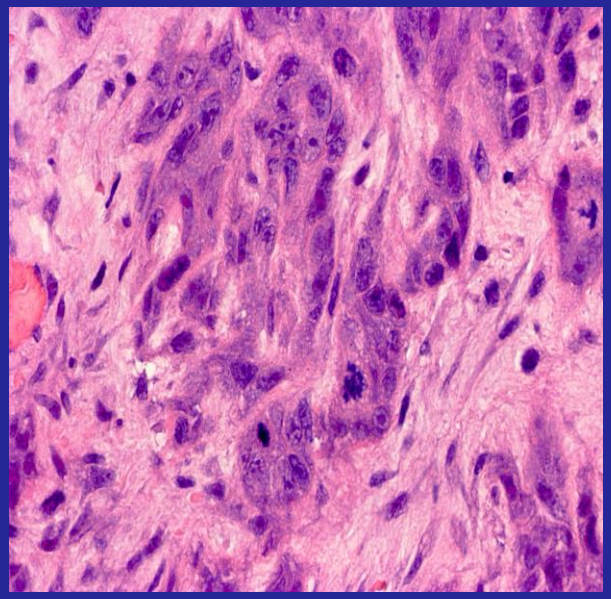
Metals (chromium, cadmium, nickel subsulfid, arsenic)

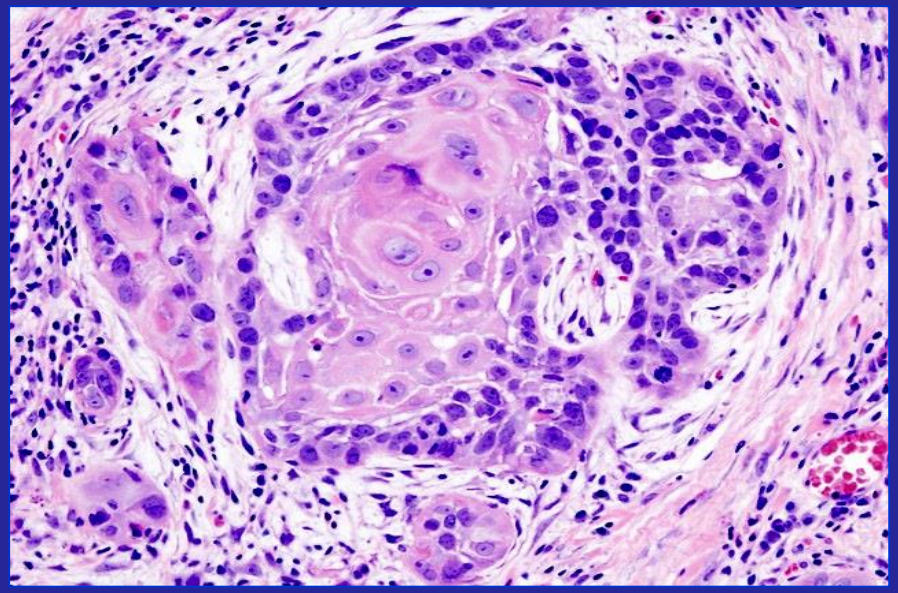
Acetaldehid-induced DNA-adduct-formation following alcohol ingestion in oral squamous cells



100 x ↑

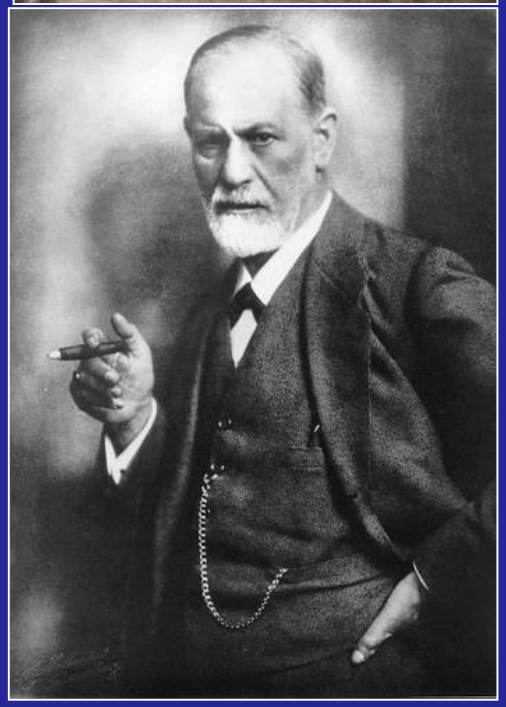
Exophytic Endophytic Ulcerative





90 %

Cancer of lip



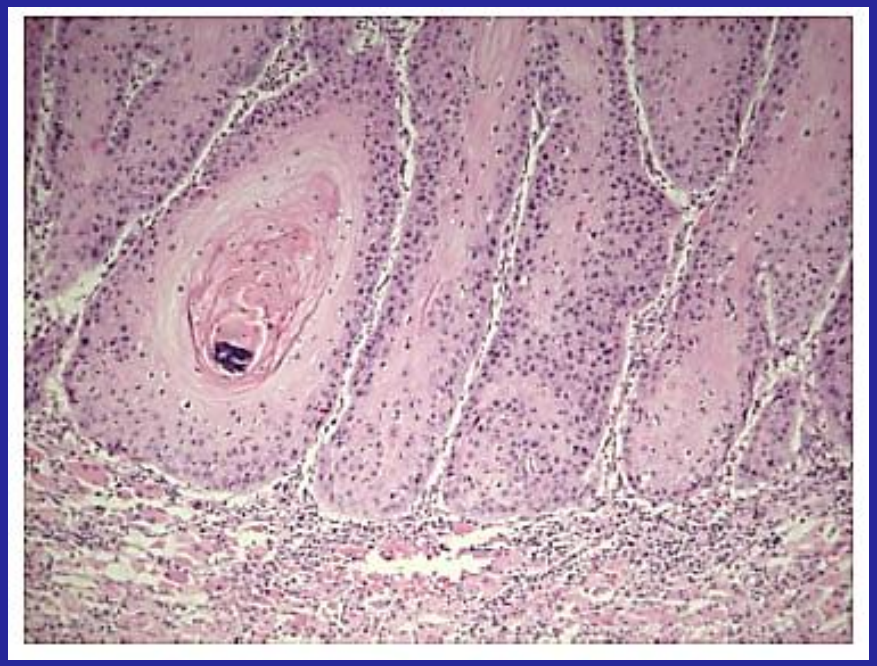
Other factors

Frequency is decreaased by
- vitamins A, C, E
- carotenoids

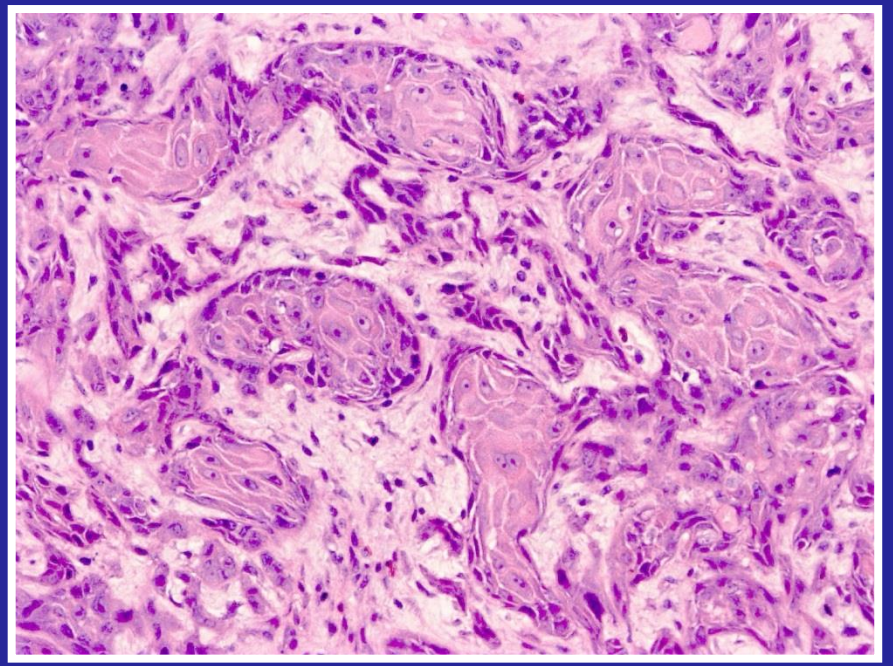
Not justified:
regular eating of vegetables
- (no decreased cancer morbidity among vegetarians)

Growth patterns

Expansive front



Invasive front



TNM-staging

T1 - diameter: </= 2 cm

T2 - diameter: 2 – 4 cm

T3 - diameter > 4 cm

T4 - more than 4 cm + local invasion

N1 - ipsilateral, solitary, diameter max. 3 cm

N2a - ipsilateral, solitary, diameter 3 – 6 cm

N2b - multiple, ipsilateral, diameter max. 6 cm

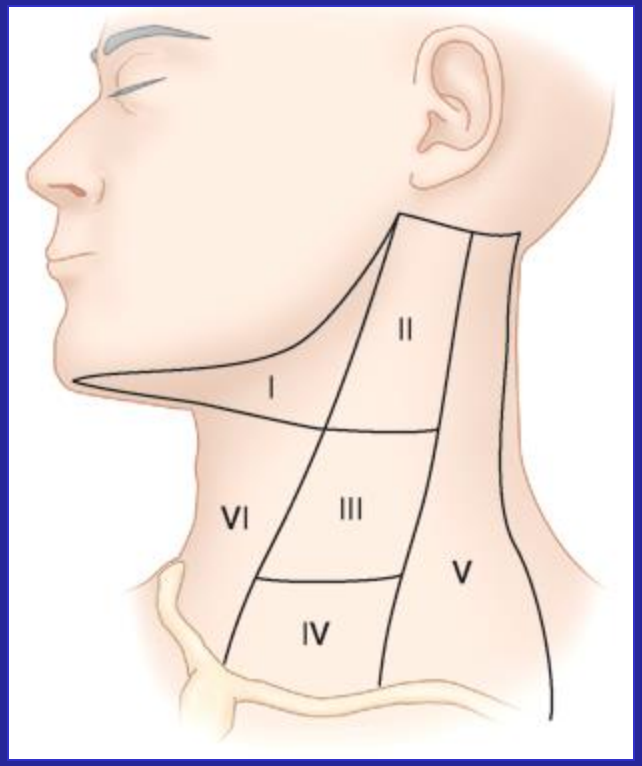
N2c - bilateral, or contralateral, max. 6 cm

N3 - any lymph node, > 6 cm

(Level of lymph nodes is also important! – lower levels: worse prognosis)

M1 - distant metastasis (rare; mainly lung)

Levels of cervical lymph nodes



I – submental/submandibular

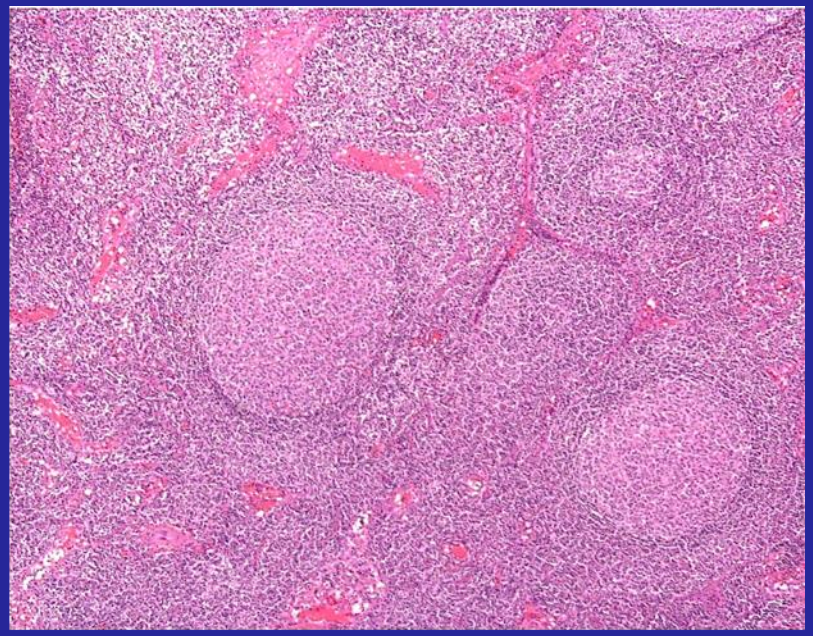
II – upper cervical/jugular

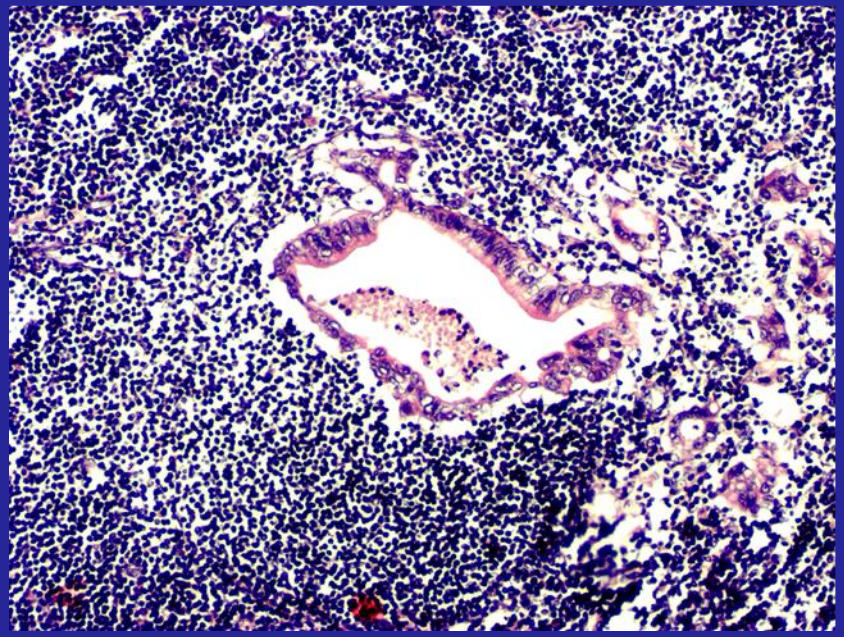
III – middle cervical/jugular

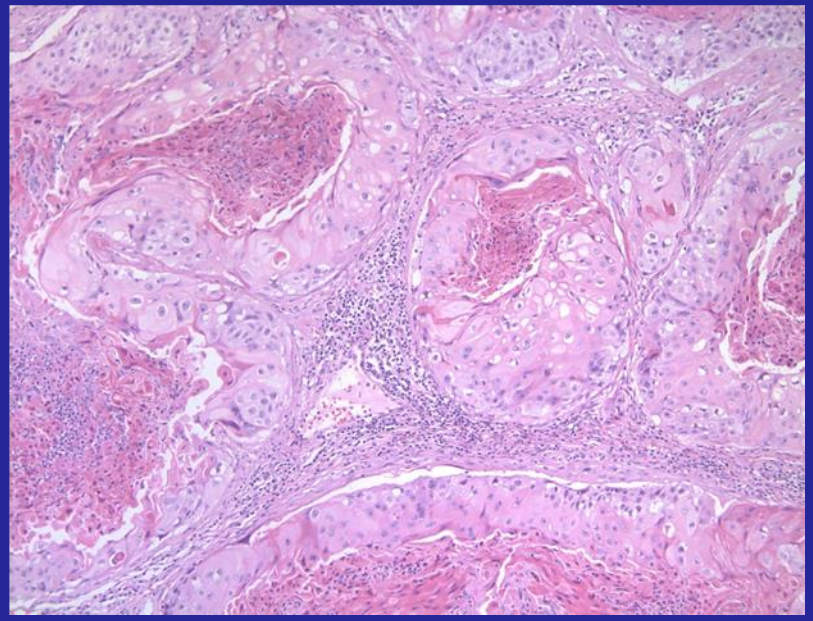
IV – lower cervical/jugular

V – supraclavicular

VI – pretracheal/prelaryngeal

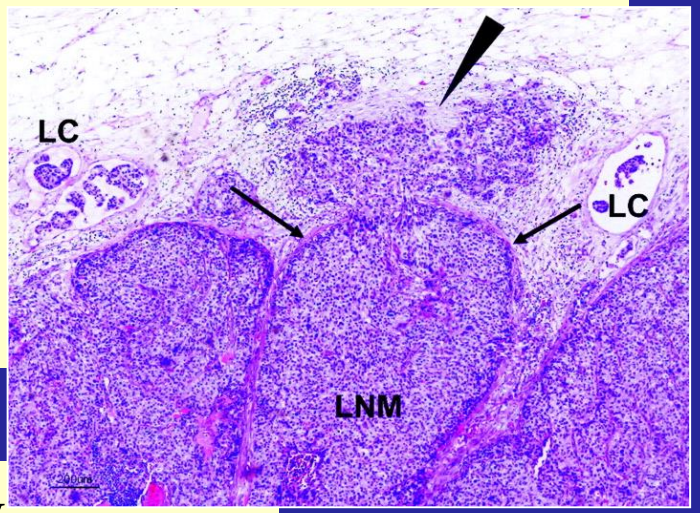






Factors determining prognosis

Grade
TNM-stage
Growth pattern
Extracapsular spread from ymph node metastases
Localization
Distant metastases (rare– lung)



Different metastasizing capacity

Lip- generally low metastatic capacity

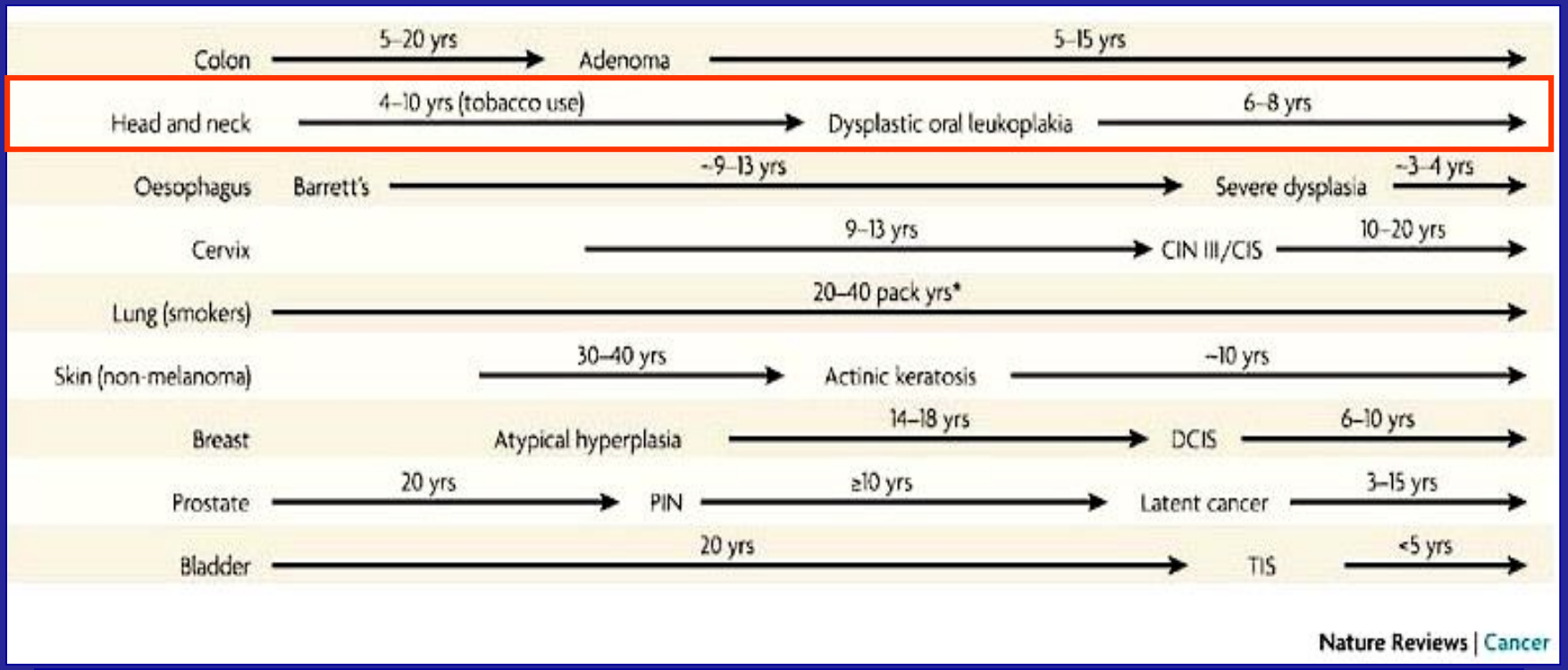
(submental, submandibular lymph nodes)

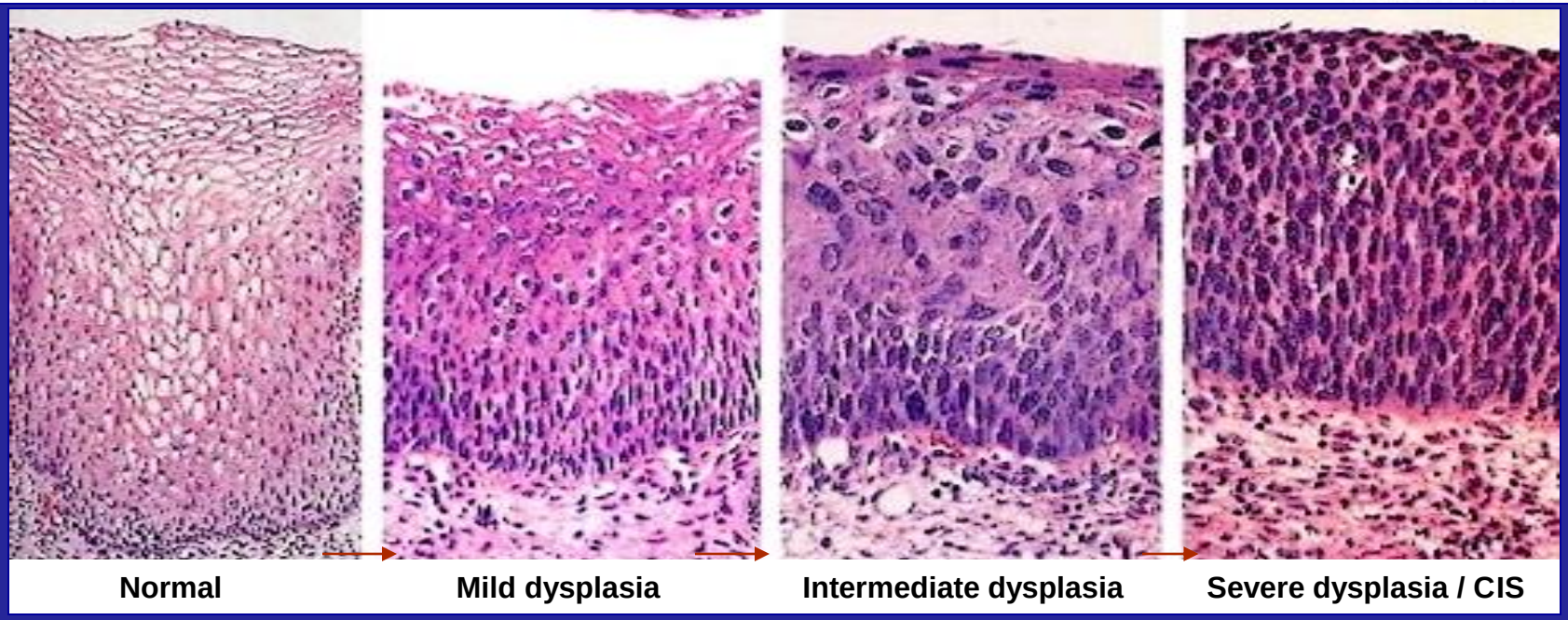
Palate - generally low metastatic capacity

(buccinator, submandibular, jugular ln.)

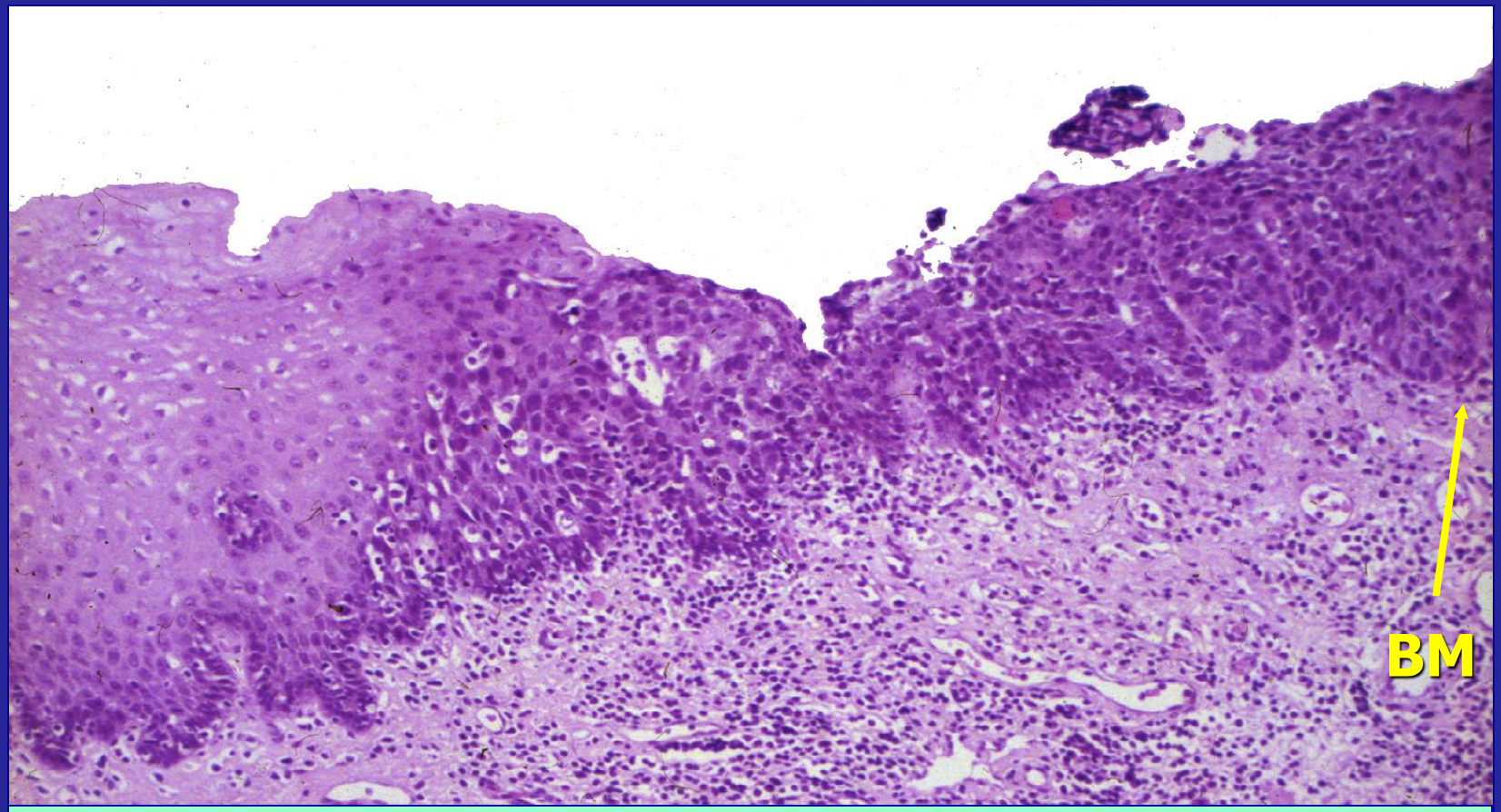
Other intraoral tumors– submandibular, jugular ln.

Midline tumors – frequent bilateral met.


Colon
5–20 yrs
Adenoma
5–15 yrs
Head and neck
4–10 yrs (tobacco use)
Dysplastic oral leukoplakia
6–8 yrs
Oesophagus
Barrett's
~9–13 yrs
Severe dysplasia
~3–4 yrs
Cervix
9–13 yrs
CIN III/CIS
10–20 yrs
Lung (smokers)
20–40 pack yrs*
Skin (non-melanoma)
30–40 yrs
Actinic keratosis
~10 yrs
Breast
Atypical hyperplasia
14–18 yrs
DCIS
6–10 yrs
Prostate
20 yrs
PIN
≥10 yrs
Latent cancer
3–15 yrs
Bladder
20 yrs
TIS
<5 yrs
Nature Reviews | Cancer

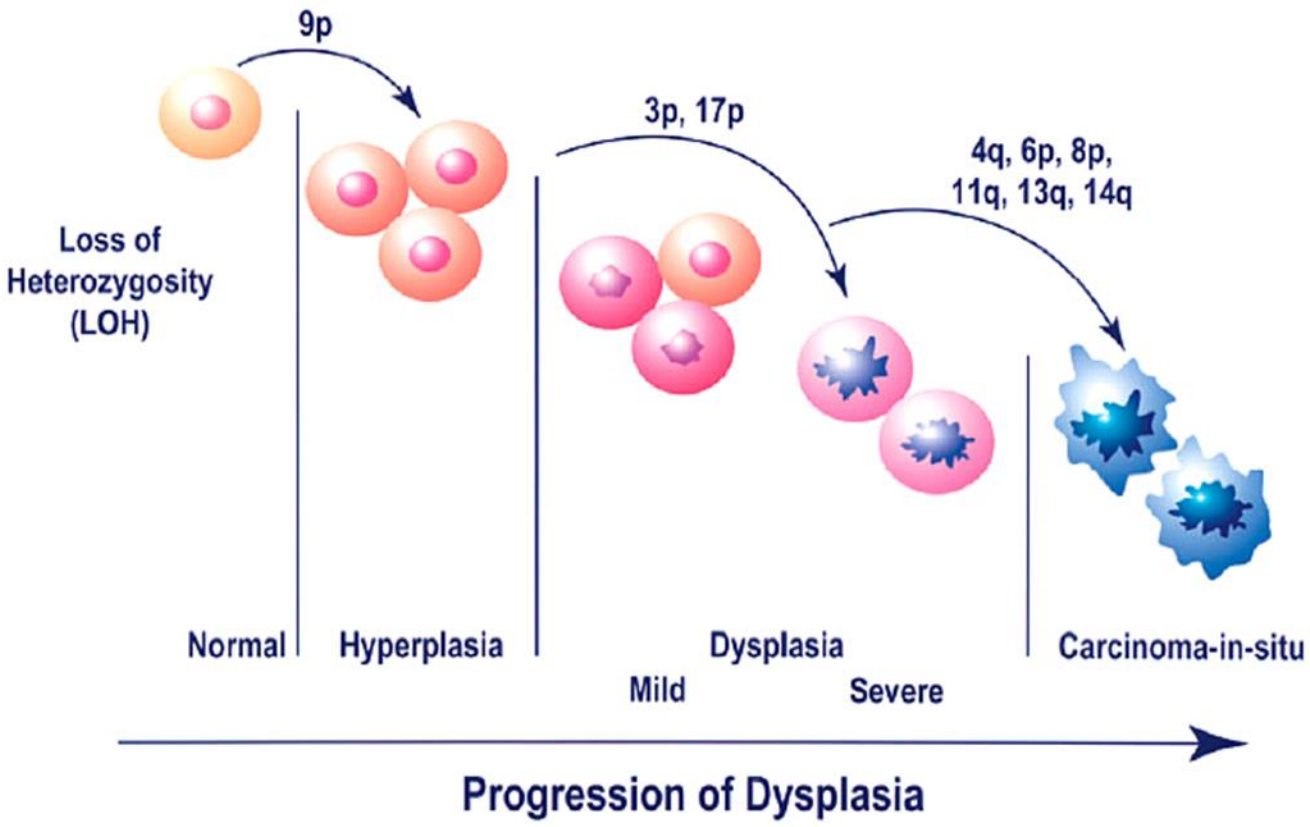

Normal
Mild dysplasia
Intermediate dysplasia
Severe dysplasia / CIS

Major molecular alterations during natural history of oral cancer



------	9p21 LOH	3p21, 17p13 LOH	11q13, 13q21,	5p, 8, 4q27, 10q23 LOH
	p16 inactivation	p53 mutation	14q32 LOH	PTEN inactivation
		(50%)	cyclin D1 amplif.	

Molecular Model of Dysplasia and Carcinogenesis



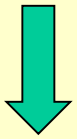
HPV (16, 18)

– identified in more than 50 % in oropharyngeal cancers

– 25-30% of mouth and throat cancers are caused by it

– 5-year survival is much better than the virus-negative cases (80% vs. 60%)

Feature	HPV-negative HNSCC	HPV-positive HNSCC
Incidence	Decreasing	Increasing
Aetiology	Smoking, excessive alcohol use	Oral sex
Age	Above 60 years	Under 60 years
Field cancerization	Yes	Unknown
TP53 mutations	Frequent	Infrequent
Predilection site	None	Oropharynx
Prognosis	Poor **(Hungary: 40%)**	Favourable



distinct entity

Verrucous carcinoma

Elderly men

Etiology: smoking, HPV

Exophytic, irregular surface

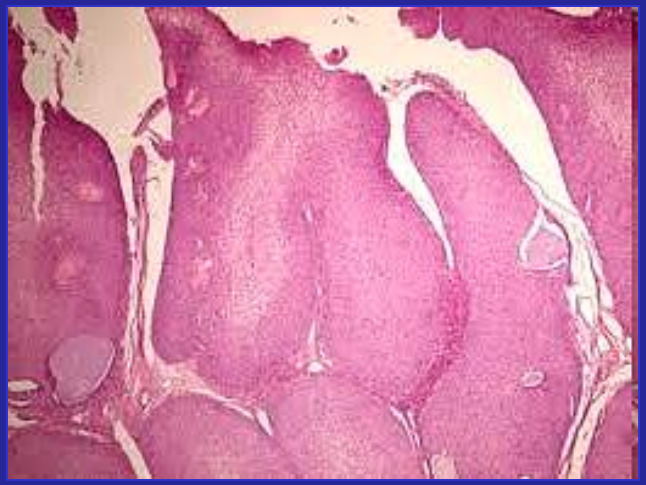
Manly in posterior location

Slowly growing, mainly expansive

Good prognosis (rare lymph node metastases, no distant met.)

(5-year survival > 90 %)

Radioresistant



Preneoplastic conditions

(more frequently undergo malignant transformation than the corresponding normal tissues - increased cancer risk)

Oral cancers: 10 – 60% are preceded by premalignant lesions

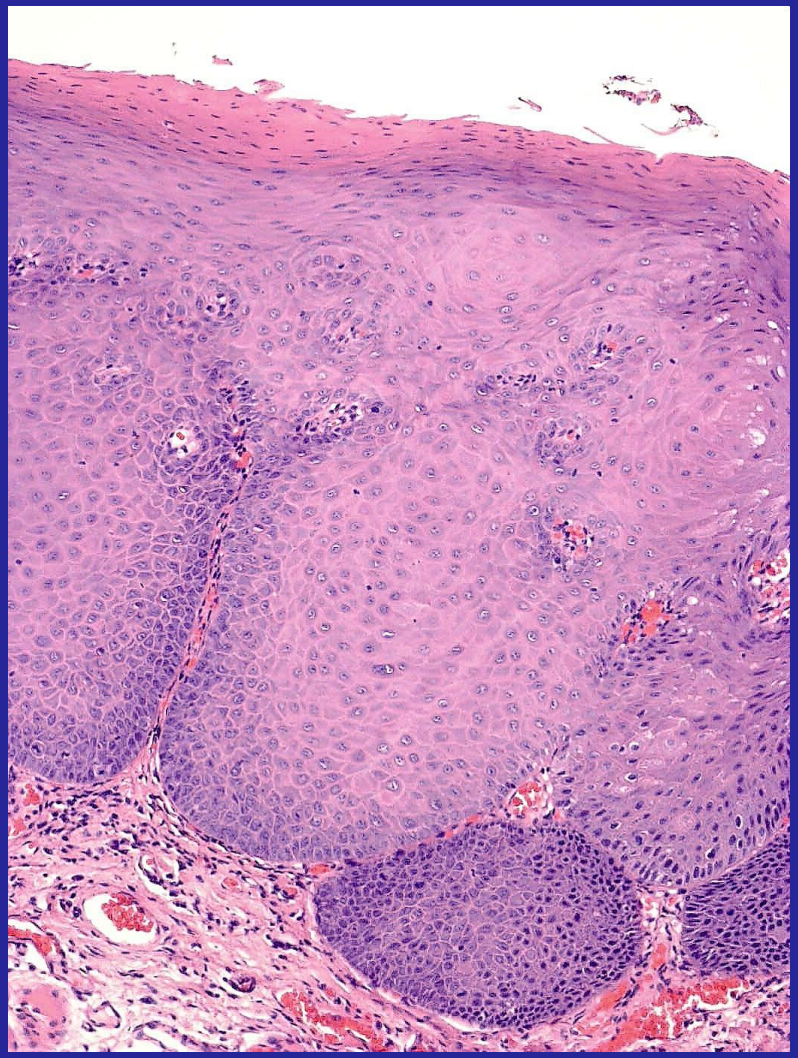
1/3 of cases develop *de novo*

Leukoplakia: 3-6 % is transformed over a 10-year period

Leukoplakia w/severe dysplasia: 40%

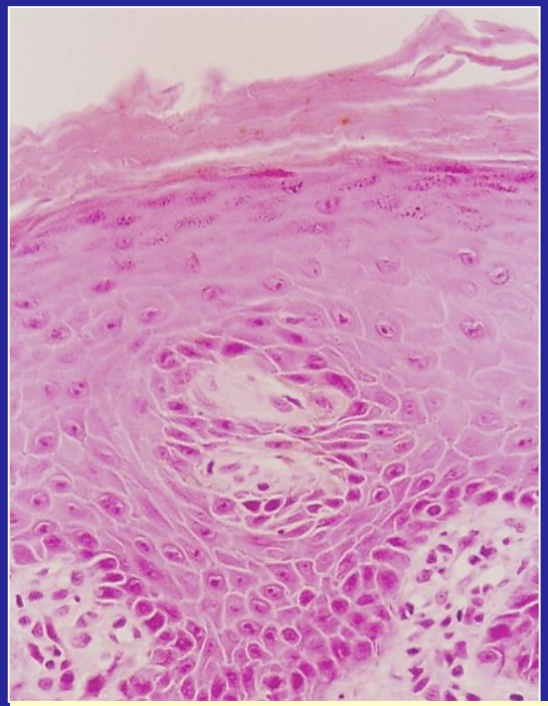
Proliferative verrucous leukoplakia: 70 %

Erythroplakia (carcinoma in situ): 50 % become invasive

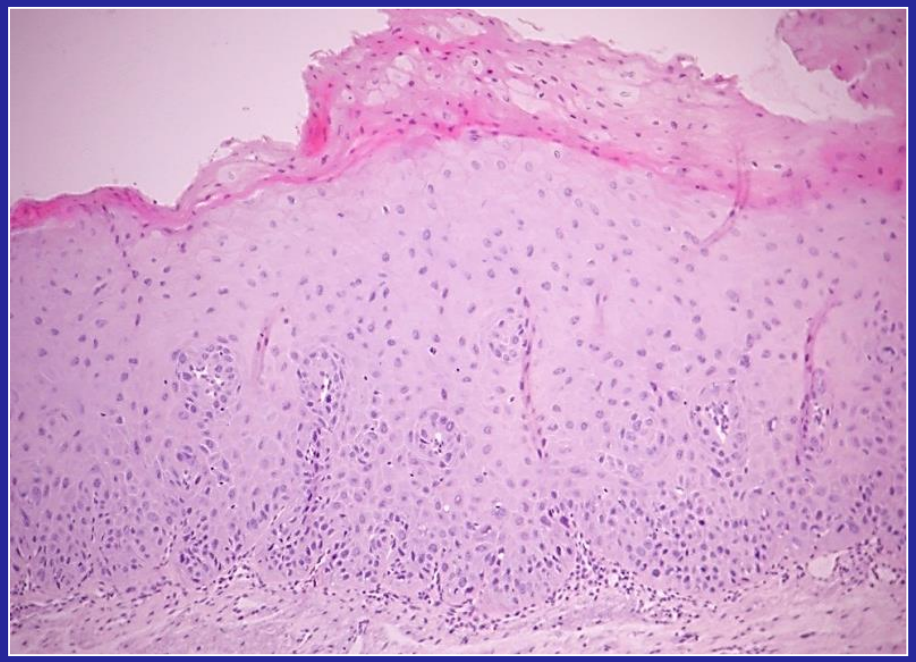


nodular leukoplakia

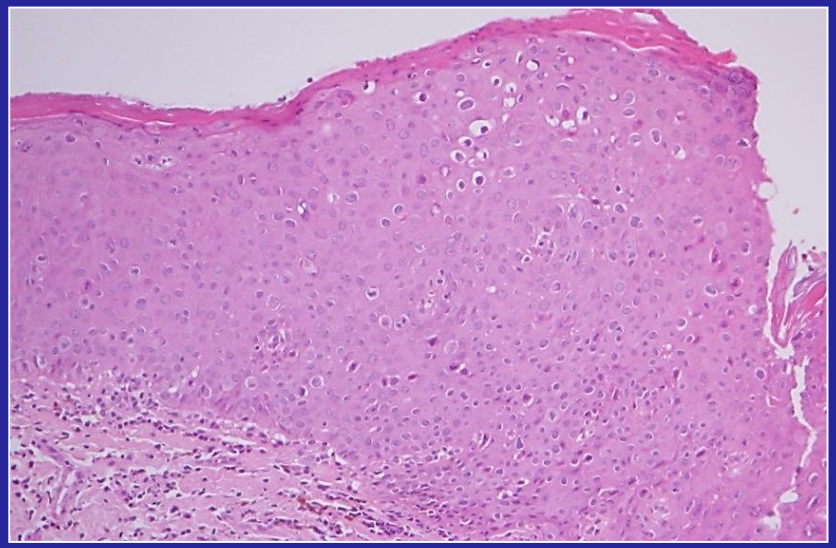
erosive leukoplakia



mild dysplasia

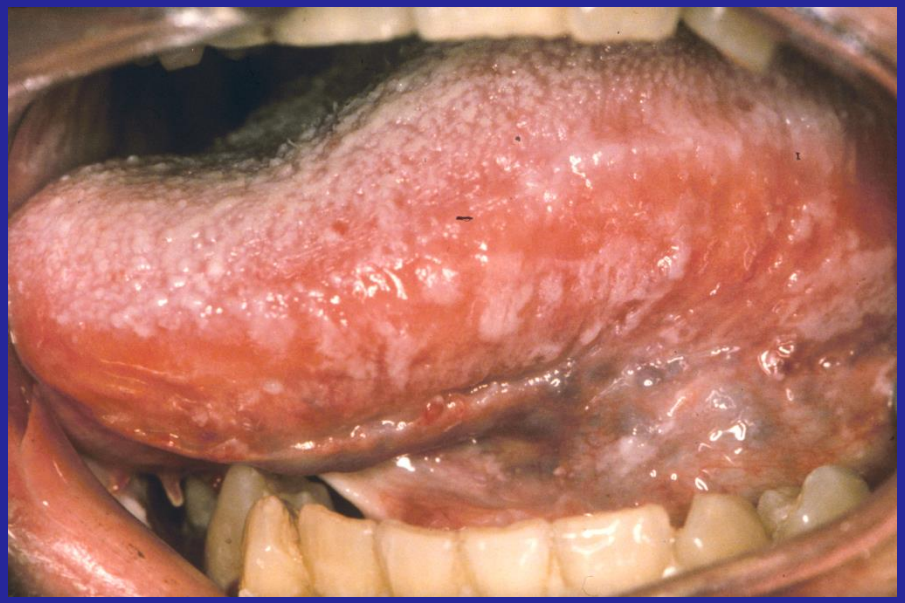


intemediate dysplasia



severe dysplasia


cc in situ



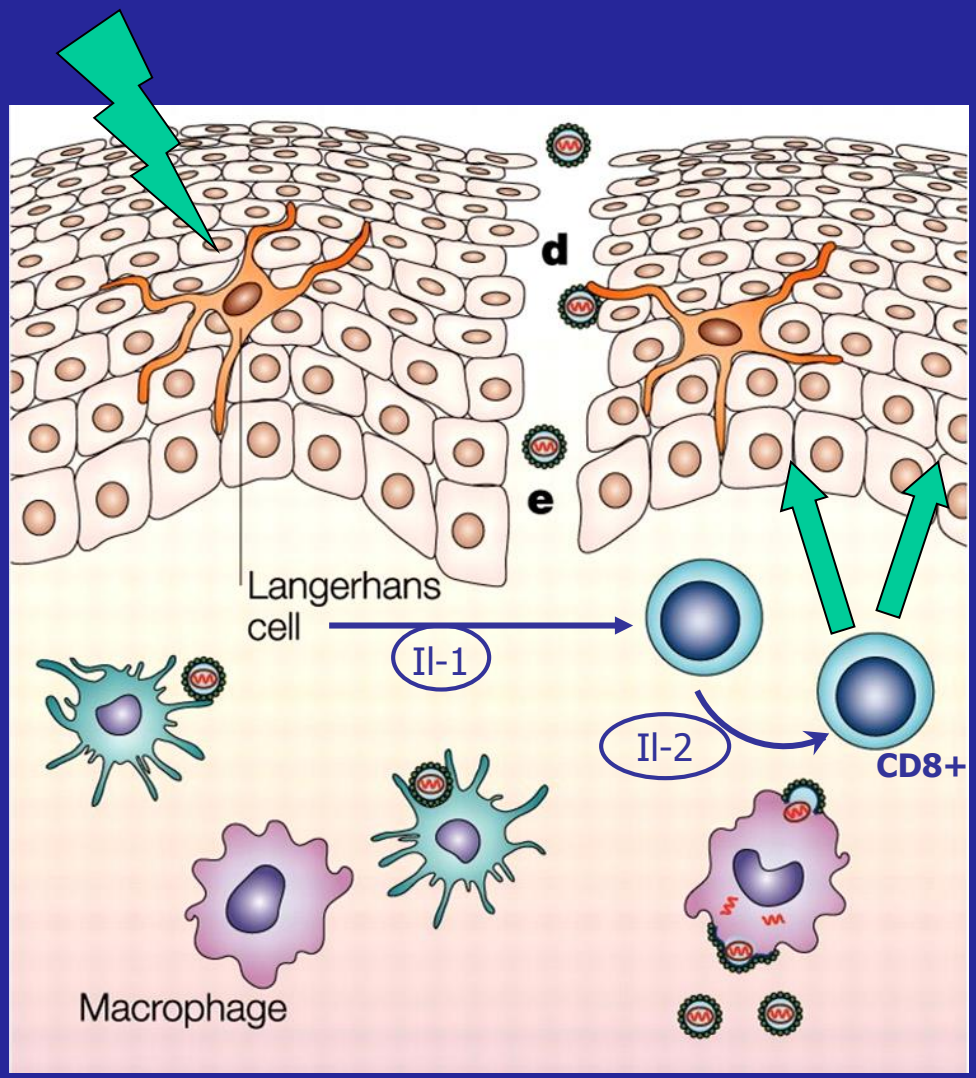
Hairy leukoplakia

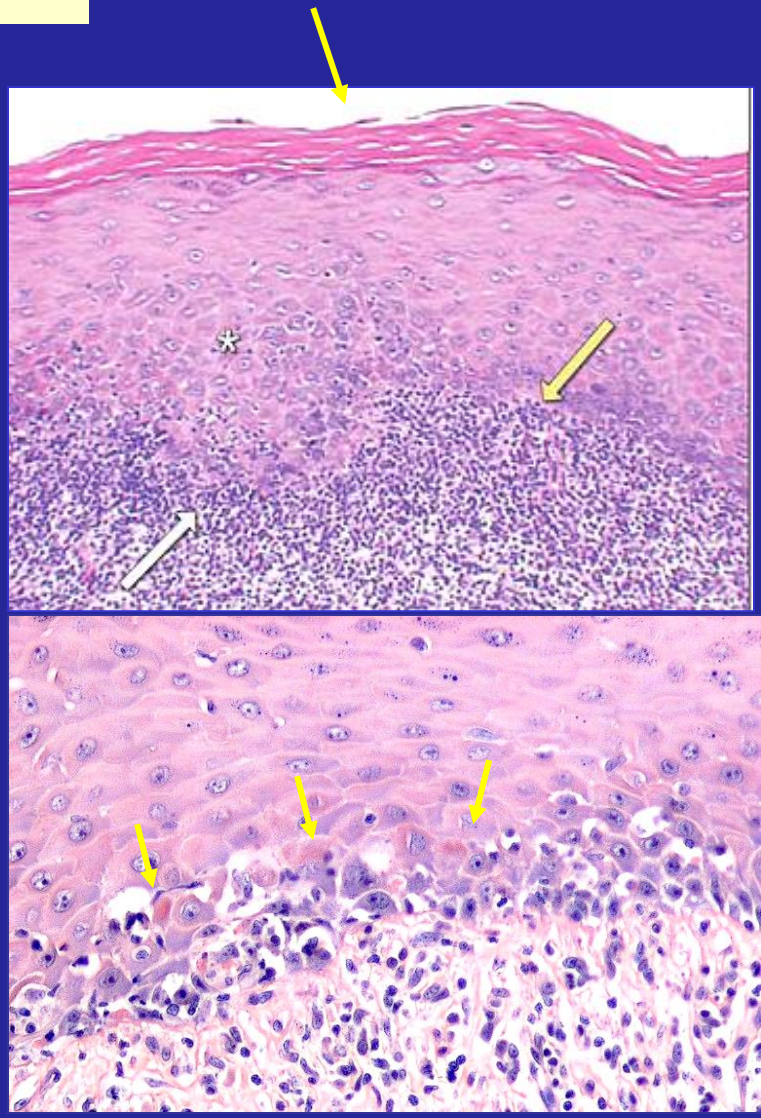
Preneoplastic conditions (WHO)

- Sideropenic dysphagia (in case of chronic iron deficiency: Plummer-Vinson syndrome, or Paterson-Kelly syndrome)
- Oral lichen planus (→ 0.4 - 5.6 %) + high risk of developing new tumors
- Syphilis, st. III. (interstitial glossitis w/atrophy + leukoplakia)
- Oral submucous fibrosis (India, Southeast Asia) (→ 7 - 13 %) (more aggressive than the others)
- Discoid lupus erythematosus (→ 2.5 %)
- Xeroderma pigmentosum
- Epidermolysis bullosa hereditaria (AD, AR)

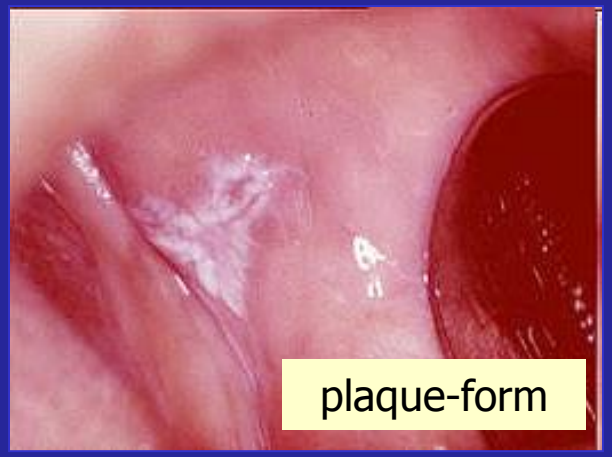
Discoid lupus erythematosus

Lichen planus





IF: fibrinogen!



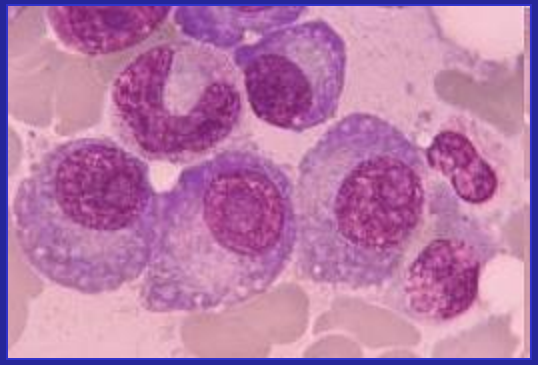
erosive

bullous

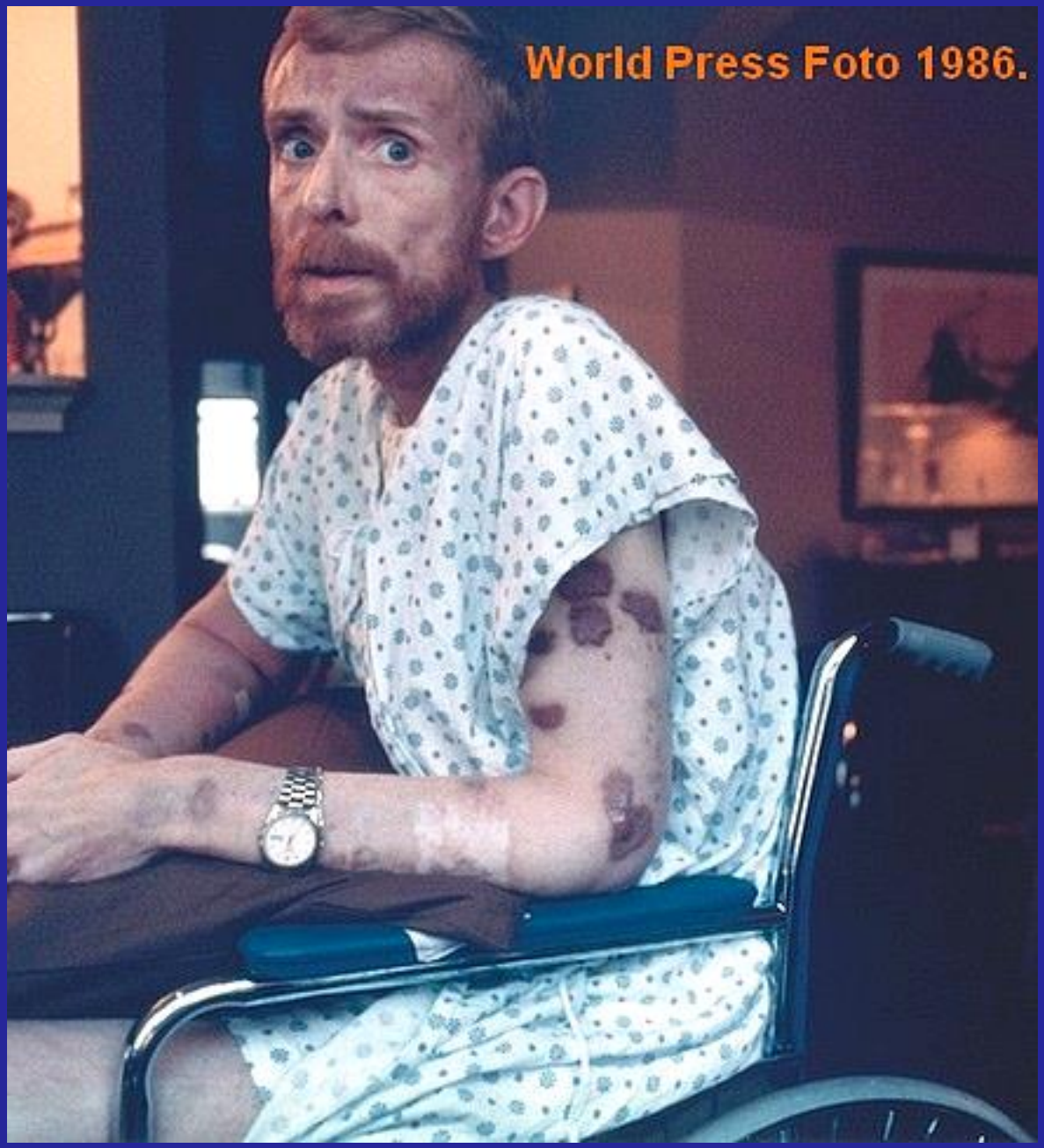
Other neoplasms

melanoma

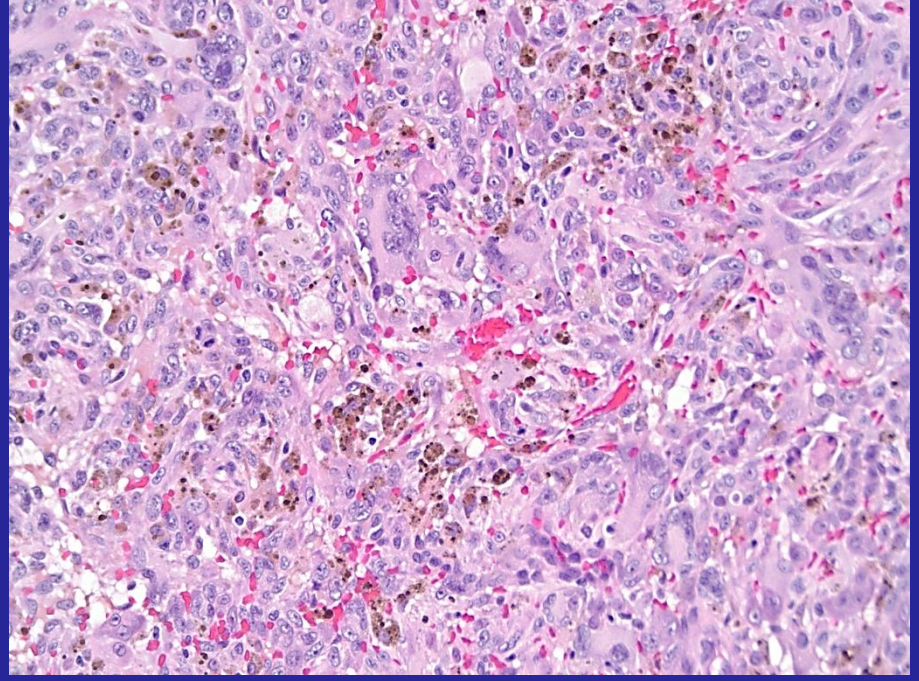
Kaposi-sarcoma

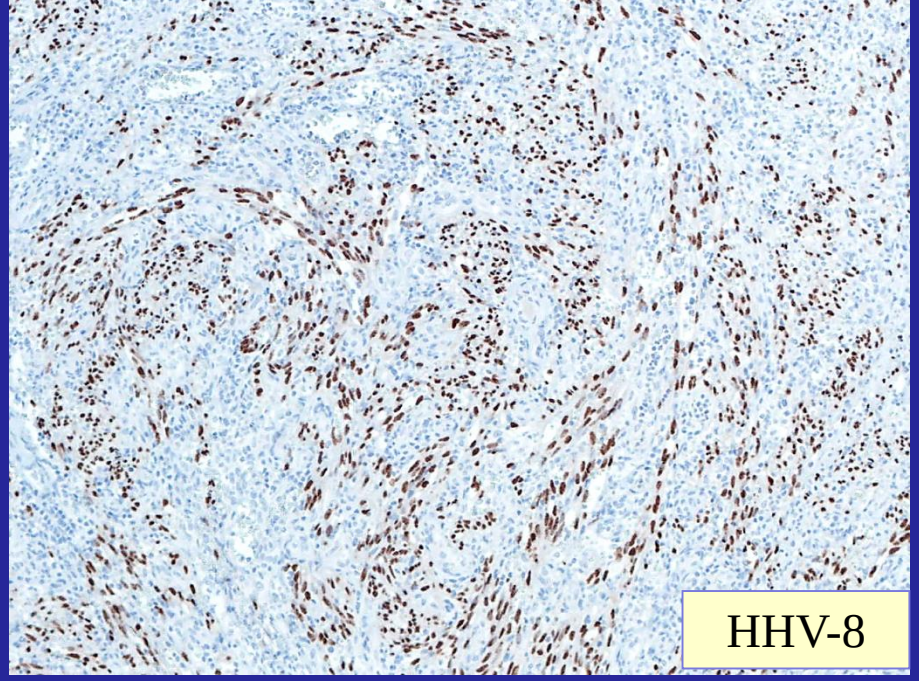


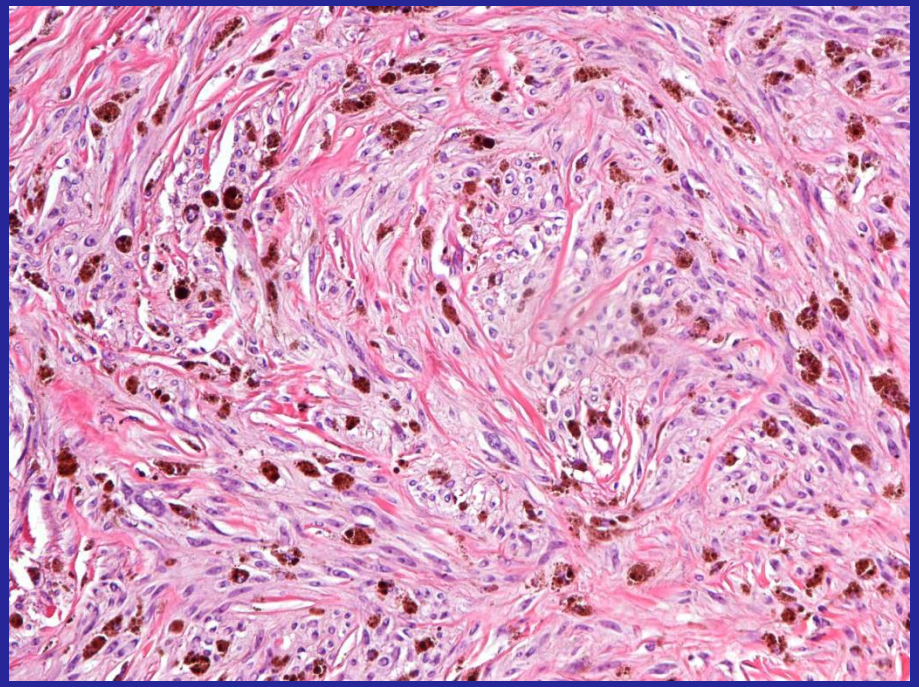
plasmocytoma

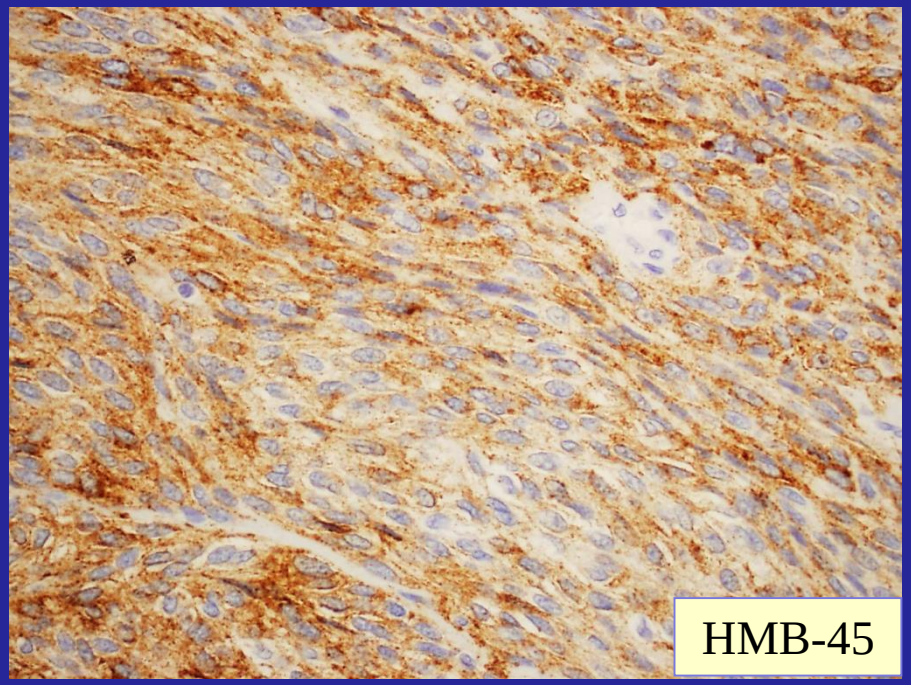

World Press Foto 1986.


WIZSCIENCE.COM




HHV-8




HMB-45

Focal epithelial hyperplasia (Heck-disease)

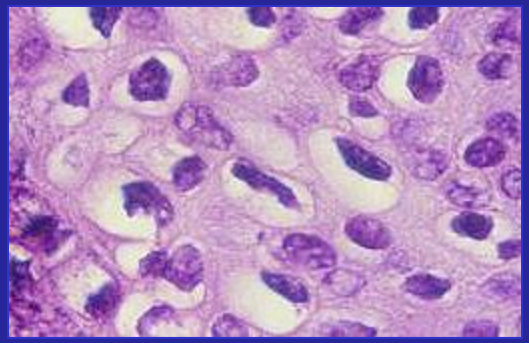
Children, young adults

Multiple

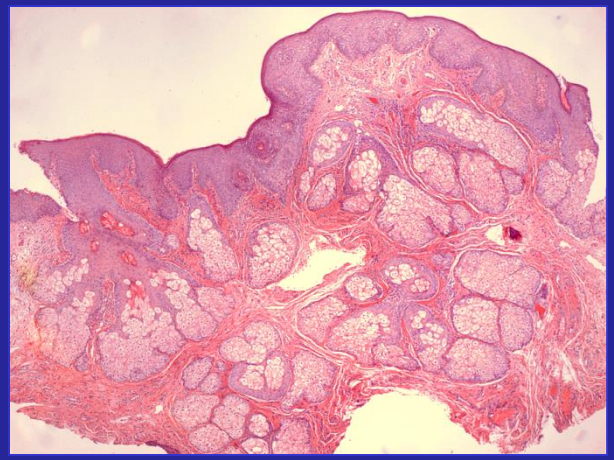
HPV 12, 32

No malignant potential

May regress spontaneously over time



Fordyce granules



Sebaceous hyperplastic islands

Symptomless or mild symptoms

Cosmetical, differential diagnostic problem