Management von Hauttumoren im ORL-Bereich

Sommerschule 2017 SGORL

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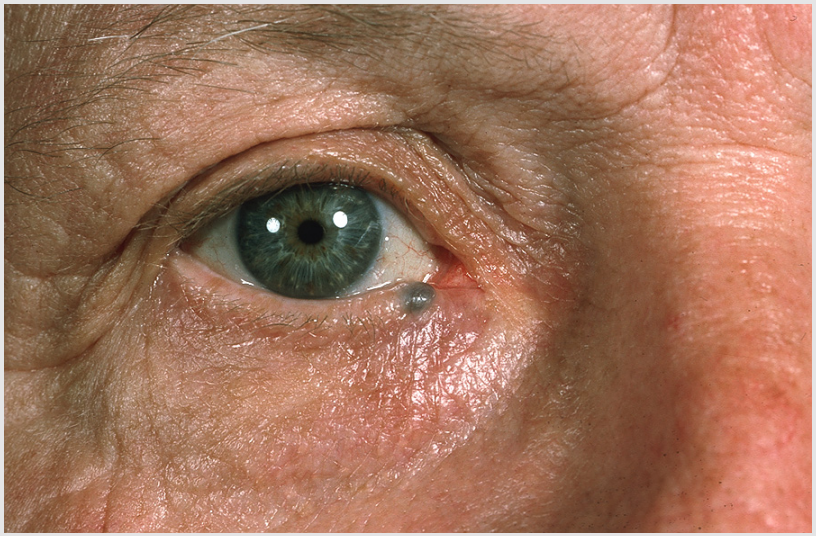
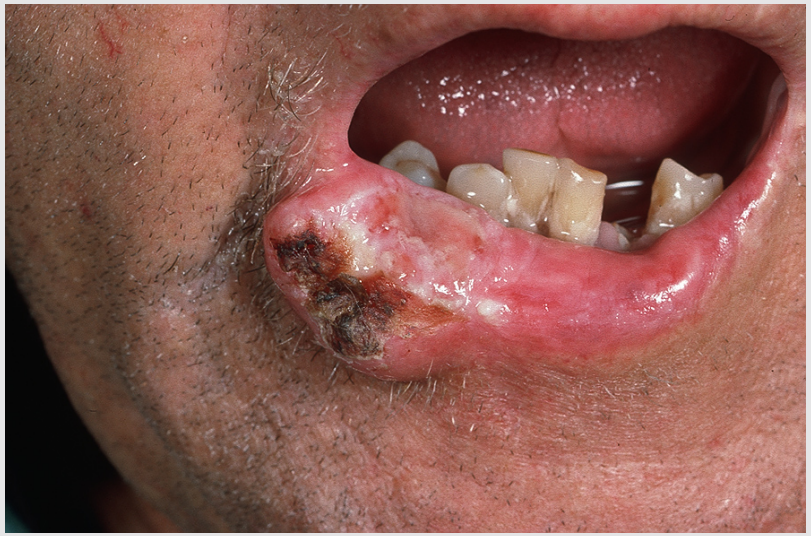
HIRSLANDEN
KLINIK ST. ANNA

BENIGN VS. MALIGNANT





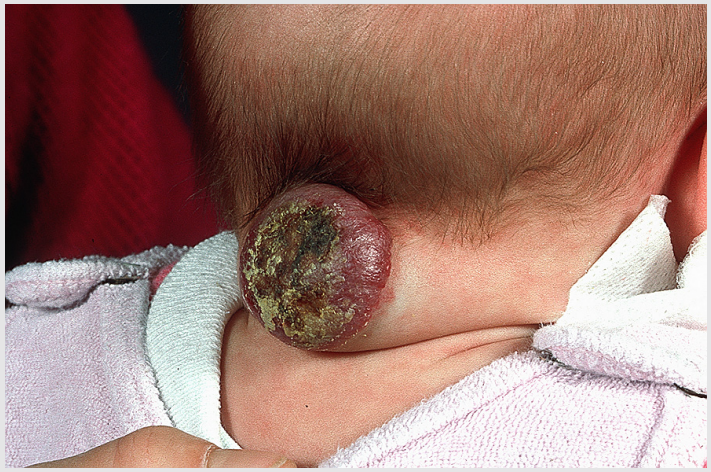
Typical benign:

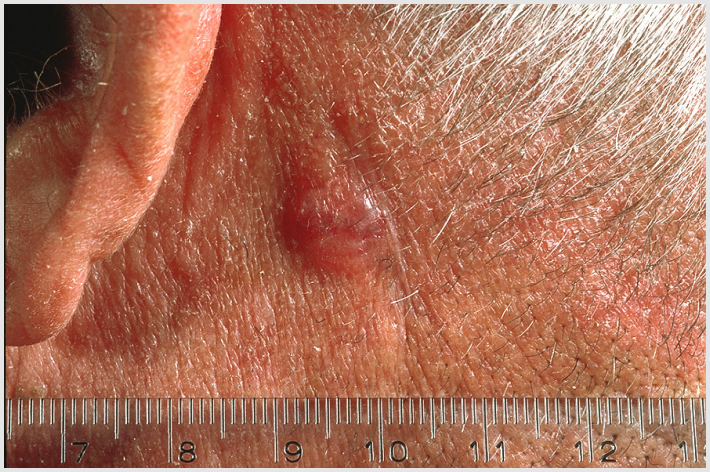
- symmetric
- well defined
- regular surface

Typical malignant:

- irregular
- not well defined
- ulcerous

BUT!





To differentiate between benign and malignant skin tumors can be challenging!

NON-MELANOMA SKIN CANCER

Basal cell carcinoma (BCC)

- Superficial
- Nodular
- Infiltrative
- Micronodular

Squamous cell carcinoma (SCC)

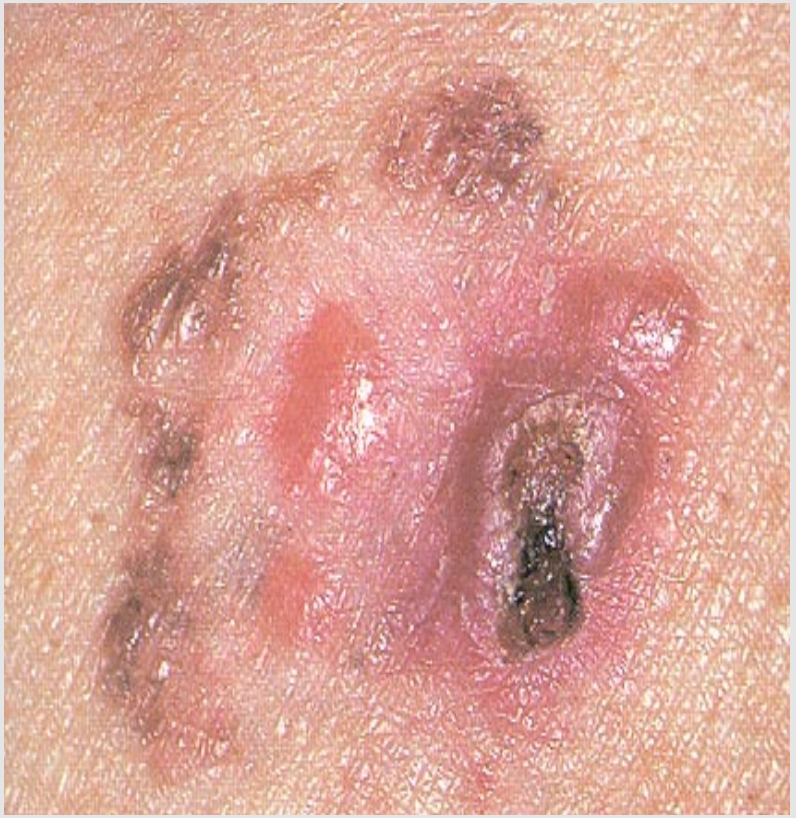
- Well-, mod-, poorly-diff
- Verrucous
- Spindle cell
- Desmoplastic
- Basosquamous
- Clear cell

Merkel cell carcinoma

others

MELANOMA

- Superficial spreading
- Nodular
- Lentigo maligna
- Acral lentiginous
- Mucosal



NMSC EPIDEMIOLOGY

Rising incidence[1]

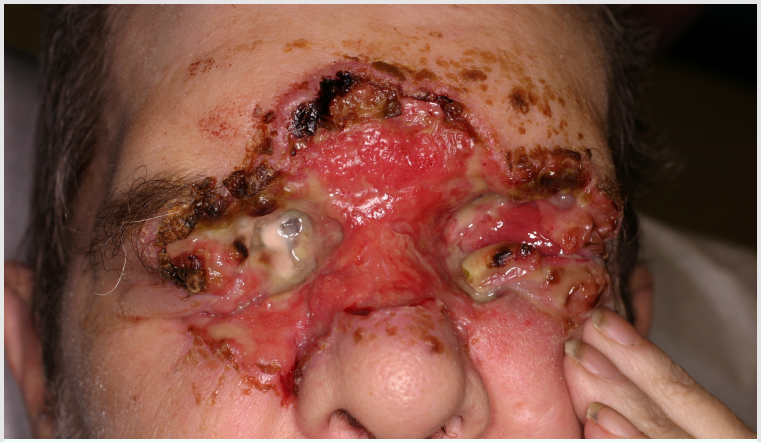
- 1.0-1.3M new cases/year
- Increasing 2-3% per year
- Expected to double in 20 yrs

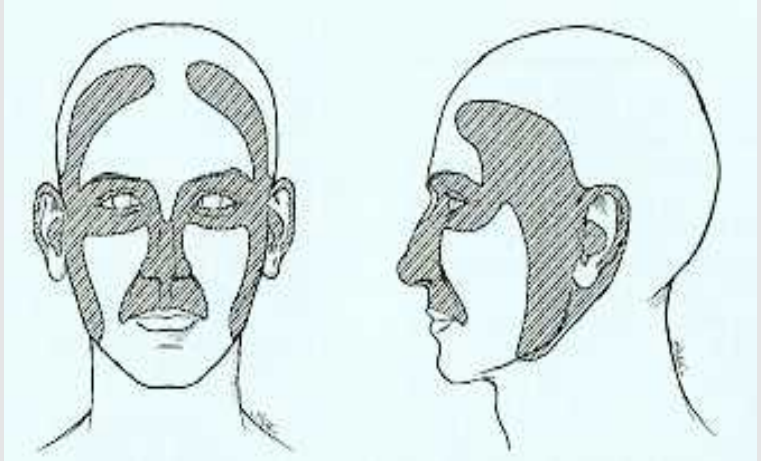
Lifetime risk of NMSC

- 25-33% BCC
- 7-11% SCC

Demographics

- Male : Female ratio = 3-4 : 1
- BCC:SCC ratio = 4 : 1



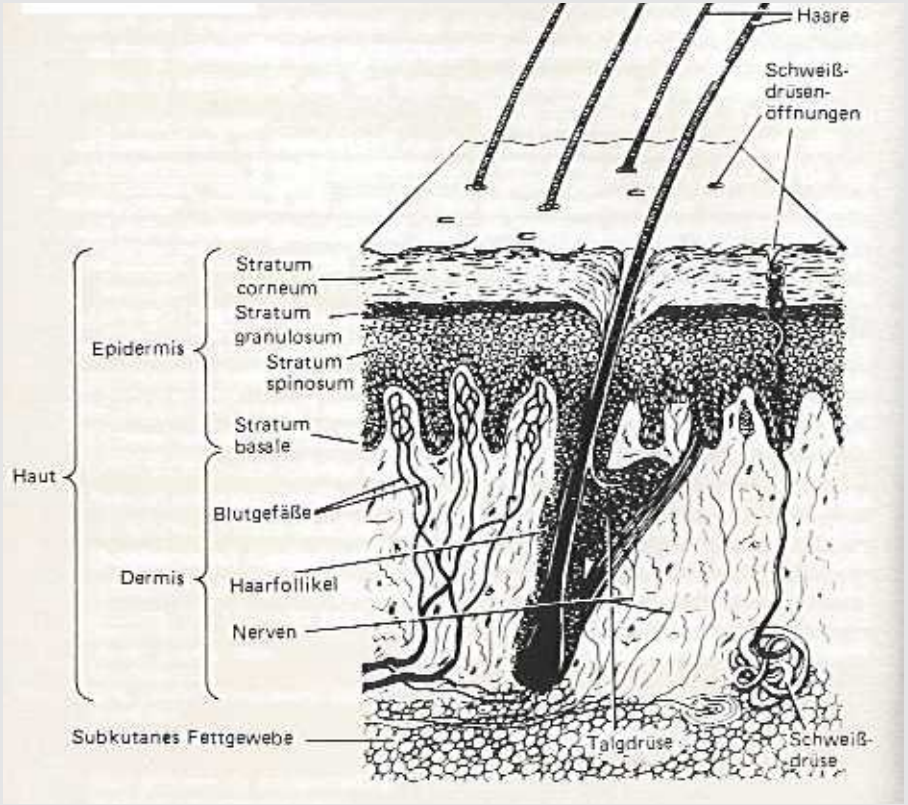


[1]Alam M et al, *New Engl J Med* 2001

DEFINITION

BCC is believed to arise from the stratum basale layer of the epidermis

SCC originates from the stratum granulosum



UV EXPOSURE

UVA and UVB tumorgenesis

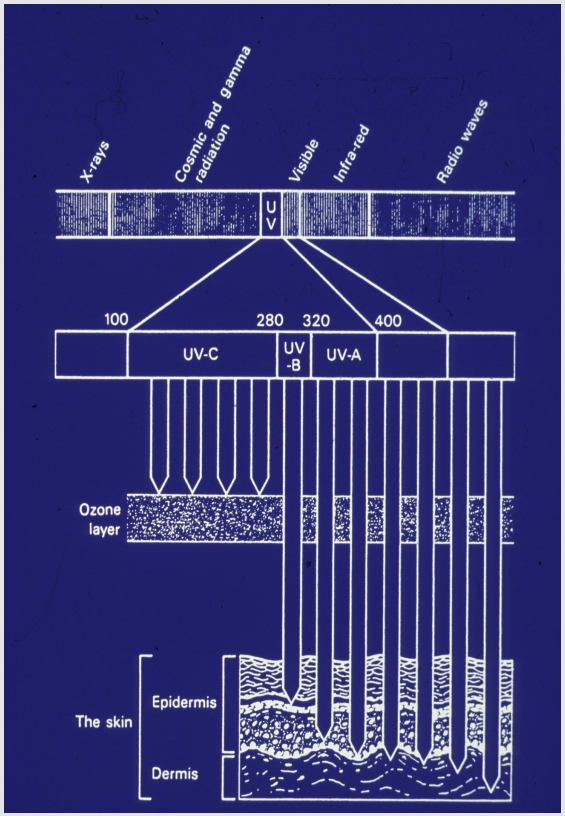
- P53 pyrimidine dimer formation
- Loss of *Fas-Fas* ligand interaction

Exposure variance[1]

- Intense, intermittent (BCC)
- Chronic (SCC)

Elevation of risk

- Sunbathing
- Artificial tanning beds
- Ozone depletion



[1]Zak-Prelich M et al. *Dermatol Surg* 2004

ENVIRONMENTAL RISK FACTOR

UV exposure

- 10% ozone thinning - 300K cases[1]

Latitude of habitation

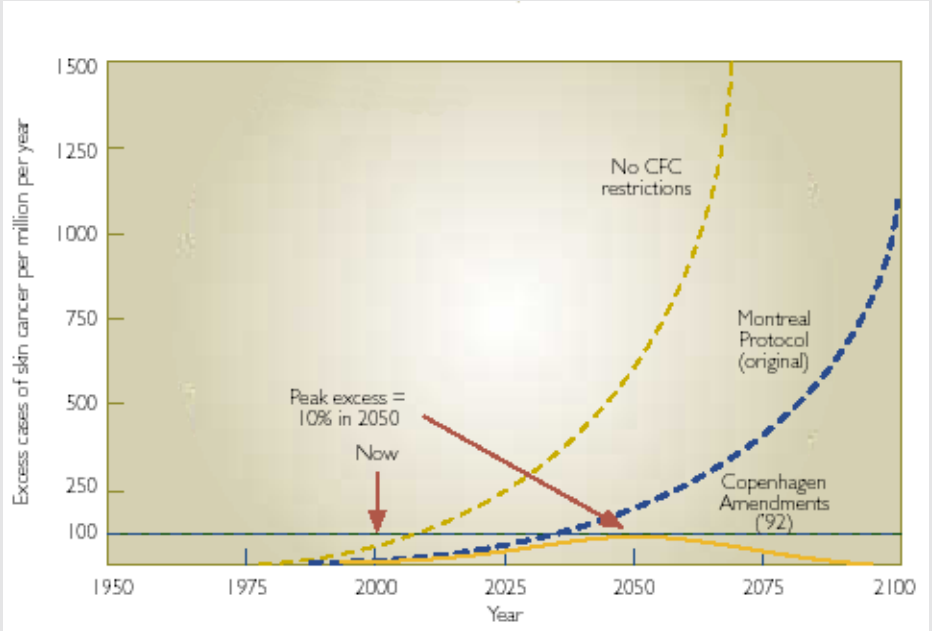
- 2x risk per 8-10 degrees
- Ozone or lifestyle or both?

Radiation exposure

- Childhood cancer survivors
- Nuclear reactors/ weapons

Chemical exposure

- Arsenic, Coal tar, etc.



Slaper H et al. *Nature 1996*

[1]WHO ultraviolet radiation and the INTERSUN program

IMMUNOSUPPRESSION

Significant increase in incidence

- SCC predominates
- BCC:SCC ratio switched

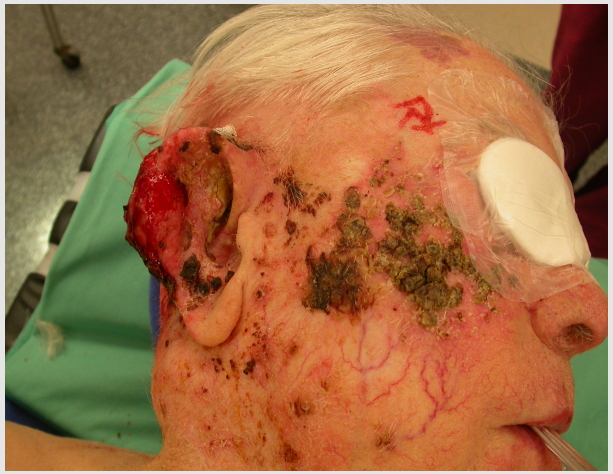
Transplant patients

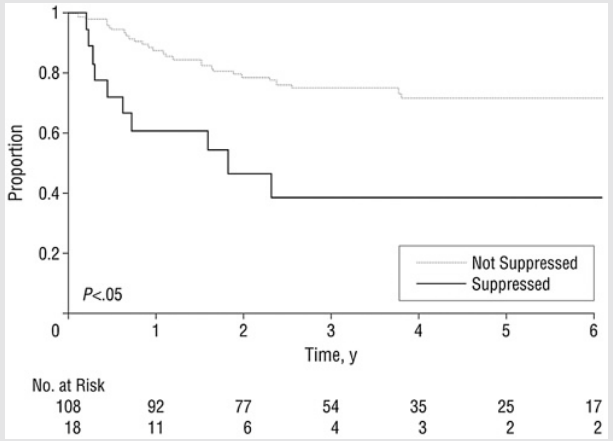
- Cardiac (45% SCC by 10 years)[1]
- Renal (81% NMSC by 20 years)[2]
- Liver

CLL, NHL

HIV, HPV (5 , 8, 38)

- Less impact on BCC incidence





Veness MJ et al, *Cancer* 1999

[1]Berg D et al. *J Am Acad Dermatol* 2002;[2]Ramsey HM et al. *Br J Dermatol* 2002

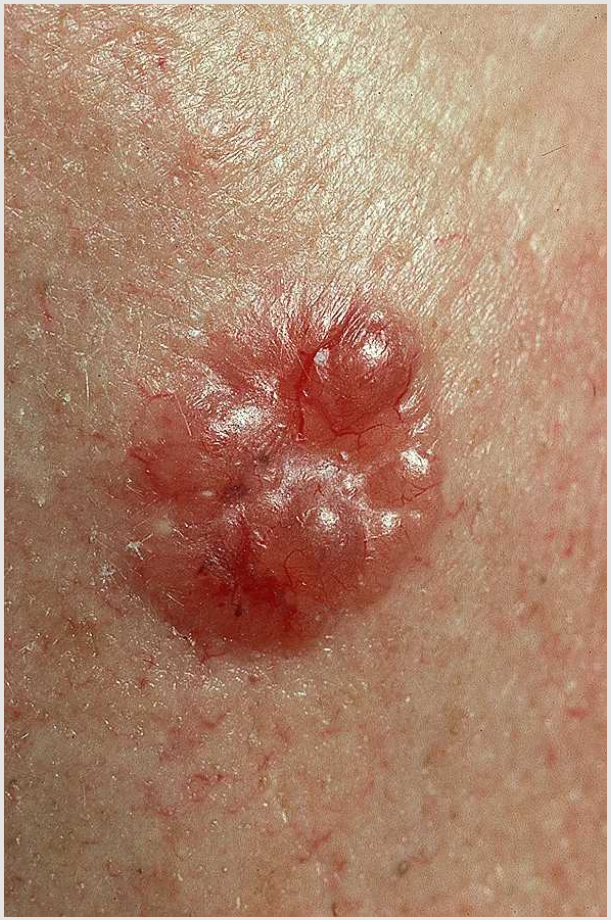
BCC

No metastases (semi-maligne)

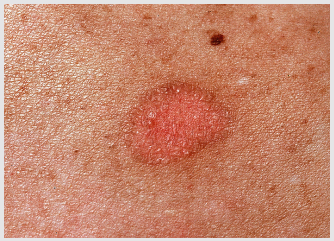
Most common malignant tumor in the western world

75% of all patients are >40y

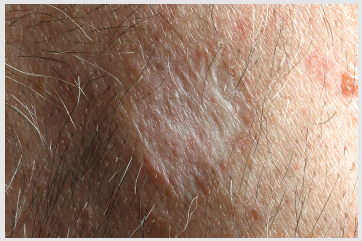
Genetic variant: Gorlin-Goltz syndrome



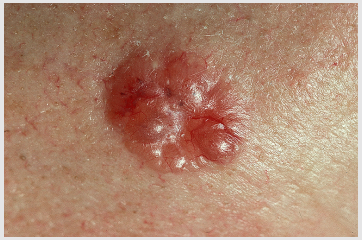
VARIANTS



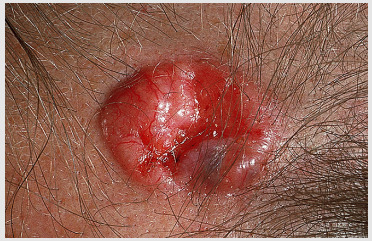
Superficial spreading



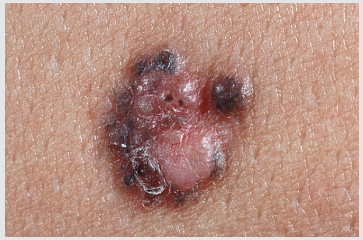
sclerosing



nodular



ulcerated



pigmented

TREATMENT BCC

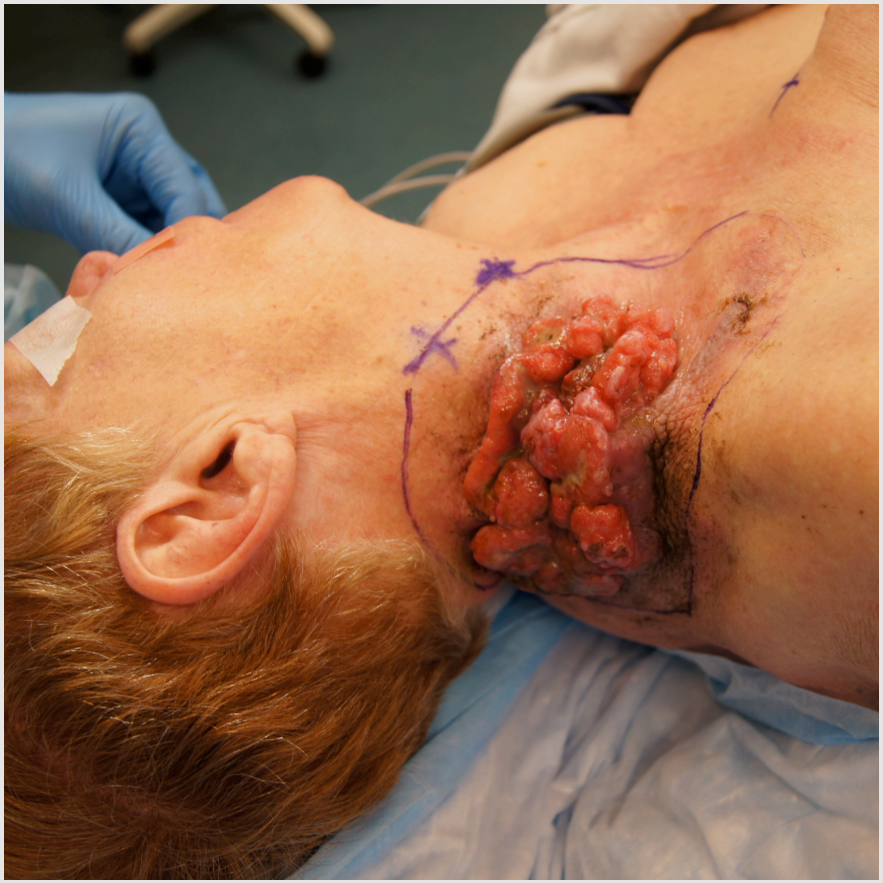
	recurrence within 5 years:
En bloc resection (margins vary; 2-5mm)	10%
Mohs‘ surgery	1.5%
Curettage	7.5%
Radiotherapy	8-9%

Rowe D J Dermatol Oncol 1989

Superficial BCCs:

cryotherapy, photodynamic therapy (PDT), cytotoxic agents (imiquimoid), immunotherapy (hedgehog inhibitor)

TREATMENT BCC

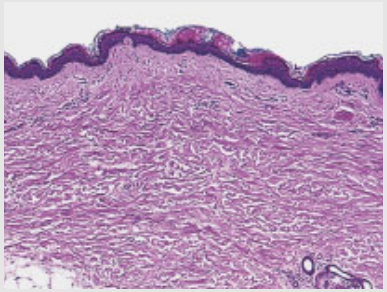


SCC

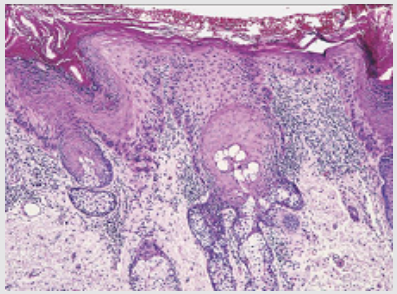
Premalignant lesions

solar keratosis

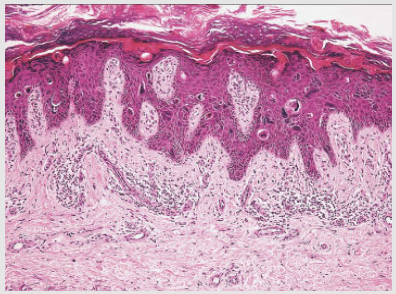
Bowen‘s disease



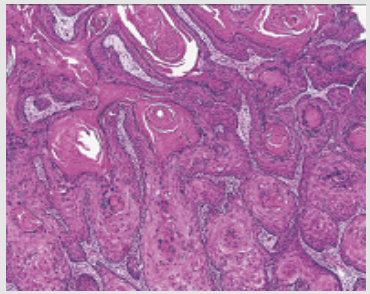
normal



keratosis



Bowen‘s disease



SCC

SOLAR KERATOSIS

>40y strong solar exposition

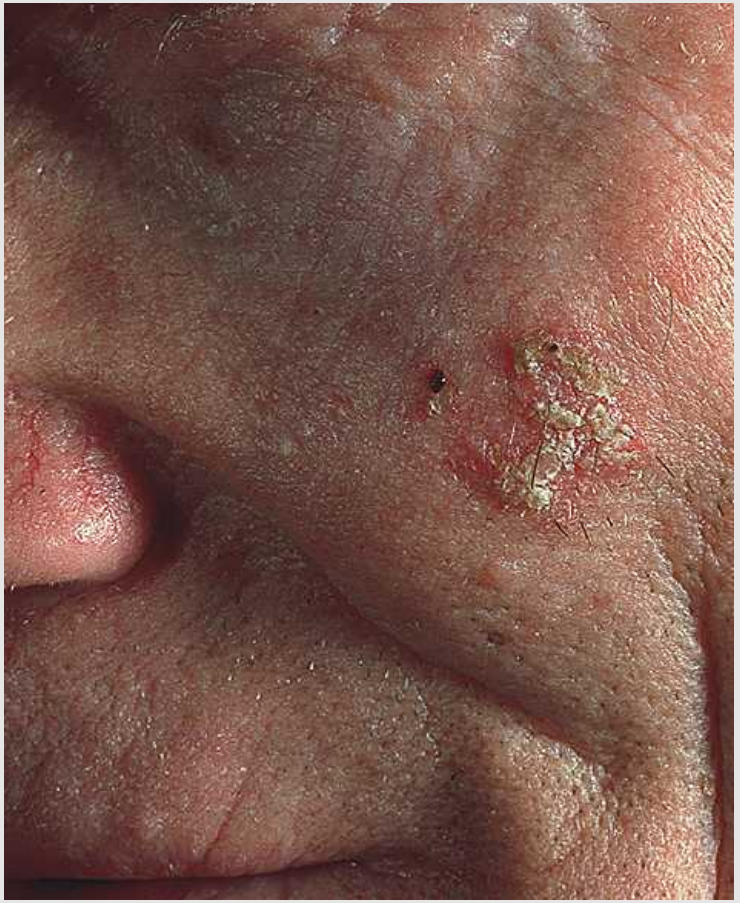
USA: 10-25% of all >40y

Australia: 40 - 50% of all >40y

etiology:

Cumulative effect UV-exposure

P53-gene mutation



SOLAR KERATOSIS

- Transition into SCC:

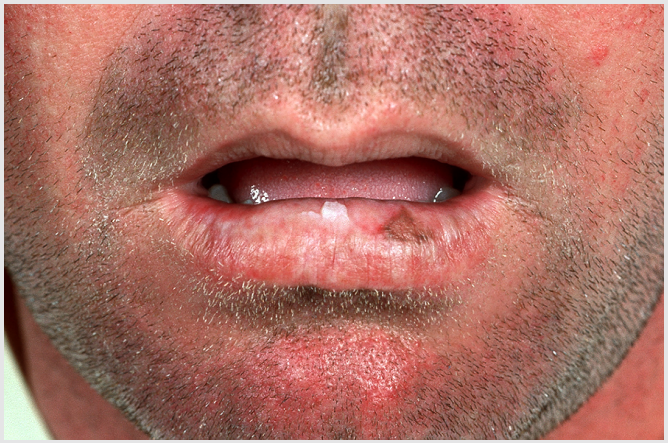
  ~ 8% per ann

  GlogauRG, J Am Acad Dermatol 2000; 42:23-4

- Spontaneous regression:

  ~ 26% per ann

  Marks R, Br J Dermatol 1986; 649-55



TREATMENT

cryotherapy

retrospective trials	98.8%
prospective trials	70%

Photodynamic therapy (PDT)

remission	90%

cytotoxic agents (5-Fluorouracil)

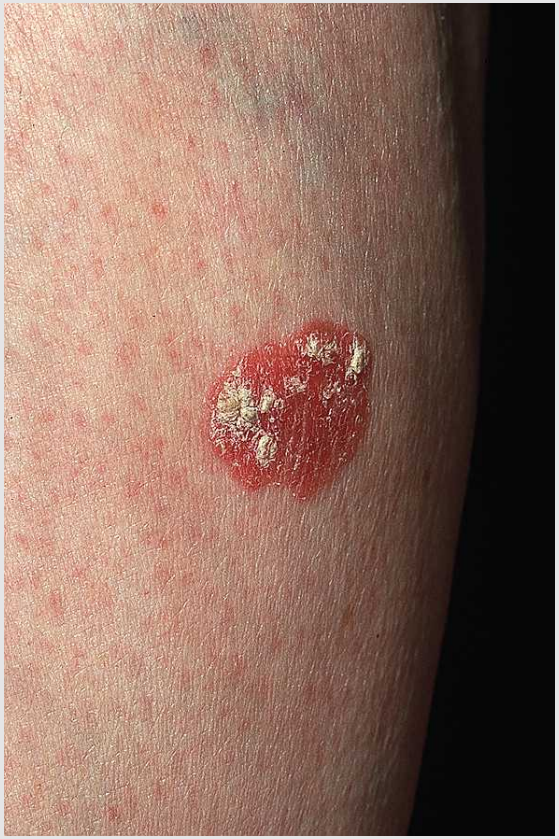
Curettage

BOWEN'S DISEASE

Intraepidermal carcinoma (Carcinoma-in-situ)

Persistent redish plaque

All over the body

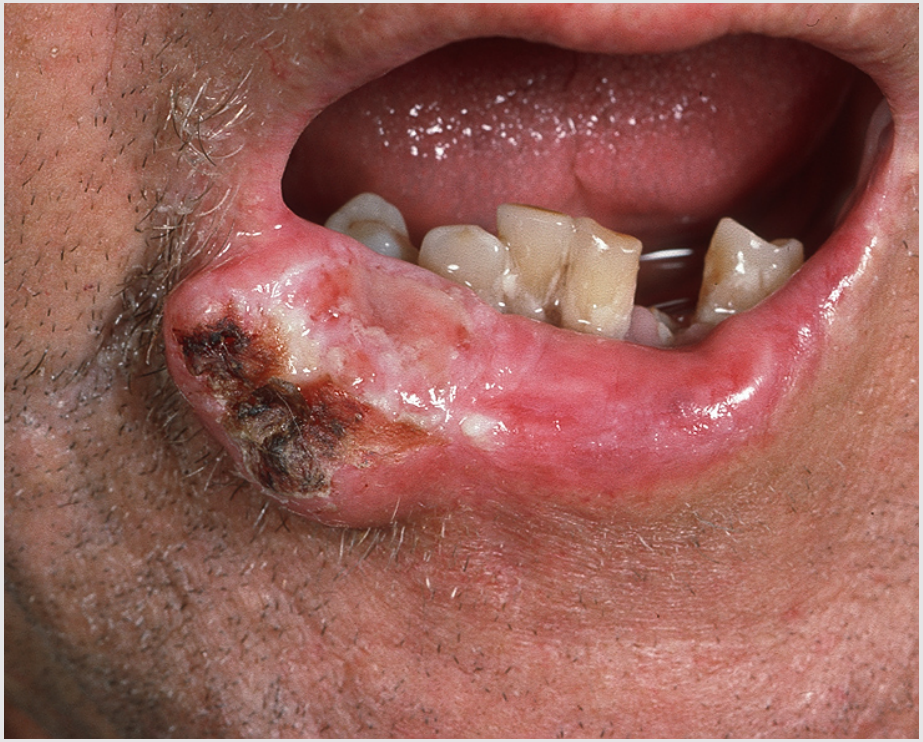


Treatment:

- Resection
- Cryotherapy
- Cytotoxic agents
- PDT

SCC

- Keratinocytes as origin
- 10x less frequent than BCC
- Inzidence CH: 25-30/100k/ann
- Verrucous, later ulcerous or exophytic

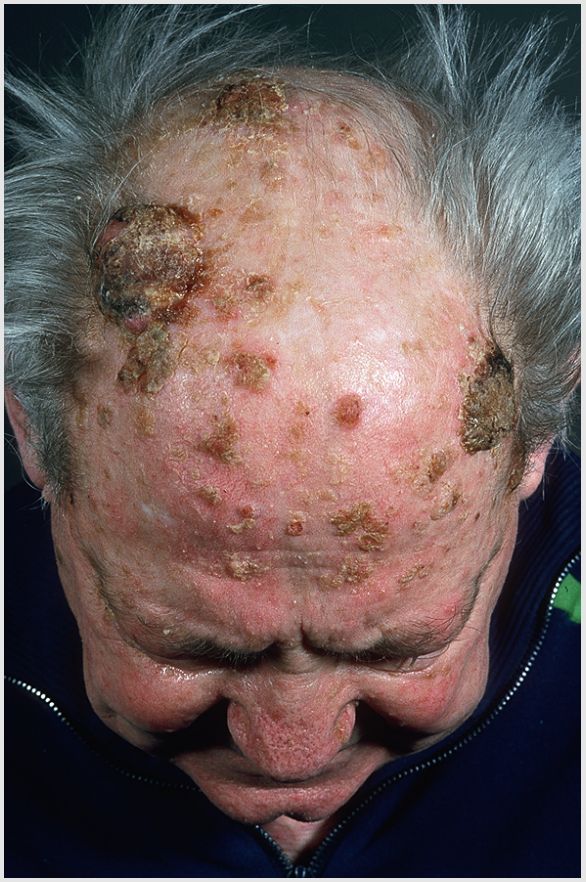


SCC

Favourable localizations
-uper face
-scalp
-lower lip
Often originated from keratosis

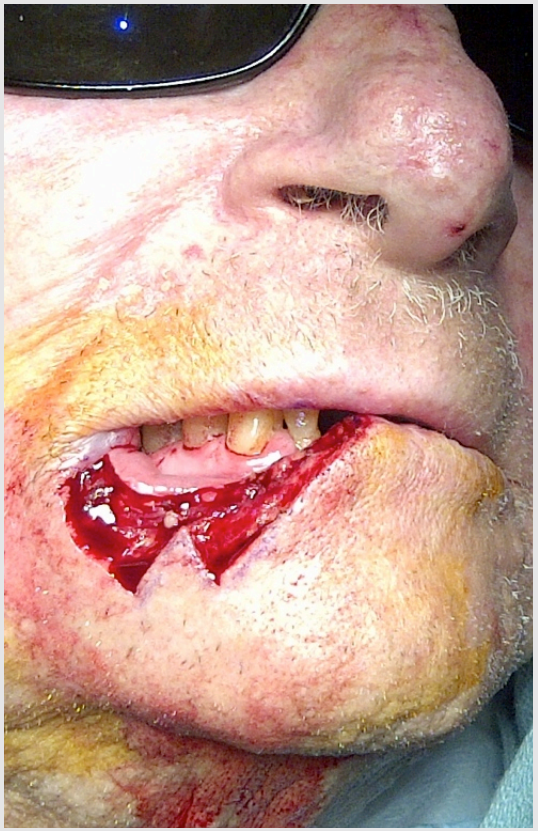
Treatment:
Surgical resection
Radiatio

Risk for metastases:
- <2mm thickness- no
- 2-6mm thickness- intermediate (5%)
- >6mm thickness- high (20%)



SCC

- Min. margins for untreated lesions
  - Primary SCC: 5 mm
- Min. margins for recurrent/aggressive lesions
  - SCC: 1-2cm

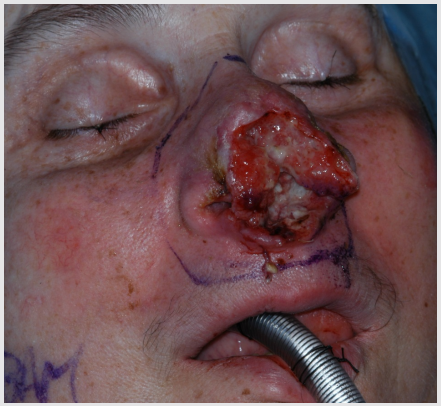


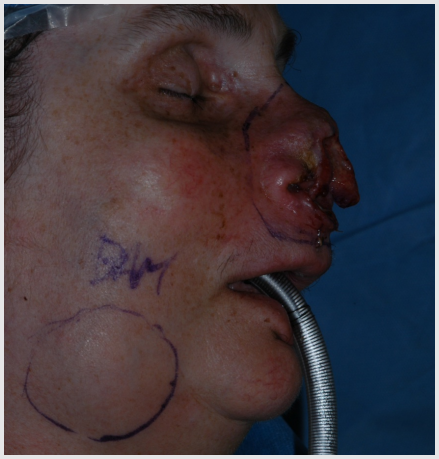
AGGRESSIVE SCC

- Clinical features
  - Recurrent lesions
  - Regional metastases
  - Size > 4cm
  - Deep invasion
  - PNI

3 y DSS drops from 100% to 70% if one of these elements is present

- Histopathology features
  - SCC
    - Poorly/undifferentiated
    - Spindle cell, desmoplastic, basosquamous





PERINEURAL INVASION

- V2 most commonly affected
- Most (60%) asymptomatic
- Maintain high index of suspicion
  - Forehead and temple
  - Periauricular region
- Histologic evaluation of nerve branches
- Retrograde dissection of involved major nerves
- Adjuvant procedures
  - Mastoidectomy, maxillectomy, mandibulectomy
  - Orbital exploration or exenteration
- Adjuvant radiation
  - Follow course of the main nerve to skull base

LYMPH NODE METASTASES

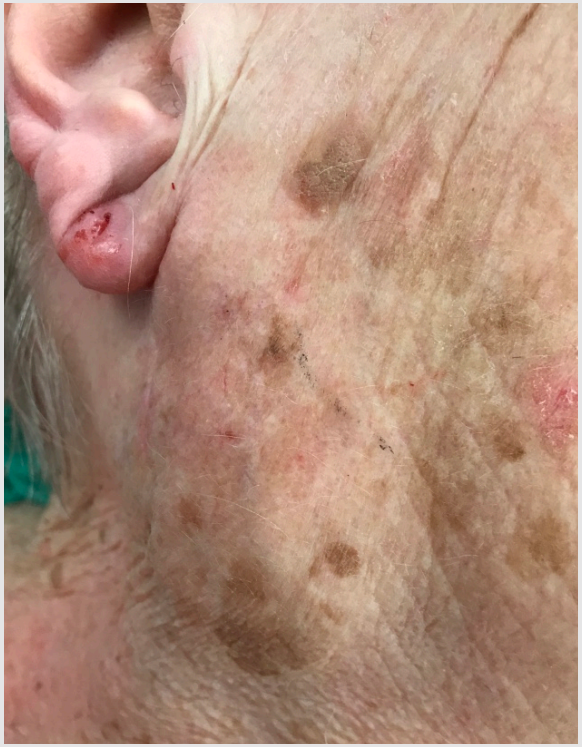
Reported incidence 0.1-21%[1] → ≈5%

Delayed appearance

- 10-19 months after treatment for primary
- Nearly all metastases evident by 3 years
- Elicit cutaneous SCC history in patients with "unknown" primary

Location of nodal metastases

- 35% limited to parotid
- 30% limited to cervical nodes
- 35% involved both



[1]Moore BA et al. *Laryngoscope* 2005

LYMPH NODE METASTASES

High risk factors for lymphatic spreading

• Size> 2cm	20-30%
• Invasion into subcutaneous fat (>5mm)	16-45%
• Poorly differentiated	12-32%
• Perineural invasion	40-47%
• Lymphovascular invasion	40%
• Location near parotid or lip	10-30%
• Local recurrence	25-62%
• SCC in preexisting scars	40%

D'Souza J *Head Neck Surg* 2011

SURGERY OF NODAL BASIN

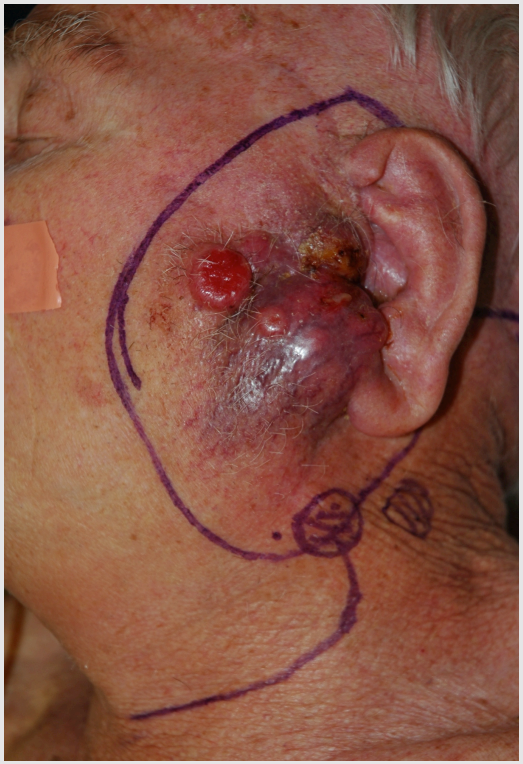
Sentinel node biopsy for high-risk patients in clinical N0-neck (ongoing multicentric trial)

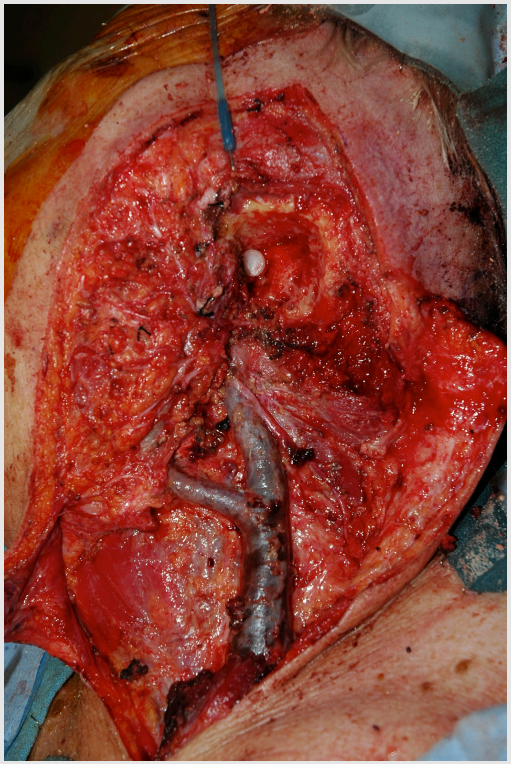
ND if direct invasion of the parotid gland or fascia

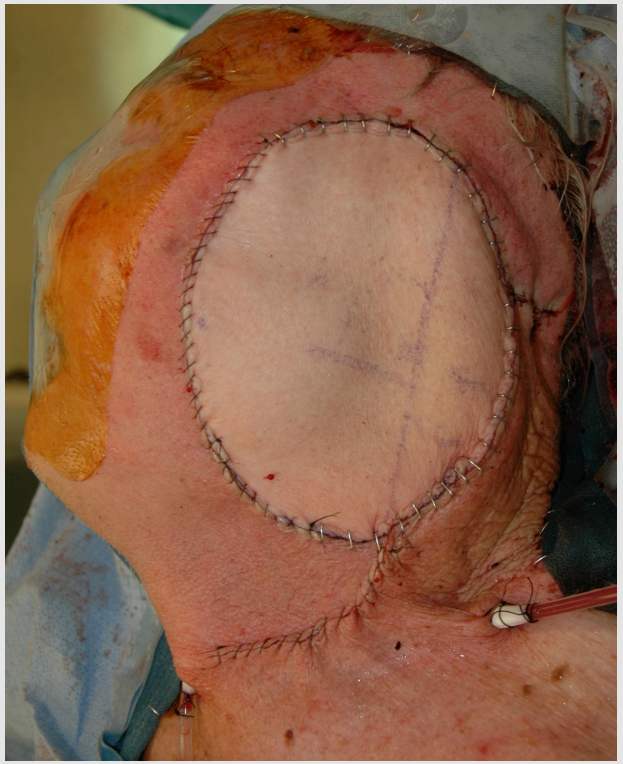
ND if clinical evidence of nodal metastases

Eventually free tissue transfer

SCC







ADJUVANT RADIATION TX

Large, recurrent tumors
(especially > 4 cm)

Close or positive margins

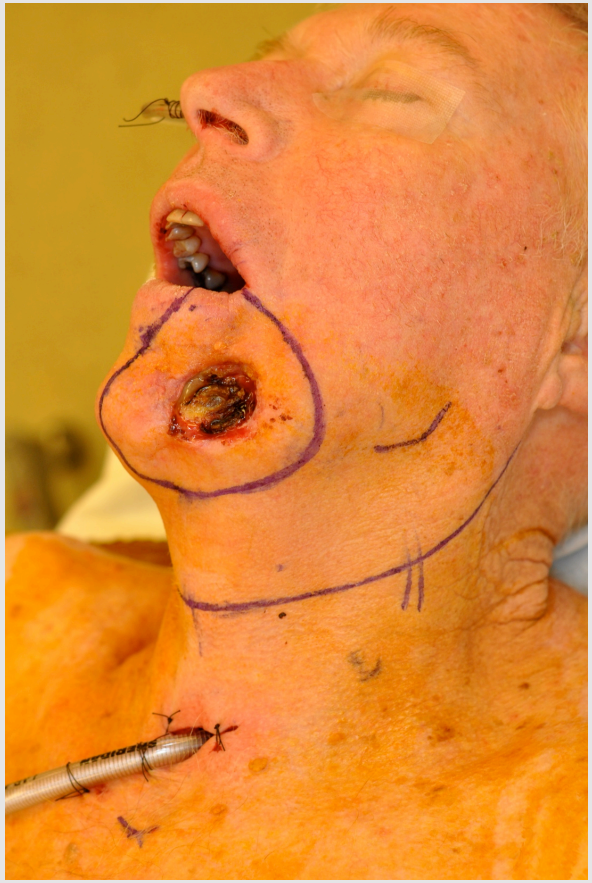
Aggressive histology

- Spindle cell SCC
- Poorly differentiated SCC

Perineural invasion

Multiple positive nodes

Extracapsular spread

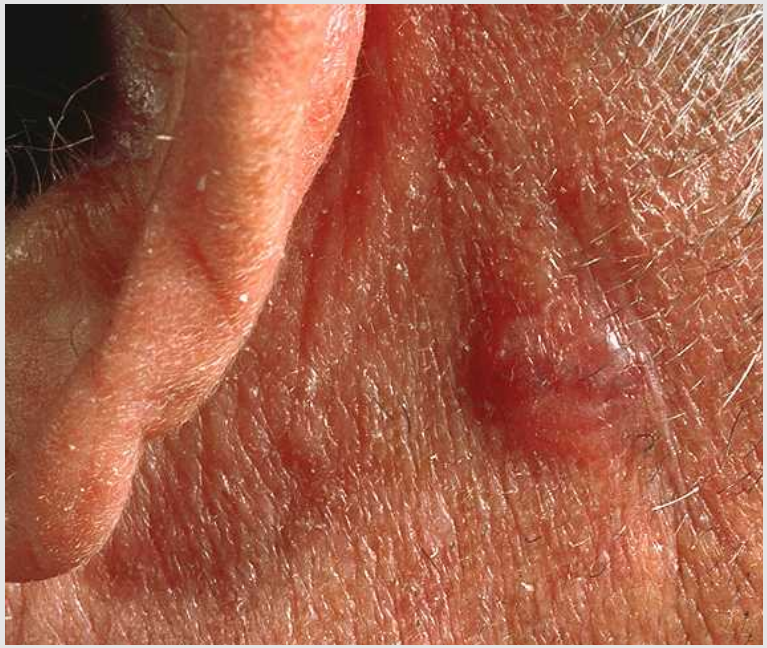


MERKEL CELL CARCINOMA

Malignant neuroendocrine tumor originated from mechanoreceptors at epidermis-dermis

- Skin coloured, red
- All over
- Rapid growth
- Metastasized at dx in 30-50%!

Treatment:
Wide (margin >1cm) surgical resection and RT
Radiosensitive
SNB for cN0 neck

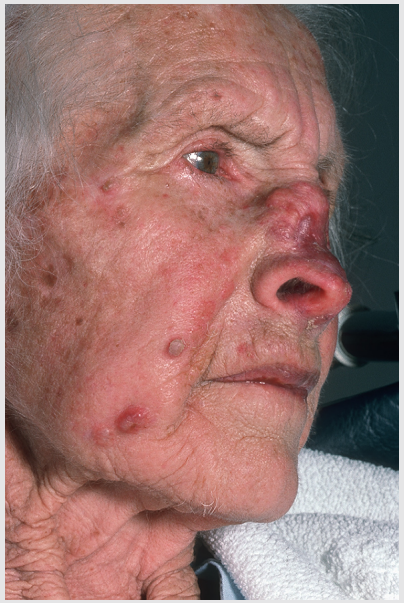


OTHERS

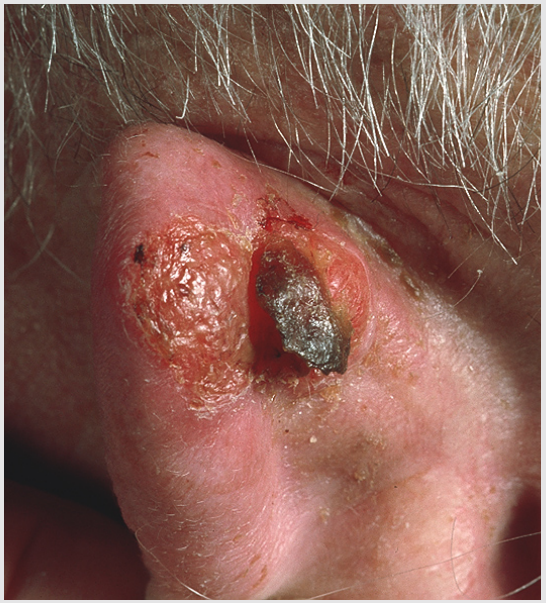
Sweat gland carcinoma
- Often metastasizes

Sebaceous carcinoma
- Rarely metastasizes

Treatment:
Wide surgical resection

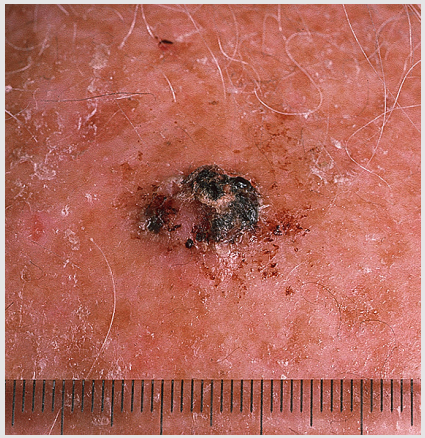


Sweat gland carcinoma

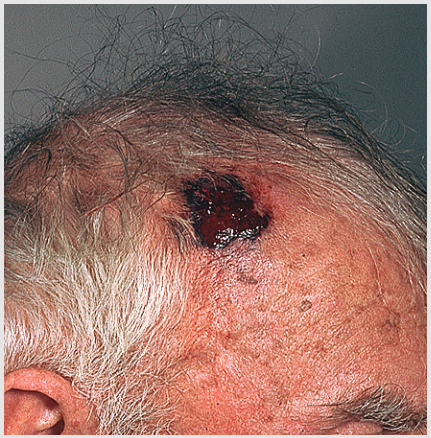


Sebaceous carcinoma

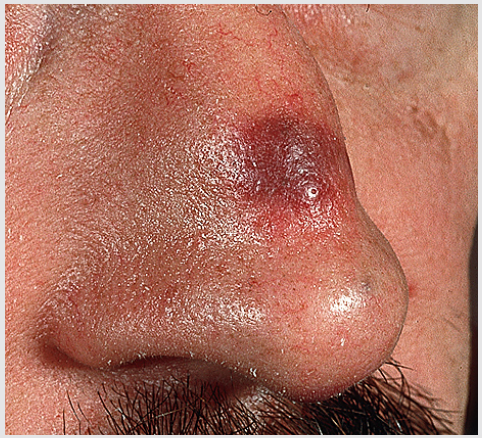
OTHERS



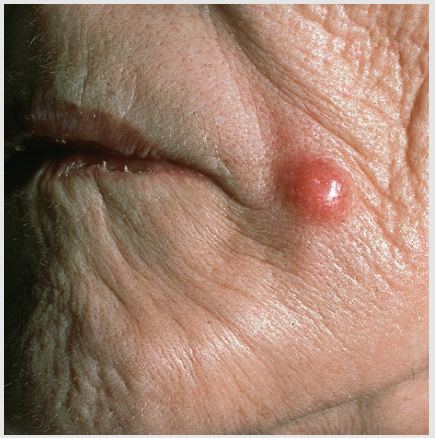
Malignant fibrous histiocytoma



Angiosarcoma



Kaposi sarcoma



Cutaneous metastases

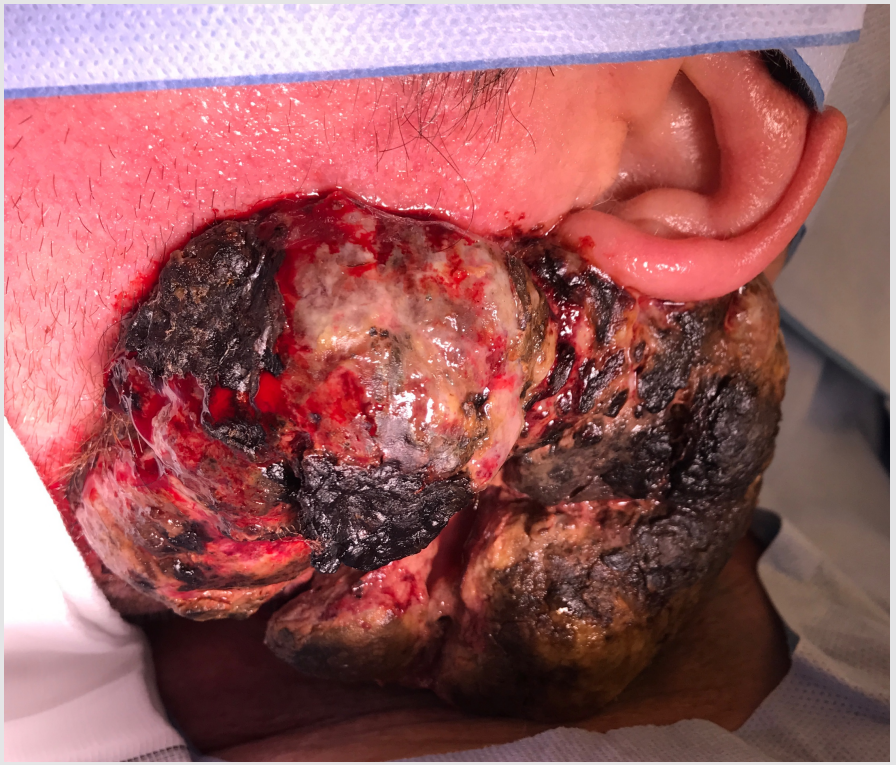
MELANOMA

Fastest rising cancer worldwide 3%/yr

Mortality increase 2nd only to lung

5% skin cancer, 75% skin cancer death

Risk of developing melanoma- 1/75 in 2000, 1/1500 in 1935



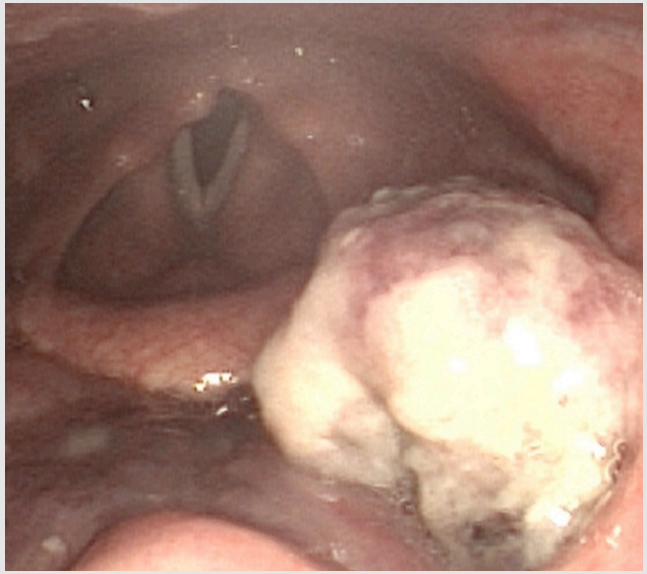
MELANOMA

20% of melanomas occur in the H&N

More aggressive than melanoma of the extremities

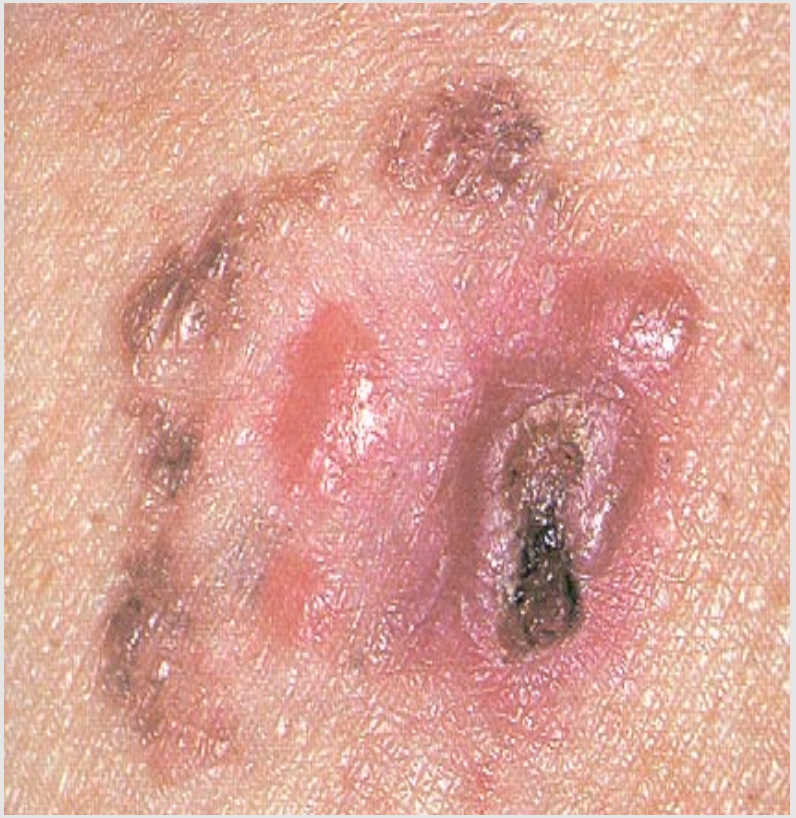
Subsites

- Face 51%
- Scalp 26%
- Neck 16%
- Ear 9%



MELANOMA

- Superficial spreading
- Nodular
- Lentigo maligna
- Acral lentiginous
- Mucosal



STAGING

Breslow classification

- Vertical thickness of lesion in millimeters

Clark's classification

- Anatomic level of local invasion

I Lesions involving only the epidermis (in situ)

II Invasion of the papillary dermis, papillary-reticular dermal interface not reached

III Reticular dermis not penetrated

IV Reticular dermis invaded but not into subcutaneous tissue

V Subcutaneous tissue invaded

CLASSIFICATION PRIMARY AJCC TNM 2009

Tx: Primary cannot be assessed (eg shave Bx, regressed melanoma)

T0: No evidence of primary

Tis: In situ melanoma

T1: <= 1mm thick

- T1a without ulceration and mitoses < 1/mm2
- T1b with ulceration or mitoses >= 1/mm2

T2: >1mm & <= 2mm with/without ulceration

T3: >2mm & <= 4mm with/without ulceration

T4: >4mm with/without ulceration

New AJCC staging system available end of 2017

CLASSIFICATION PRIMARY NEW UICC TNM 2016

pT1a and pT1b:

- pT1a ≤ 0.8mm
- pT1b > 0.8mm -1mm

DEPTH OF INVASION

Nodal disease

Clark's level	
I	<1%
II	2-5%
III	20%
IV	40%
V	70%

Breslow depth	
<=0.75	<1%
0.76–1.49	25%
1.5-4.0	57%
>4.0	>70%

NODAL TERMINOLOGY

Satellite mets

A skin met occurring within 2cm of the primary

In-transit mets

An intralymphatic met occurring >2cm from the primary but before the first echelon of regional lymph nodes

Micrometastases

Mets diagnosed after elective/sentinel lymphadenectomy

Macrometastases

Clinically detectable LN mets confirmed by therapeutic lymphadenectomy, or when any LN met exhibits gross extracapsular extension

WORK UP AND TREATMENT

cN0 Hals	neck ultrasound, evt. CT/MR
cN+ Hals	PET/CT, MRI brain if would influence management
cM1	LDH

Treatment:

- How wide and how deep?
- Lancet 1907: Sampson-Handley 5cm margin

RESECTION MARGINS

Surgical margin no more than 2cm

1cm vs 2cm unanswered

More data available on 2cm margins

Excisions greater than 2 cm offer no advantage

1 or 2cm margins may be difficult to achieve on the face

Melanoma-in-situ	0.5cm
Melanoma <2mm	1.0cm
Melanoma ≥2mm	2.0cm

MANAGEMENT OF N0 NECK

Sentinel node biopsy

Stage	0	in situ melanoma (Tis N0 M0)
	IA	< 1mm without ulceration and Clark II/III (T1a N0 M0)
	IB	< 1mm with ulceration or mitotic activity or Clark IV/V (T1b N0 M0)
		1.01- 2mm without ulceration or mitotic activity (T2a N0 M0)
	IIA	1.01- 2mm with ulceration (T2b N0 M0)
		2.01- 4mm without ulceration (T3a N0 M0)
	IIB	2.01- 4mm with ulceration (T3b N0 M0)
		>4mm without ulceration (T4a N0 M0)
	IIC	>4mm with ulceration (T4b N0 M0)

MANAGEMENT OF N+ NECK

Neck Dissection

Recurrence after modified radical neck dissection low:

- 26% (Fisher, 1989)
- 34% (O'Brien, 1991)

Poor prognosis, < 20% at ten years

ADJUVANT THERAPIES

Immunotherapy

- Interferon
- Vaccines
- Novel agents

Chemotherapy

Bio-Chemotherapy

Targeted Therapy

- RAS/RAF/MAPK

Radiation

ROLE OF RADIOTHERAPY

Considered to be a radio-resistant tumour

Hypofractionation suggested

- radioresistance overcome by increasing dose per fraction

patient convenience

not associated with increased morbidity

no survival difference with conventional Rx

INDICATIONS FOR RTX

Primary

- Recurrent disease following re-excision

Nodal

- Multiple nodes
- Extracapsular disease
- In-transit disease
- Recurrent disease

FOLLOW-UP

Varies from 3-6 monthly x 5 years

Including neck ultrasound

PET/CT depending on depth and nodal status

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