Skin tumors

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Embryology

Epidermis				dermis
Ectoderm			mesoderm	Mesoderm
Neural crest	Merkel cells	keratinocytes	Langerhans	
Melanocytes				
pigmentation	Mechanoreceptor (light touch sensation)	structural and immunological backbone of the epidermis	Immunity	

A. Epidermis

1. Keratinocytes

a. Primary cell in epidermis

b. Start in basal layer (stratum germinativum or basale)

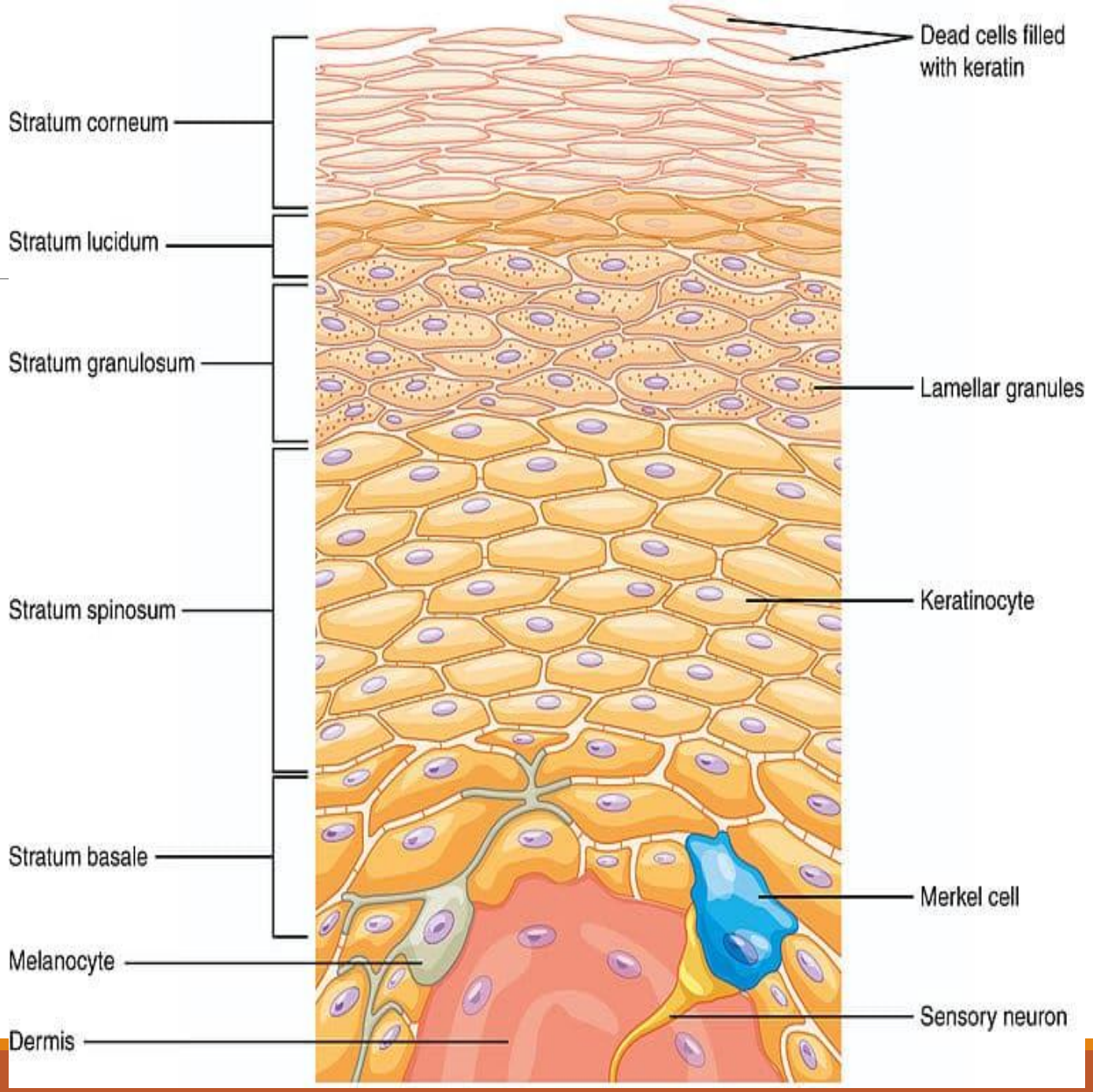
2. Melanocytes

a. Found in basal layer

b. Protect against ultraviolet (UV) radiation

3. Merkel cells: Mechanoreceptors

4. Langerhans cells: Antigen-presenting cells in stratum spinosum



B. Dermis

1. Cell types: Fibroblast, macrophage, and mast cell

2. Papillary dermis

a. Similar thickness to epidermis

b. High content of type III collagen, less type I

c. Site of collagenase activity.

d. Intertwines with the rete ridges of the epidermis.

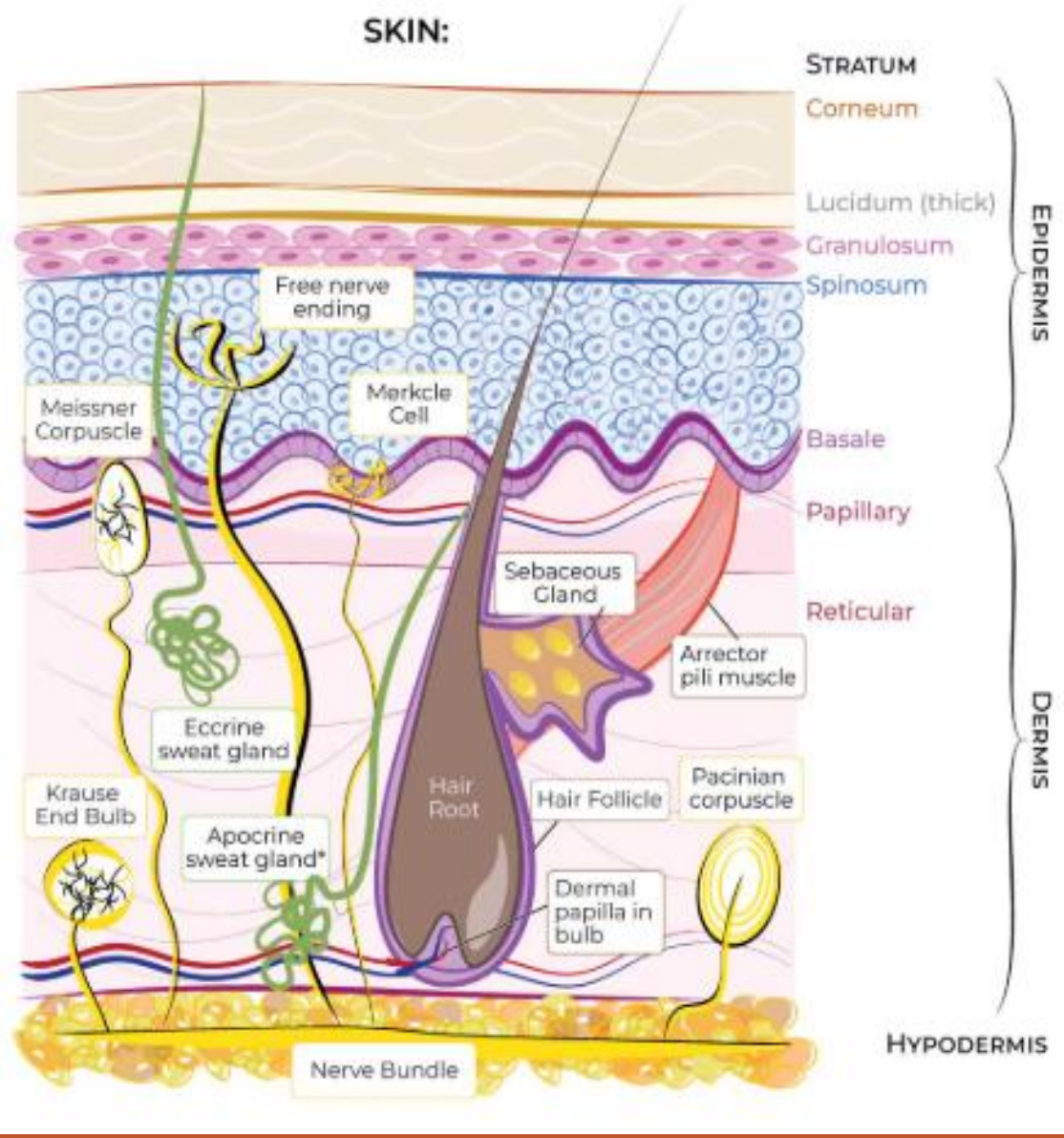
e. Contains terminal networks of Meissner corpuscles and capillaries.

3. Reticular dermis

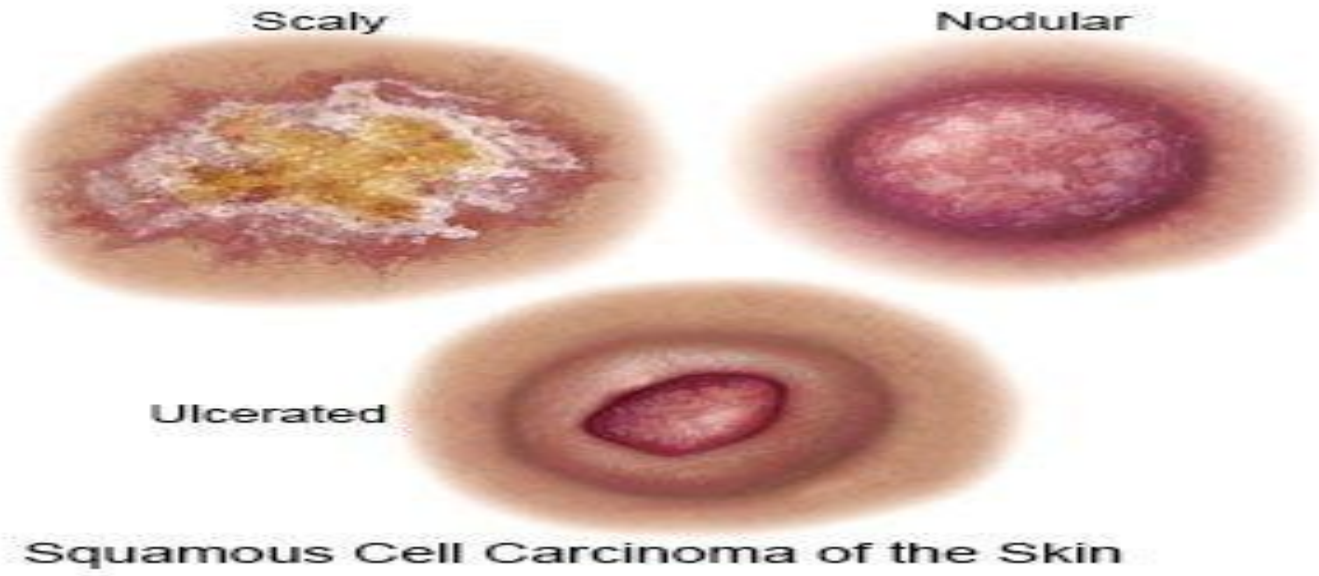
a. Majority of the dermal layer

b. Mostly type I collagen bundles with elastic fibers between

c. Contains roots of the hair, sebaceous glands, sweat glands, receptors, nails, and blood vessels



Squamous cell carcinoma



Squamous Cell Carcinoma of the Skin

Epidemiology

- 2nd most common skin tumor after BCC

- sex: M> F
- Age; typically affect individuals >60 years old

- Higher incidence in white people (it's strongly related to cumulative sun exposure)

Risk factors:

-cumulative UV exposure (from sun exposure, tanning beds & PUVA therapy for psoriasis)

- most significant risk factor

- especially in patients with light skin tones, recurrent sunburns/ recreational tanning or in area close to equator , PUVA phototherapy

- **Chronic inflammation: burn scar , pressure ulcers, chronic sinus tract, osteomyelitis)**
- **Chemical carcinogens: coal tar & arsenic OR ionizing radiation**
- **Chronic immunosuppression: HIV, long term glucocorticoid**
- **Inherited disorder: albinism, xeroderma pigmentosum, epidermolysis bullosa , Fanconi anemia , bloom syndrome**
- **Smoking**
- **Viral infection: HSV, HPV (type 16,18) ➔ anogenital & periungual SCC**
- **Some of drugs: voriconazole, azathioprine, hydrochlorothiazide & dabrafenib (BRAF inhibitors)**
- **Family Hx of cSCC**

Precursor & early lesions

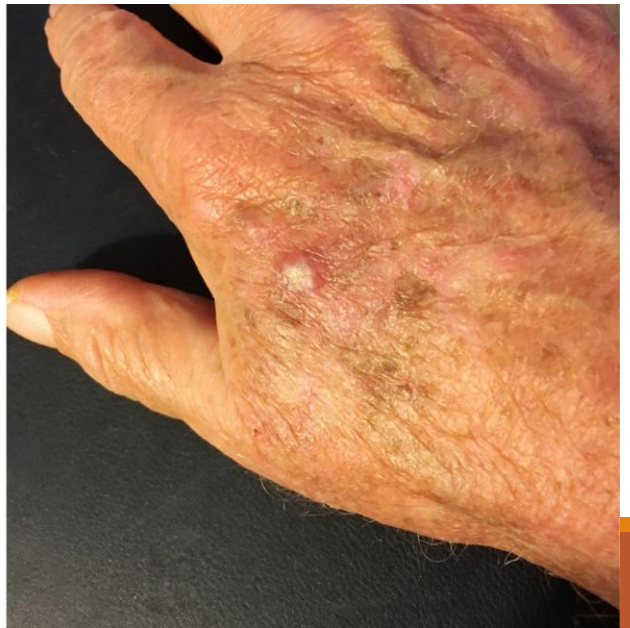
ACTINIC KERATOSIS (AKS) = SOLAR KERATOSES

-The most common in situ variant of SCC

-Seen in sun exposed area: face, forearms, dorsum of hand, lower legs & bald scalp

-appearance: erythematous macules & papules with coarse, adherent scale

-20% will transform into SSC ,while 60-65% of all SCC arise from Aks



Small lesion w/ rough surface (sandpaper like texture) → brown/ erythematous & scaly

BOWEN'S DISEASE (CSCC IN SITU)

-it's an SCC confined to the epidermis → full thickness cytologic atypia of the keratinocytes

-commonly seen sun exposed areas such as head, neck below the knees in elderly women

- Appearance: solitary erythematous, well demarcated, scaly patch/ plaque + asymptomatic (grow slowly)

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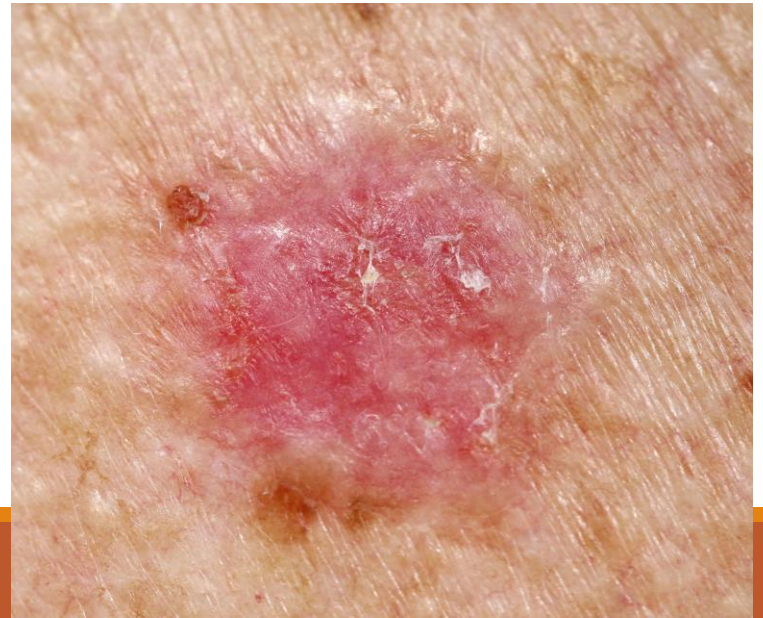


Sub types & variants

Marjolin's ulcer

Chronic wounds --- 10 -25 years→ SSC

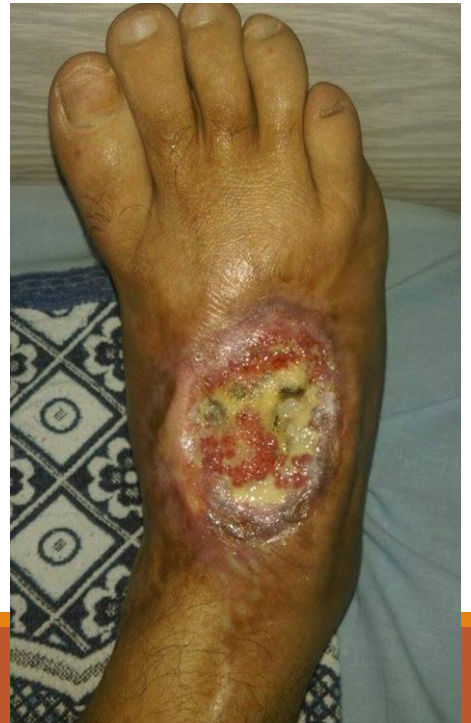
Commonly metastasize

rolled/ everted wound margins, excessive granulation tissue, rapid increase in size & bleeding on touch

Occurs in areas with: - ulcers

- scars (e.g.: burn scar)

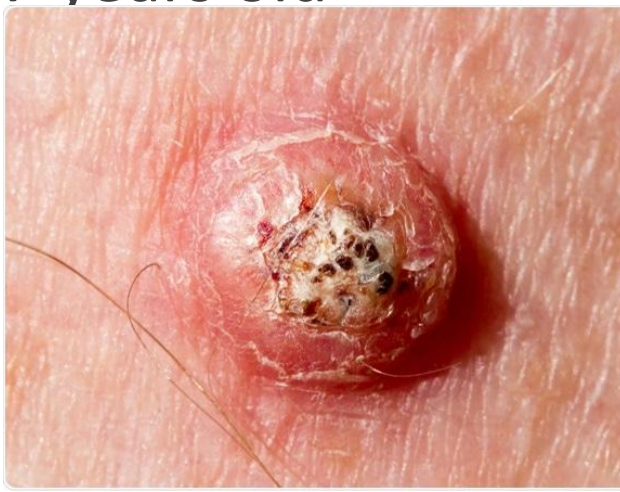
- osteomyelitic fistulas



Keratoacanthoma

- Low risk histological variant of SCC

-Usually found on face/ limbs of chronically sun damaged 50-77 years old white skinned individuals



-Maybe caused by:

*HPV in hair follicle during growth phase + sun exposure

* smoking & chemical carcinogenic exposure

- Typically has rapid 6 week growth phase → involution over next 6 months → rapidly growing nodule with central keratin plug (crateriform tumor)→ typically 1-2 cm; can grow up to 20cm

- 5-10 % can progress to SCC

Macroscopically:

The appearance of SCC may vary from smooth nodular, verrucous, papillomatous to ulcerating lesions. All ulcerate eventually as they grow. The ulcers have a characteristic everted edge and are surrounded by inflamed, indurated skin.

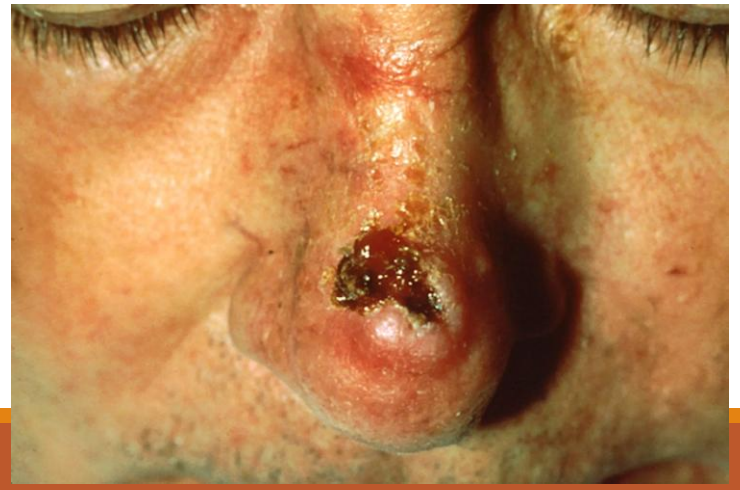
Ulcerative SCC

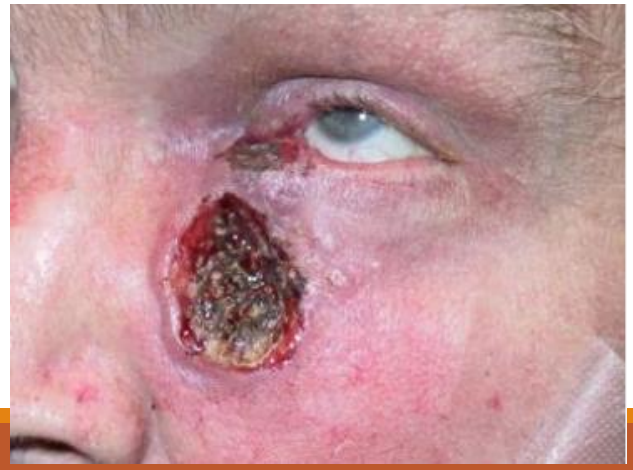
- Most common type
- Grows rapidly , invade locally & has very aggressive growth
- Appear ~~with raised border & central ulceration (~~**~~SCCs arising spontaneously (de novo) begin as small nodules on the skin. As they enlarge, the center becomes necrotic, sloughs, and the nodule turns into an ulcer)~~**
- Location:

*typically on sun exposed areas: - dorsal aspect of forearms & hands(m.c)

- head & neck (including ears& lips)

- If spread to lymph node in head & neck → < 50% survival rate

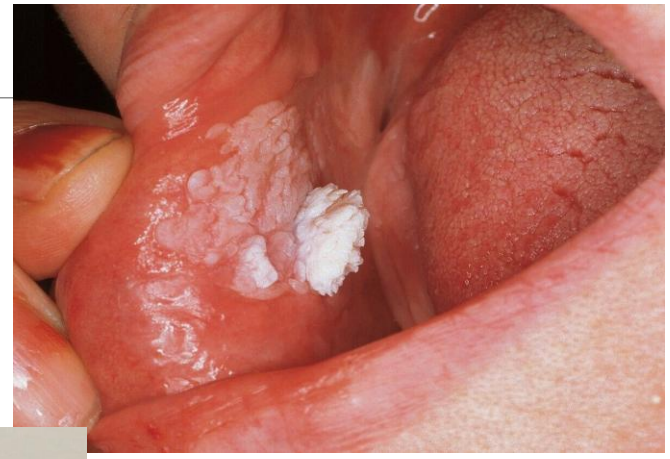




Verrucous SCC

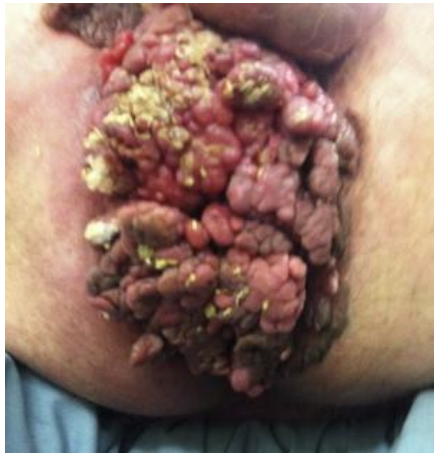
Slow growing ,well defined, exophytic, cauliflower like growths & less likely to metastasize

site:

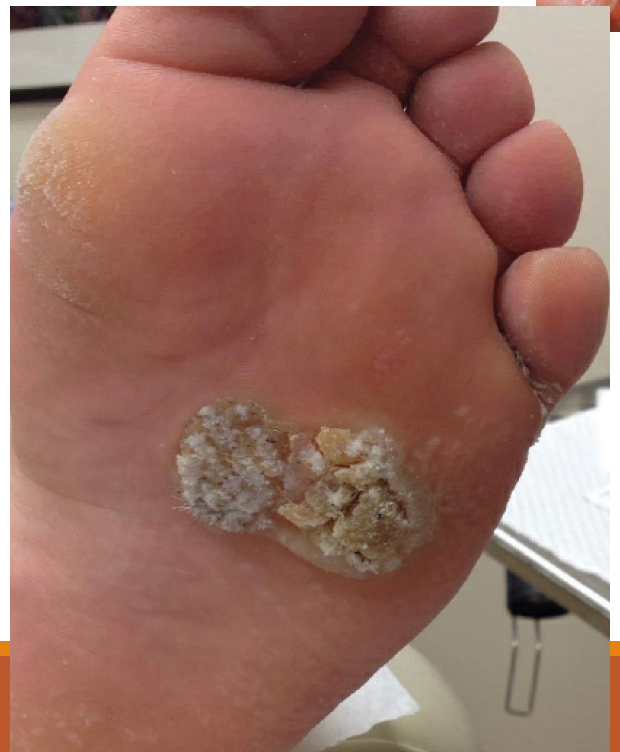


oral cavity (most frequent)→ oral florid papillomatosis

anogenital →



Planter foot (epithelioma cuniculatum)



Prognosis: (depend on)

1 Invasion:

a. **Depth:** the deeper the lesion, the worse the prognosis.

<2 mm, metastasis is highly unlikely

>6 mm, 15 per cent of SCCs will have metastasized.

b. Surface size: lesions >2 cm have a worse prognosis than smaller ones.

2 Histological grade: the higher the Broders' grade, the worse the prognosis.

3 Site: SCCs on the lips and ears have higher local recurrence rates than lesions elsewhere and tumours at the extremities fare worse than those on the trunk.

4 Etiology: SCCs that arise in burn scars, osteomyelitis skin sinuses, chronic ulcers and areas of skin that have been irradiated have a higher metastatic potential.

5 Immunosuppression: SCC will invade further in those with impaired immune response.

6 Microscopic invasion of lympho-vascular spaces or nerve tissue carries a high risk of metastatic disease.

The overall rate of metastasis is 2 per cent for SCC → most common sites for metastasis: lymph nodes(80%), lungs, liver, brain & bone

*** can spread through nervous, lymphatic or vascular systems**

*** perineural invasion can manifest as pain, numbness , weakness**

Diagnosis:

A comprehensive clinical examination in patients with suspected cSCC should include:

-Examination of the lesion; dermoscopy can support visual inspection

-Examination of the draining lymph nodes;

-A full-body skin examination to assess for concurrent precancerous lesions and other skin cancers

-A skin biopsy is required for diagnostic confirmation and risk stratification.

-Biopsy all lesions suspicious for cSCC.

-The biopsy specimen should include the deep reticular dermis.

<u>If suspect malignancy;</u>

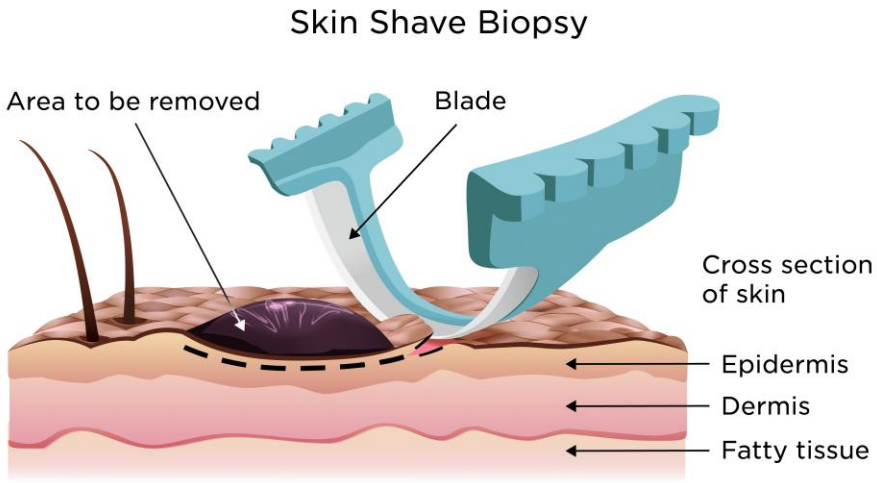
-Imaging

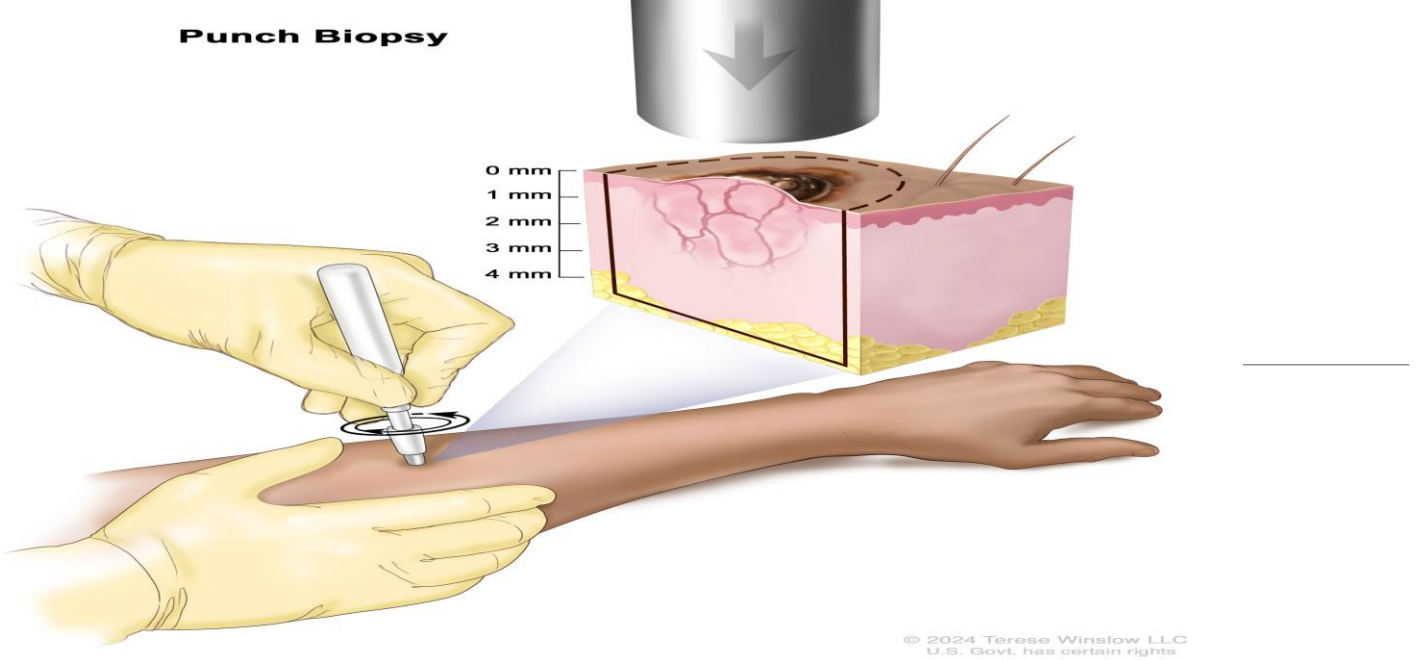
CT with IV contrast: for suspected spread to soft tissue, bone, or lymph nodes

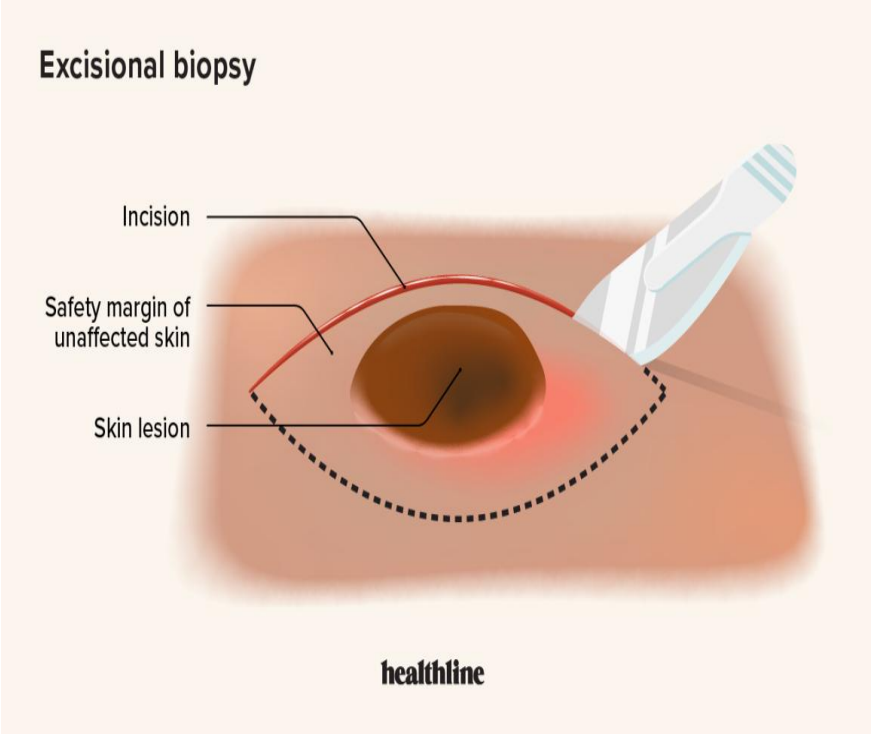
PET-CT or ultrasound: for lymph nodemetastasis [14]

MRI: for suspected perineural, brain, or eyeinvolvement [1]

-Sentinel lymph node biopsy







Techniques:

- Shave biopsy for a raised lesion
- Punch biopsy of the most abnormal area of a large lesion
- Full-thickness excisional biopsy is preferred for lesions with pigmented features of cSCC to rule out melanoma.
- Consider complete excision (with appropriate margins) as a diagnostic and therapeutic procedure for small lesions.
-Ensure adequate sample size and depth for histopathological examination; if not, a repeat biopsy may be required

High risk features of cSCC

Table 1. NCCN Risk Stratification[a]

Characteristic	NCCN risk group: Low	High	Very high
History and physical			
Location and size	Trunk, extremities <2 cm	Trunk, extremities 2 to <4 cm; head, neck, hands, feet, pretibial, and anogenital (any size)	≥4 cm (any location)
Borders	Well-defined	Poorly defined	NA
Primary vs recurrent	Primary	Recurrent	NA
Immunosuppression	Negative	Positive	NA
Site of prior RT or chronic inflammatory process	Negative	Positive	NA
Rapidly growing tumor	Negative	Positive	NA
Neurological symptoms	Negative	Positive	NA
Pathological findings			
Degree of differentiation	Well or moderately differentiated	NA	Poor differentiation
Histologic features: acantholytic (adenoid), adenosquamous (showing mucin production), or metaplastic (carcinosarcomatous) subtypes	Negative	Positive	Desmoplastic SCC
Depth: thickness or level of invasion	≤6 mm and no invasion beyond subcutaneous fat	NA	>6 mm or invasion beyond subcutaneous fat
Perineural involvement	Negative	Positive	Tumor cells within the nerve sheath of a nerve lying deeper than the dermis or measuring ≥0.1 mm
Lymphatic or vascular involvement	Negative	Negative	Positive

Abbreviations: NA, not applicable; NCCN, National Comprehensive Cancer Network; RT, radiotherapy; SCC, squamous cell carcinoma.

[a] Adapted from NCCN 2022 guidelines. Any tumor with 1 or more high- or very high-risk features was categorized as high risk or very high risk, respectively.

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Table 3 Summary of High-Risk Features of cSCC.

- Size (greater than 2 cm in greatest dimension)
- Thickness (greater than 2 mm)
- Perineural invasion
- Lymphatic or vascular invasion
- Histologic subtype (desmoplastic or adenosquamous carcinoma, invasive Bowen disease, or a cSCC arising in an area of chronic inflammation)
- Poor differentiation
- Immunosuppression
- HPV infection
- High-risk anatomic location (ear, lip)
- Drainage areas
- Inadequate tumor resection or tumor with tendency towards recurrence
- Expression of tumor genes

Abbreviations: cSCC, cutaneous squamous cell carcinoma; HPV, human papillomavirus

Table 3 Eighth Edition of the TNM Staging Manual of the AJCC for Cutaneous Epidermal Carcinoma (SCC) of the Head and Neck and Nonmelanoma Skin Cancer Other Than Merkel Cell Carcinoma of the Head and Neck.

AJCC TNM Staging Manual for Squamous Cell Carcinoma of the Head and Neck (Eighth Edition)		
T	TX	Primary tumor cannot be assessed (after curettage...)
	T0	No evidence of primary tumor
	Tis	Carcinoma in situ
	T1	Greatest dimension up to 2 cm
	T2	Greatest tumor dimension > 2 cm but < de 4 cm
	T3	Greatest tumor dimension ≥ 4 cm or minimal erosion of the bone or perineural invasion or deep invasion[a]
	T4	Tumor with extensive cortical or medullary bone involvement **(T4a)**, invasion of the base of the cranium or invasion through the foramen of the base of the cranium **(T4b)**
N	NX:	Nearby lymph nodes cannot be assessed (prior resection for another reason, body habitus...)
	N0	No involvement of nearby lymph nodes as determined clinically/radiologically
	N1	Metastasis **in an isolated ipsilateral lymph node ≤ 3 cm in greatest dimension, ENE (−)**
	N2	N2a: metastasis **in an isolated ipsilateral lymph node 3-6 cm in greatest dimension, ENE (−)**
		N2b: metastasis in multiple ipsilateral lymph nodes less than 6 cm, ENE (−)
		N2c: metastasis in bilateral or contralateral lymph nodes, less than 6 cm, ENE (−)
	N3	N3a: metastasis **in a lymph node greater than 6 cm, ENE (−)**
		N3b: metastasis in **any lymph node(s) and ENE (+)**
M	M0	Absence of distant metastasis
	M1	Distant metastasis

AJCC TNM Staging System for SCC of Head and Neck (Eighth Edition)			
T1	N0	M0	Stage I
T2	N0	M0	Stage II
T3	N0, N1	M0	Stage III
T1	N1	M0	Stage III
T2	N1	M0	Stage III
T1-T3	N2	M0	Stage IV
Any T	N3	M0	Stage IV
T4	Any N	M0	Stage IV
Any T	Any N	M1	Stage IV

Sites on the lower lip are included, eyelid carcinoma is excluded. Tumors of the vulva, pens, perineal region, and other sites other than the head and neck are excluded.
In boldface, aspects most relevant to staging.
Abbreviations: ENE extranodal or extracapsular extension defined as extension through the lymph node capsule in the surrounding connective tissue with or without stromal reaction; SCC squamous cell carcinoma; SLNB sentinel lymph node biopsy.
[a] Deep invasion defined as thickness greater than 6 mm or invasion deeper than subcutaneous fat. For a tumor to be T3, perineural invasion should be present in nerves greater than 0.1 mm, deeper than the dermis, or clinical and radiological involvement of affected

T stage	Primary tumor (T)
T1	0 high-risk factors*
T2a	1 high-risk factor*
T2b	2–3 high-risk factors*
T3	4 high-risk factors or bone invasion*

*BWH high-risk factors include tumor diameter ≥2 cm, poorly differentiated histology, perineural invasion of nerve(s) ≥0.1 mm in caliber, or tumor invasion beyond subcutaneous fat (excluding bone invasion, which upgrades tumor to BWH stage T3).
BWH, Brigham and Women's Hospital; CSCC, cutaneous squamous cell carcinoma.

Treatment

1) Surgical excision : is the only means of providing accurate information on histology and clearance. The margins for primary excision should be tailored to surface size in the first instance.

-4-mm clearance margin should be achieved if the SCC measures <2cm;

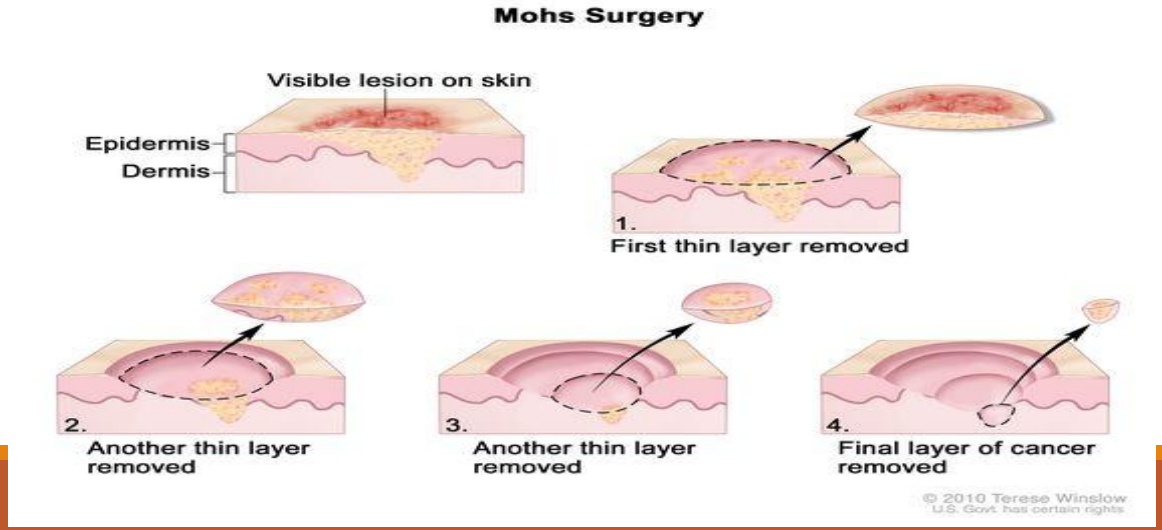
-1-cm clearance margin if the SCC measures >2cm

-95% of local recurrence and regional metastases occur within 5 years, thus follow-up beyond this period is not indicated

2) Mohs surgery : Sequential horizontal excision with frozen section testing.

-Highest cure rate for SCC: 94% to 99%.

- Indications, include recurrent, high-risk SCC, and/or lesions in aesthetically sensitive areas (nose, eyelid, lip, etc.)



3)Field therapies (topical creams, PDT, laser therapy)
are used much less in SCC than in BCC treatment, because of higher risk associated with missed deep tumor portions, and the risk of scarring obscuring SCC recurrences.

4) Radiation therapy is typically reserved as primary therapy for those who are poor surgical candidates (unresectable lesions or for the very elderly), and as adjuvant therapy after surgical resection for large, high-risk tumors.When used as primary therapy, cure rates may approach 90%.Cosmetic damage and long-term risk of radiation must be considered

5) Systemic therapy

Consider if curative RT or resection is not feasible for:

High-risk locally advanced or metastatic SCC

Management of positive margins

Systemic therapy includes:

Immune checkpoint inhibitors (e.g., pembrolizumab, cemiplimab)

Chemotherapy(e.g., cisplatin, carboplatin, 5-FU, paclitaxel)

Epidermal growth factor receptor inhibitors (e.g., cetuximab)

Regional lymphadenectomy

1. Indicated for clinically positive (palpable) nodes.

2. FNA: Confirm spread of SCC to palpable lymph node.

3. ELND (elective lymph node dissection): Indicated for a tumor extending down to parotid capsule or a large lesion contiguous v
draining nodal basin.

4. SLN biopsy: Sentinel lymph node dissection may be used in high risk cases with clinically negative nodal disease

Adjuvant radiation therapy: Used post excision for high risk cutaneous SCC

For localized cSCC:

High risk CSCC: MMS (preferred)

alternative :

- Surgical excision with wide margins; consider delayed closure until R0 resection is confirmed.
- RT ± systemic therapy for patients who cannot undergo resection

** need adjuvant RT if perineural is involved

Low risk cSCC: - surgical excision (4-6mm margin)

- MMS
- RT (if cant undergo resection)

** for small, superficial lesions+ cant undergo resection: C&E in non hair bearing areas / cryotherapy

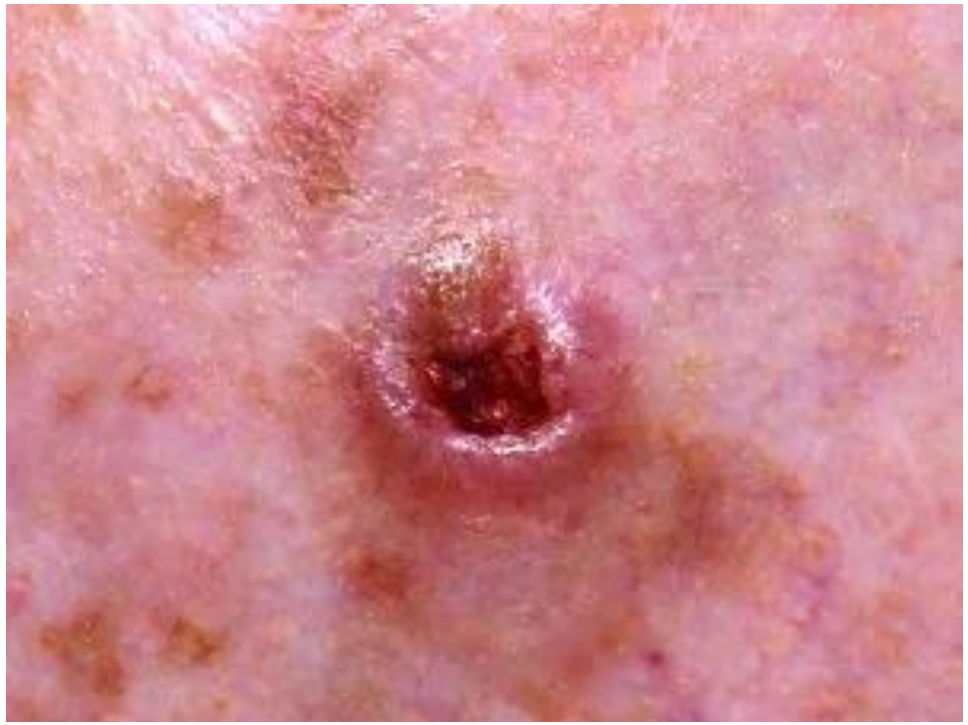
Locally advanced or metastatic cSCC

- Specialist referral and multidisciplinary care are recommended to consider the following options:
- Surgical resection ± lymphadenectomy
- Adjuvant RT
- Systemic therapy
- Palliative care
- Enrollment into clinical trials

Basal cell carcinoma (BCC) = rodent ulcer

Epidemiology:

- Most common tumor diagnosed in USA (1M cases/ year)
- Most common form of skin cancer in white people
- Sex: M>F (2:1)
- In middle aged/elderly



Risk factors:

1.Sun exposure : 36% of BCCs originate from the area of previously diagnosed actinic keratosis (AKs), but have distinct cells of origin. (strongest predisposing factor)

2. Advancing age

3. Fair complexion

4. Long-term exposure to psoralens and UVA therapy (i.e., PUVA therapy for psoriasis)

5. Immunosuppression, most commonly seen in transplant patients

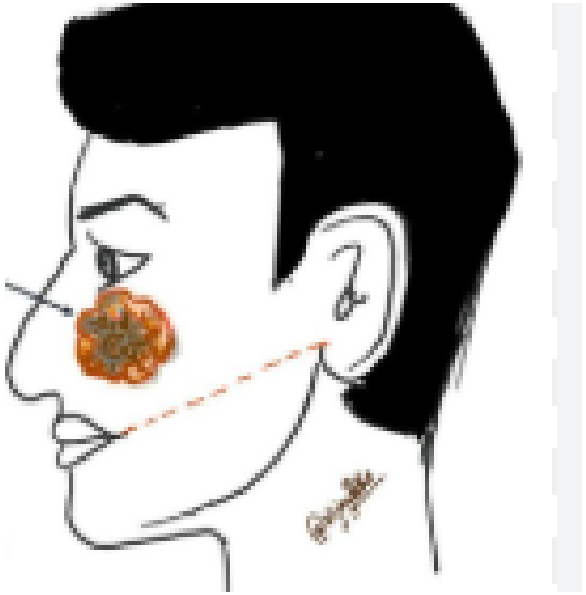
6. Nevus sebaceus of Jadassohn, a superficial skin lesion typically in the head and neck regions, presents as an irregular, raised, yellow to pink, non-hair bearing raised mass. They are usually present at birth or develop in early childhood, and approximately 15% undergo malignant transformation to BCC.

7. Arsenic exposure

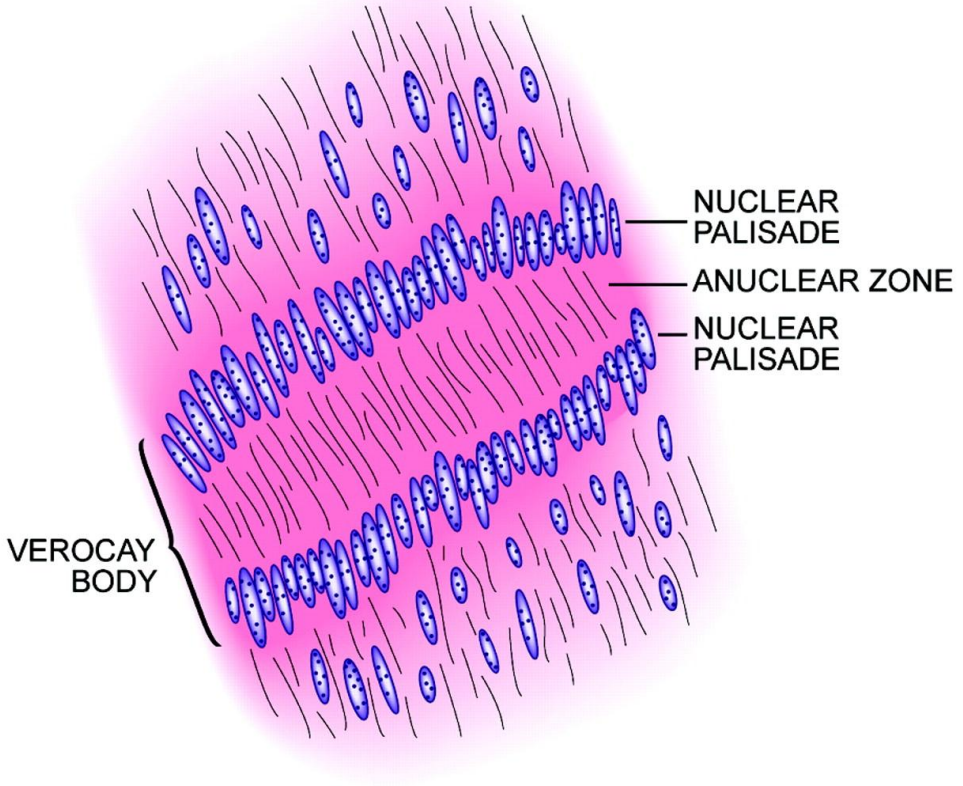
BCC disease:

Origin: basal keratinocytes at basal layer of epidermis (at dermo-epidermal junction

Most common in areas with high Concentration of pilosebaceous follicles➔ > 90% are found on head % neck (above a line from lobe of ear to the corner of mouth)



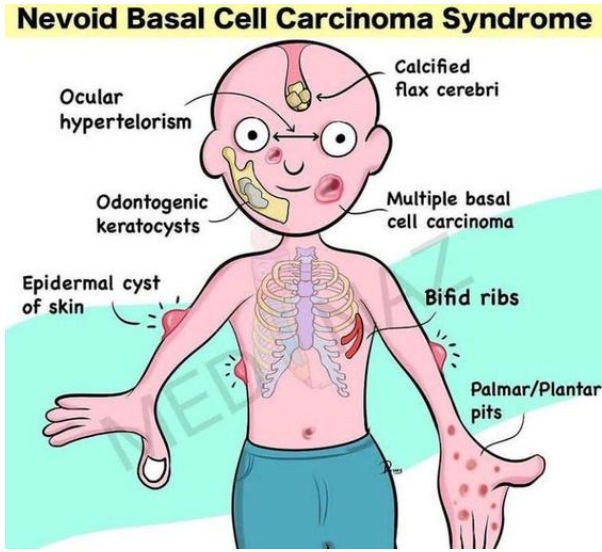
Pathology:
palisading nuclei



Syndromes associated with BCC:

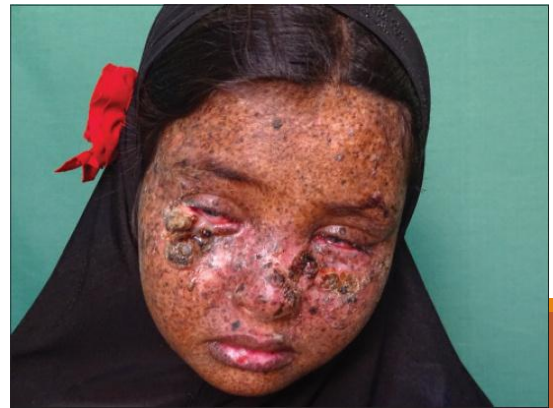
a. **Basal cell nevus syndrome (Gorlin's syndrome)** → **mandibular cyst , palm pits , multiple BCC**

seen early in childhood with malignant



b. Xeroderma pigmentosum (XP): Patients have increased incidence of BCC, SCC, and malignant melanoma

c. Albinism

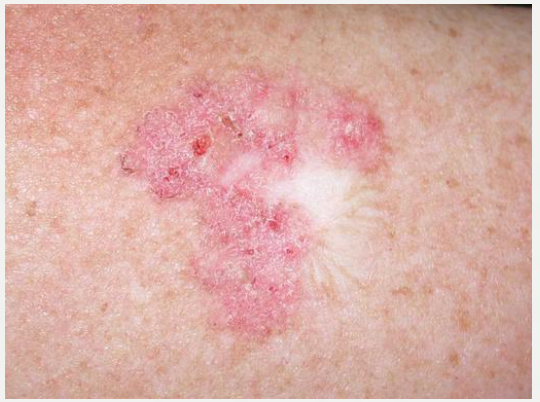


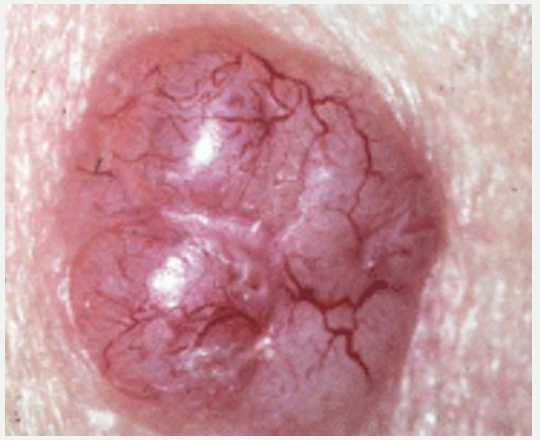
Pathology

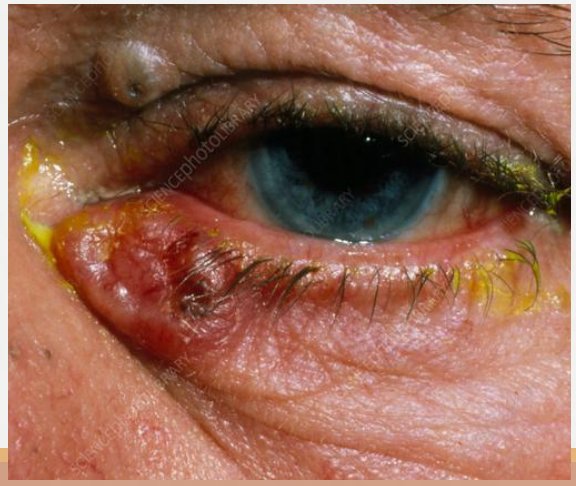
Macroscopic, the tumour has raised, rolled but not everted edges. It consists of pearly nodules over which fine blood vessels can be seen to course (telangiectasia)

BCC can be divided into localised *(nodular, nodulocystic , cystic, *pigmented and naevoid) and generalised lesions. These lesions can be superficial (multifocal or superficial spreading) or infiltrative (*morphoeic, ice pick and cicatrising)

• Nodular and nodulocystic variants account for 90 per cent of BCC.







Prognosis

There are ‘high risk’ and ‘low risk’ BCCs.

High-risk BCCs are:

1. Large (>2 cm);

2. Located at sites where direct invasion gives access to the cranium (near the eye, nose and ear)

3. Recurrent tumours

4. Tumours forming in the presence of immunosuppression;

5. Micronodular or infiltrating histological subtypes.

Treatment

Treatment can be surgical or non-surgical.

Treatment of BCC varies according to size, location, type, and high- or low-risk. Treatment options include surgical excision, medical, or destructive therapies. Surgical excision should include 4 mm margins for small, primary BCC on cosmetically sensitive areas, and 10 mm margins otherwise.

Mohs' micrographic surgery : Sequential horizontal excision with immediate frozen section testing by dedicated Mohs dermatopathologist.

Indications include morpheaform BCC and/or lesions in aesthetically sensitive areas (nose, eyelid, lip,ears, etc.)

Other destructive techniques include cryosurgery and laser ablation.

Radiation therapy can be used as adjuvant therapy following surgery, or as primary therapy in poor surgical candidates with low-risk lesions,deeply invasive BCC

Topical Pharmaceuticals

Topical imiquimod or 5-fluorouracil have been used for periods of 6 to 16 weeks for small, superficial BCC of the neck, trunk or extremities.

3

Melanoma

Least common ,most aggressive 💀

Epidemiology:

Most common cause of skin cancer-related death

Incidence is higher among individuals who are:

- Non-Hispanic White
- Male
- ≥ 75 years of age

Risk factors

Phenotypic include fair skin, freckling, light eye color, and light hair color (stronger risk factor than eye color).

Darker skin is protective against melanoma.

2. Geographic: High altitudes, lower latitudes have increased UV exposure, therefore increased risk

3. Gender: Females have lower risk and better prognosis

4. Race: for African-Americans Incidence is lower, but prognosis is worse, due to delayed diagnosis and/or worse disease subtype

5. Previous melanom

Family history: Vast majority of melanomas are sporadic; however, some hereditary forms exist

a. Familial melanoma (aka hereditary melanoma):

Two or more cases of melanoma in first-degree relatives may indicate familial melanoma, autosomal dominant transference with variable penetrance.

b. Dysplastic nevus syndrome (also known as familial atypical multiple mole and melanoma [FAMMM] syndrome):

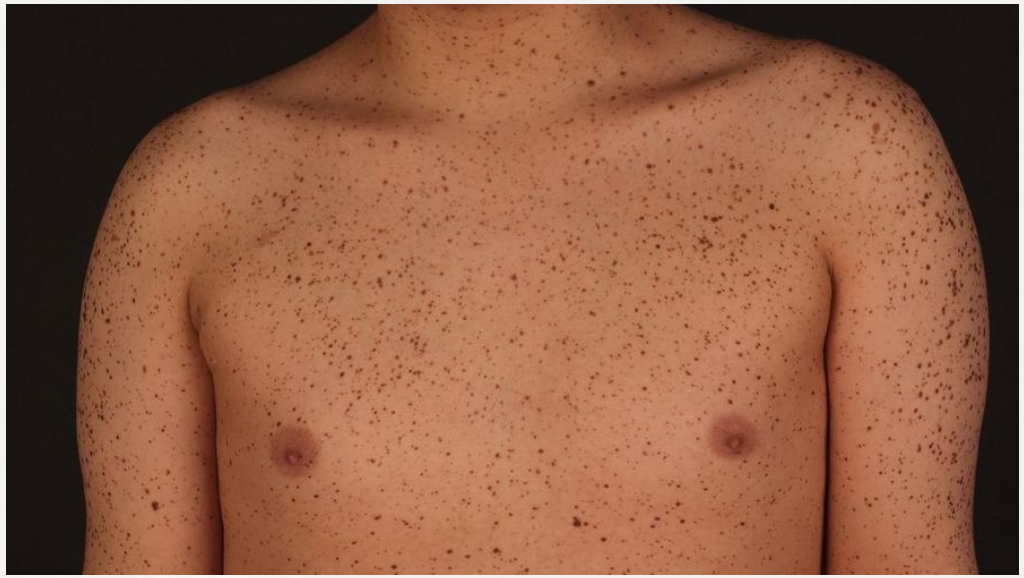
Patients have a first- or second-degree relative with malignant melanoma and typically have at least 50 melanocytic nevi. Mutations in CDKN2A typical. Patients need vigilant screening.

c. Xeroderma pigmentosum (XP)

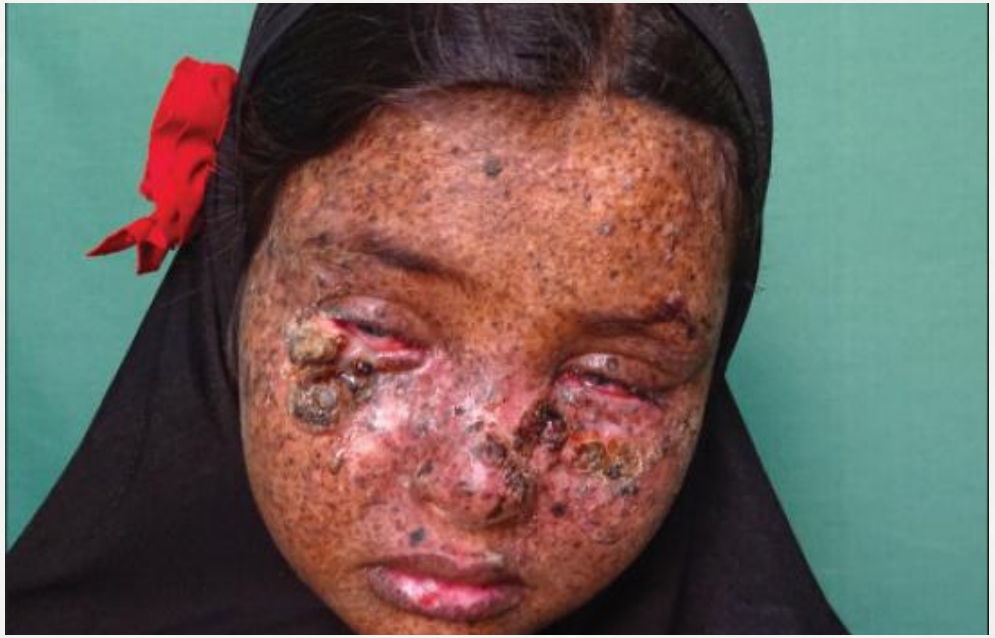
i. Heterogeneous group of syndromes; due mutations in various DNA repair genes.

ii. DNA damage by UV leads to early death secondary to metastatic spread of skin tumors.

iii. Typically presents in childhood with multiple BCCs; SCCs and melanomas typically cause death.



FAMMM



Xeroderma pigmentosum

genetic basis of melanoma?

- mutation in BRAF gene
- germline mutations in CDKN2A and CDK4 gene
- Mutation in MC1R gene

Precursor lesions

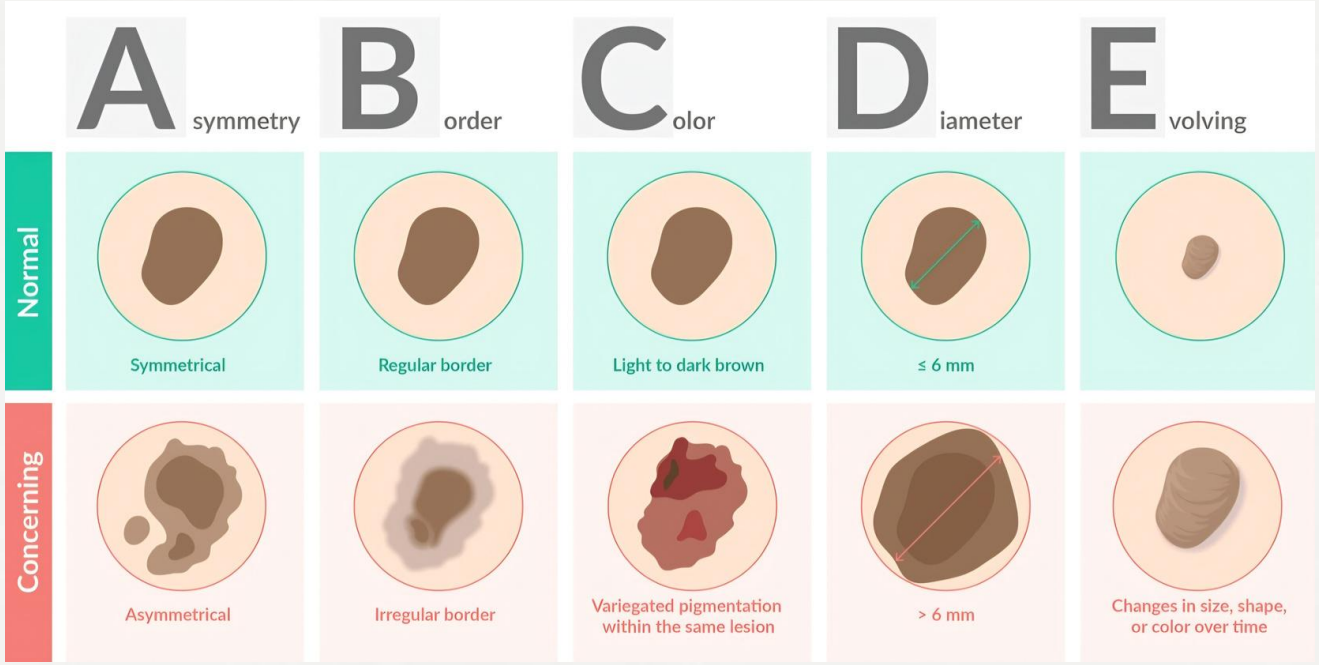
1- Congenital nevi

2-acquired melanocytic nevi

3-dysplastic atypical nevi

4- Melanoma in situ / atypical junctional melanocytic hyperplasia (AJMH)

5- Spitz nevus



ABCDE criteria

The following skin lesion characteristics are concerning for melanoma:

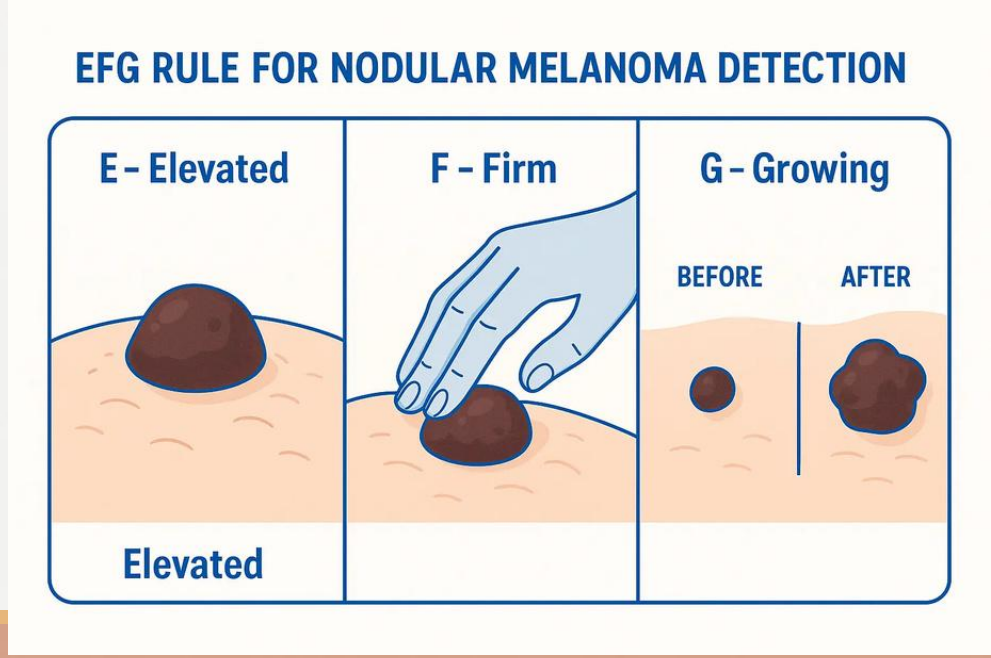
A = Asymmetry

B = Border (irregular border with indistinct margins)

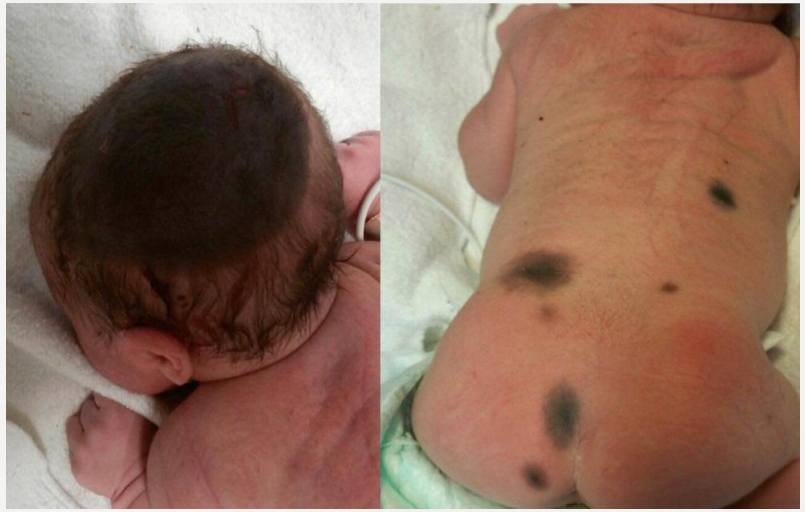
C = Color (variegated pigmentation within the same lesion)

D = Diameter > 6 mm

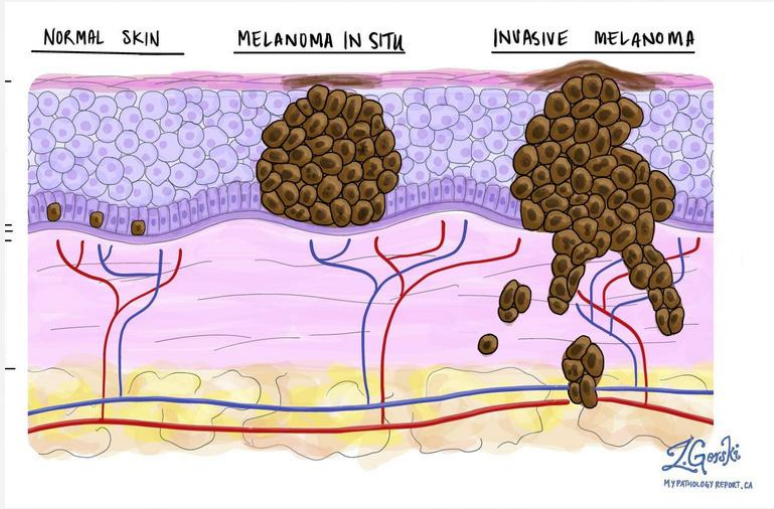
E = Evolving (a lesion that changes in size, shape, or color over time)



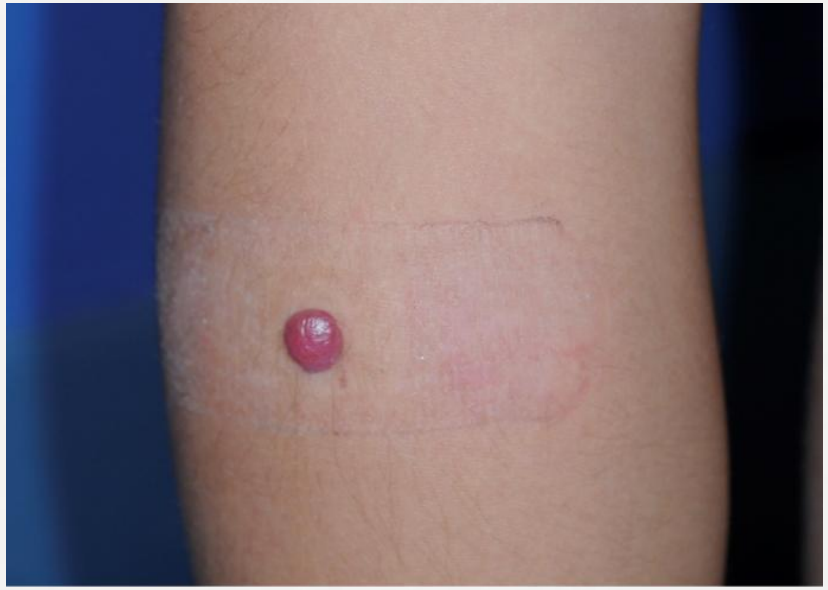
Sign	Description	Clinical Significance
E - Elevation	The lesion is **raised above the surrounding skin**, indicating that the cancerous cells have proliferated in a vertical fashion and are invading the dermis. This is often measured by the **Breslow thickness**, the most critical prognostic factor in primary melanoma.	**High risk of metastasis.** Elevated lesions have a greater Breslow thickness (depth of invasion).
F - Firmness	The lesion has a **hard or firm consistency** when palpated (felt). This firmness is a result of the densely packed malignant cells and the associated inflammatory/fibrotic reaction in the underlying tissue.	**Suggests deeper tumor infiltration** and loss of the soft, doughy quality of a benign mole.
G - Growth	The lesion shows **progressive enlargement, change in size, shape, or color** over a short period (weeks to months). This also includes the development of satellite lesions or ulceration. This is the "Evolving" element from the ABCDE criteria, but is often emphasized separately.	**Indicates aggressive behavior**. Rapid growth is characteristic of advanced malignant proliferation.



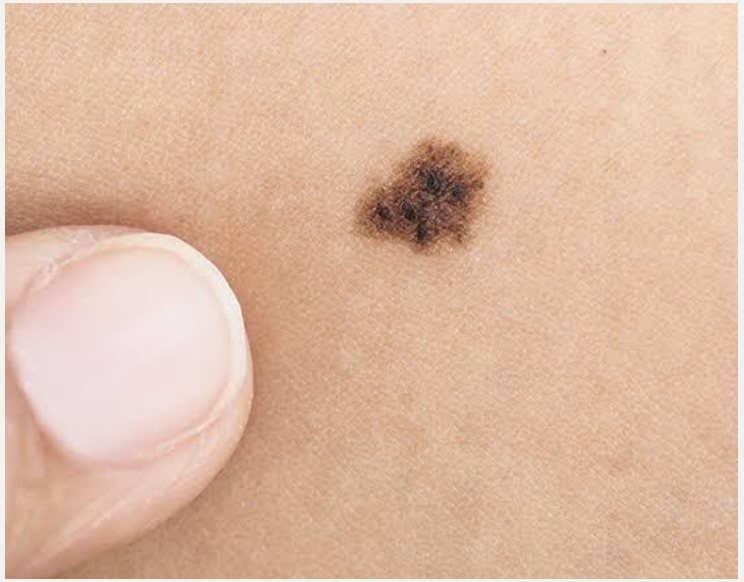
Congenital nevi



Melanoma in situ



Spitz nevus



dysplastic atypical nevi

Classification of melanoma types

1. Superficial spreading melanoma

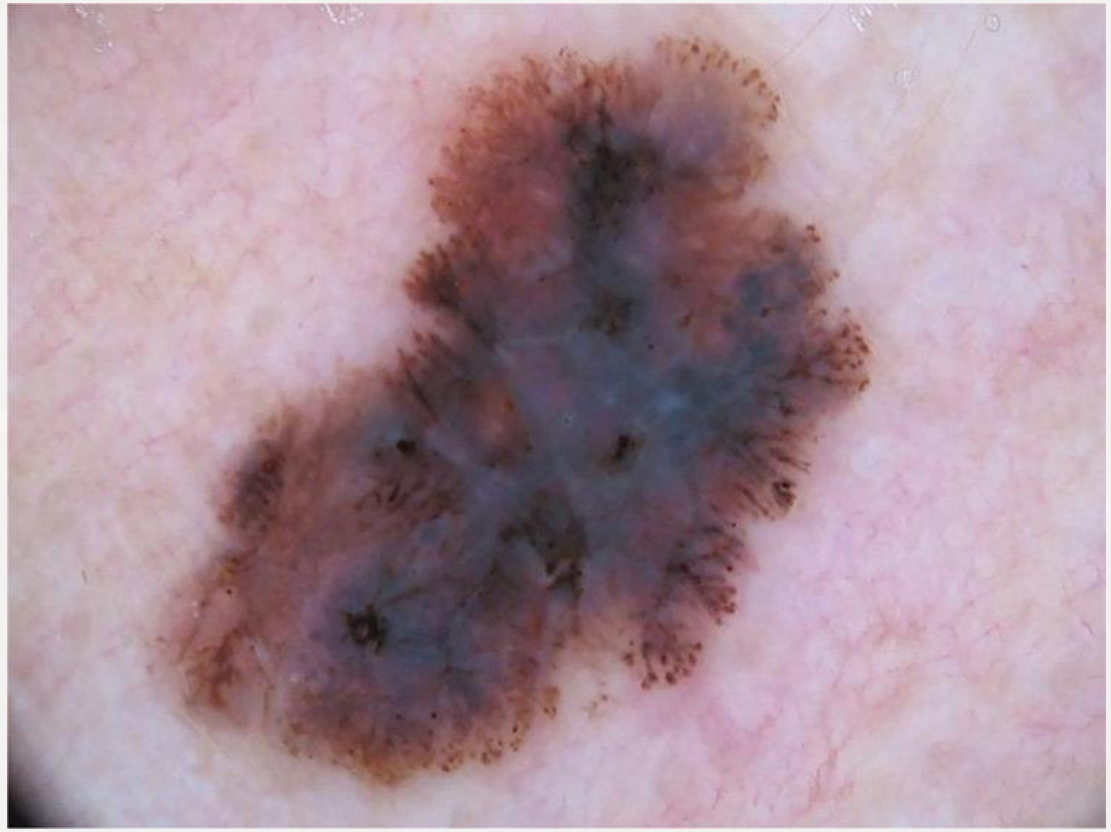
• This accounts for 50% to 70% of melanomas and typically arises from a precursor melanocytic nevus.

• equallyAffects both genders

• . Median age at diagnosis is 50 years

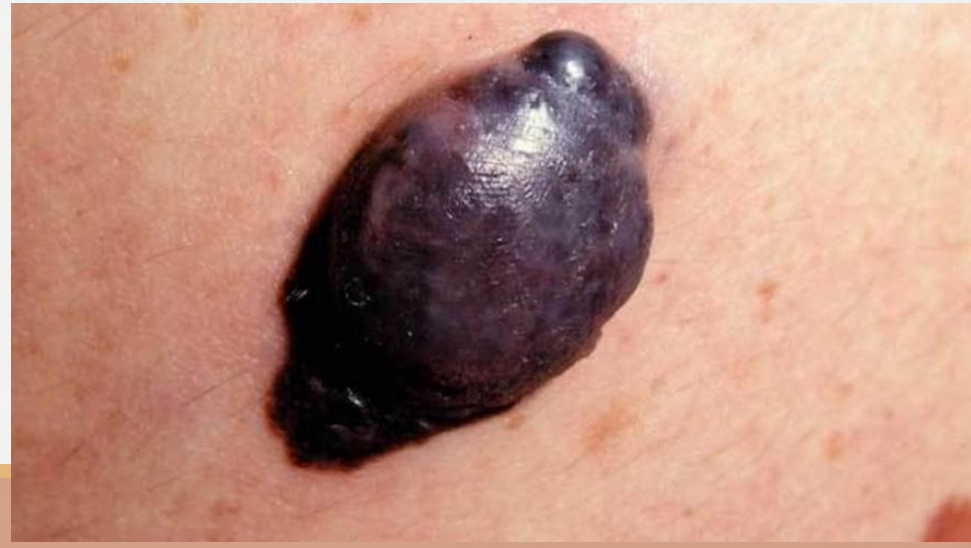
• most common sites lower legs in women are Upper back in men and

• vertical growth phase late Radial growth phase early,



Nodular melanoma

Second most common: 15% to 30% cases
. Most aggressive type
Typically do not arise from preexisting nevi
. Men are affected twice as frequently as women
Median age at diagnosis is 50 years
No clear association with sunlight exposure
Resemble blood blisters or other noncancerous lesions
Have regular, symmetrical borders
They typically appear as blue/black papules, 1–2cm in diameter, and because they lack the horizontal growth phase, they tend to be sharply demarcated. Up to 5% are amelanotic
Vertical growth phase is a hallmark feature;
no radial growth



Lentigo maligna melanoma (LMM)

Lentigo maligna = is an in situ cutaneous melanoma that has invaded the dermis or beyond (i.e., that is no longer in situ), is known as lentigo maligna melanoma

was previously also known as Hutchinson's melanotic freckle

They are positively correlated with prolonged, intense sun exposure, affecting women more than men. They account for between 5% and 10% of MM. LMM are thought to have less metastatic potential than other variants as they take longer to enter a vertical growth phase. Nonetheless, when they have entered the vertical growth phase their metastatic potential is the same as any other melanoma.

The median age at diagnosis is 70 years.

Usually greater than 3 cm in diameter; irregular, asymmetric with color variegation, areas of regression may appear hypopigmented.

most common location is the cheek.

Acral lentiginous melanoma

.LM is the most common subtype of melanoma in darker skinned populations,affects the soles of feet and palms of hands.

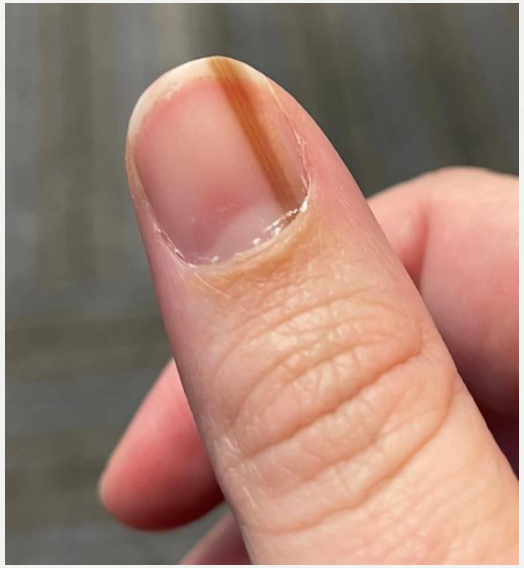
.It is rare in white-skinned individuals (2–8% of MM) but more common in the Afro-Caribbean, Hispanic and Asian population (35–60%).

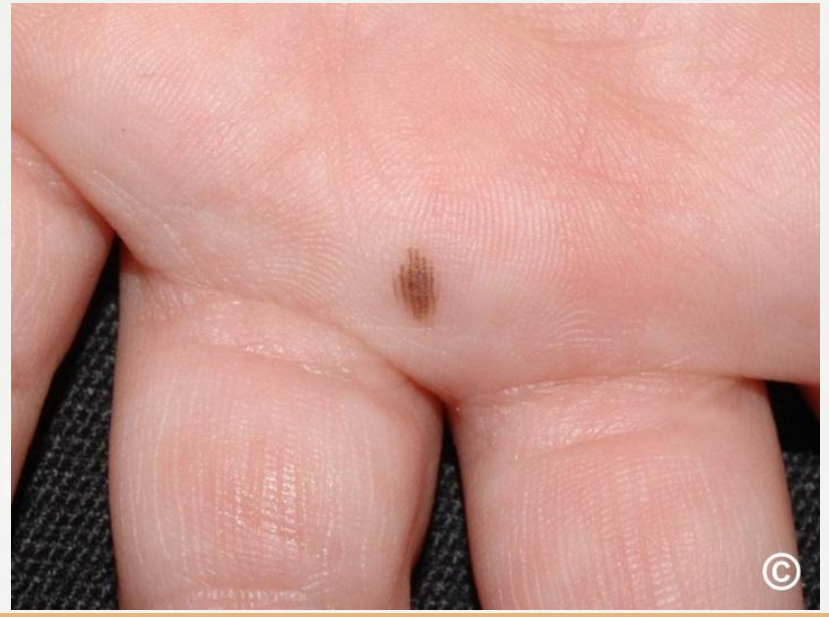
.It usually presents as a flat, irregular macule in later life. 25% are amelanotic and may mimic a fungal infection or pyogenic granuloma.

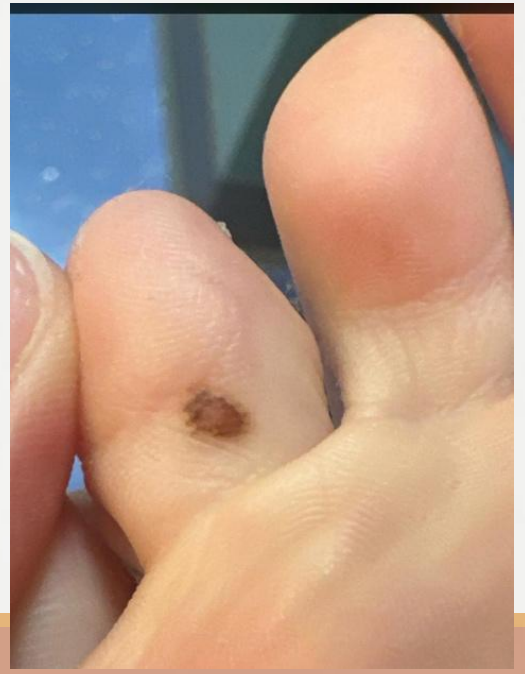
. Irregular pigmentation, large size (>3 cm) common

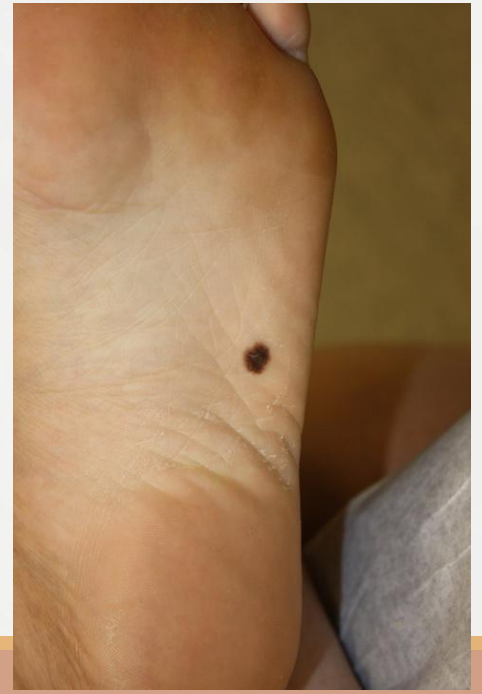
. Most common site is great toe or thumb

. Long radial growth phase, transition to vertical growth phase occurs with high risk of metastasis.









Diagnosis and staging of melanoma.

Physical examination is only 60% to 80% sensitive for diagnosing melanoma.

Full-body photography to monitor atypical nevi may increase sensitivity.

B. Common clinical features of melanoma lesions: (ABCDE)

1. Asymmetry
2. Border irregularity
3. Color variation
4. Diameter >6 mm
5. Enlarging/evolving lesion

Diagnosis of primary melanoma is made by histologic analysis of full-thickness

biopsy specimens• Excisional biopsy is preferred for lesions **<1.5 cm** in diameter. If possible, excise lesion with **1- to 3-mm margins.**

• Incisional biopsy is appropriate when suspicion is low, the lesion is large (>1.5 cm) or is located in a potentially disfiguring area (face, hands, and feet),or when it is impractical to perform complete excision.

.Incisional biopsy does not increase risk of metastasis or affect patient survival.

• Permanent sectioning is used to determine tumor thickness

• Avoid shave biopsies, since they forfeit the ability to stage the lesion based on thicken

• Clinically suspicious lymph nodes should undergo fine-needle aspiration (FNA)

• Orientation of biopsy incisions should also take definitive surgical therapy into consideration.

• Extremity biopsies should use longitudinal incisions.

• Transverse incisions are sometimes preferable for preventing contractures over joints.

• Head and neck incisions should be placed within relaxed skin tension lines,keeping facial aesthetic units in mind.

Major prognostic factors:

*TNM : Tumor thickness, Nodal status, and Metastases

1. Clark level is based on invasion through the histologic layers of the skin; it is more subjective

2. Breslow thickness is reported in millimeters; thus, it is more accurateand reproducible than Clark level and is a better prognostic indicator

AJCC staging of cutaneous melanoma (2018) [27][30]

	Tumor characteristics (T)	Regional spread (N)	Distant metastasis (M)
Stage 0 melanoma	• Tumor in situ	• None	• None
Stage I melanoma	• IA: Breslow depth < 0.8 mm without ulceration • IB: Breslow depth < 0.8 mm with ulceration, Breslow depth 0.8–1.0 mm with or without ulceration, or Breslow depth 1.0–2.0 mm without ulceration		
Stage II melanoma	• IIA: Breslow depth 1.0–2.0 mm with ulceration, or Breslow depth 2.0–4.0 mm without ulceration • IIB: Breslow depth 2.0–4.0 mm with ulceration, or Breslow depth > 4.0 mm without ulceration • IIC: Breslow depth > 4.0 mm with ulceration		
Stage III melanoma	• Any Breslow depth	• Present	
Stage IV melanoma	• Any Breslow depth	• May or may not be present	• Present

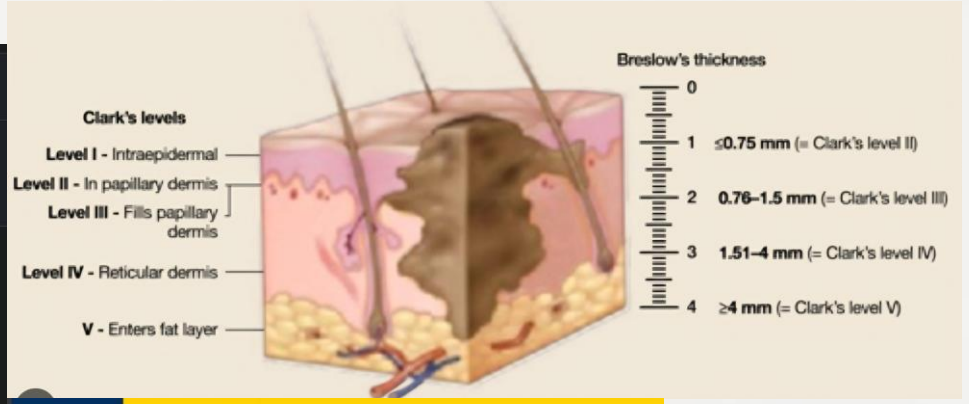


TABLE 13-3 Melanoma Thickness Grading

Clark level	Skin layer/depth	5-y survival (%)
I	In situ	100
II	Papillary dermis	88
III	Papillar-reticular dermis	66
IV	Reticular dermis	55
V	Subcutaneous	22
Breslow depth (mm)		**5-y survival (%)**
<0.76		89
0.76–1.49		75
1.5–2.49		58
2.5–3.99		46
>3.99		25

Other prognostic factors

1. Anatomic location: Trunk lesions generally carry worse prognosis than those on the extremities.
2. Sex: For a given melanoma, women generally have a better prognosis; women are also more likely to have extremity melanomas which carry a better prognosis.
3. Ulceration is a poor prognostic sign
4. Lymph node involvement or in-transit metastases are more significant than any other prognostic factors.

melanoma treatment

Definitive management of melanoma :

1. Wide local excision is the treatment of choice.
2. Recommended surgical margins depend on tumor thickness
3. Subungual melanoma requires amputation proximal to the DIPJ for fingers and proximal to IP joint for the thumb.

Recommended surgical margins for invasive melanoma resection	
Breslow depth	Surgical margin
Tumor in situ	• 0.5–1 cm
≤ 1 mm	• 1 cm
> 1 mm and ≤ 2 mm	• 1–2 cm
> 2 mm	• 2 cm

Sentinel lymph node biopsy (SLNB)

SLNB is performed in conjunction with wide local excision of the primary tumor. Lymphatic mapping is performed to determine the first lymph node that drains the primary tumor site (sentinel node). SLNB-positive patients undergo staged regional lymphadenectomy and may be candidates for adjuvant therapy.

Preoperative nuclear imaging is performed with radiolabeled colloid solution (technetium-99) injected intradermally at the primary tumor.

This can be done on the day of or day prior to surgery.

Lymphoscintigraphic imaging localizes the sentinel node basin(s) (some tumor sites can drain to multiple basins).

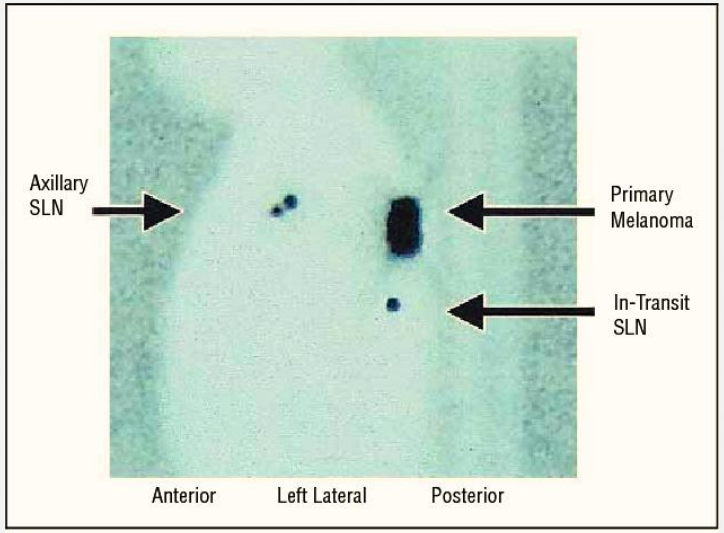
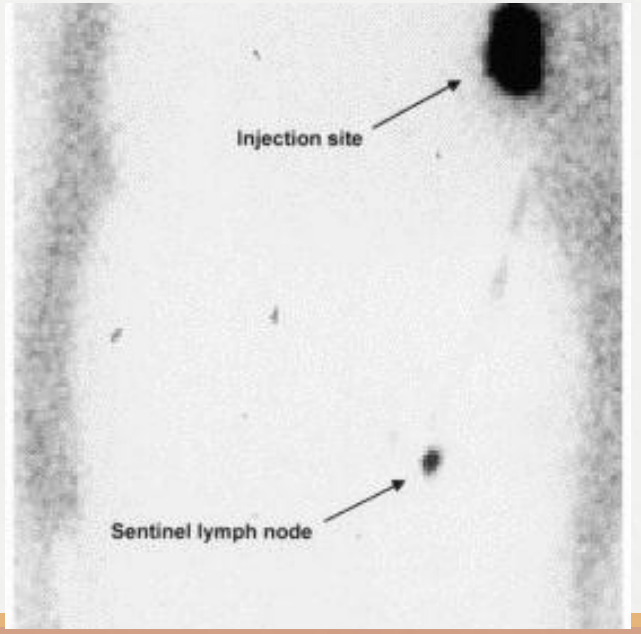
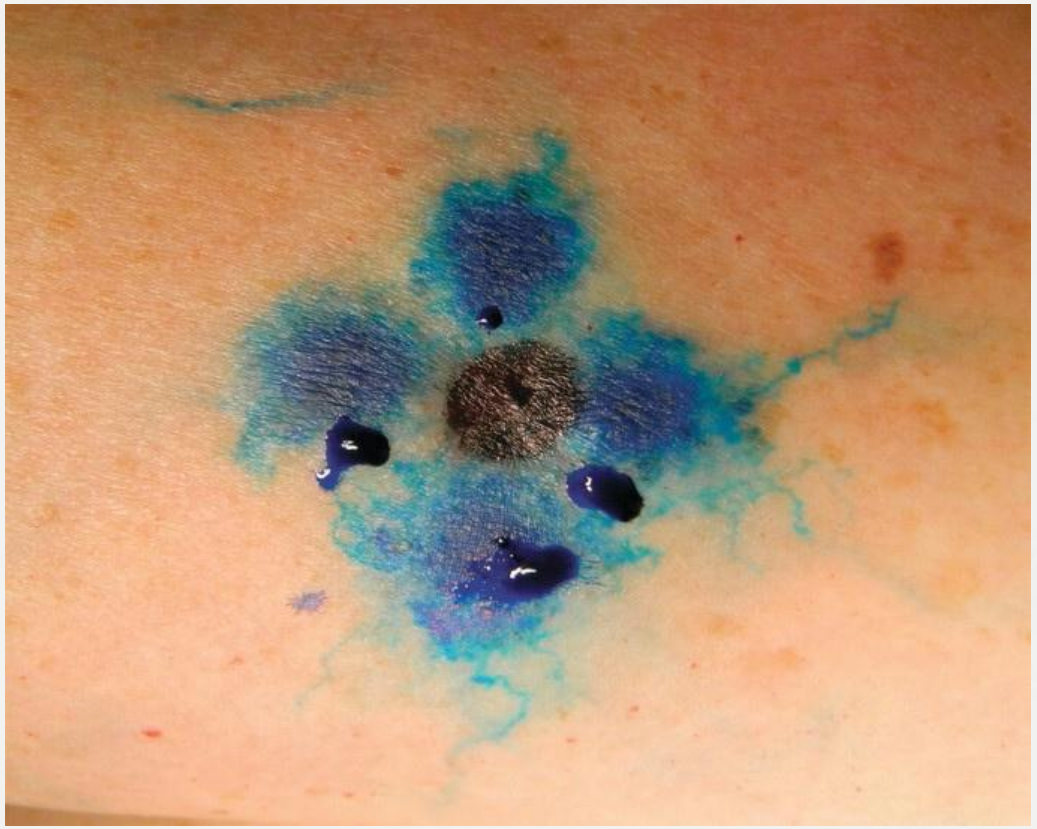


Figure 1. Lymphoscintigram of a patient with a primary melanoma in the left scapular region, demonstrating axillary nodal drainage and an interval sentinel lymph node (SLN) in the subcutaneous tissues of the back.



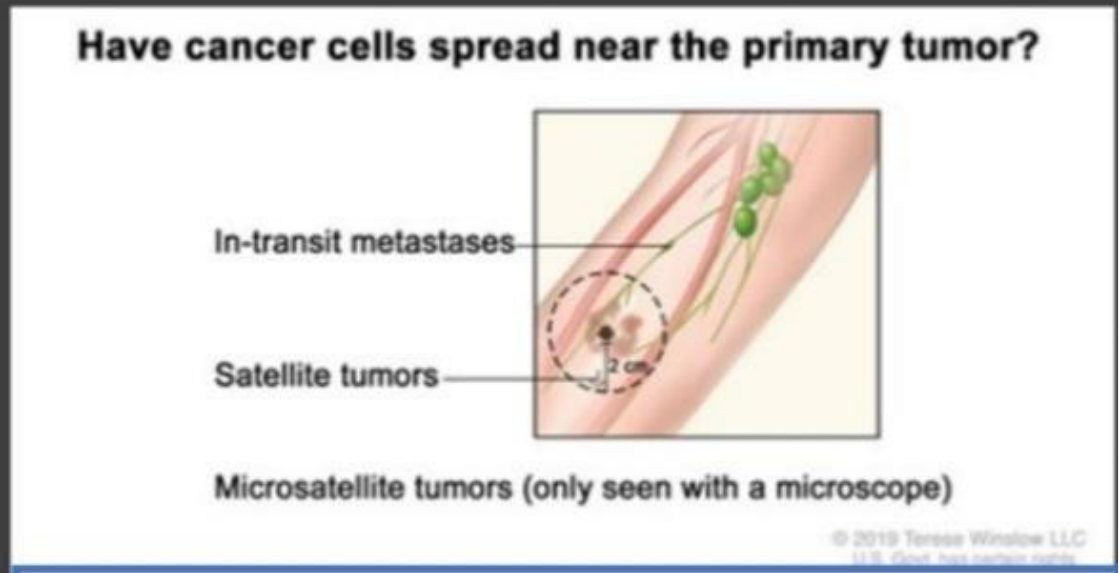
In the operating room, a lymphangiography dye (lymphazurin or methylene blue) can be injected intradermally at the periphery of the primary tumor site prior to excision of the primary tumor.

1. Mark edges of the lesion before injection to avoid obscuring them with the dye and take care with the dye because spills are difficult to manage.
2. Potential sentinel nodes will appear blue when exploring the nodal basin, giving secondary confirmation to localization with Geiger counter detection of Tc99.
3. Dye injection may briefly interfere with pulse-oximeter readings; alert anesthesiologist at the time of injection.
4. Caution: Risk of allergy or anaphylaxis with dye injection
5. Following excision of the primary tumor All radioactive (“hot”) and/or blue nodes are excised.
6. Histologic analysis of sentinel node with immunohistochemical staining identifies micrometastases. Permanent sections are required; frozen sections cannot reliably differentiate normal from neoplastic melanocytes



D. Surveillance and treatment of melanoma recurrence

1. Guidelines vary depending on stage of melanoma
2. **Asymptomatic patients** should be seen every 3 to 4 months for 2 years then every 6 months for 3 years, then annually. The most accurate way to detect metastatic disease is to take a thorough history
3. **Chest x-ray and liver function tests** (LDH and alkaline phosphatase)are usually sufficient; more extensive workups including computed tomo-graphic (CT) scans have not altered outcomes.
4. **Local recurrence** typically occurs within 5 cm of the original lesion, usually within 3 to 5 years after primary excision; most often this represents incomplete excision of the primary tumor.



The most common sites of recurrence are the skin, subcutaneous tissues, distant lymph nodes, then other sites (lung, liver, brain, bone, GI tract).

Mean survival with disseminated disease is 6 months. Respiratory failure and CNS

Chemotherapy:

Complete remission is rare. a. Dacarbazine (DTIC),
carmustine , cisplatin, and tamoxifen in combination are most frequently used.
Isolated hyperthermic limb perfusion for extensive cutaneous disease(melphalan and tumor necrosis factor) is used at some centers

Cytokine :

therapy has been demonstrated to produce relatively high levels
of tumor response, albeit transient. FDA-approved regimens
include interferon-α (IFN-α) for stage III disease and interleukin2 (IL-2) for stage IV disease; however, these therapies demonstrate little or no improvement in overall survival.

Immunotherapy :

Immunotherapy drugs called checkpoint inhibitors use the body's own immune system to fight cancer. Some people who use checkpoint inhibitors have had very encouraging results, but they do not work for everyone with advanced melanoma.

Targeted therapy:

Selective cell-signaling inhibitors (e.g., vemurafenib
If a person has a BRAF mutation, they will get both a BRAF inhibitor and a MEK inhibitor. commonly used combinations include vemurafenib and cobimetinib
Drugs for NRAS and C-KIT mutations may be available through clinical trials

Less common skin cancers

Merkel cell carcinoma: a rare, rapidly progressive neuroendocrine neoplasm that typically manifests as a painless, firm, nontender, red-blue nodule on the head or neck .It is four times more common in women than men.

Risk factors include

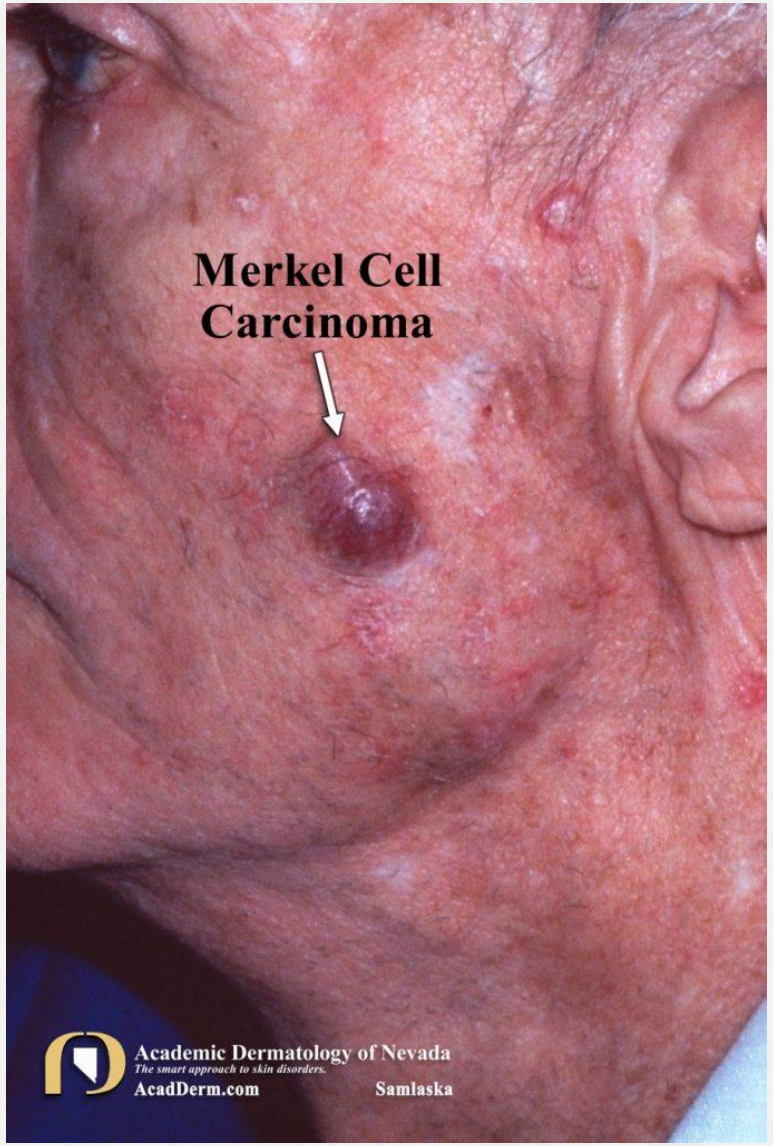
age over 65; history of extensive sunlight exposure; fair skin; and immunosuppression (HIV; organ transplants).

Recent research has implicated Merkel cell polyomavirus in 80% of MCC cases Presents as a purple to red papulonodule or indurated plaque; 50% involve the head and neck, 40% the extremities, and 10% the trunk.

MCC is aggressive, with radial spread, high local recurrence, and regional and systemic metastasis.

Treatment involves local excision with wide (up to 3 cm) margins; SLN biopsy, and postoperative radiation started several weeks later.

Poor prognosis; 50% survival at five years.



The End

THANK YOU FOR LISTENING