

Sommerschule, école d'été 2017

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epidemiology, carcinogenesis

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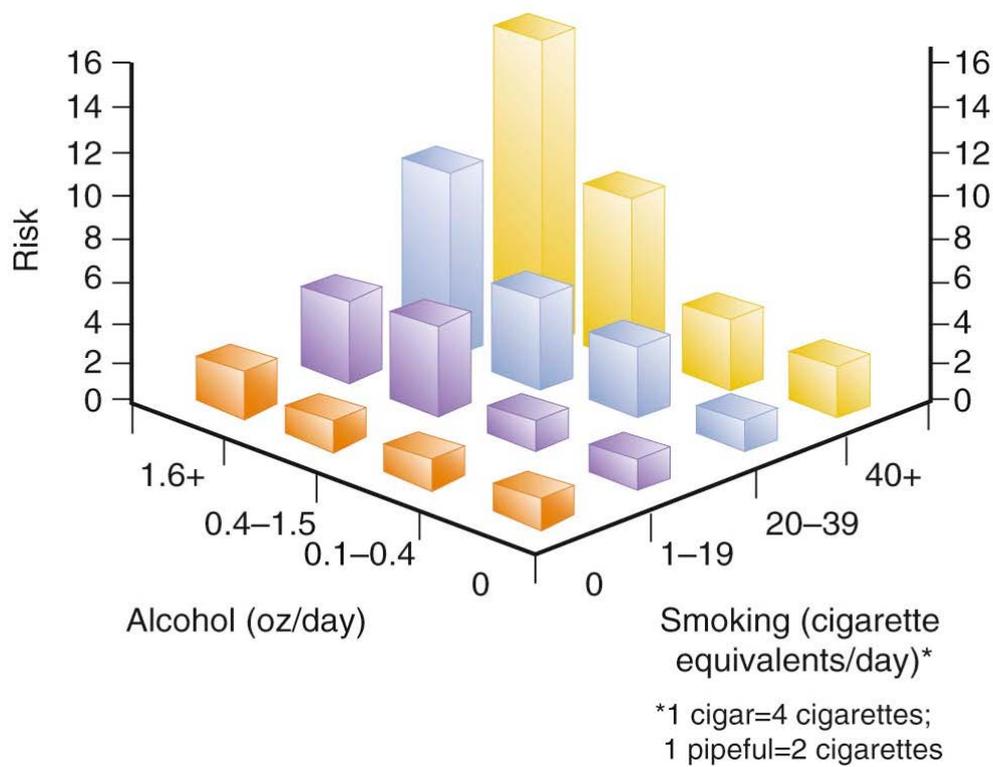
introduction

- majority of H&N Neoplasms arise from the mucosa of upper aerodigestive tract (oral cavity, pharynx, larynx, nasal cavity, sinuses)
- also originate from salivary-, (para-)thyroid glands, soft tissue, bone & skin
- most common type is SCC & papillary thyroid cancer
- rare: salivary gland cancers and sarcomas
- surgery => radiotherapy => chemotherapy => immunotherapy

etiology

cancer = result from interplay between host and environment

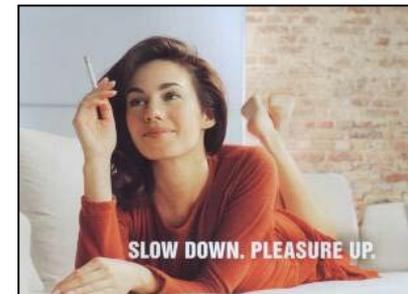
- alcohol, tobacco (90%) & HPV exposure are key causative factors
- risk of cancer proportional to duration and intensity
- synergistic effect of C2 and tobacco
- HIV, immunosuppression after transplantation
- ionizing radiation



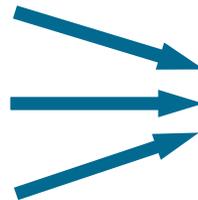
carcinogenesis by tobacco

damage dosage proportional / recovery according to abstinence

Odds ratio:	non-smoker:	1x
	7 cigarettes/day	2x
	25 cigarettes/day	16x



- benzpyrene
- methylcholanthrene
- nitrosamine
- many others



DNA-damage

- risk assessment by packyears
(py = number of packages cigarettes/day x years)

consequences of smoking on treatment success

- worse survival
- higher incidence of recurrent disease
- higher incidence of secondary primaries

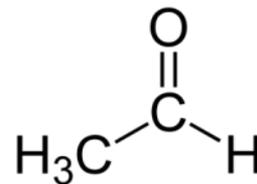
- worse therapy response
- stronger side effects of therapy

- higher risk of complications
- delayed wound healing
- higher co-morbidity

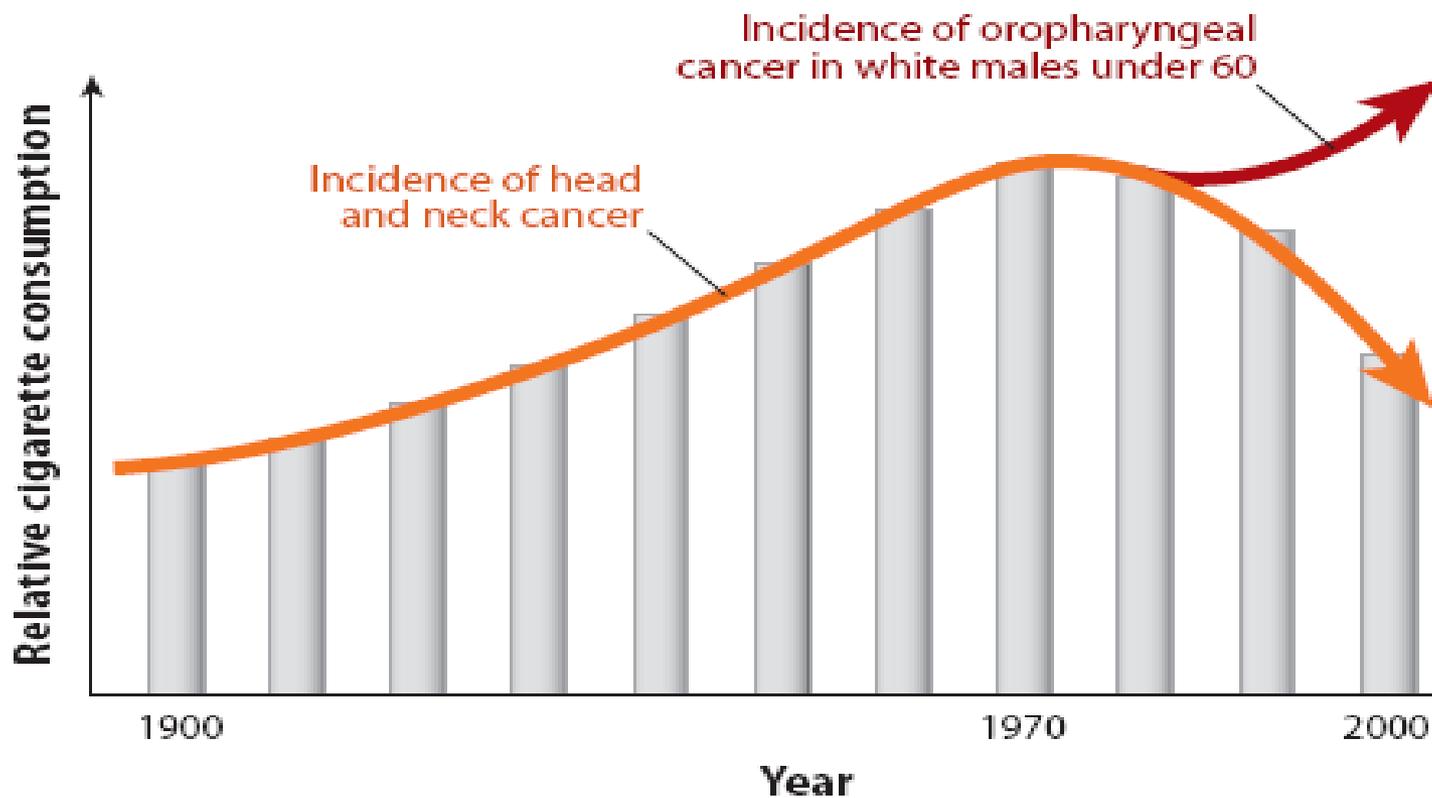
carcinogenesis by alcohol

Acetaldehyde

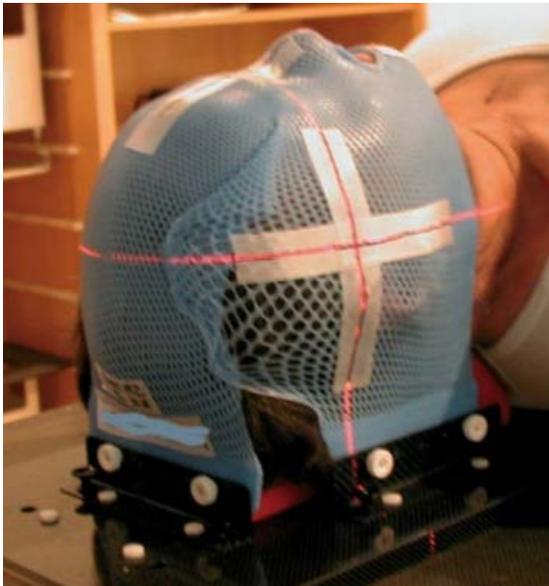
First metabolite of ethanol metabolism
Accumulation in saliva
Carcinogenic effect on mucosal surface
ALDH2-deficiency in people from Asia



HPV epidemiology



carcinogenesis by ionizing radiation



- secondary primaries within target volume
- aggressive behavior
- delay
- carcinomas, sarcomas
- bad prognosis

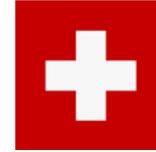
global epidemiology

HN Cancer 5th most common cancer type (HNSCC 6th most common)

- significant geographic variation (4-45/100'000)
- ethnic aspects, industrialization, environment, social context
- male:female ratio (SCC) 2-15:1
- male:female ratio (thyroid ca) 1 :3
- highest incidence of oral cavity & pharyngeal Cancer in South East Asia [chewing Tabacco and betel nuts (quid, «paan»), reverse smoking]
- highest incidence of nasopharyngeal cancer in South East Asia and North East Africa (EBV)



“national” epidemiology



- ~ 5% of all malignancies in Switzerland
- ~ 22 new cases/year/100'000 inhabitants
- 90% males; incidence in females rising
- 6. decade of life

global etiology

- highest incidence of laryngeal, hypopharyngeal Ca in Italy, France, Spain (↑ )
- lower incidence in less developed countries
- exposition to «environmental carcinogens» (↑ risk for oral cavity cancer, leukoplakia, fibrosis and lichen planus)
- ? environmental pollution, toxic substances at place of work, nutrition, viral infections, genetic predisposition

global epidemiology

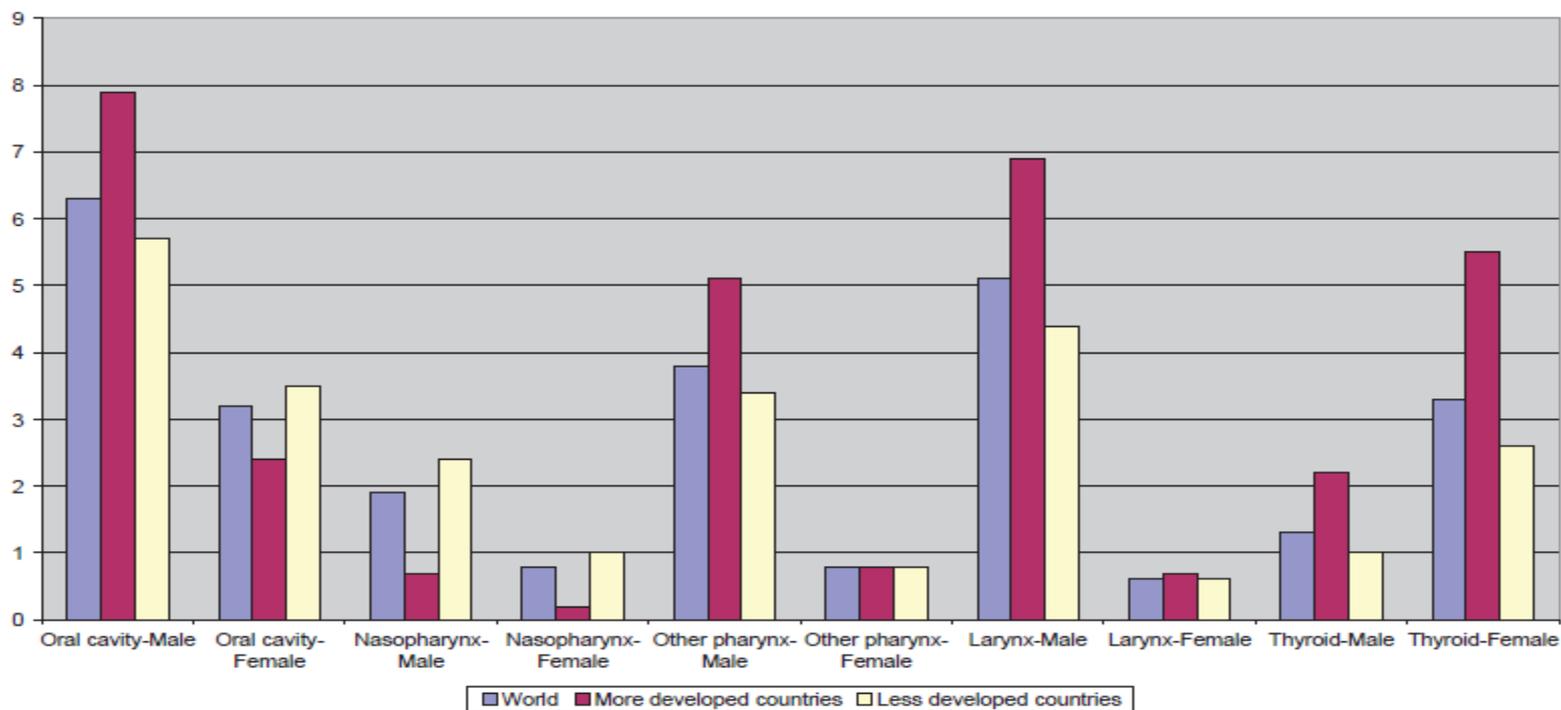


Figure 1.3 Incidence of head and neck cancers in more and less developed countries (per 100,000). *Source: From Ref. 5.*

global epidemiology

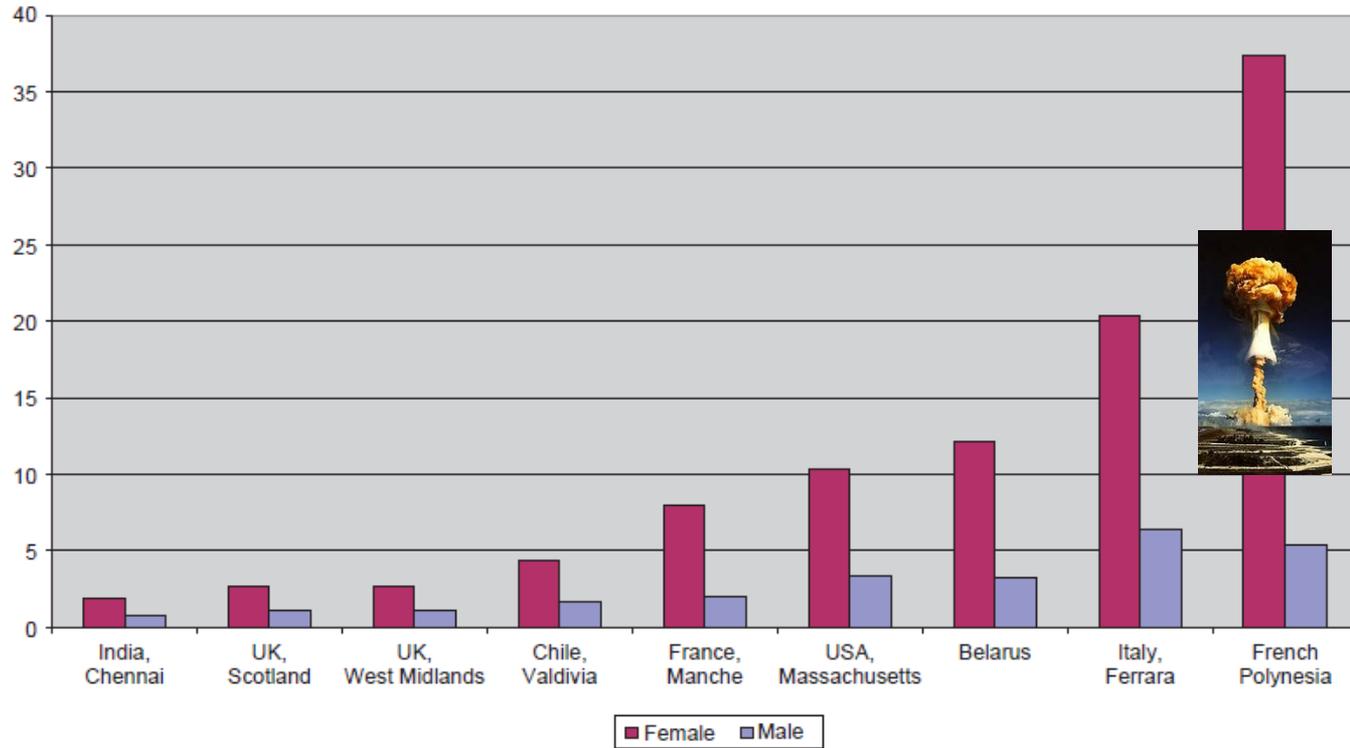


Figure 1.2 World variations in incidence of thyroid cancer (per 100,000). Source: From Ref. 1.

Table 1.1 Incidence and Mortality of Cancer Worldwide 2002 (5)

Rank	Cancer	Number of cases	Deaths
1	Lung	1,352,132	1,178,918
2	Breast	1,151,298	410,712
3	Colon and rectum	1,023,152	528,978
4	Stomach	933,937	700,349
5	Prostate	679,023	221,002
6	Liver	626,162	598,321
7	Cervix uteri	493,243	273,505
8	Oesophagus	462,117	385,892
9	Bladder	356,557	145,009
10	Non-Hodgkin lymphoma	300,571	171,820
11	Leukaemia	300,522	222,506
12	Oral cavity	274,289	127,459
13	Pancreas	232,306	227,023
14	Kidney etc.	208,480	101,895
15	Ovary etc.	204,499	124,860
16	Corpus uteri	198,783	50,327
17	Brain, nervous system	189,485	141,650
18	Melanoma of skin	160,177	40,781
19	Larynx	159,241	89,956
20	Thyroid	141,013	35,375
21	Other pharynx	130,296	83,993
22	Multiple myeloma	85,704	62,535
23	Nasopharynx	80,043	50,332
24	Hodgkin lymphoma	62,329	22,812
25	Testis	48,613	8,878

survival, depending on disease stage

- small tumour => larger tumor => nodal disease => distant disease

relative 5-year-survival depending on tumour stage at initial diagnosis

Table 1.4 Relationship of Tumor Size (T) and Node Metastases (N)

Direct size relation

Larynx
Oral cavity
Salivary glands
Lip
Nasal cavity and sinuses

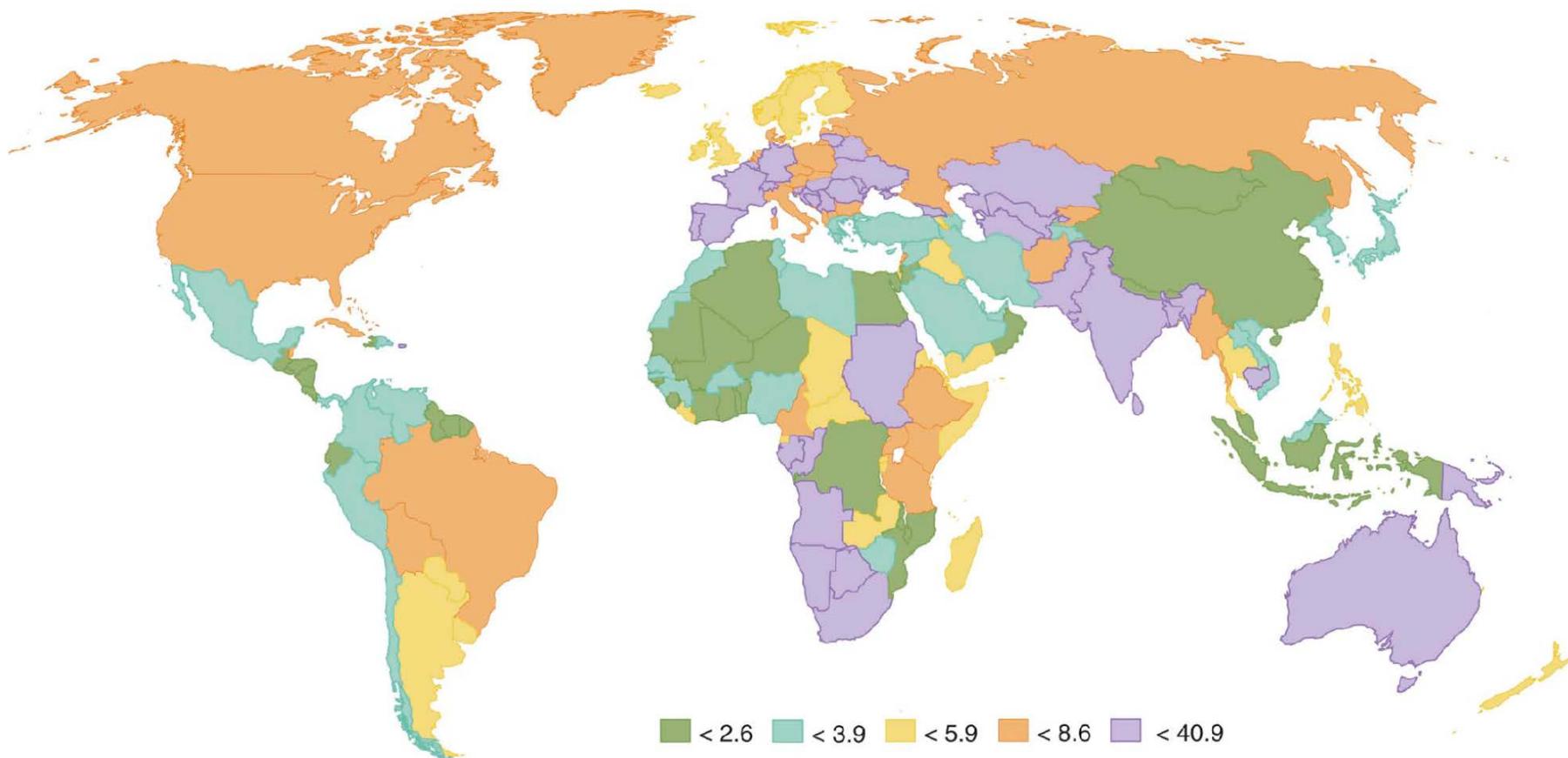
No size relation

Oropharynx
Nasopharynx
Hypopharynx
Thyroid

Table 1.5 Five-Year Relative Survival Rates in U.S.A. by Extent of Disease at Diagnosis, 1996–2002 (2)

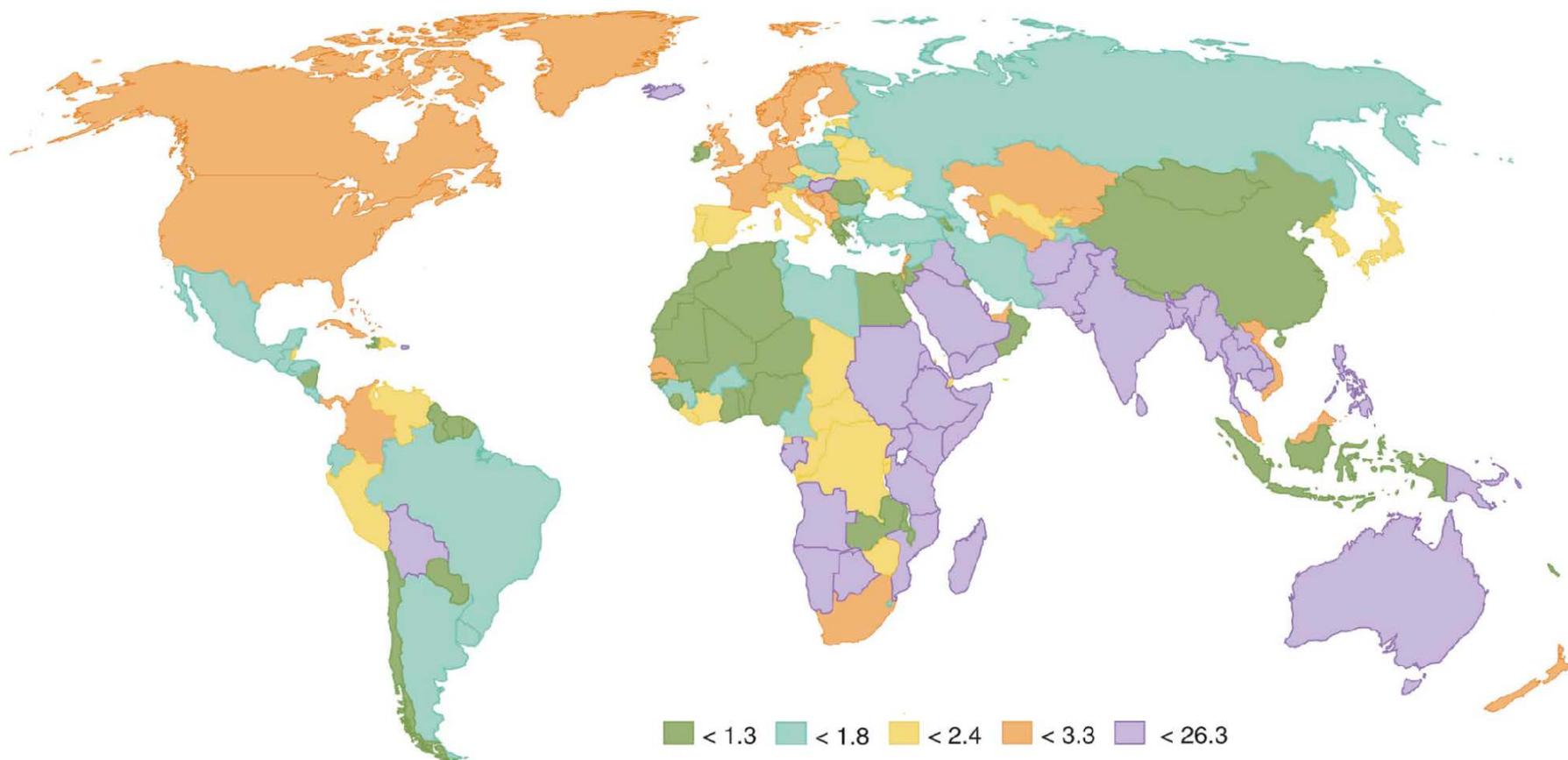
Site	All Stages %	Local %	Regional %	Distant %
Larynx	64.1	83.5	50.4	13.7
Oral cavity & pharynx	58.8	81.3	51.6	26.4
Thyroid	96.7	99.7	96.9	56.4

oral cavity, incidence/100'000 men



(From Ferlay J, Bray F, Pisani P, Parkin DM, Eds. GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide, Version 2.0, IARC CancerBase no.5, Lyon, IARC Press, 2004.)

oral cavity, incidence/100'000 women



(From Ferlay J, Bray F, Pisani P, Parkin DM, Eds. GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide, Version 2.0, IARC CancerBase no.5, Lyon, IARC Press, 2004.)

global epidemiology

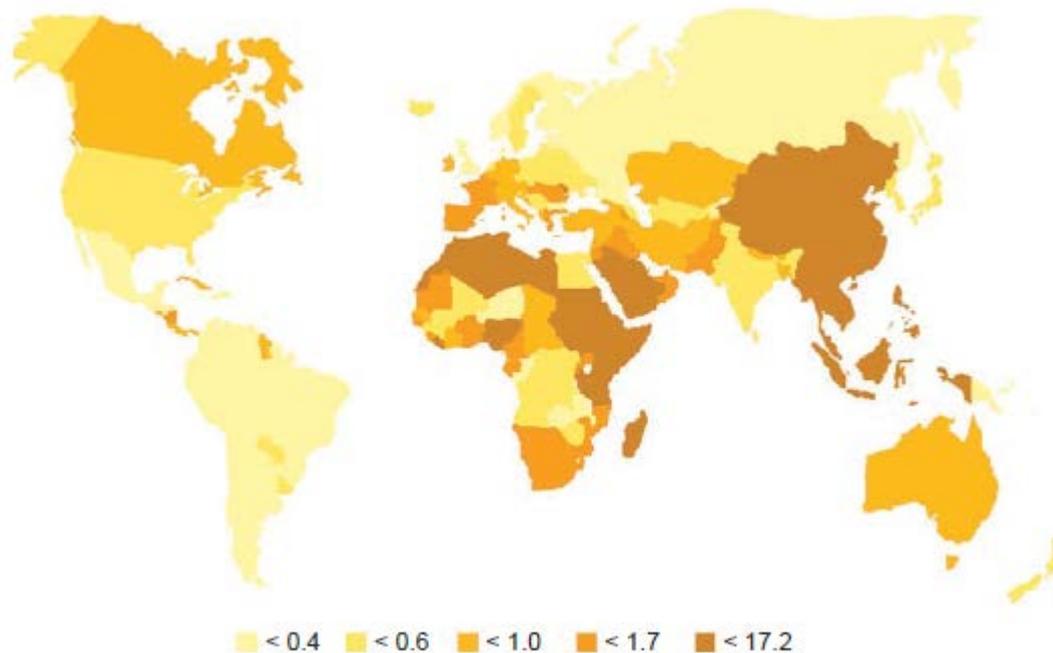


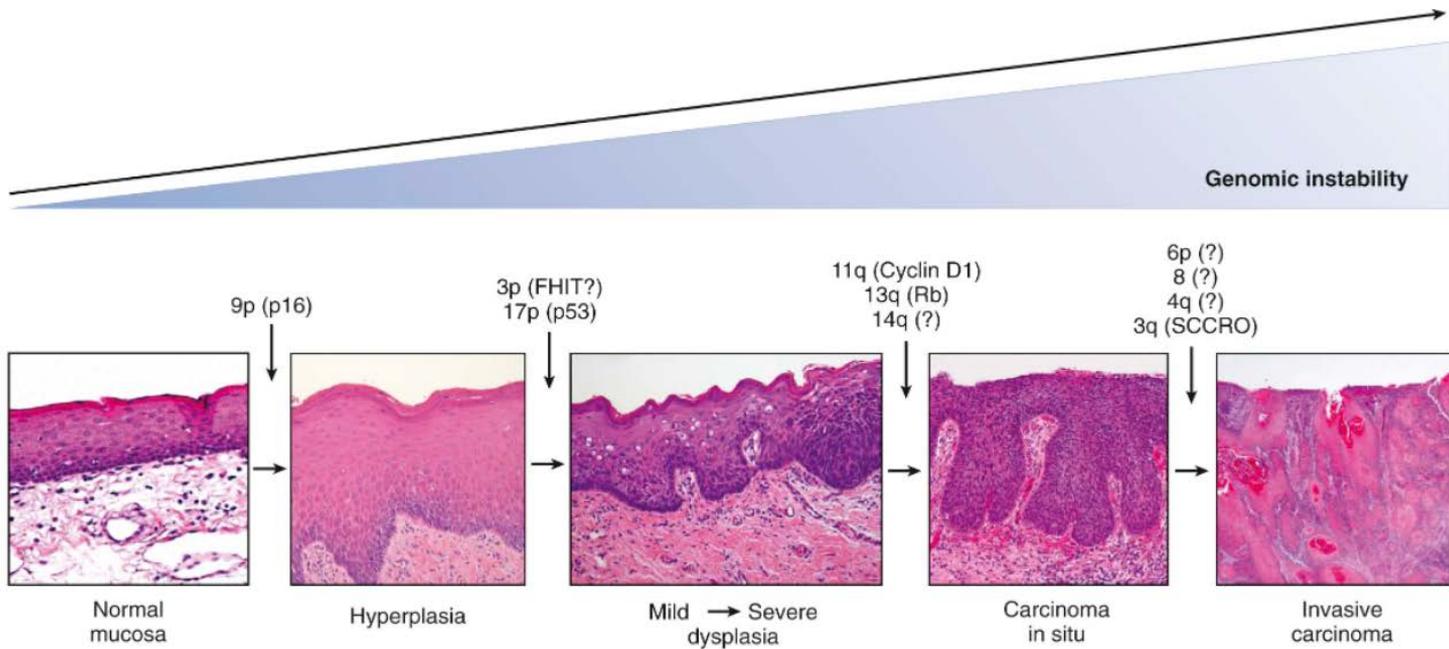
Figure 1.5 Worldwide variations in male incidence of nasopharyngeal cancer. *Source:* From Ref. 5.

tumour biology

- imbalance between mutagenic signals and protective mechanisms
- activation of oncogenes / inactivation of tumour suppressor genes
inhibition of apoptosis
- genetic aberrations develop randomly → cell become immortal →
indefinite cell division → clonal selection
- evasion of immune system
- principle of field cancerization
- knowledge on different genetic alterations enable targeted therapies

tumour biology

- principle of field cancerization
- knowledge on different genetic alterations enable targeted therapies



major symptoms

- hoarseness
- sore throat
- cervical nodes

diagnostic workup

triple endoscopy

HRCT or MRI

FDG-PET

- in case of high risk for distant metastasis (T>2; N>2a)
- CUP

TNM-system

- T tumour size / extension
- N cervical lymph nodes
- M distant disease
(lungs, bones, liver, ec.)

therapy

primary and lymph nodes

treatment decision

tumour dependent factors:

location, extension, assumed resection defect, possibilities of reconstruction

postsurgical QoL, swallowing, breathing, speaking, esthetical appearance