Skin Tumors

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Skin embryology

A. Epidermis: Ectoderm

B. Dermis: Mesoderm

C. Other cells

1. Melanocytes: Neural crest
2. Merkel cells: Neural cells
3. Langerhans cells: Mesenchymal

Skin histology

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

هل ال langerhans cells بصير فيها tumors ؟؟

No

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

Skin malignancies

A. Generally grouped into three types (listed from most common to least)

B. Basal cell carcinoma (BCC)

C. Squamous cell carcinoma (SCC)

D. Melanoma

E.Merkel Cell Carcinoma

Basal Cell Carcinoma (BCC)
(rodent ulcer)

Rodent ulcer = BCC الإسم الثاني لل
Why? Bcz most of BCC types can get ulcer
*Rodent ulcer> morphological classification

Incidence

Basal cell carcinoma represents the most common tumor diagnosed in the United States,with an estimated one million new cases occurring each year. and the nodular variant is the most common subtype.

- **Epidemiology**

the most common form of skin cancer in white people. It occurs usually in elderly subjects, in males twice as commonly as in females

- The strongest predisposing factor to BCC is ultraviolet radiation.
- It occurs in the middle aged or elderly with 90 per cent of lesions found on the face

Risk factors

1. Sun exposure (increased with lower latitudes, high altitude): 36% of BCCs originate from the area of previously diagnosed actinic keratosis (AKs), but have distinct cells of origin.

2. Advancing age

3. Fair complexion

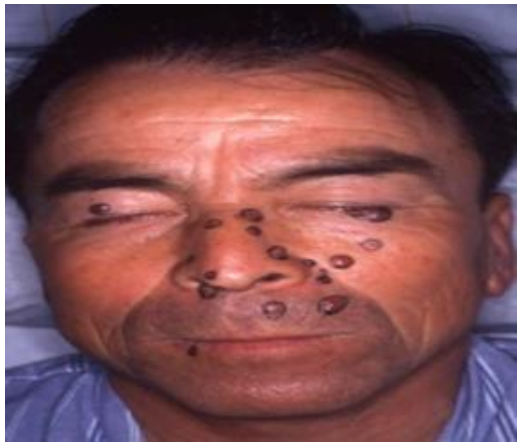
4. Long-term exposure to psoralens and UVA therapy (i.e., PUVA therapy forpsoriasis)

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–hairbearing raised mass. They are usually present at birth or develop in early childhood, and approximately 15% undergo malignant transformation to BCC.

7. Arsenic exposure

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

BCC disease biology and characteristics

A. Basal keratinocytes are the cell of origin, residing in the basal layer of the Epidermis at the dermoepidermal junction.

C. BCC is most common in areas with high concentrations of pilosebaceous follicles and thus **>90%** are found on the **head** and **neck** , above a line from the lobe of the ear to the corner of the mouth.

D. Metastasis is **rare**—termed “barely a cancer” by some researchers

E. Morbidity is caused by invasion of the tumor into underlying structures, including the sinuses, orbit, and brain. Typically, only a problem if neglected for many years.

BCC divided into 4 types (pathological classification):
1.Nodular

Pathology

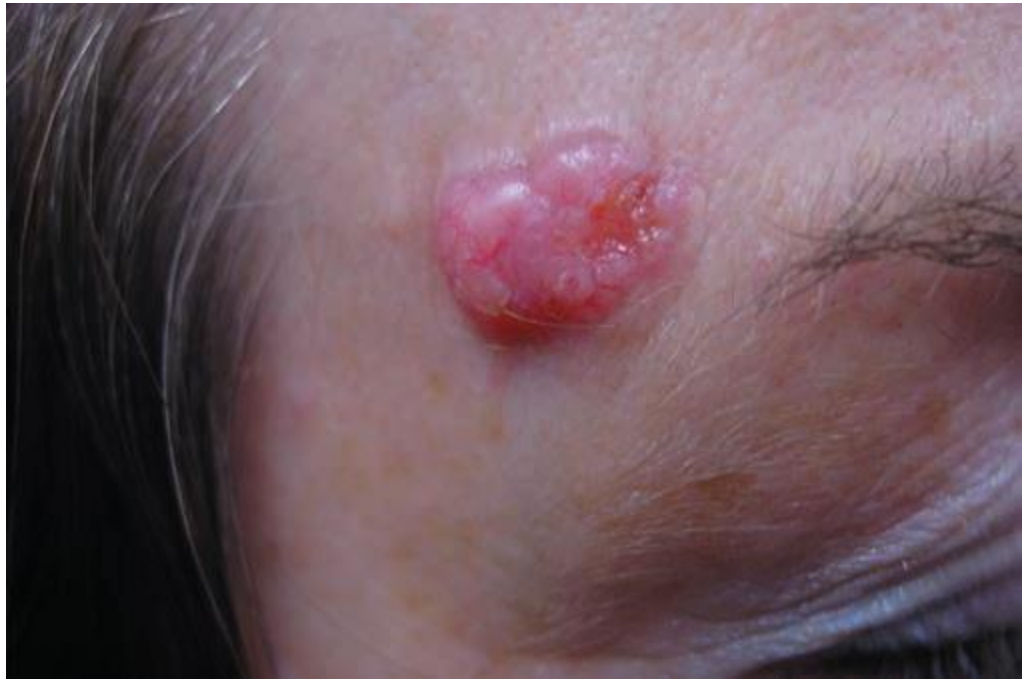
2.pigmented
3.scaring
4.superficial spreading

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)

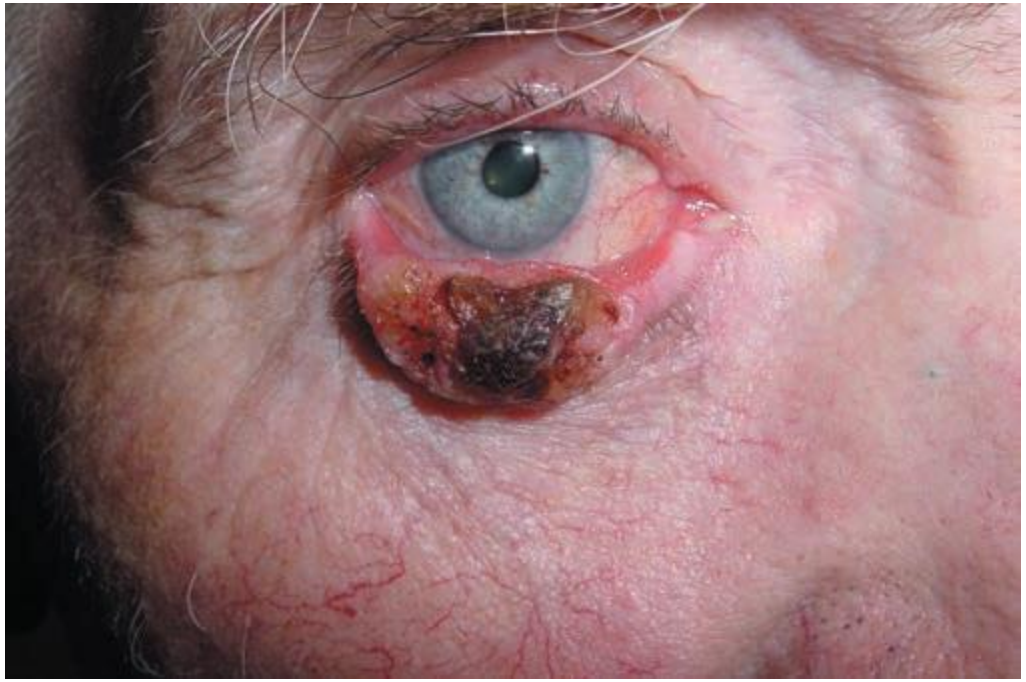
BCC can be divided into localised ***(nodular, nodulocystic , cystic, *pigmented and naevoid)** and generalised lesions. These lesions can be **superficial (multifocal or superficial spreading) or infiltrative (*morphoeic, ice pick and cicatrising)**

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

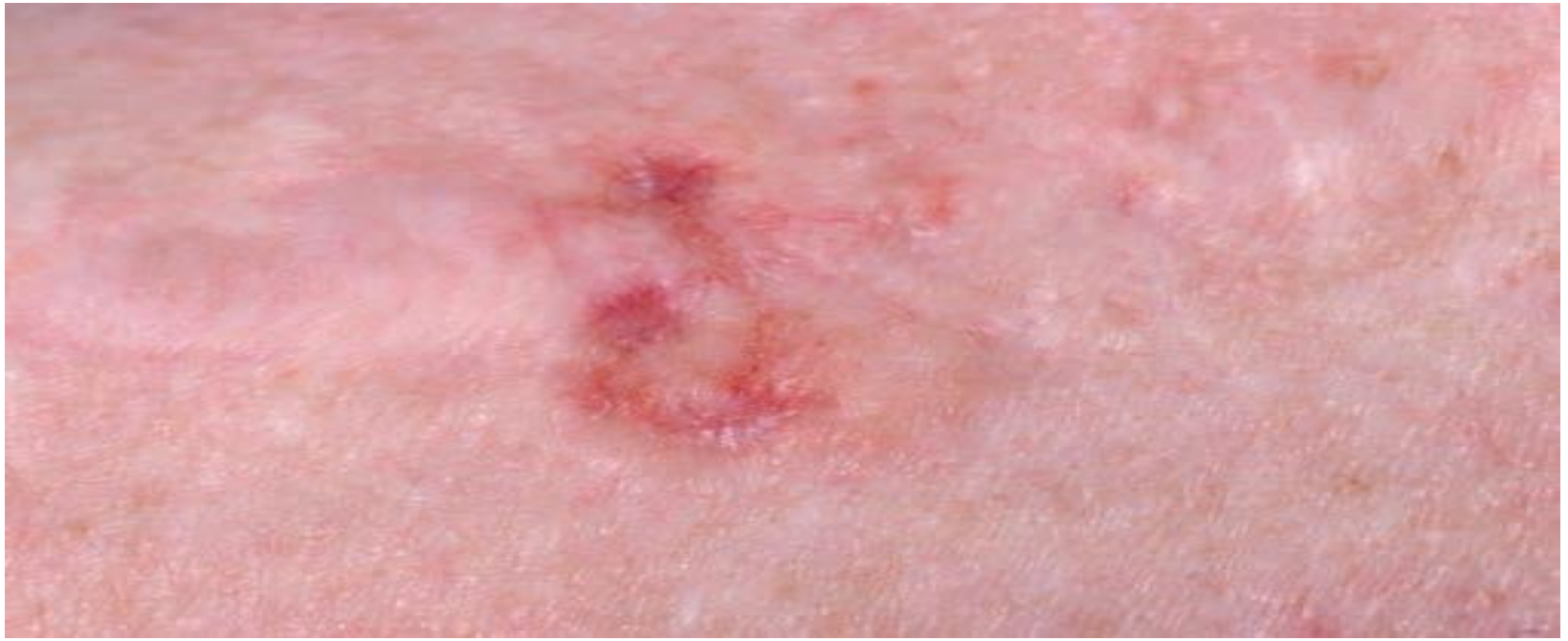
- **(definite dx is by histopathology**



A nodulocystic basal carcinoma (BCC). Note the characteristic pearly papules with telangectasia



*An ulcerating BCC on the lower eyelid.



A recurrent morphoeic 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 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.

For cosmetic causes

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.

2.
Squamous cell carcinoma

- Second most common skin cancer after BCC.
- It is strongly related to cumulative sun exposure, especially in white people, it is more common in men than in women.
- It is a malignant tumor, has direct, blood and lymphatic spread.

Risk factors :

1. UV radiation: Sun exposure and tanning booth use, PUVA therapy for psoriasis.
2. chronic inflammation (burns, pressure ulcers, chronic sinus tracts, pre-existing scars, osteomyelitis,)

Marjolin's ulcer: SCC arising in a chronic wound

3. Viral infection: Some types of human papillomavirus (HPV16,18); herpes simplex virus...especially in oral cavity
4. Chemical carcinogens: such as coal tar, and arsenic .
5. Radiation : Ionizing R
6. Immunosuppression : HIV
7. Genetic predisposition : albinisim, xeroderma pigmentosum.
8. smoking.

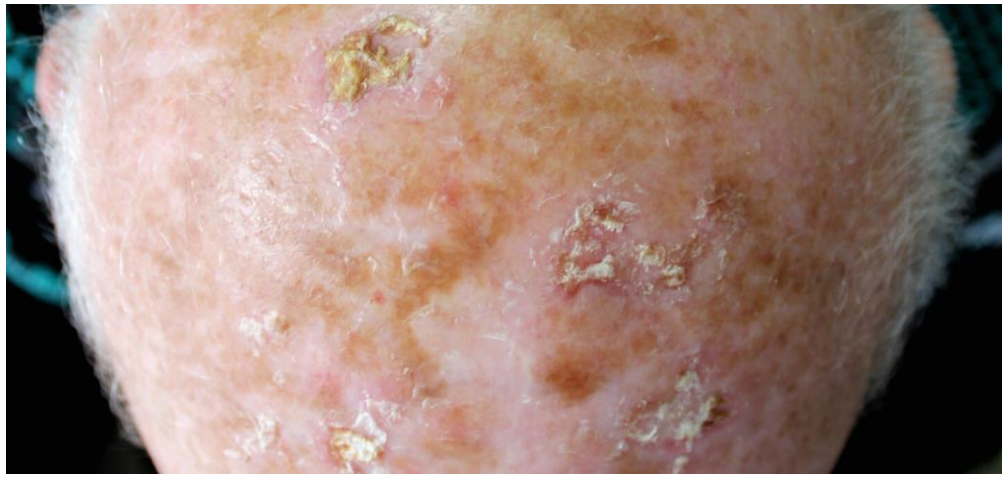
Variants of SCC

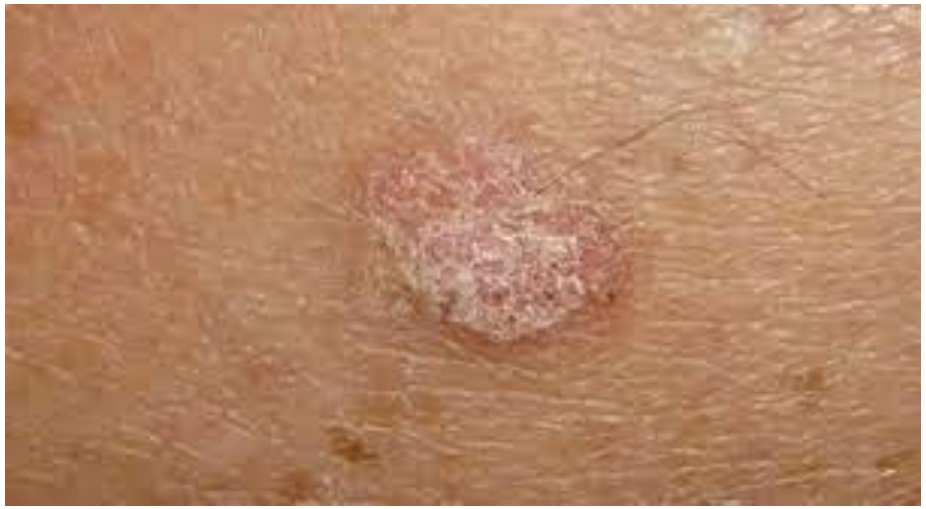
1. Actinic keratoses (AKs, or solar keratoses)

- The most common in situ variant of SCC is actinic keratosis

Erythematous macules and papules with coarse, adherent scale and seen in sun exposed areas especially the face, forearms, dorsa of hands, lower legs and bald scalp.

- Histologically resembles SCC (biopsy needed for diagnostic confirmation)
- It is estimated that approximately 10% of actinic keratoses will transform into invasive squamous cell carcinoma, in turn, 60-65% of all SCC arise from sites of Aks





2. Bowen’s disease (SCC in situ)

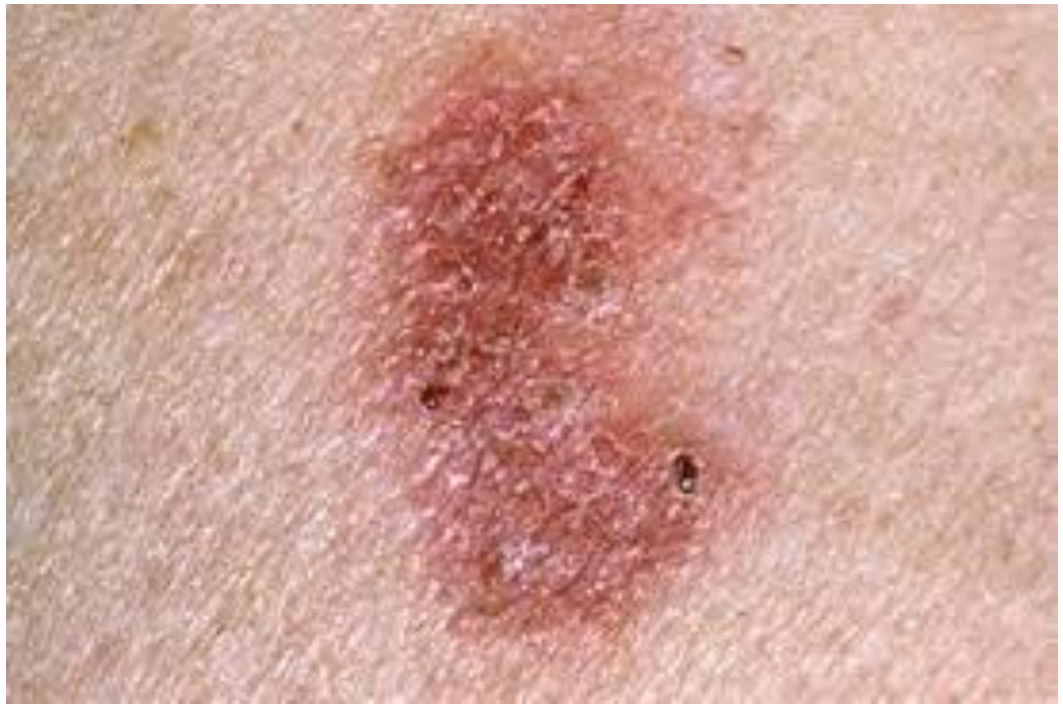
Consederd beginning of SCC

Bowen’s disease is an SCC confined to the epidermis, and is common below the knees in elderly women

Exhibits full-thickness cytologic atypia of the keratinocytes

Usually, a solitary patch of red scaly skin, although multiple areas may occur;

Bowen’s disease is asymptomatic .



3. Marjolin’s ulcer

- SCC arising in areas of chronic wounds (burn, pressure ulcer, fistula, osteomyelitis tracks) are known as Marjolin’s ulcers.
- Commonly metastasize to lymph nodes.
-The period between the initial injury and the development of marjolin’s ulcer is 10 - 25 year .(acute majorline ulcer is extremely rare)

Ulcer in post burned lesion

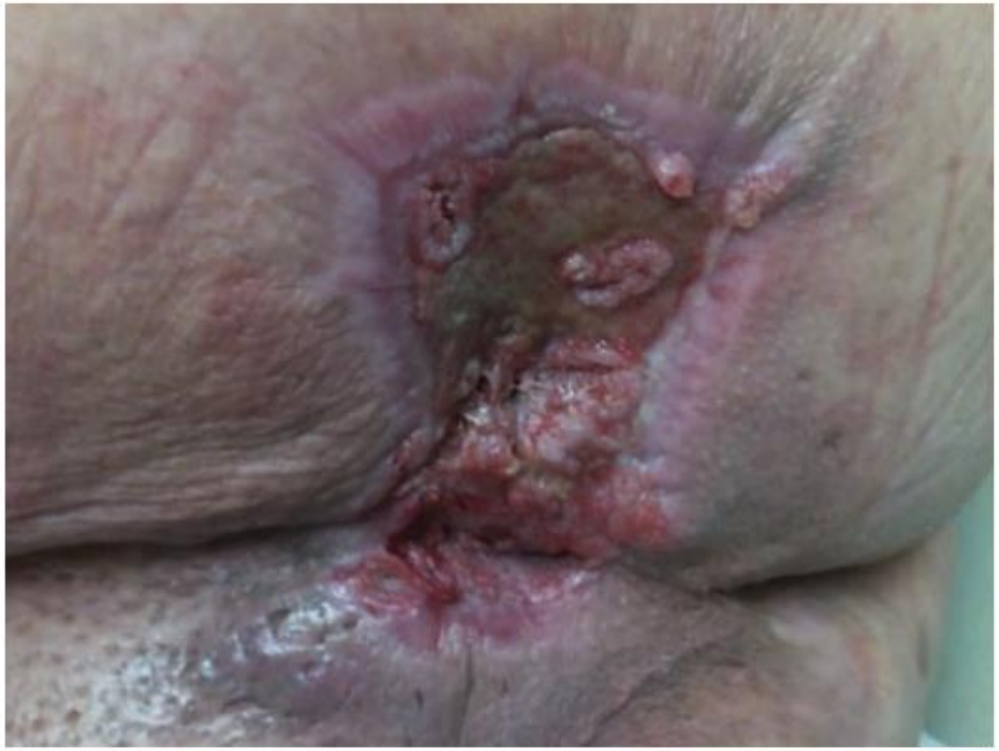
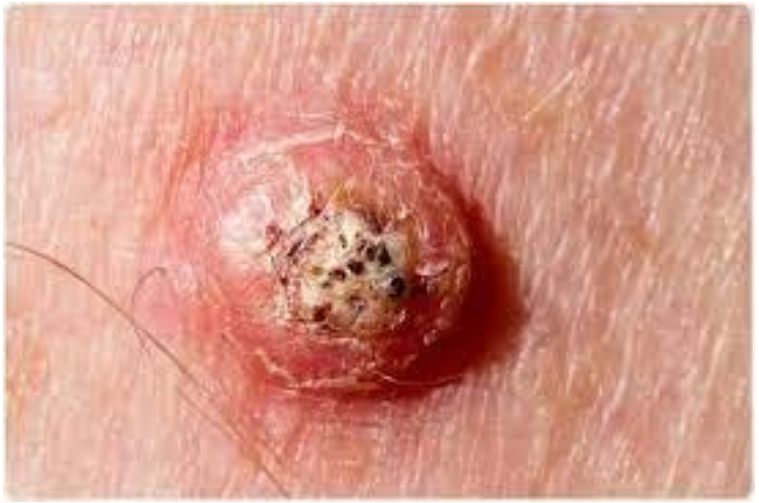


Figure 16-9. Squamous cell carcinoma forming in a chronic wound.

4. Keratoacanthoma

- It is now being accepted as a subtype of SCC that is characterized by a rapidly growing nodule with a central keratin plug.
- usually found on the face or limbs of chronically sun-damaged 50- to 70-year-old white-skinned individuals
- Etiology is unknown but they may be caused by HPV in a hair follicle during the growth phase and are also associated with smoking and chemical carcinogen exposure
-Typically has a rapid 6-week growth phase followed by involution over the next 6 months. However, can progress to SCC in 5% to 10% of cases.

Tx :excision

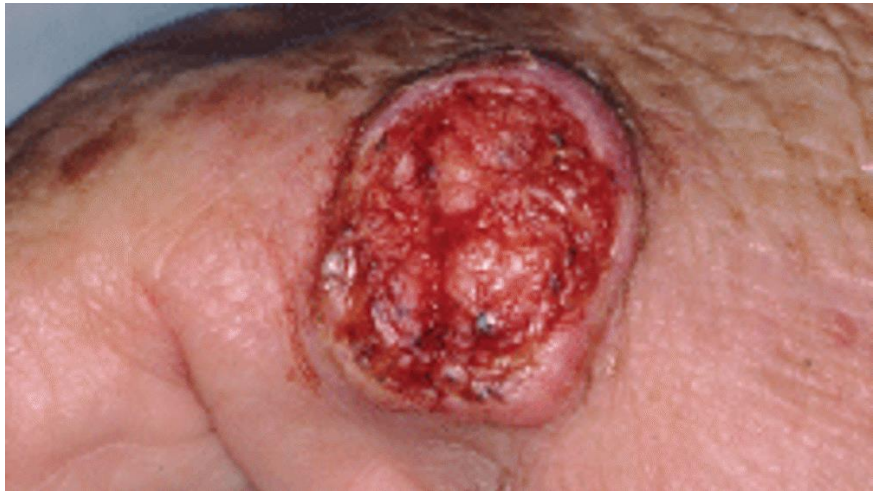


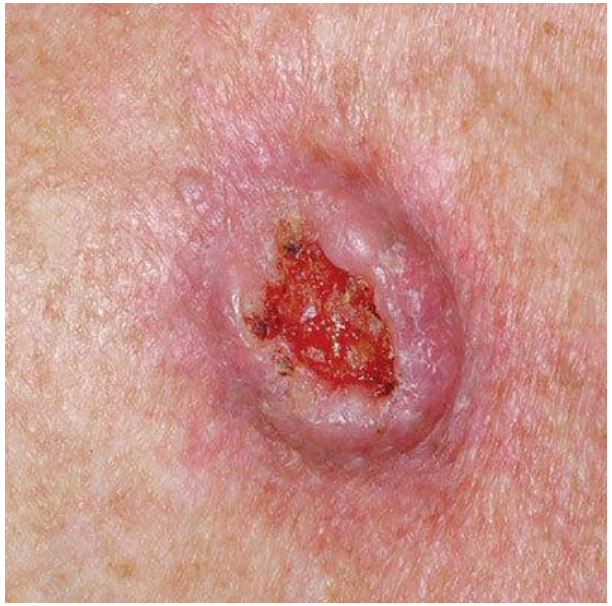
Macroscopically:
The appearance of SCC may vary from smooth nodular, verrucous, papillomatous to ulcerating lesions. All ulcerate eventually as they grow. The ulcers have a characteristic everted edge and are surrounded by inflamed, indurated skin.

Ulcerative scc (most common)

- Grows rapidly and is locally invasive.
- Has very aggressive growth, raised borders, and central ulceration.
- <50% 5-year survival if spread to lymph nodes in the head and neck

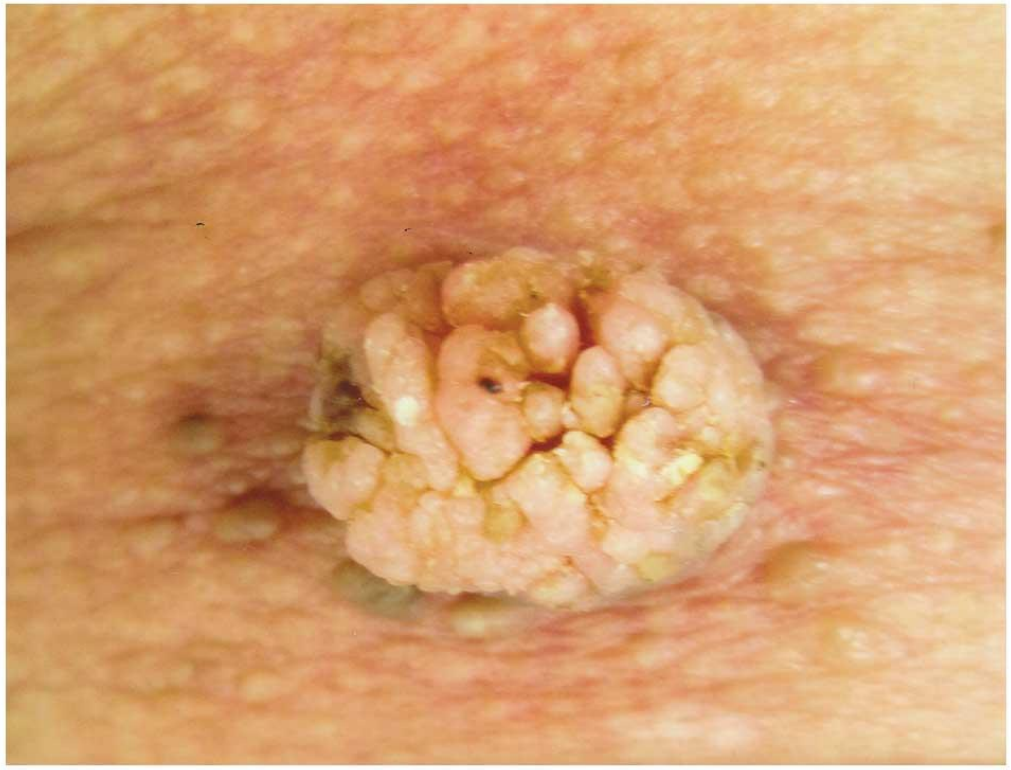
SCCs arising spontaneously (de novo) begin as small nodules on the skin. As they enlarge, the center becomes necrotic, sloughs, and the nodule turns into an ulcer.

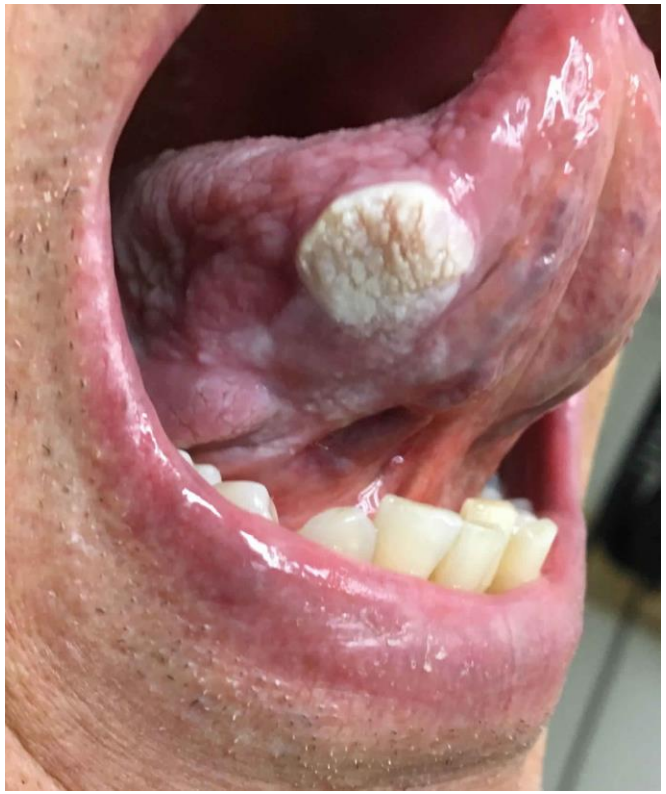




Verrucous scc

Slow-growing, exophytic, and less likely to metastasize.
The most frequently affected site is the oral cavity.





Prognosis

There are several independent prognostic variables for SCC:

1 Invasion:

a. Depth: the deeper the lesion, the worse the prognosis. For SCC <2 mm, metastasis is highly unlikely; whereas if >6 mm, 15 per cent of SCCs will have metastasised.

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 Aetiology: SCCs that arise in burn scars, osteomyelitis skin sinuses, chronic ulcers and areas of skin that have been irra- diated have a higher metastatic potential.

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

6 Microscopic invasion of lymphovascular spaces or nerve tissue carries a high risk of metastatic disease.

The overall rate of metastasis is 2 per cent for SCC – usually to regional nodes –

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 <2 cm;

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

- 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.)

Field therapies بسموه Photodynamic sensitized drugs or molecular targeted drugs
Why? Bcz the drugs targeted directly on lesion or molecules

3. Field therapies

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.

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.

Regional lymphadenectomy

1. Indicated for clinically positive (palpable) nodes.
2. FNA: Confirm spread of SCC to palpable lymph node.
3. ELND: Indicated for a tumor extending down to parotid capsule or a large lesion contiguous with a 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 postexcision for high-risk cutaneous SCC.

3
Melanoma

Least common ,most aggressive

Risk factor

1. 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 melanoma

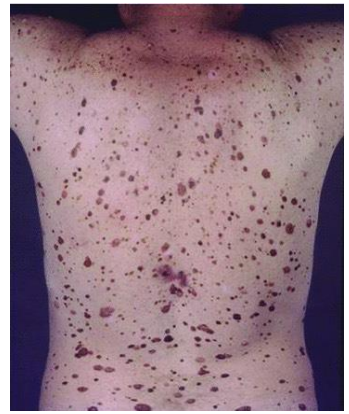
Family history: Vast majority of melanomas are sporadic; however, some hereditary forms exist

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.

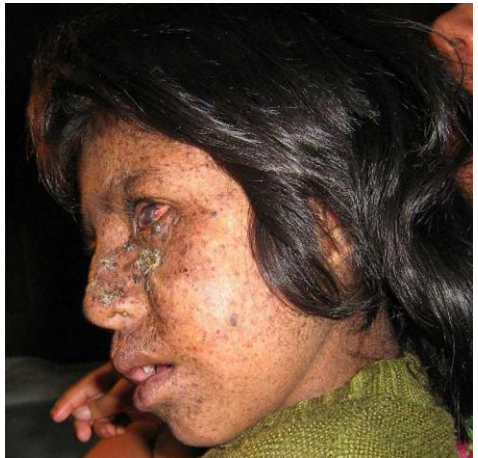


c. Xeroderma pigmentosum (XP)

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.



Precursor lesion

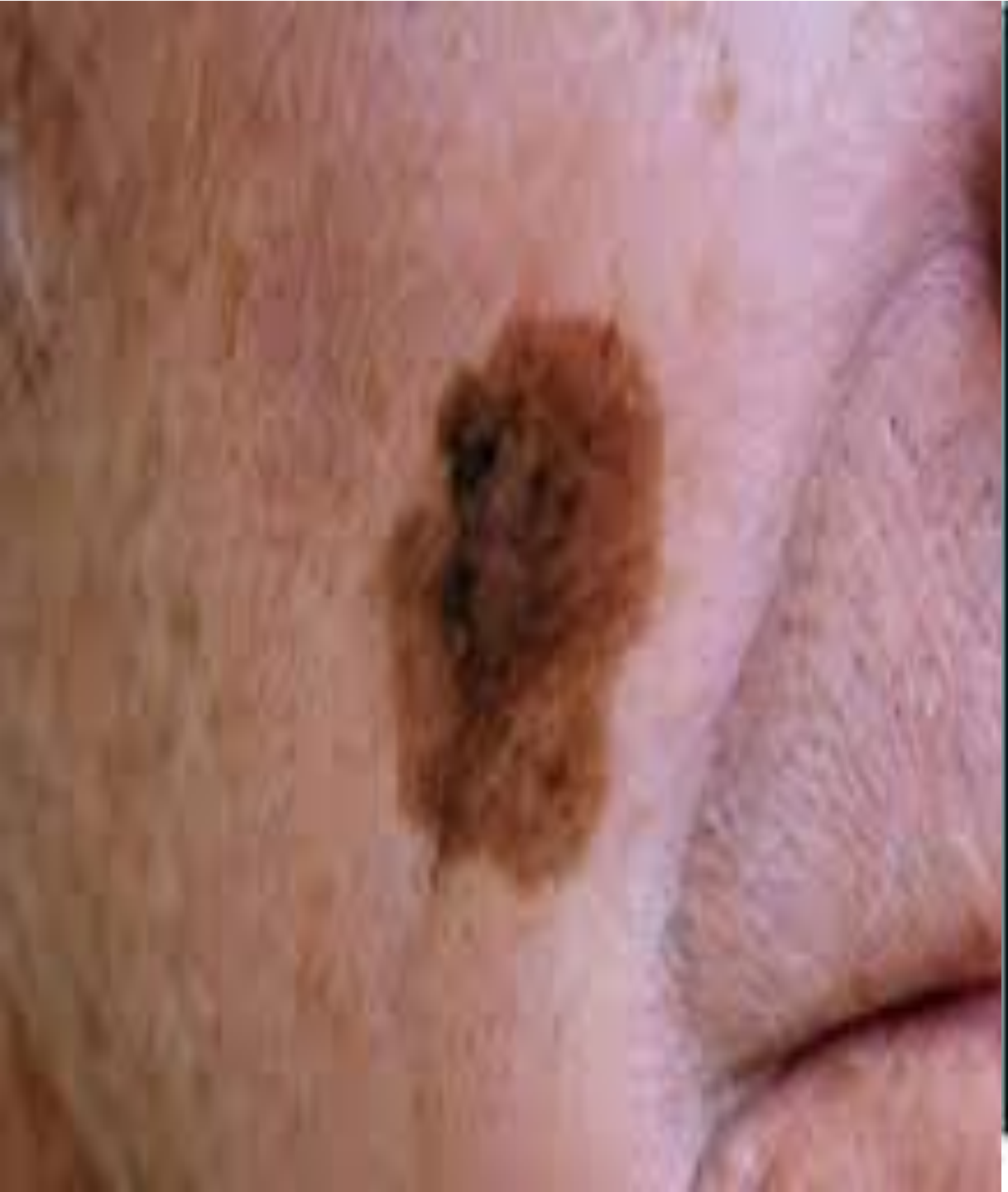
1- Congenital nevi

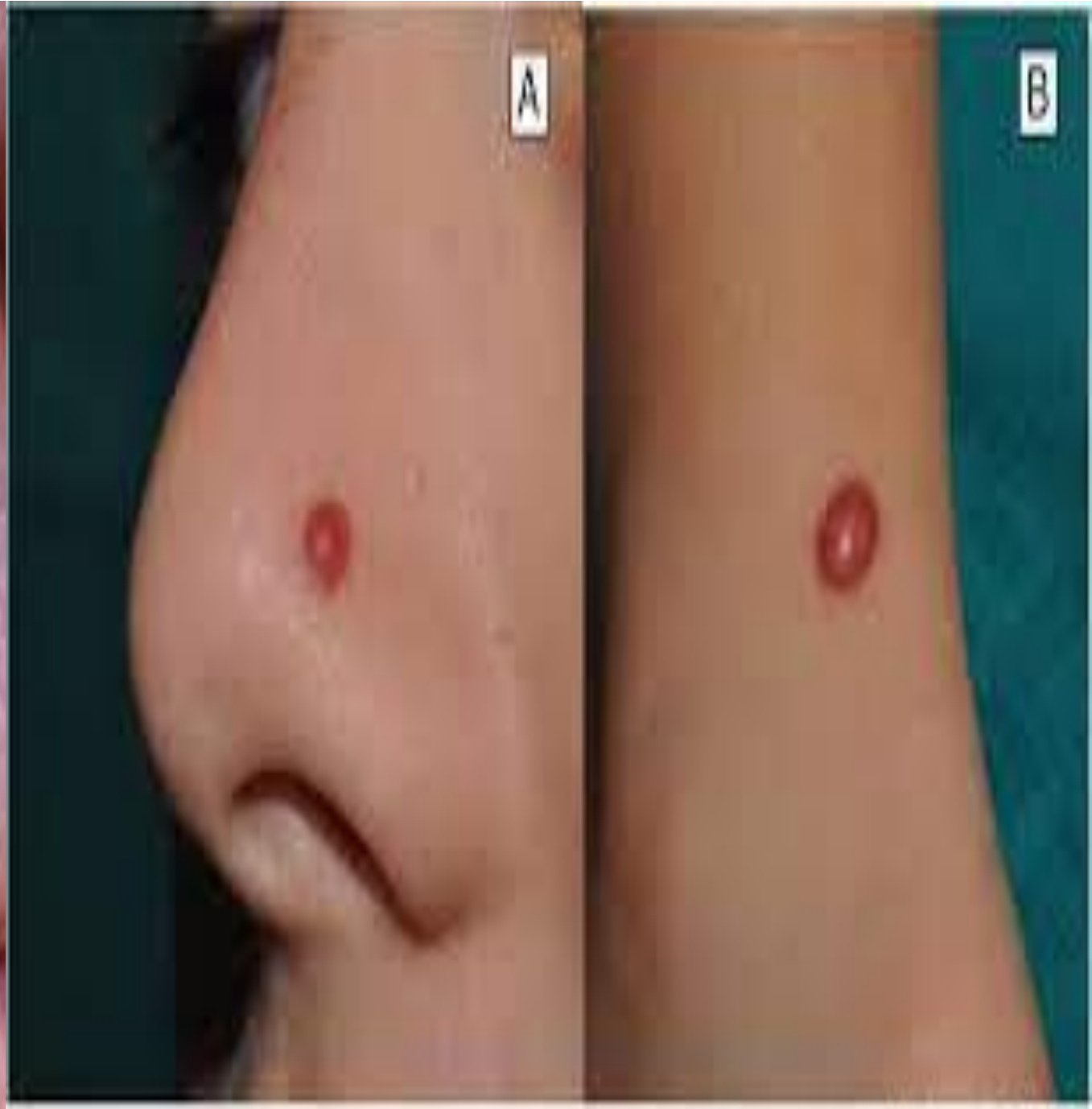
2-acquired melanocytic nevi

3-dysplastic atypical nevi

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

5- Spitz nevus




A
B

Spitz nevus

In situ

genetic basis of melanoma?

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

Signs of melanoma

ABCD signs

Asymmetry	Are the halves of each spot different?	
Border	Are the edges uneven, scalloped or notched?	
Colour	Are there differing shades and colour patches?	
Diameter	Is the spot greater than 6 mm across, or is it smaller than 6 mm but growing larger?	

EFG signs

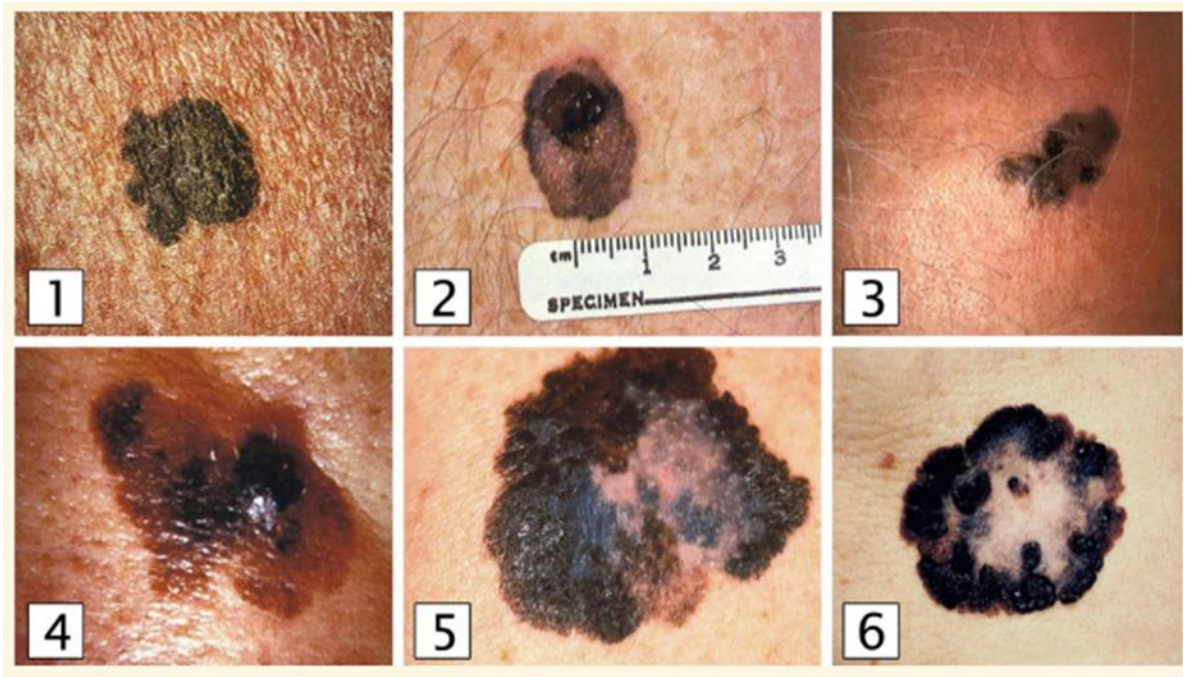
Some types of melanoma, such as nodular and desmoplastic melanomas (see page 12), don't fit the ABCD guidelines.

Elevated	Is it raised?	
Firm	Is it firm to touch?	
Growing	Is it growing quickly?	

Classification of melanoma types

1. Superficial spreading melanoma

- This accounts for 50% to 70% of melanomas and typically arises from a precursor melanocytic nevus.
- Affects both genders equally
- . Median age at diagnosis is 50 years
- Upper back in men and lower legs in women are most common sites
- Radial growth phase early, vertical growth phase late



Superficial spreading melanoma can have a variable presentation. According to the ABCDE criteria, these include irregular margins and subtle asymmetry (image 1). In images 2–6, prominent findings are irregular pigmentation and an expanding lesion.

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

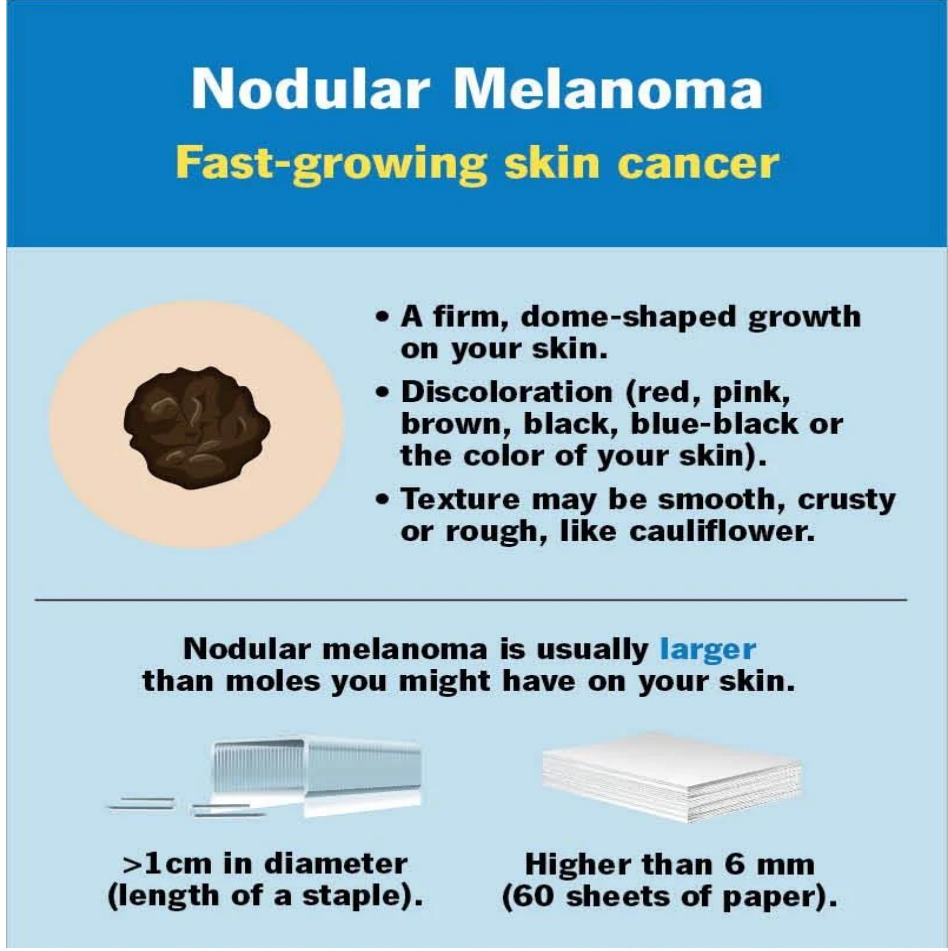
No clear association with sunlight exposure

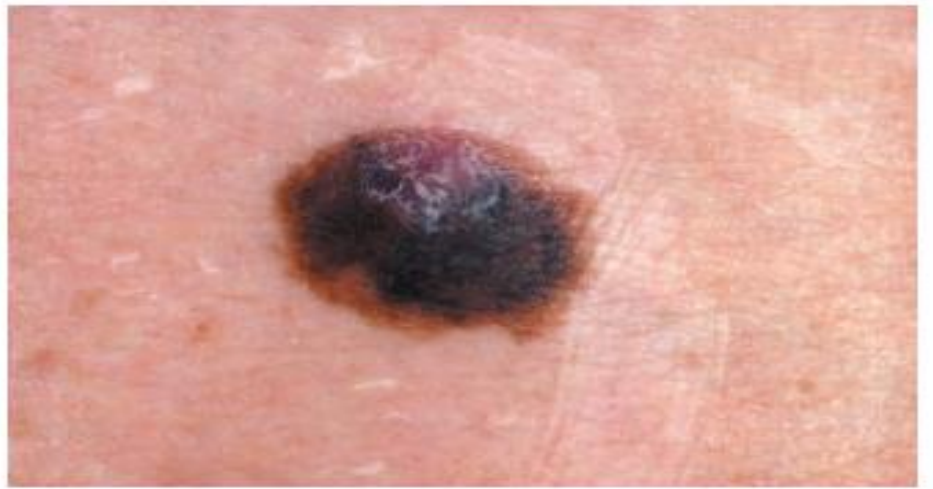
Resemble blood blisters or other non-cancerous lesions

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.

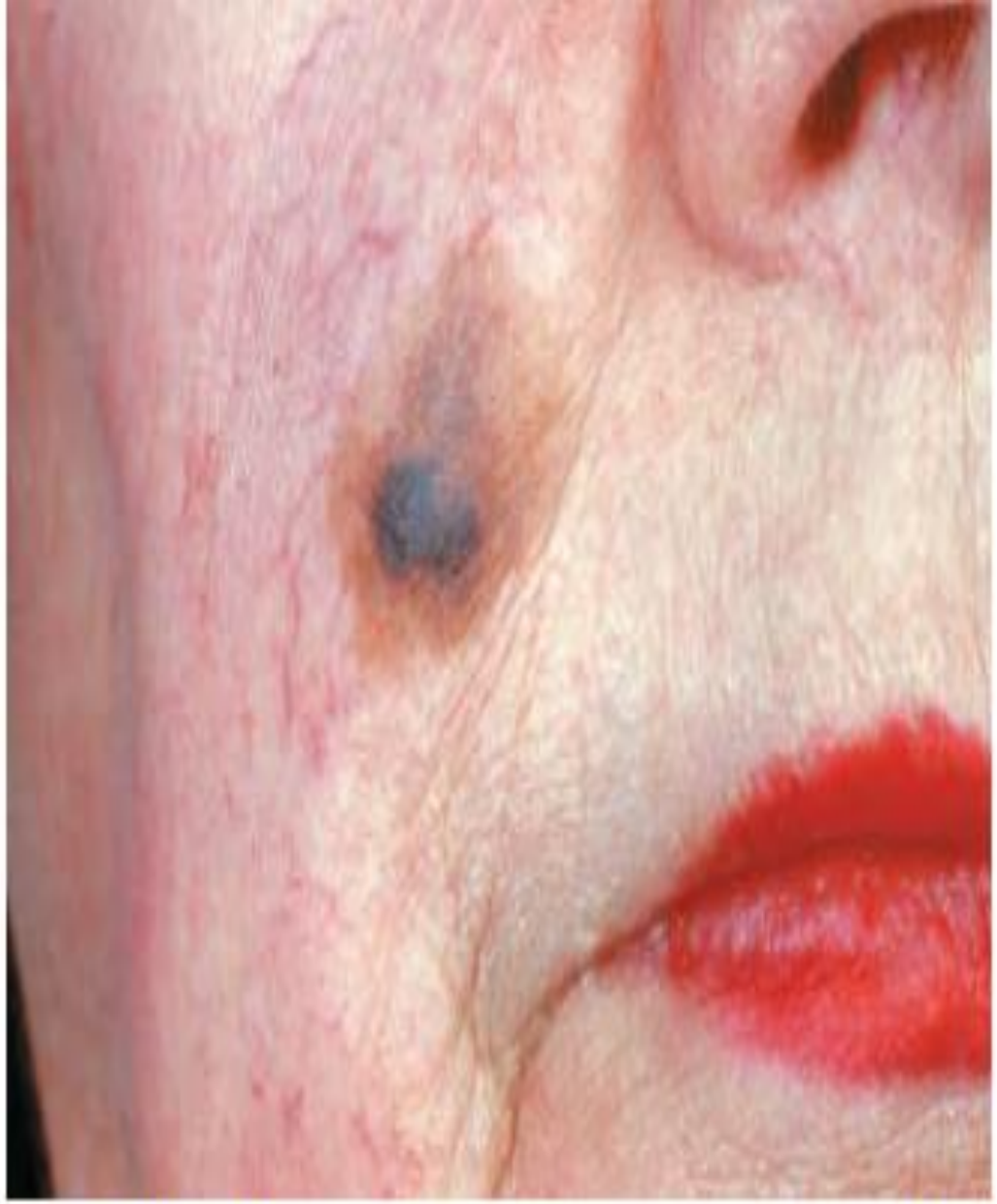


Figure 40.39 Lentigo maligna melanoma (courtesy of St John's Institute for Dermatology, London, UK).

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.

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

e. Most common site is great toe or thumb

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

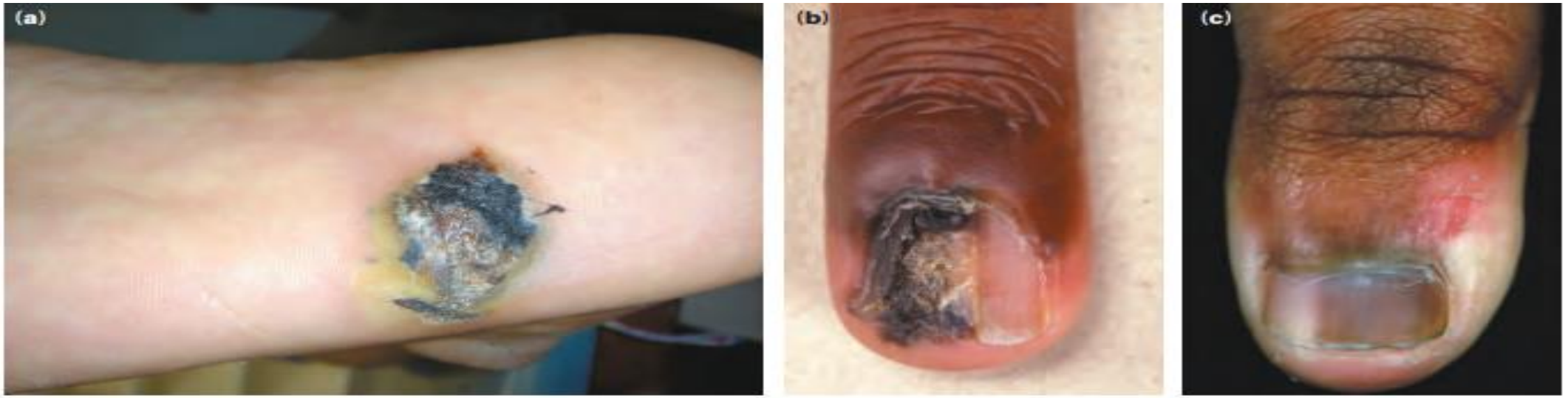


Figure 40.40 (a) Acral lentiginous melanoma on the sole of the foot (courtesy of Mr AR Greenbaum). (b) Subungual melanoma – probably a superficial spreading melanoma. Note the swelling proximal to the nail fold. (c) Benign racial melanonychia. ((b) and (c) courtesy of St John's Institute for Dermatology, London, UK.)

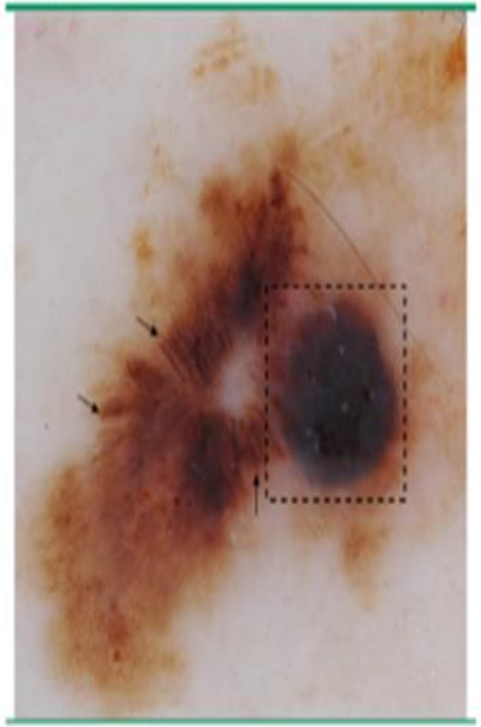
Superficial spreading - early radial growth (great prognosis) (1

Lentigo maligna - radial growth (also good prognosis) (2

Nodular - early vertical growth (poor prognosis) (3

Acral lentiginous - arises on palms and toes, not associated with UV exposure (4

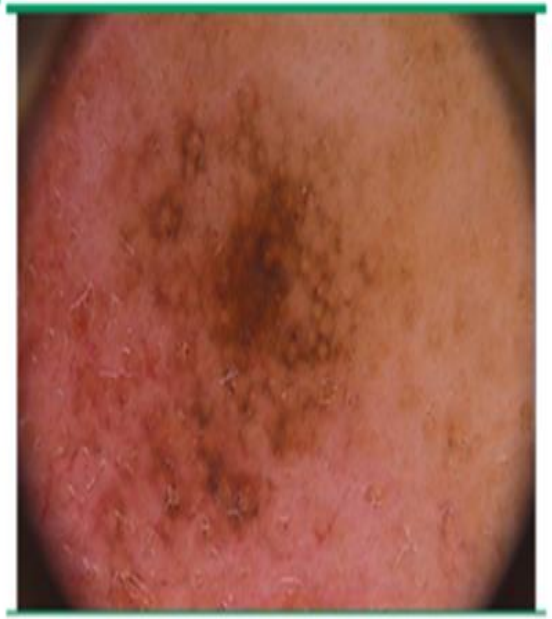
Dermoscopy of superficial spreading melanoma



Melanoma 0.90 mm. Atypical network, peripheral streaks (solid arrows), blue white-veil, and off-centered blotch (dashed square) are observed.

Malignant melanoma in situ, superficial spreading

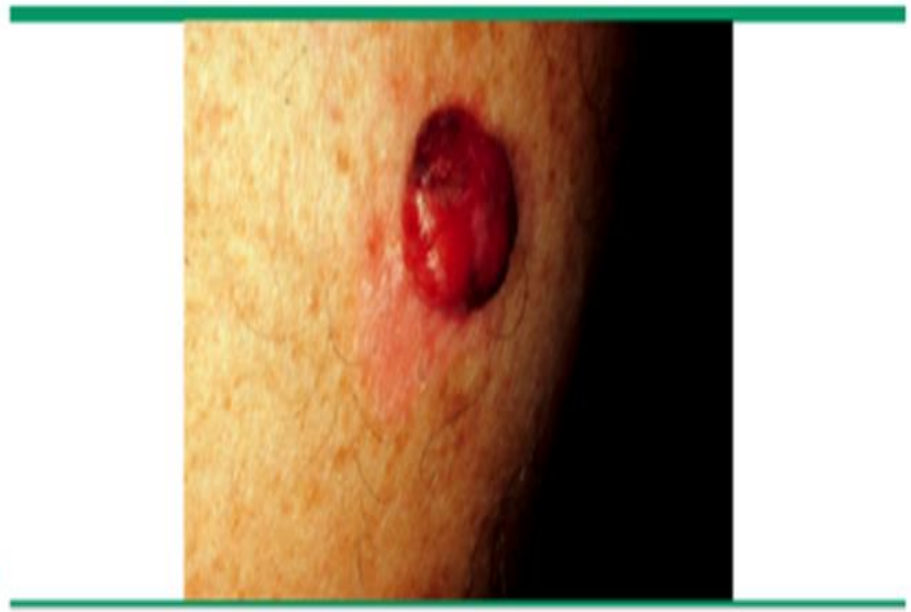
Dermoscopy of lentigo maligna melanoma



A 69-year-old woman was evaluated for an enlarging pigmented lesion of her right cheek. Two biopsies were performed with the help of dermoscopy to outline the borders of the lesion. Pathology revealed a lentigo maligna melanoma. On this dermoscopic image (x50), one can see slate-gray dots and globules leading to annular-granular pattern which is typical of lentigo maligna melanoma.

Lentigo maligna melanoma

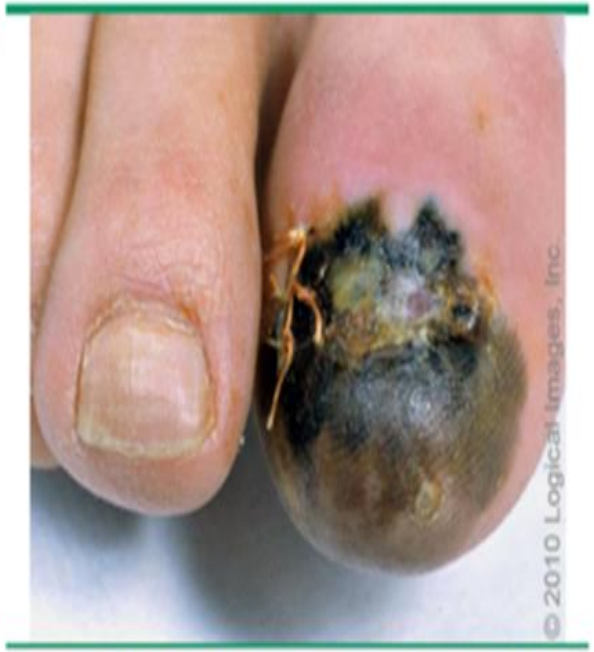
Nodular melanoma



Nodular melanomas present a discrete nodule, usually with dark pigmentation, although they may be amelanotic, as depicted above.

Nodular melanoma

Subungual acral lentiginous melanoma



Destruction of the nail bed by the tumor is present in this patient with subungual melanoma involving the toe. Note the presence of pigment involving the periungual skin (Hutchinson's sign).

Acral lentiginous melanoma

Diagnosis and staging of melanoma

A. 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 accurate and reproducible than Clark level and is a better prognostic indicator.

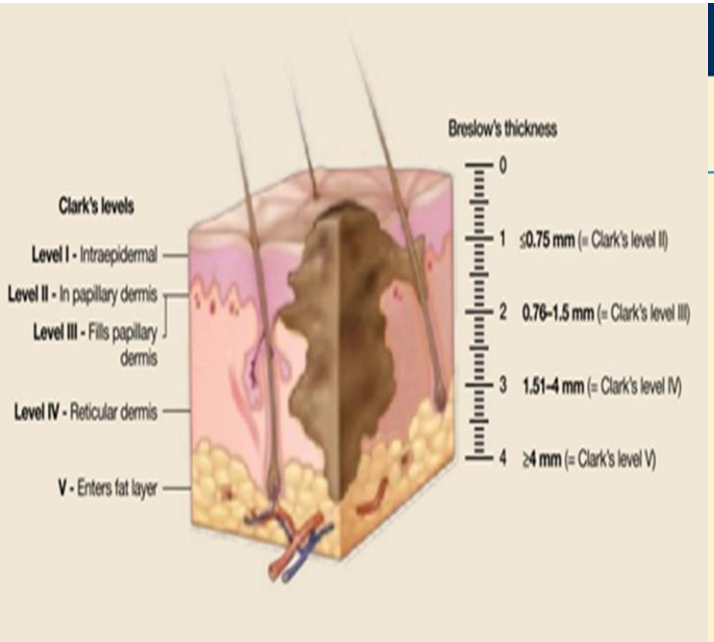


TABLE 13-3 Melanoma Thickness Grading

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

TABLE 13-4 AJCC Melanoma Staging System (1998)

TNM DEFINITIONS

Primary Tumor	
Tx	Unknown, cannot be assessed
T0	No evidence of primary tumor
Tis	Melanoma in situ (AJMH, Clark II)
T1	<0.75 mm (Clark II)
T2	0.76–1.50 mm (Clark III)
T3	1.51–4 mm (Clark IV)
T4	>4 mm or satellitosis within 2 cm of primary (Clark V)
Regional Lymph Node Involvement	
NX	Unknown, cannot be assessed
N0	Negative
N1	Metastasis 3 cm or less in greatest dimension in any regional lymph node(s)
N2	Metastasis >3 cm in greatest dimension in any regional lymph node(s) and/or in-transit metastasis
Distant Metastasis	
MX	Unknown, cannot be assessed
M0	No distinct metastasis
M1	Distant metastasis

STAGING

Stage 0	Tis, N0, M0
Stage I	T1, N0, M0 T2, N0, M0
Stage II	T3, N0, M0
Stage III	T4, N0, M0 Any T, N1, M0 Any T, N2, M0
Stage IV	Any T, Any N, M1

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.

TABLE 13-5 Recommended Surgical Margins for Melanoma Excision

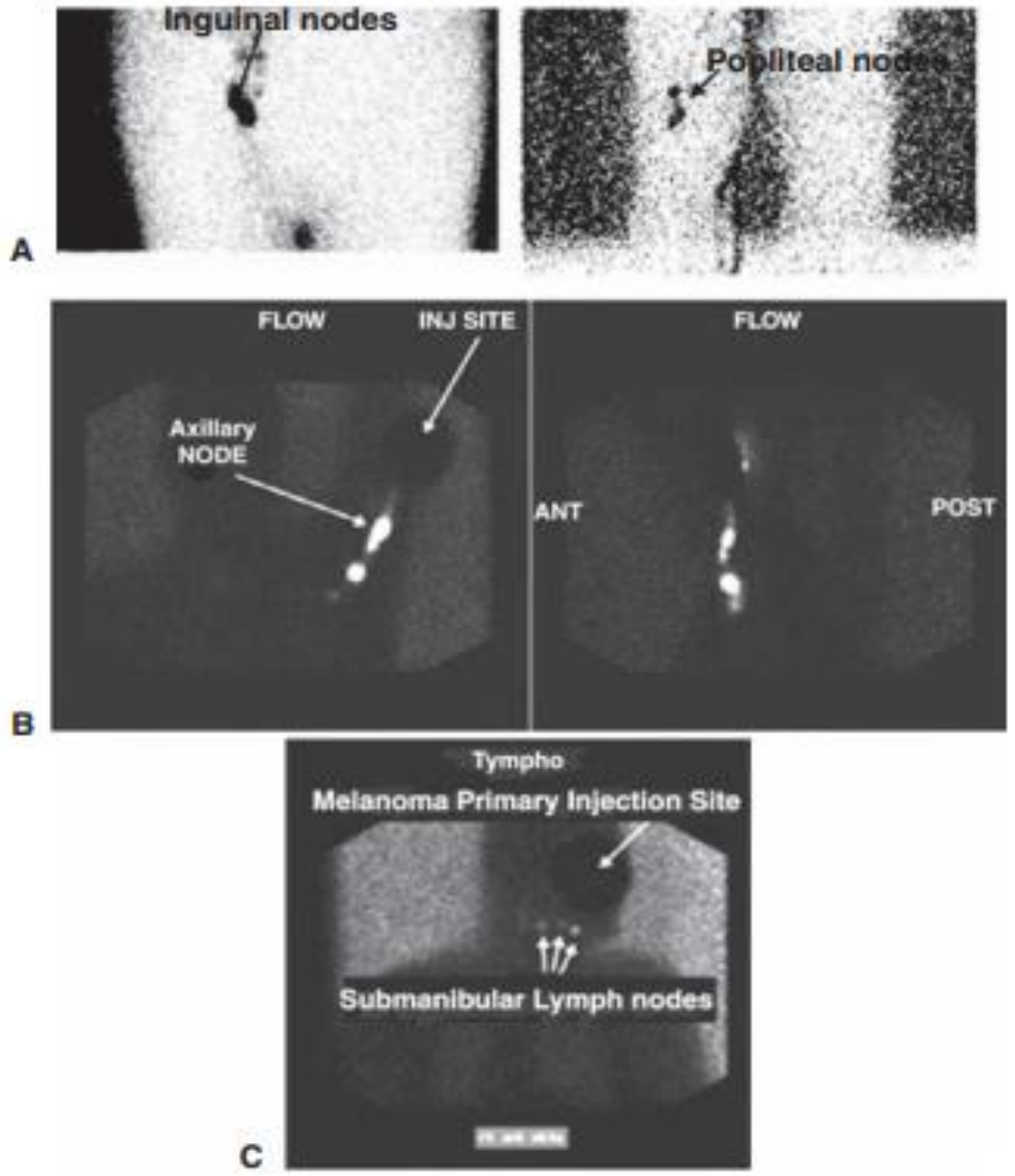
Melanoma thickness (mm)	Margin (cm)
In situ	0.5
<1	1
1–4	2
>4	2–3 (controversial)

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).



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.

i. 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.

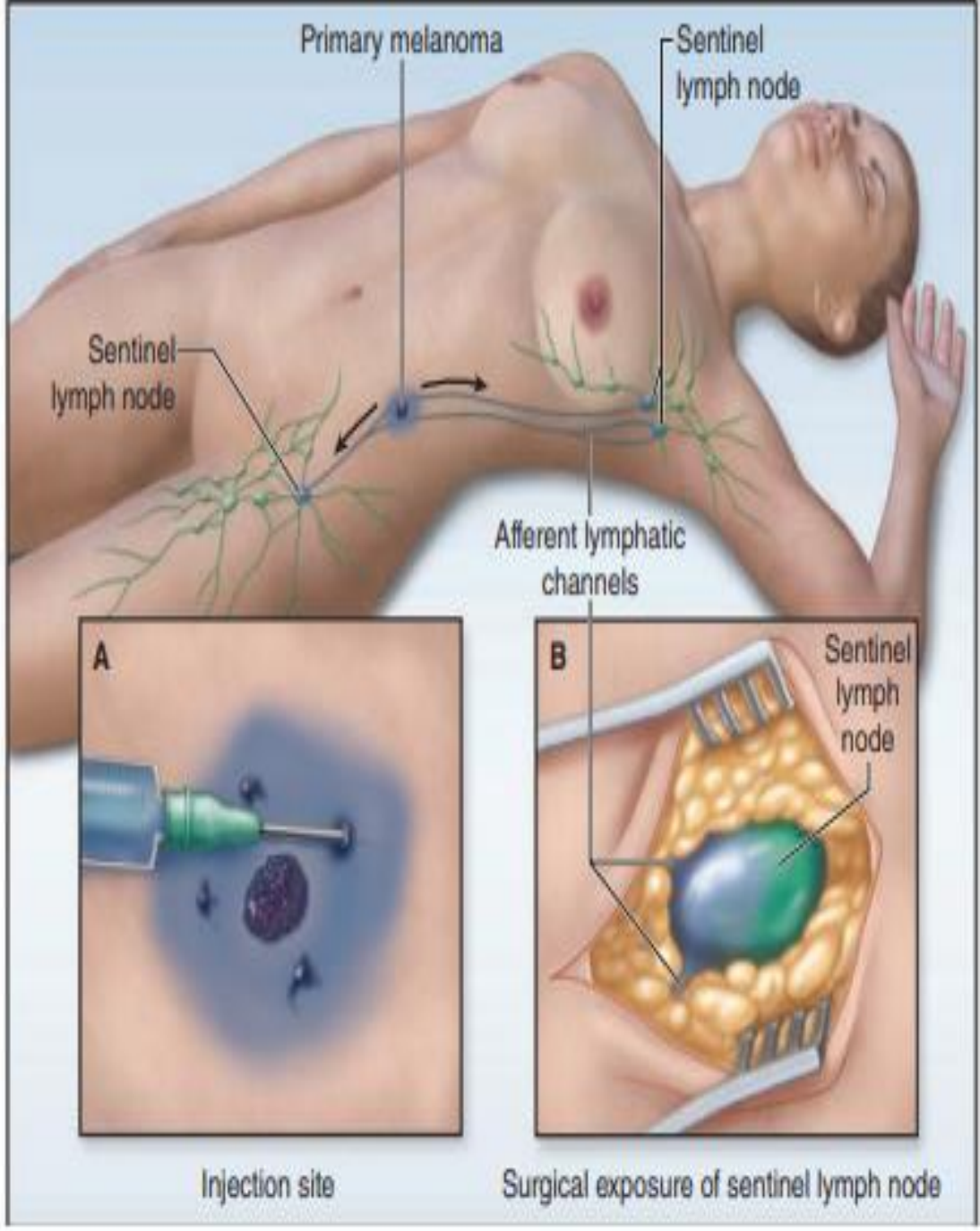
ii. Potential sentinel nodes will appear blue when exploring the nodal basin, giving secondary confirmation to localization with Geiger counter detection of Tc99.

iii. Dye injection may briefly interfere with pulse-oximeter readings; alert anesthesiologist at the time of injection.

iv. Caution: Risk of allergy or anaphylaxis with dye injection

f. Following excision of the primary tumor All radioactive ("hot") and/or blue nodes are excised.

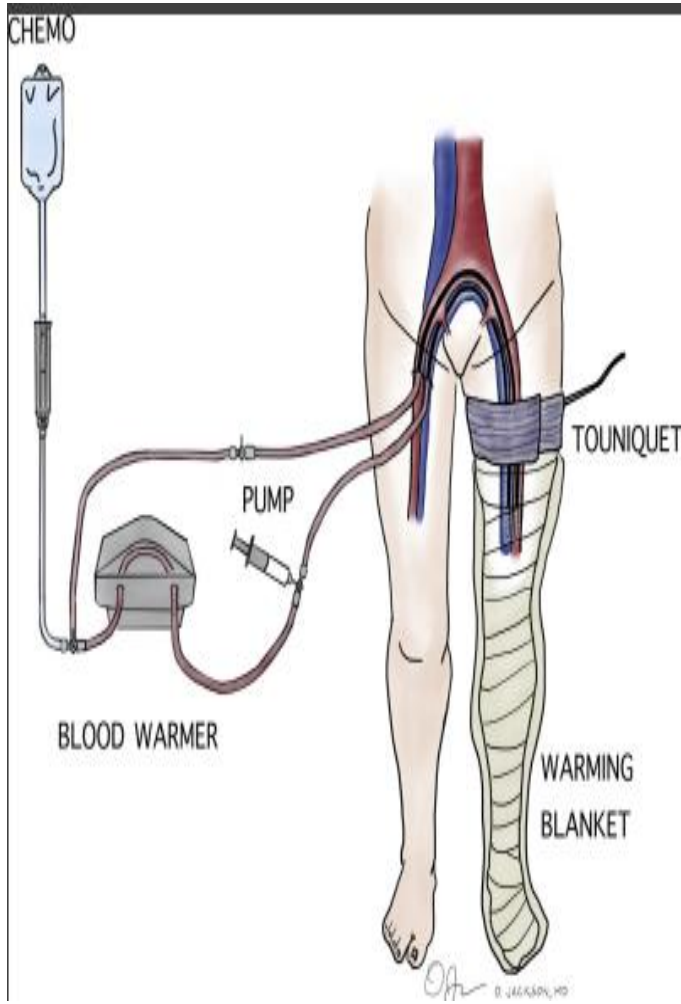
g. Histologic analysis of sentinel node with immunohistochemical staining identifies micrometastases. Permanent sections are required; frozen sections cannot reliably differentiate normal from neoplastic melanocytes.



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 interleukin-2 (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

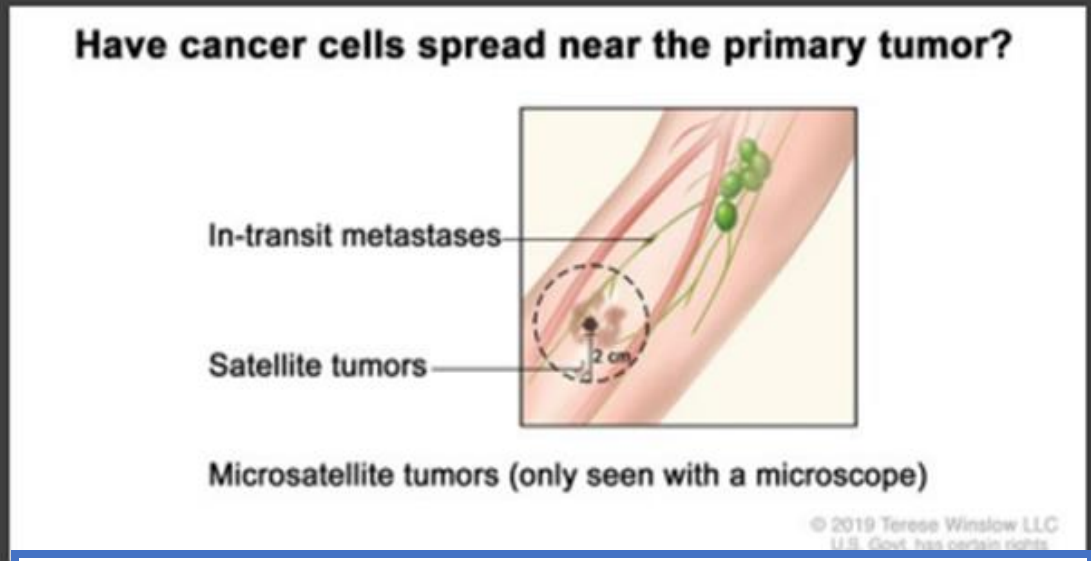
Drugs for NRAS and C-KIT mutations may be available through clinical trials

Vemurafenib

MECHANISM	Small molecule inhibitor of *BRAF* oncogene ⊕ melanoma. VEmuRAF-enib is for V600E-mutated *BRAF* inhibition.
CLINICAL USE	Metastatic melanoma.

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 complications are the most common causes of death

Less common skin cancers

Merkel cell (dermal mechanoreceptor) tumour This is an aggressive malignant tumour of Merkel cells and usually affects the elderly. 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.

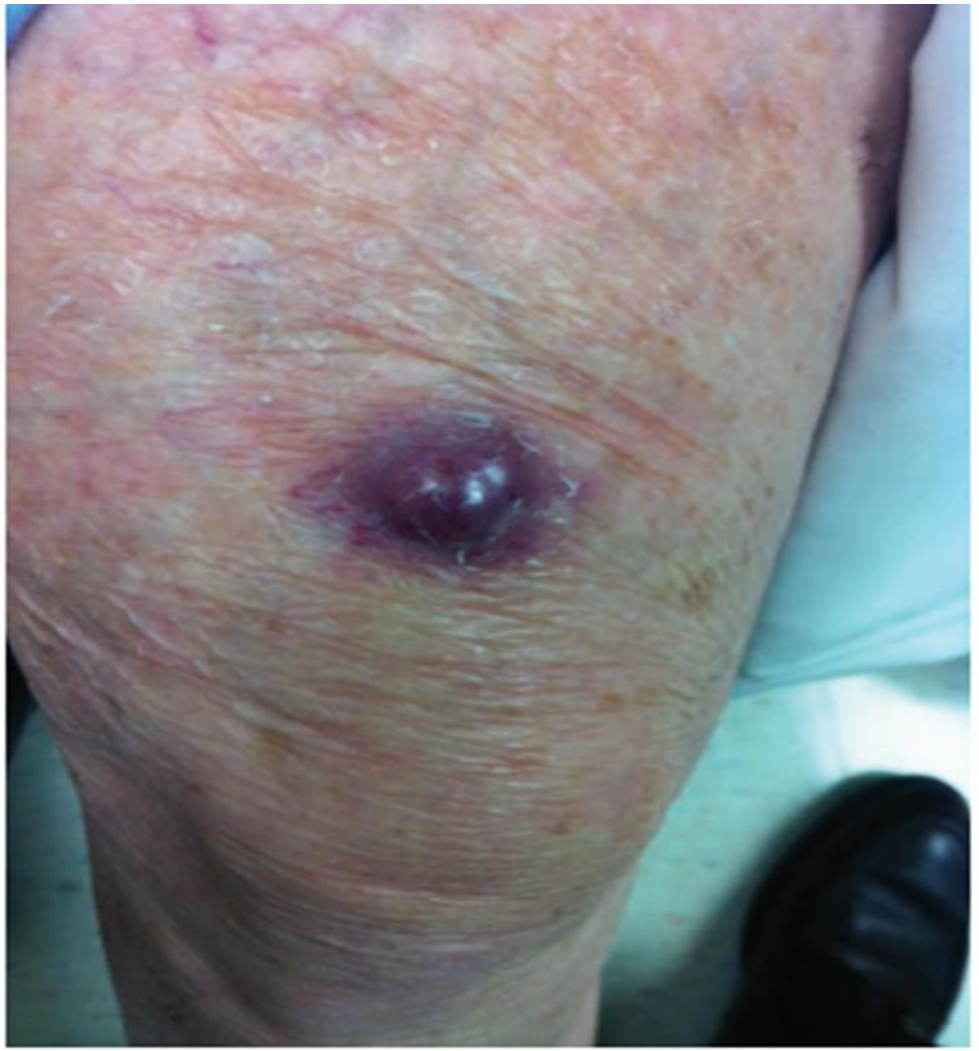


Figure 16-17. Merkel cell carcinoma seen just above the left knee in a 44-year-old female.

THANK YOU

Sources and references :

- Schwartz’s Principles of Surgery eleventh edition.
- Bailey & Love's Short Practice of Surgery
- uptodate
- Past material