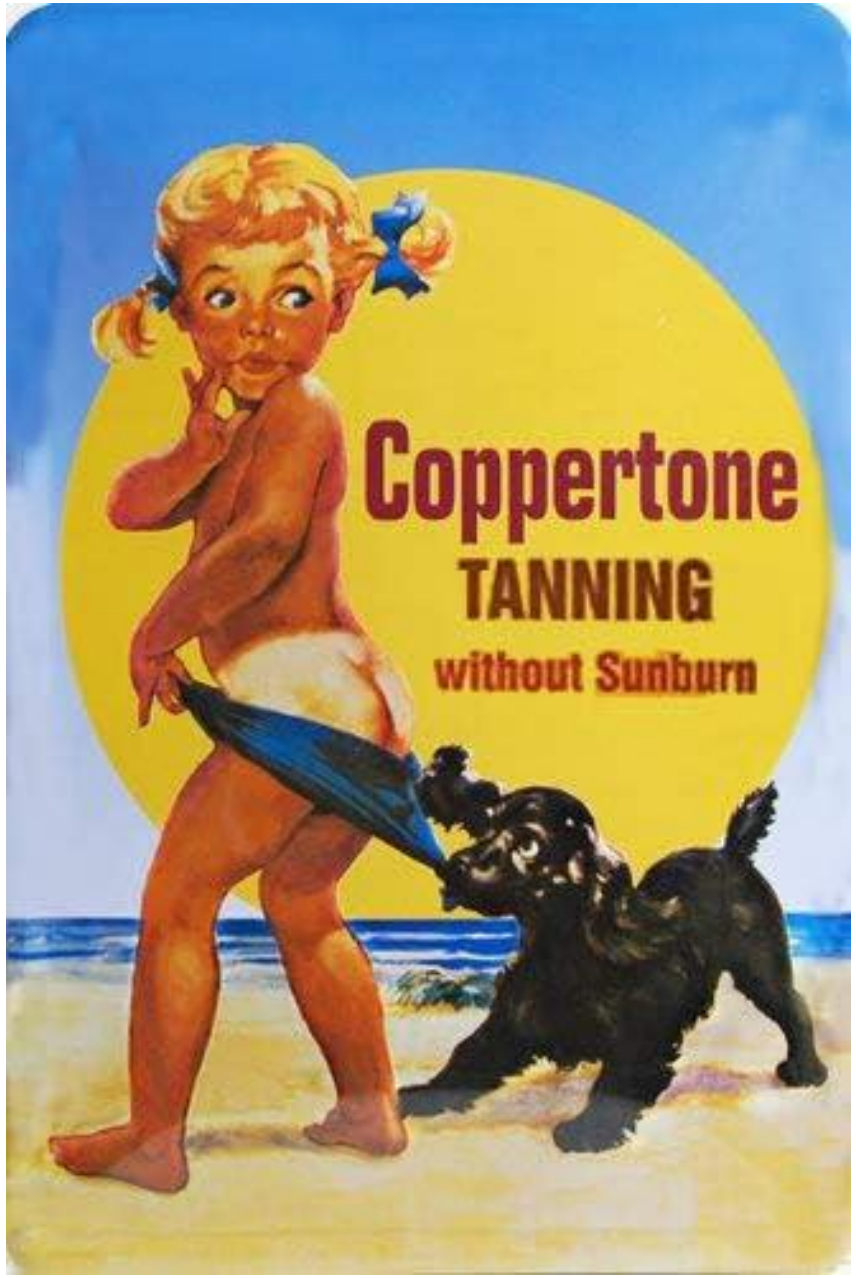

What the Coppertone Girl Didn't Know –Neoplasms

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Dermatology Nurse Practitioner, MA

Disclosures

Advisory Board

- Bristol Myers Squibb -Psoriasis
- Incite -Vitiligo
- JDNPPA -Dermatology
- UCB -Psoriasis

Speaker Panel

- American Association of Nurse Practitioners -Dermatology
- Dermatology Nurses' Association -Dermatology
- MauiDerm NP+PA -Dermatology
- Nurse Practitioner Association for Continuing Education -Dermatology

Objectives

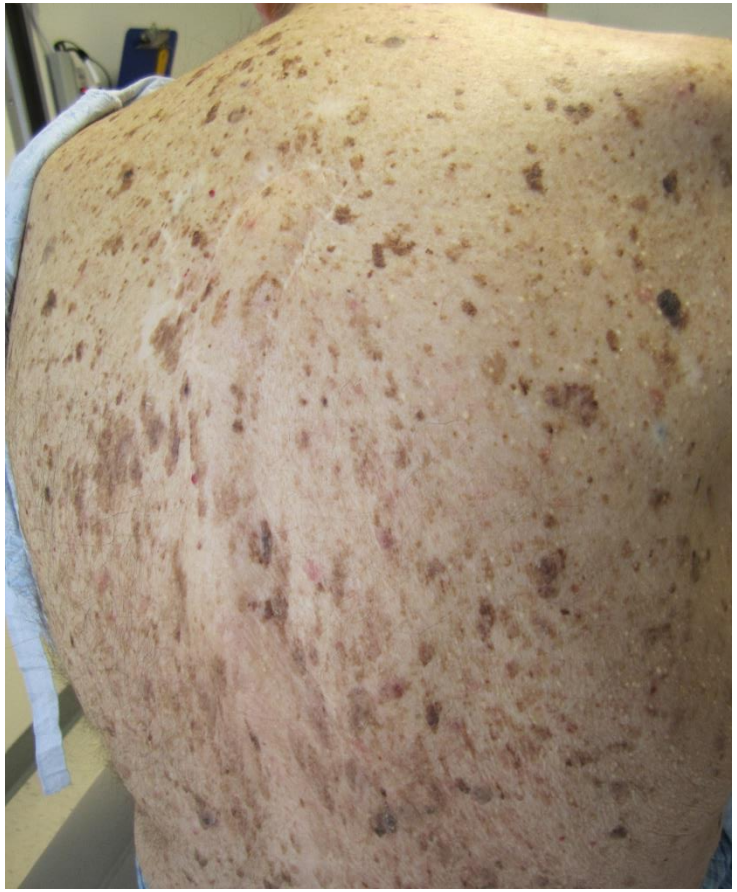
Upon completion of this presentation the participant will

- Classify common features of benign skin lesions
- Recognize risk factors for developing skin cancers
- Identify suspicious features which may indicate a malignant lesion
- Discuss appropriate management of non-melanoma skin cancers
- Describe interventions to optimize outcomes in patients with melanoma

Benign Lesions

Seborrheic Keratosis

- benign
- most common tumor of the skin
- well-demarcated, elevated or "stuck on” appearing papules or plaques
- skin-colored to shades of yellow, gray, brown, or black
- "waxy” or “greasy” surface
- can develop anywhere except palms, soles, mucous membranes



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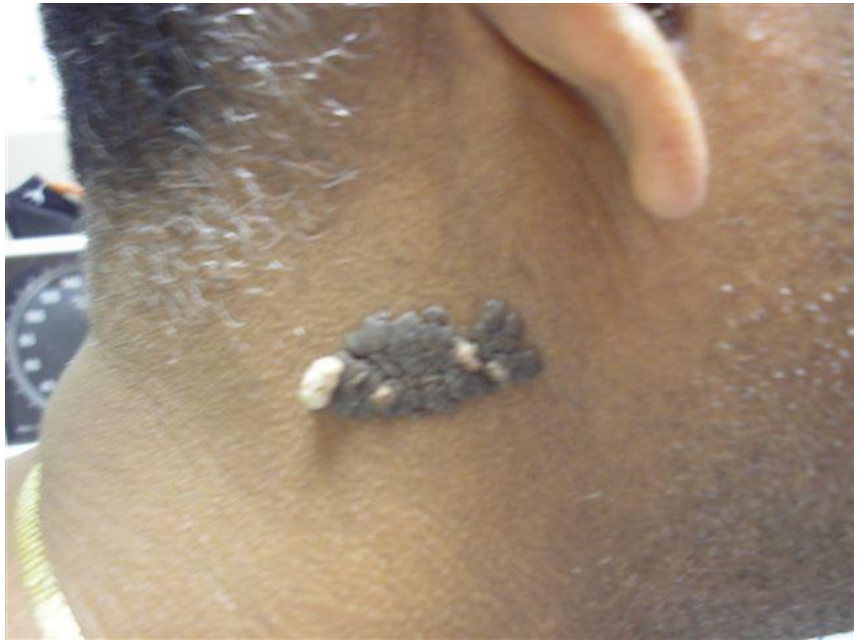
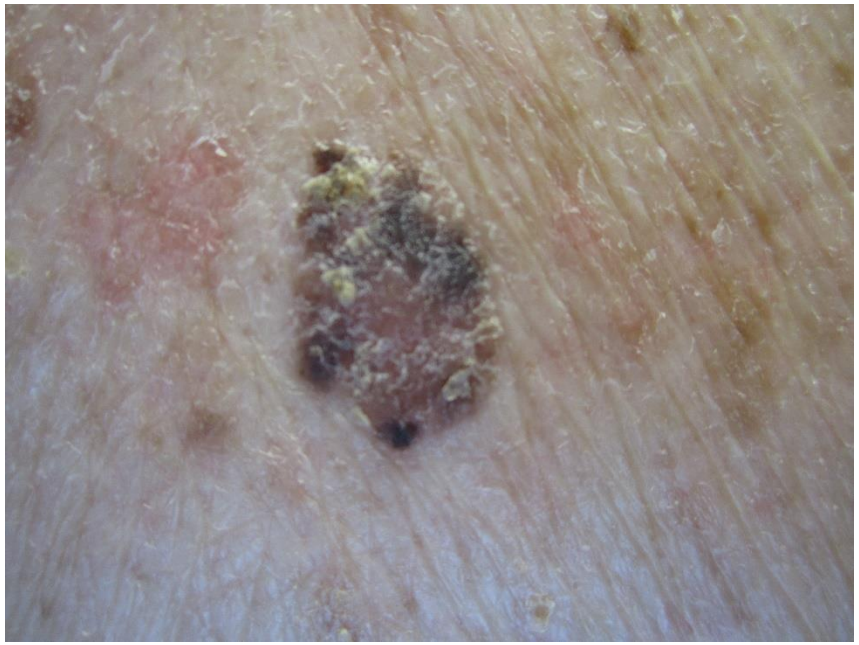
Seborrheic Keratosis: subtypes

hyperkeratotic, irritated/inflamed, reticulated, pigmented

reticulated SK (variation in color w ridges)





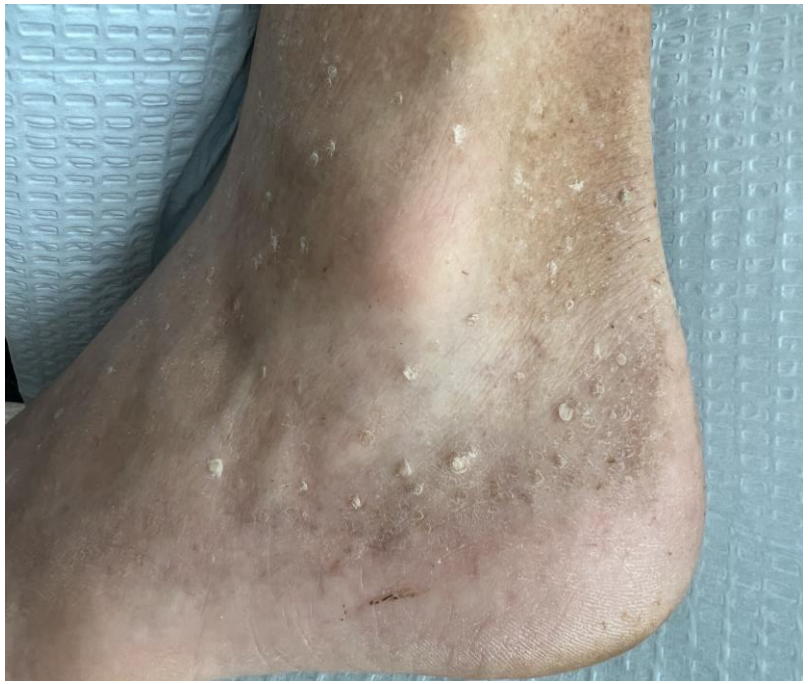
Seborrheic Keratosis: variants

Dermatosis Papulosa Nigrans

1 – 2mm dark papules concentrated around the eyes & malar cheeks

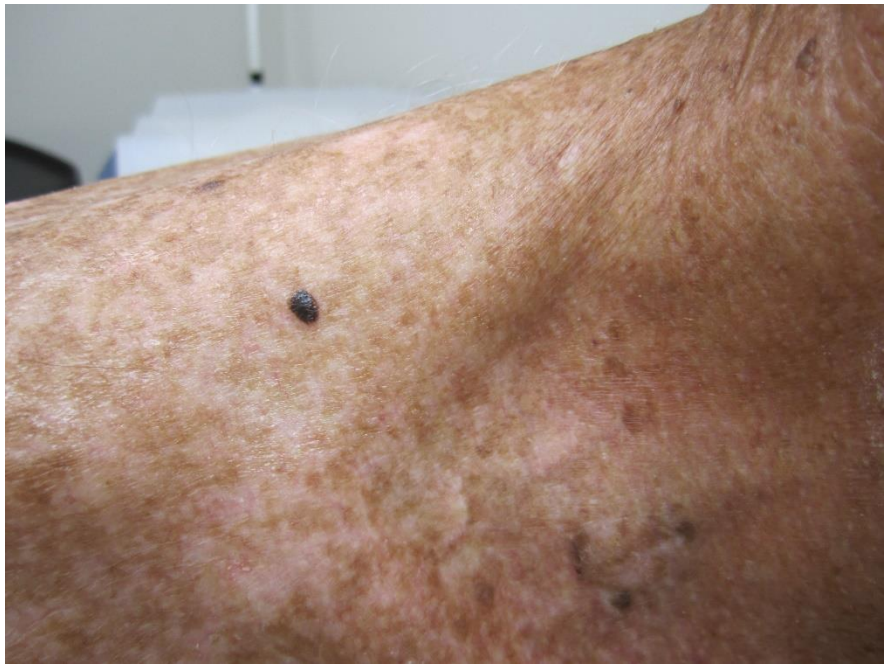
Stucco keratosis

small white papules
distal parts of the lower limbs



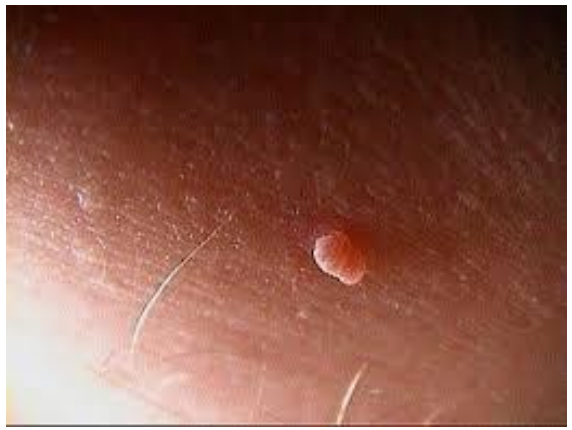
Seborrheic Keratosis: ddx

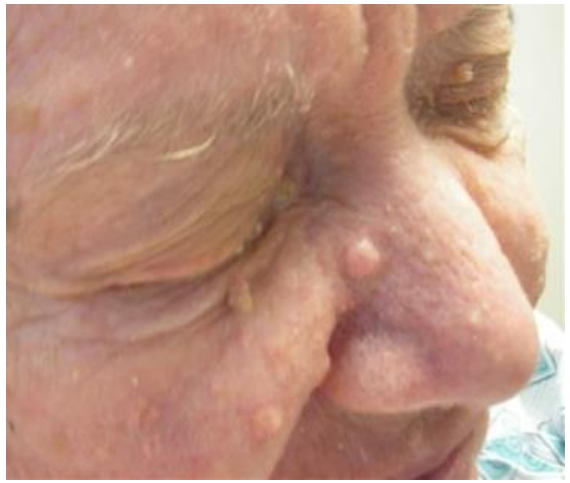
- Melanoma
- Verruca
- Actinic keratosis
- Lentigo maligna
- Melanocytic nevus
- Squamous cell carcinoma
- Pigmented basal cell carcinoma



Acrochordon

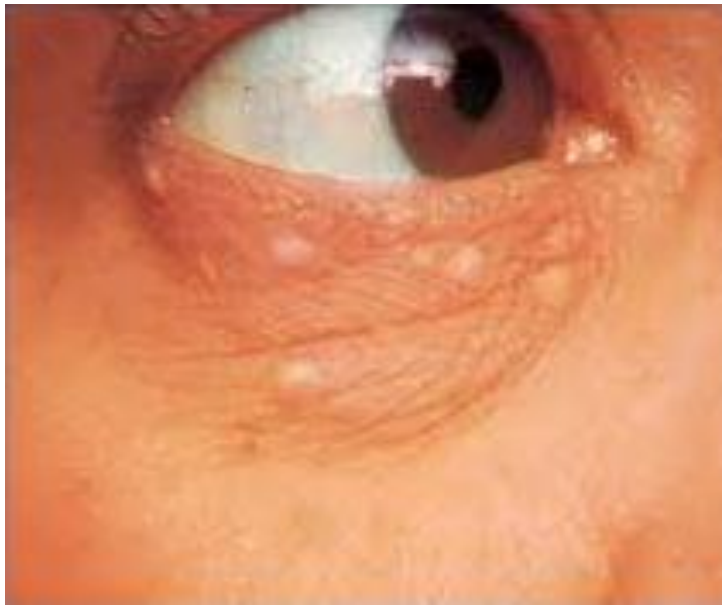
- Tags: common benign fleshy papules occurring in the skinfolds
- >30 yrs, obese
- easily irritated
- tender when traumatized, twisted, torn, thrombosed
- Acrochordons: 1-5 mm
- skin-colored – brown papule
- soft, fleshy pedunculated





Syringoma

- Small, benign, firm, skin-colored - yellow papules
- F, eyelids, upper chest, vulva
- asymptomatic, stable, persistent



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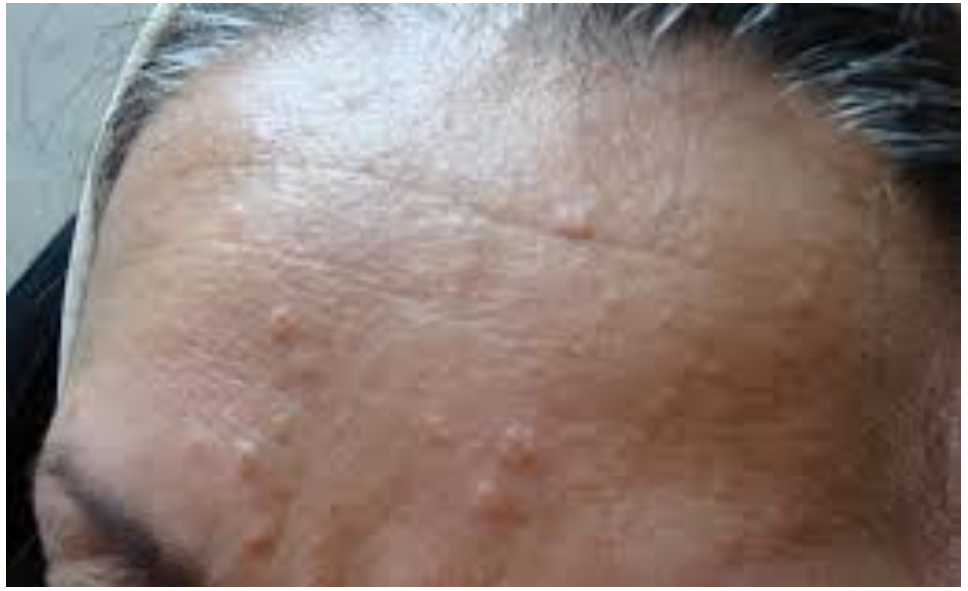
Sebaceous Hyperplasia

- common benign enlarged sebaceous gland
- middle age – older adults
- 1-4 mm soft skin-colored – pale yellow smooth umbilicated papule
- asymptomatic, persistent
- may be associated with emollient moisturizers, make-up, sunscreens
- Ddx: early BCC, Molluscum Contageosum



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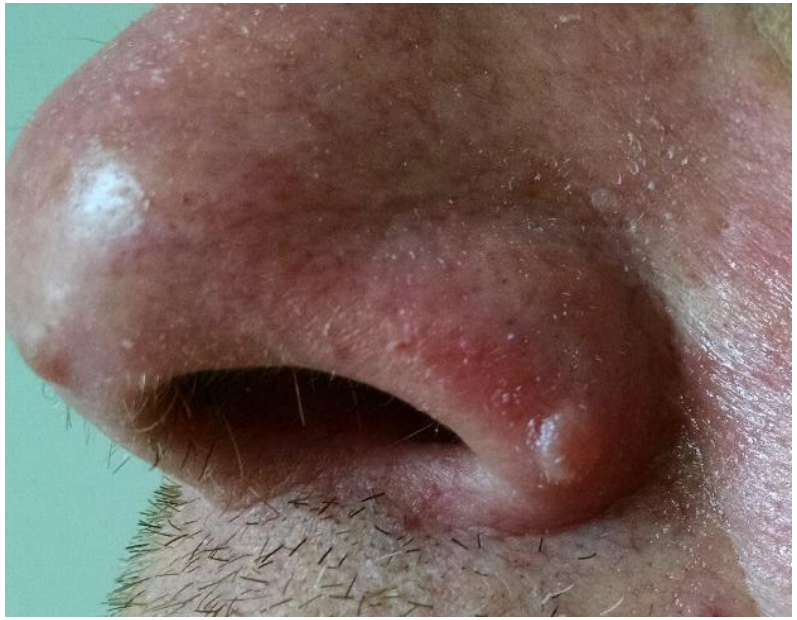
Fibrous papule

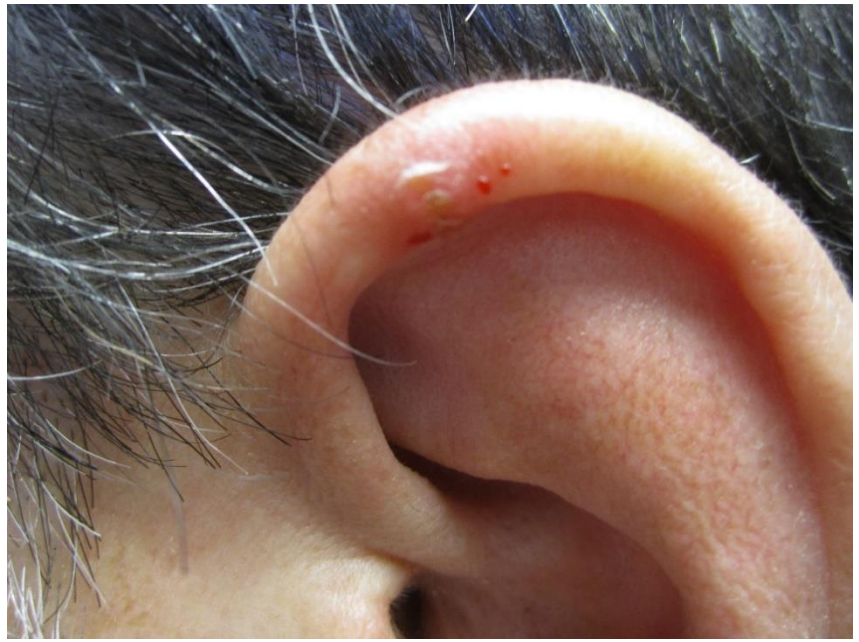
DDx

- BCC
- Keratoacanthoma
- Molluscum Contageosum

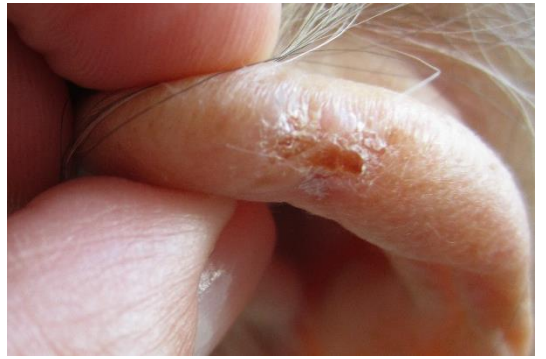


Chondrodermatitis Nodularis Helicis

- Inflammatory condition of the helical ear cartilage
- 2-4 mm firm tender pink – red papule with central keratotic punctum
- irritated – exquisitely tender papule
- lateral edge of the helix or antihelix
- >40 yrs
- sleeps on the affected side; CPAP mask; ball cap
- DDx: wart, Actinic Keratosis, BCC, SCC (Keratoacanthoma, SCCis)



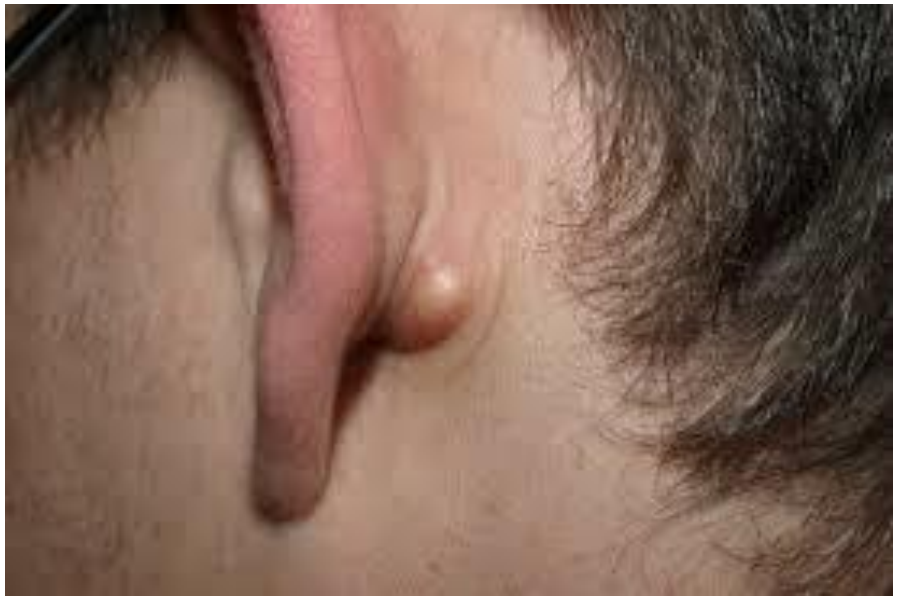
CNH



BCC

Cyst

- common, benign lesion that has a firm consistency, a pore-like opening (central punctum) and contains macerated keratin and lipid-rich debris
- asymptomatic, waxes & wanes, but may be painful if ruptured or infected
- 0.5 – 5 cm scalp, postauricular, posterior neck, truncal nodule
- epidermal cyst walls are fairly fragile and prone to rupture creating acute inflammation
- DDx: milium, lipoma, BCC, amelanotic MM



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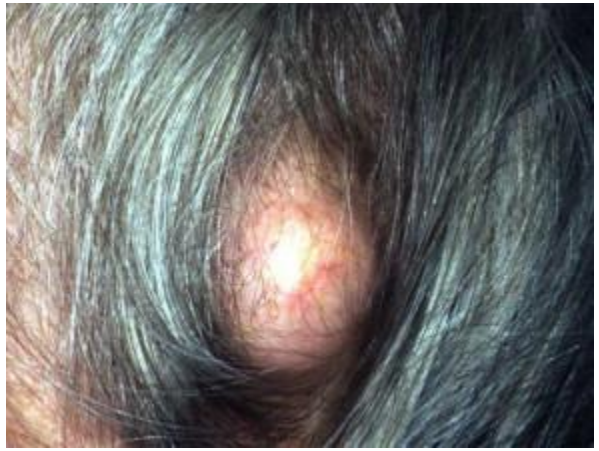
Cyst

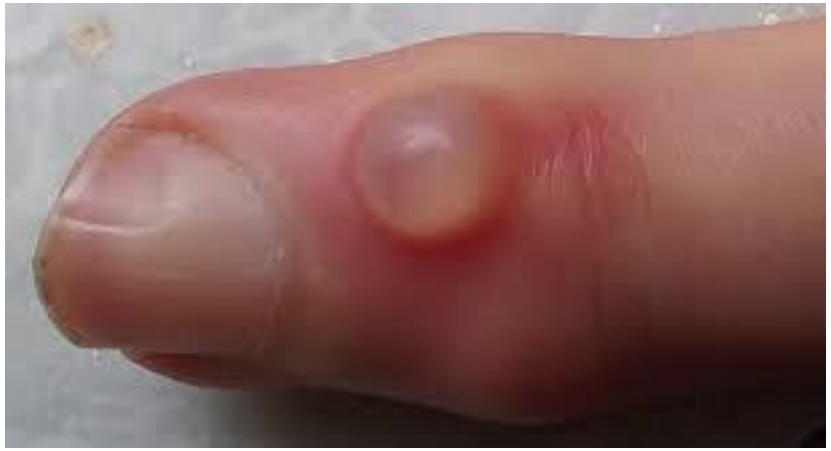
Pilar (trichilemmal) cysts

- common, benign, smooth, mobile, keratin filled cysts from the sheath of the hair follicle
- frequently multiple, may become large, tender, associated with overlying alopecia



Digital Myxoid Cyst

ddx: xanthoma, Rheumatoid nodule



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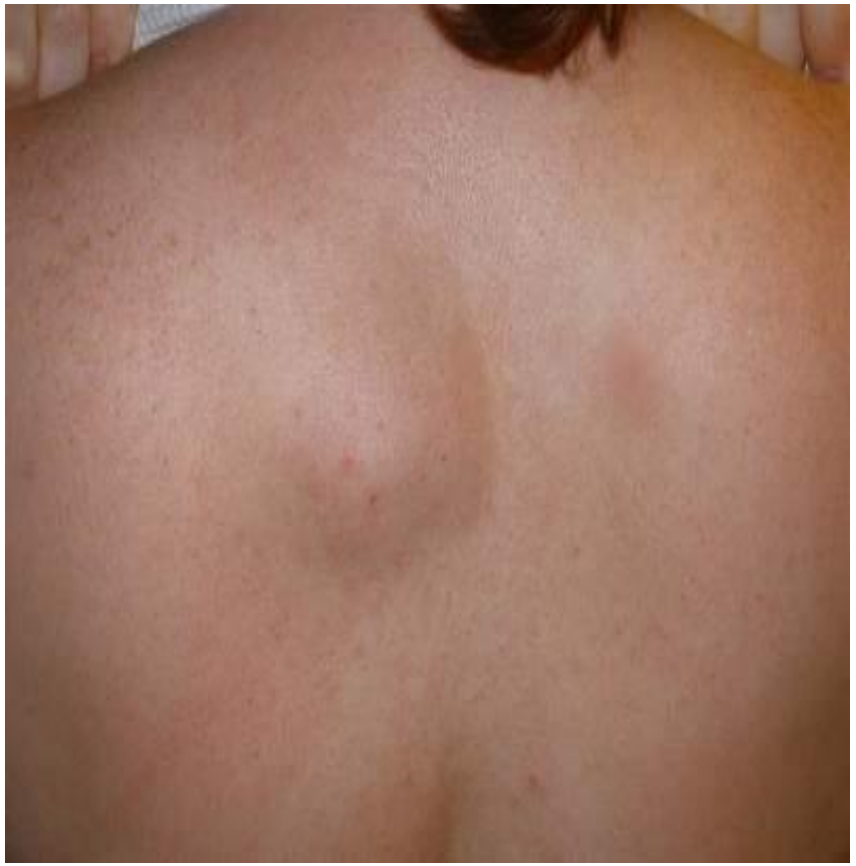
EIC: Rx

- Infection is rare but should be treated with incision & drainage, and if fluctuant, oral antibiotics (cephalexin, doxycycline, trimethoprim-sulfamethoxazole)
- Excision should be delayed until the infection has subsided
- Inflamed (non-infected) cysts may respond to intralesional triamcinolone though intralesional steroids may cause hypopigmentation hypopigmentation or atrophy.
- Incision and drainage can provide immediate reduction in pressure and discomfort, but without removing the epidermal lining, the cyst will refill with new layers of soft keratin.
- Using a punch biopsy to create a small skin opening and then using a curette to remove the cyst wall is sometimes effective.
- Alternatively, the entire cyst, along with the wall, can be excised surgically

Lipoma

- soft, painless, 1 cm - >10 cm subcutaneous mass
- most commonly seen on the trunk, but can be located anywhere on the body
- Angiolipoma: often painful, <2 cm, well-circumscribed; forearm of teens or young adults
- Angiomyolipomas: acral locations of adult males
- Liposarcomas: deep-seated tumors; thighs, retroperitoneum
- ultrasound or CT scan *before* surgery if:
  - large size (>10 cm), rapid growth, pain
  - fixation to underlying tissues, location in deep tissues, thigh, or retroperitoneal space
- Refer to Plastics, General Surgery or Derm



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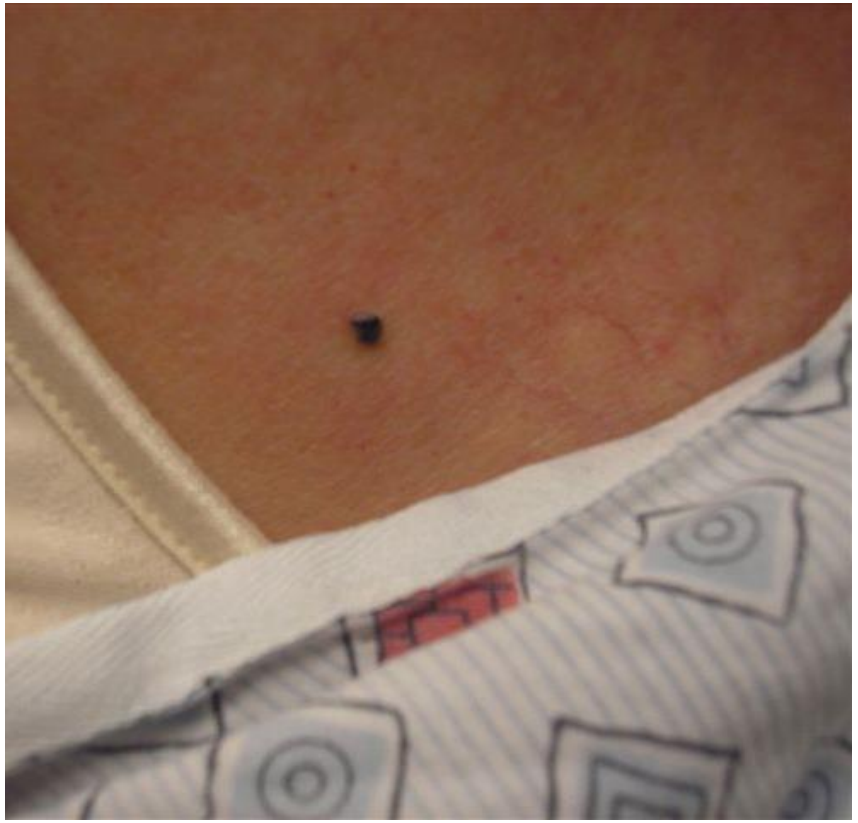
Cherry Angioma

- common type of benign acquired vascular proliferation of the skin
- etiology: aging, genetic mutation, pregnancy
- asymptomatic, can bleed with trauma
- bright red, flat 1-5 mm smooth dome shaped – polypoid papules
- head, neck, trunk, extremities
- DDx: hemangioma, insect bite, venous lake, Pyogenic Granuloma, Kaposi's sarcoma



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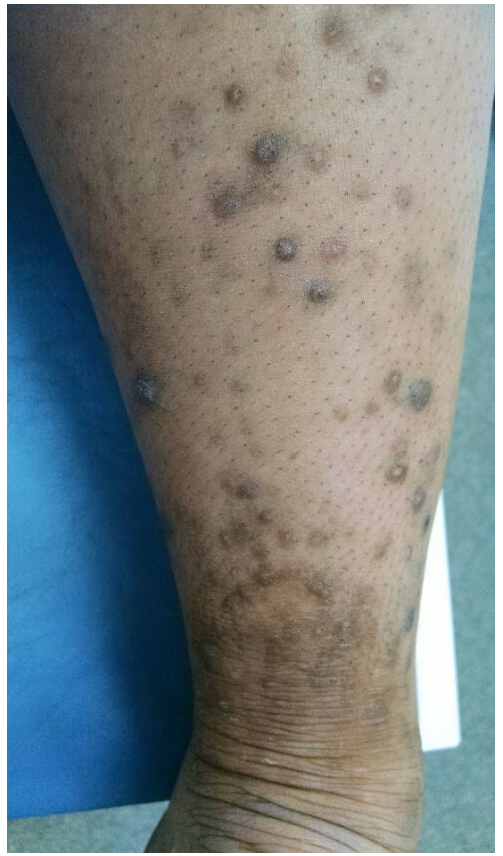
Prurigo Nodularis

- Chronic variant of Atopic Dermatitis
- nodular variant of Lichen Simplex Chronicus
- reddish, brown, hyperpigmented dome-shaped papules & nodules
- crusted, extremely pruritic, excoriated lesions at pretibial lower legs and extensor UE's
- resolve with postinflammatory hyperpigmentation
- DDx: Dermatofibroma, Lichen Simplex Chronicus, SCC, BCC, Sarcoidosis



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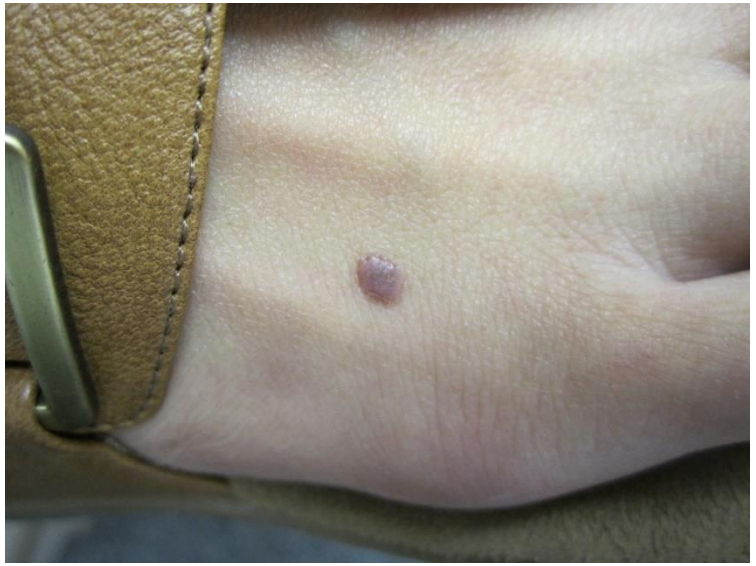
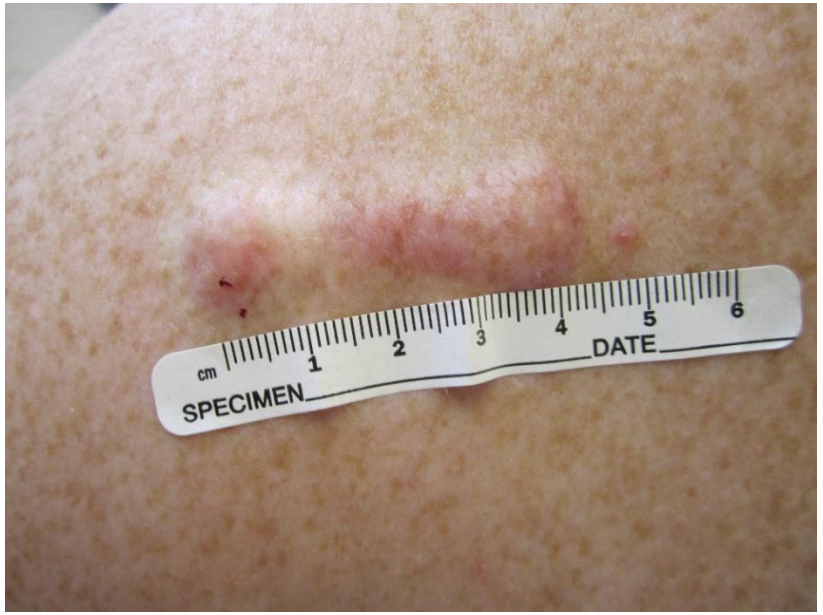
Dermatofibroma

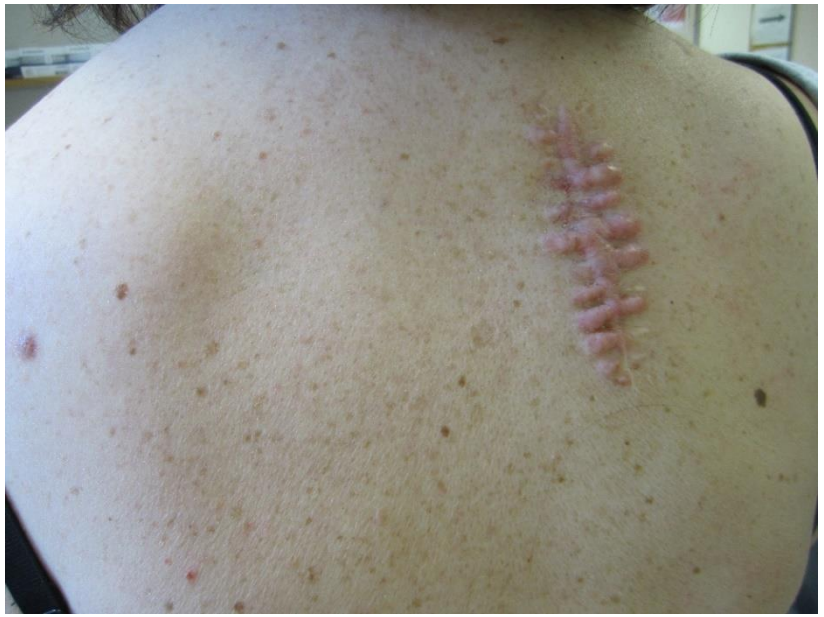
- common, benign growth of dermal fibrous tissue
- skin-colored, brown, red, purple
- smooth or scaly
- domed, flat or depressed papule or nodule
- firm, pea-sized papule which is fixed to the surrounding dermis; “dimples” with pressure
- DDx: dysplastic nevus, blue nevus, melanocytic nevus, keloid/hypertrophic scar, DFSP, Purigo Nodularis, Spitz, pigmented BCC, SCC, MCC, Melanoma



Keloid

- overgrowth of dense fibrous tissue which extends beyond the area of original injury
- randomly organized collagen fibers in a dense connective tissue matrix
- pts of Hispanic, Asian & African descent are particularly prone
- DDx: Dermatofibroma, xanthogranuloma, sebaceous cyst, lipoma, Sarcoidosis, recurrence of original tumor, Dermatofibromasarcoma Protuberans (DFSP)





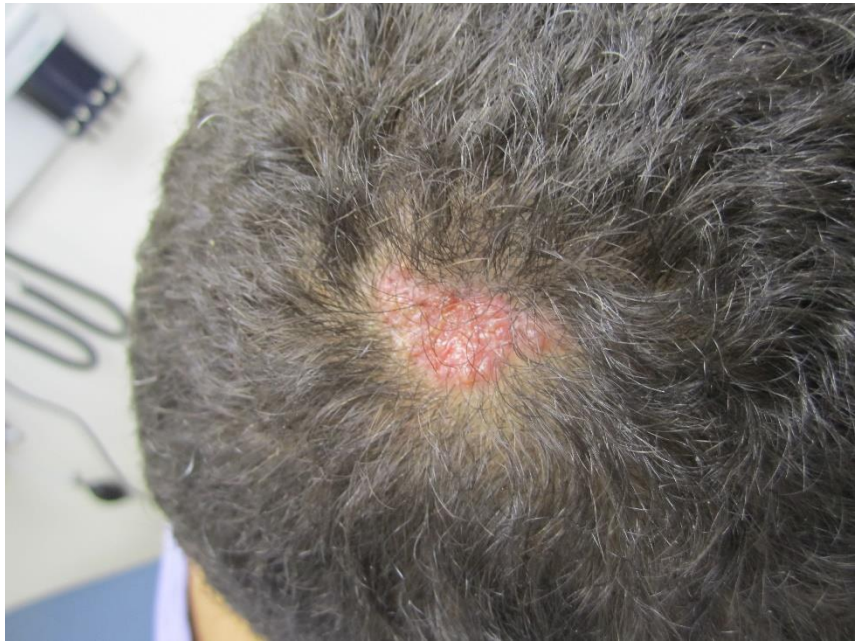
Keloid: Rx

- 2024 consensus-based recommendations for IL corticosteroid administration (ICA)
- 1st line treatment for keloids <10 cm^2 with an elevation 0.3-1 cm
- 40 mg/mL triamcinolone acetonide (TAC) using a 1 mL syringe is preferred
- consider combining other treatment options in cases in which the required cumulative dose is >80 mg of TAC per session
- suggested interval of 4 weeks between TAC treatment sessions
- consider topical anesthetics such as lidocaine/prilocaine cream before ICA. combining an intralesional corticosteroid with a local anesthetic is not recommended
- blanching is the endpoint of infiltration with injection directly into keloid tissue

https://www.dermatologyadvisor.com/news/consensus-statement-issued-for-intralesional-corticosteroid-use-keloids/?utm_source=eloqua&utm_medium=email&utm_campaign=NWLTR_DER_UPDT_RSS2-Lasso2-SLI-9467_103024_AF&hmemail=&sha256email=36ba749737ebc95b6e8b16439932cfbd83ff6b6794992dae074b889a7b90f1fc&hmsubid=&nid=&elqtrack=True

Nevus sebaceous

- congenital lesion of scalp, head, neck
- linear/ oval, skin-colored/ yellow, 1-3 cm plaque
- ~20% undergo neoplastic change and can develop benign or low-grade malignant tumors
- ~7% develop Basal Cell Carcinoma
- DDx: linear epidermal nevus



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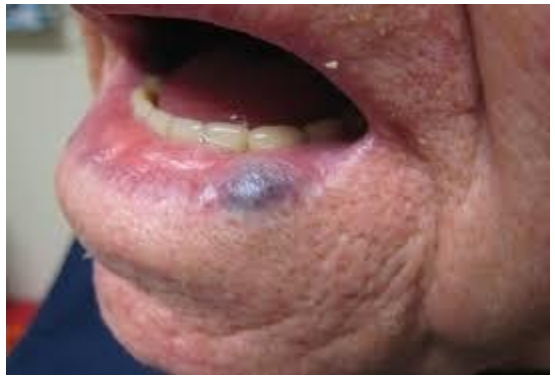
Oral Lesions

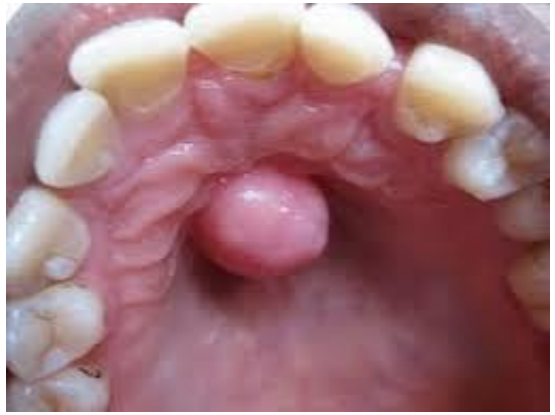
Venous Lake

- Common vascular neoplasm
- generally >60 yrs
- dark blue to purple macules or papules



Oral Fibroma

- Common oral neoplasm
- reactive fibrous hyperplasia
- from trauma or irritation
- asymptomatic, smooth, firm, solitary papules



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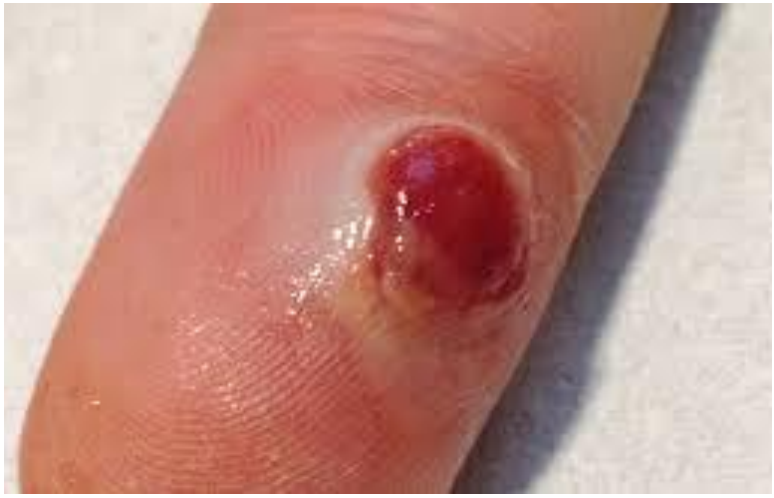
Oral Lesions

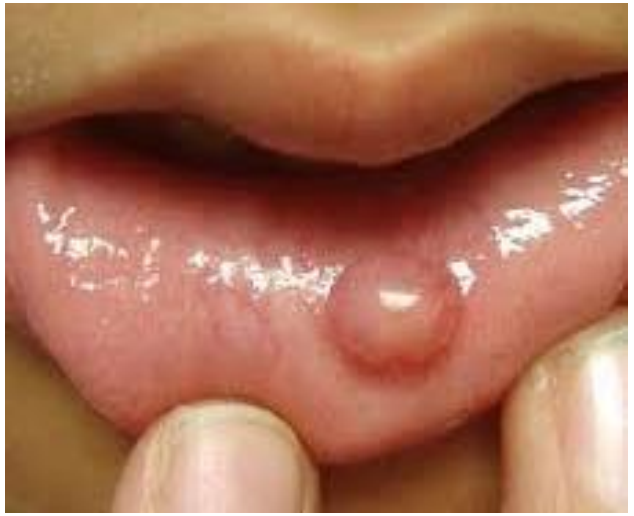
Pyogenic Granuloma

- common vascular hyperplasia of skin & mucous membranes
- associated with trauma (fingers, toes) or pregnancy/OCP hormonal factors (lips)
- benign, red, purple, rapidly growing, dome shaped papules or nodules



Mucocele Cyst

- common, mucous filled, blister-like lesion of minor salivary glands of the oral cavity
- associated with trauma; easily ruptured
- Refer to Oral Surgeon



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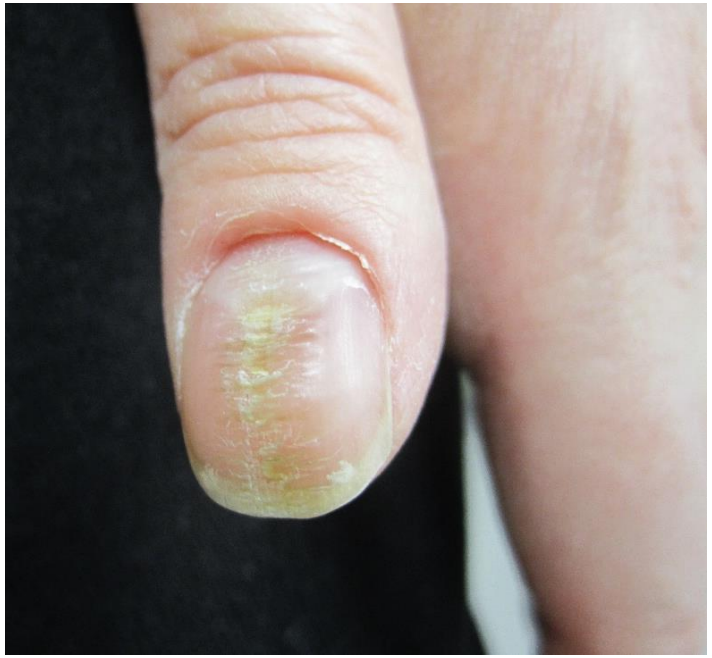
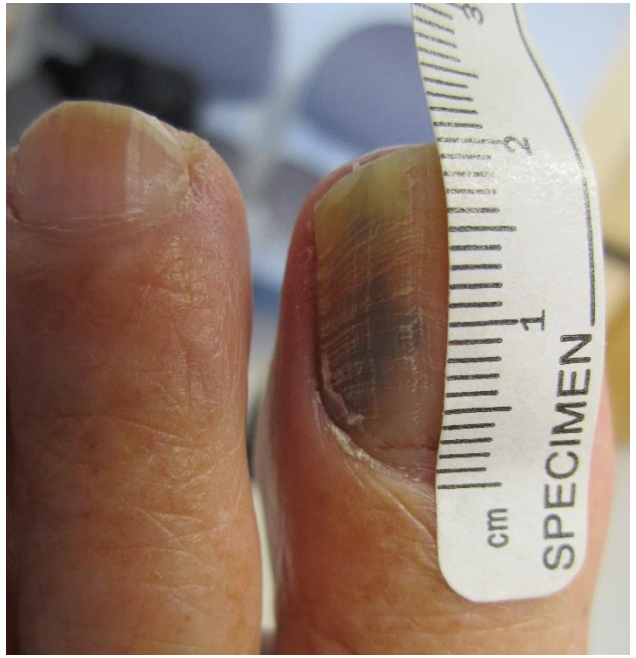
Nail Lesions

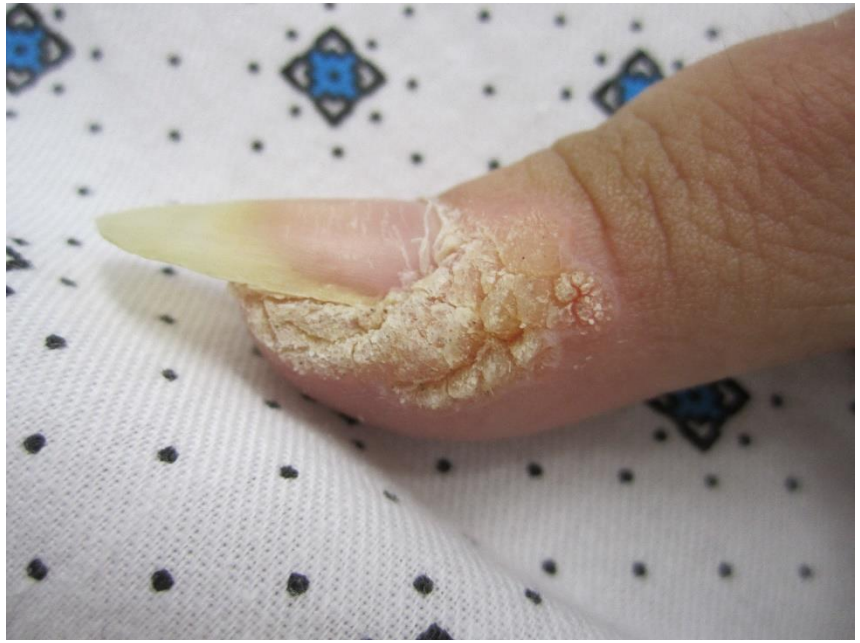


Median Nail Dystrophy (tic)

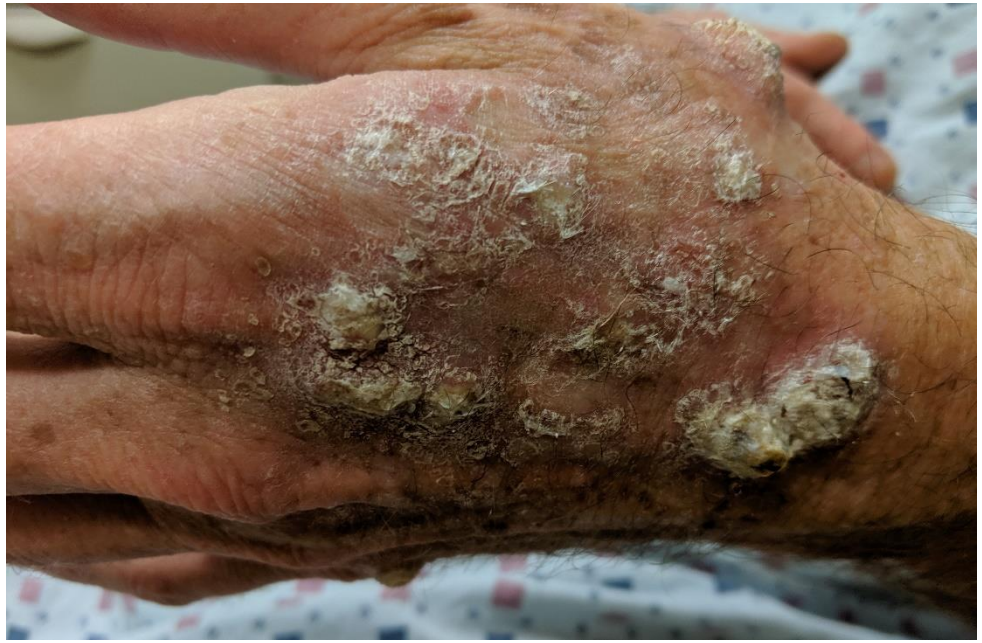


Subungual Hematoma

Nail Lesions



Subungual Wart



Squamous Cell Carcinoma

Pre-Cancerous Lesions

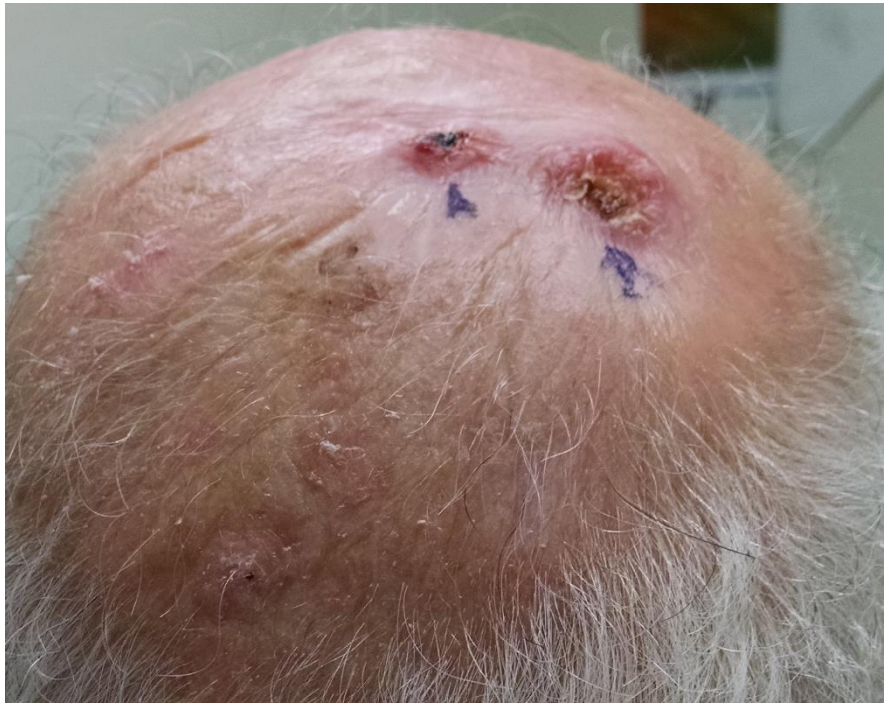
Question 1

Approximately how many (pre-cancerous) Actinic Keratoses advance to SCC?

A. 10%
B. 20%
C. 80%
D. 90%

Immunosuppression

- Increases risk for developing skin cancer
  - M > F
  - age >50
  - outdoor work/hobby
- Disease related
  - CLL: *marked increase* in recurrence, metastasis and death from NMSC
  - HIV, DM, malnutrition, substance abuse
- Drug related
  - Organ Transplant Recipient (OTR):
  - number of anti-rejection drugs, increased dose, years of treatment



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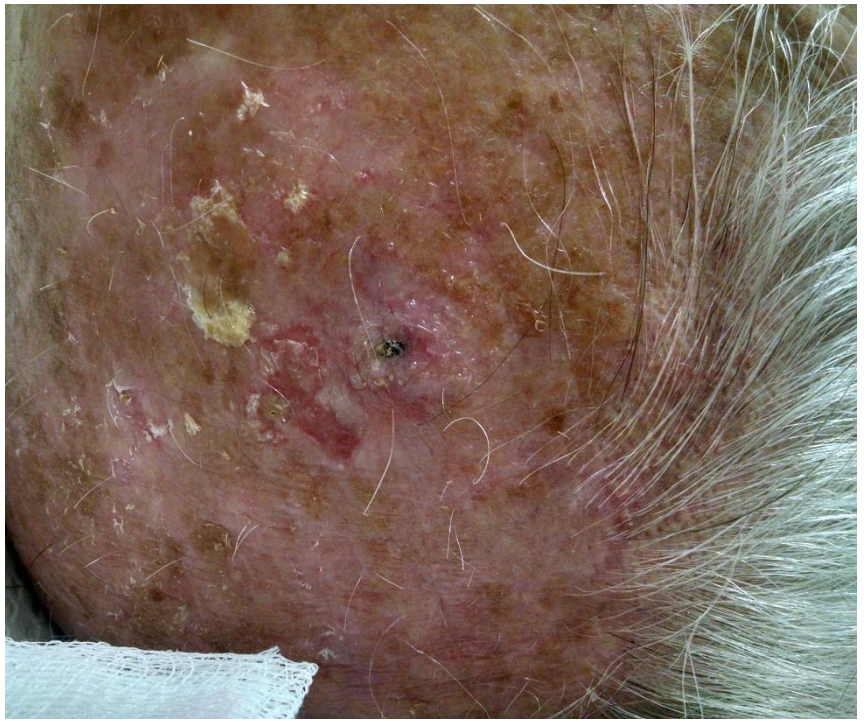
Immunosuppression

Incidence in OTR

- 40-70% of OTRs will develop NMSC
- heart & lung txp > kidney & liver txp
- *all* cardiac and renal OTRs will develop new NMSCs within 5 yrs of the 1st
- 2-3x the rate of melanoma with *increasing* incidence over time

Tumor Behavior in OTR

- *very aggressive*
- significant morbidity & mortality
- higher risk: recurrence, metastasis, recurrence after treatment of metastasis



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Actinic Keratoses (AKs)

- intra-epidermal pre-cancerous precursors to SCC

Pathogenesis

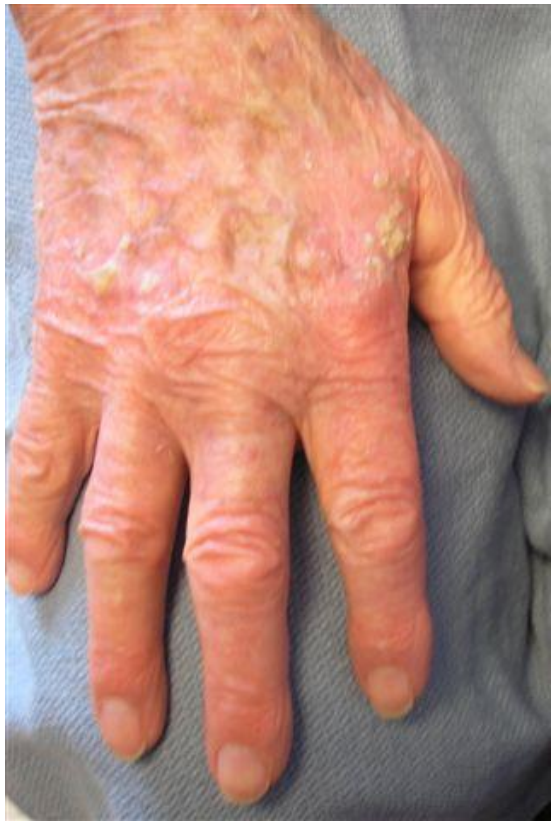
- UVR induces cellular mutations which result in formation of atypical keratinocytes

Behavior

- 20% of AKs progress into Squamous Cell Carcinoma (SCC)
- notably those at the scalp, ear, lip
- no way to know clinically which lesions will regress or progress to SCC

Biopsy

- tender, enlarging, bleeding, resistant or recurrent lesions



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AK -Treatment

Cryotherapy (liquid nitrogen)

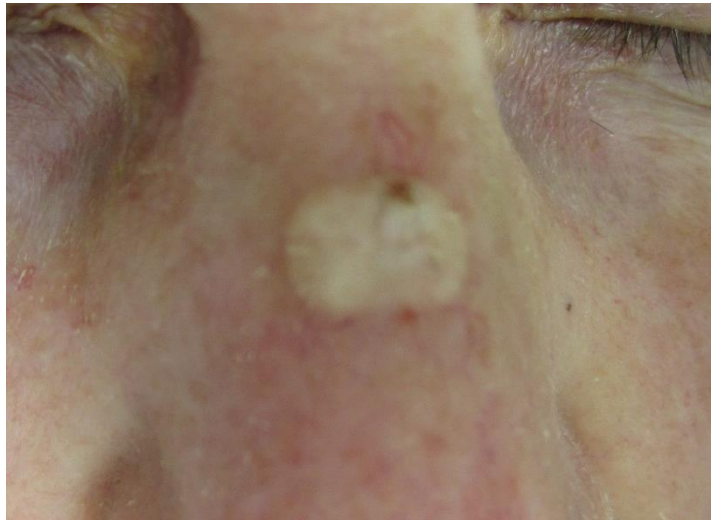
- Individual lesions

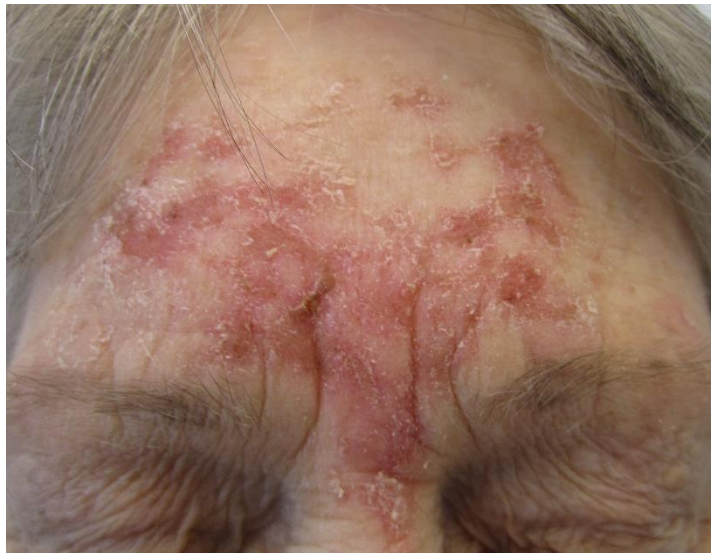
AEs: alopecia, blistering, cartilage necrosis, erosive pustular dermatosis, exuberant granulation tissue/pyogenic granuloma, hemorrhagic blistering, hyperpigmentation, hypopigmentation, infection, nerve damage, pain, permanent nail dystrophy, lacrimal duct obstruction, scarring of free nail margin, swelling

Field Cancerization

- multiple, diffuse AKs
- contiguous areas with subclinical, nonvisible sun damage
- Field therapy limits the development of SCC

tirbanibulin ointment, fluorouracil cream, imiquimod cream
Photodynamic therapy (topical 5-aminolevulinic acid + blue light)



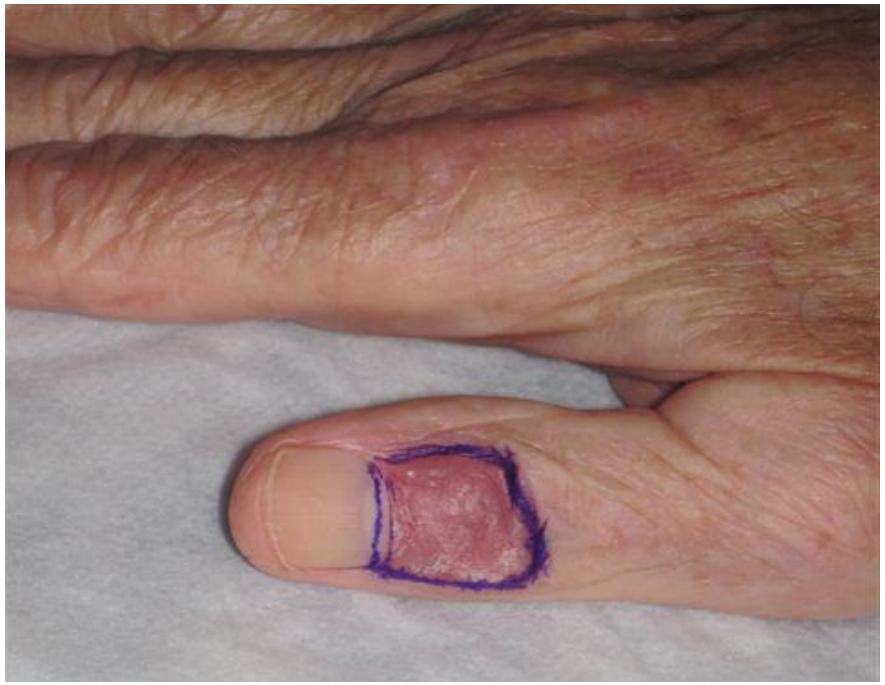


Non-Melanoma Skin Cancers

Case #1

47 yr M

- Rt thumb has been treated with betamethasone and moisturizers x 1.5 yrs for presumptive eczema



Squamous Cell Carcinoma (SCC)

malignant epithelial tumor

- arises from a proliferation of keratinocytes “squamous cells”
- constitutes 20% of all cutaneous malignancies

2nd most common skin cancer

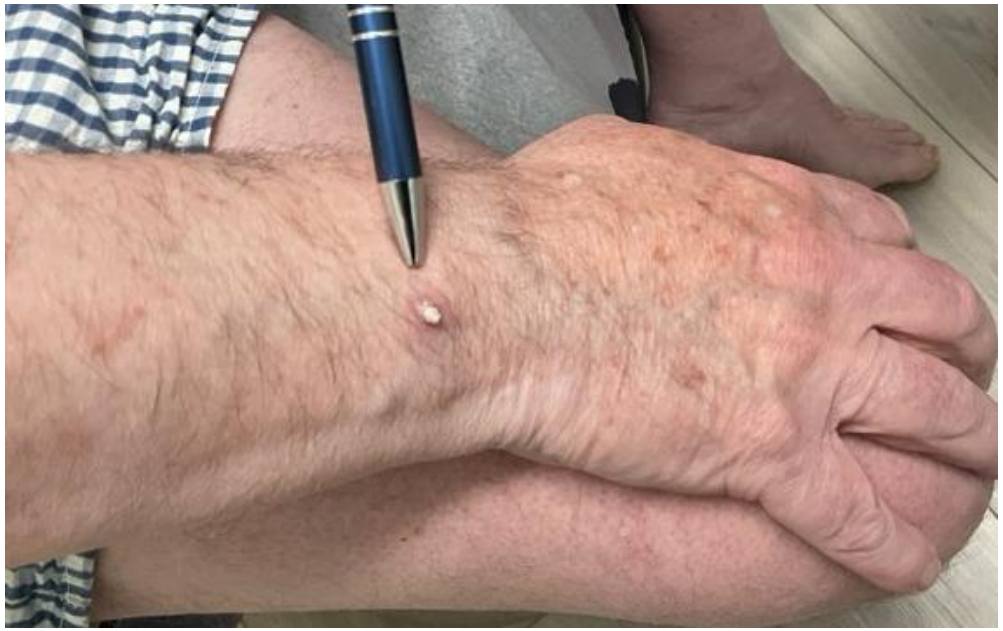
- doubled the rate over the last 40 yrs
- 50% of SCC pts will have a new SCC within 5 yrs of first

aggressiveness varies wildly

- SCC In Situ may never progress whereas
- poorly differentiated SCC have potential to metastasize

Squamous Cell Carcinoma

- epidermis is comprised of keratinocytes
- cells slowly migrate to the surface
- SCC is malignant epithelial tumor
- arising from a proliferation of keratinocytes “squamous cells”
- usually successfully treated, however;
- persistent/ recurrent tumors penetrate underlying tissues
- spread to lymph nodes, distant organs



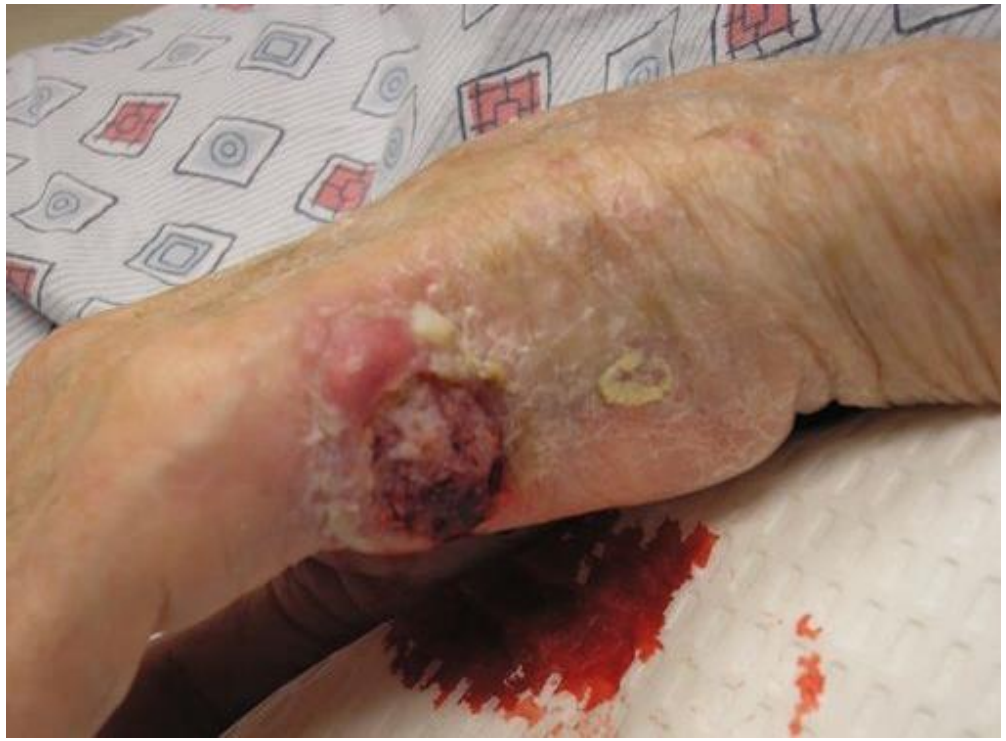
Low risk lesions

- arise from chronic UVB, heavy metals (arsenic) & chemical carcinogens (tar) exposure

Squamous Cell Carcinoma

High risk lesions

- often secondary to scarring or chronic inflammation (ie, Lupus);
- Lymphoproliferative disease (CLL)
  independent risk factor for SCC;
- HIV pts
  3x more likely to develop SCC (HPV);
- Immunosuppression (OTR) markedly increases risk of cutaneous cancers
- Peri-neural / Peri-vascular/ Single cell



Personal Photo(s) V.Lazareth NP

SCC: incidence

- SCC development in *sun exposed* skin
  - Caucasians ~70% head & neck; 15% UE's
  - multiple AKs: >20 AKs increases the risk of SCC development to 20%
- SCC development in *sun protected* skin
  - 22% of SCCs in OTRs
  - 8% of SCCs in darker skin types (most common skin ca in African-Americans)
- SCCs development at sites of chronic *inflammation & infection*
  - Trauma: burns, scars, ulcers, long-standing sores (HPV, Discoid Lupus)
  - Skin previously exposed to XRT, PUVA, chemicals (arsenic, petroleum by-products)

SCC: risk

Anti-rejection drugs

- Initial OTR treatment regime often includes 3 anti-rejection drugs
  - prednisone (>20 mg x weeks or months)
    - effect on cutaneous immune cells *increases* skin cancer risk
  - antimetabolite (azathioprine, mycophenolate mofetil)
    - effect on T-cells and B-cells *increases* skin cancer risk
  - calcineurin inhibitor (cyclosporin, tacrolimus)
    - *direct carcinogenic effect* on keratinocytes

Other medications

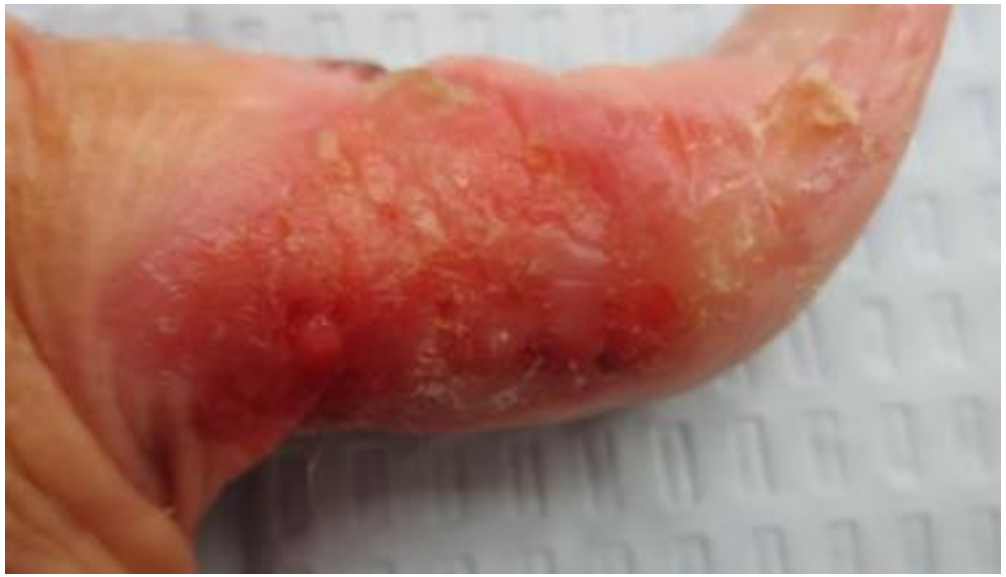
- BRAF inhibitors (for metastatic melanoma), TNF inhibitors (for psoriasis)

Pt education

- Risk of NMSC development *increases* over time post transplant, Refer to Derm

SCC: superficial (Bowens Disease)

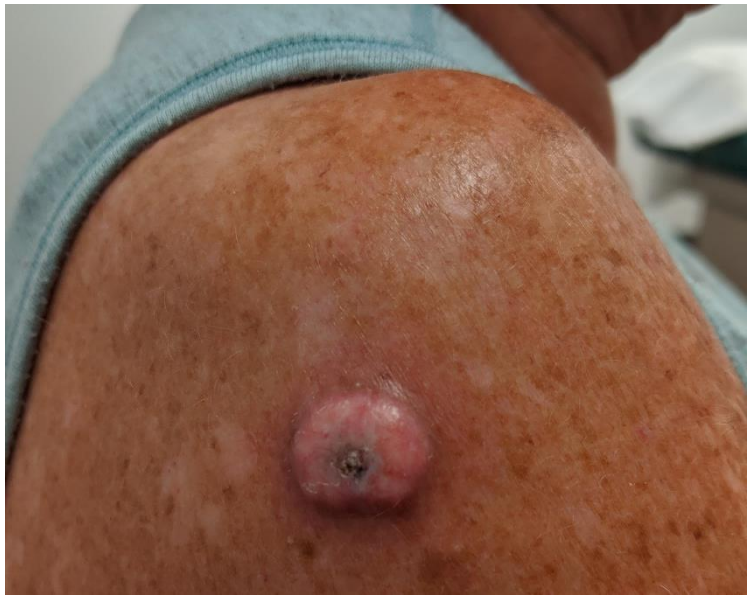
- red scaly plaque
- usually > 1cm in size
- often misdiagnosed as psoriasis, eczema
- cancer confined to the epidermis
  - non-invasive at this stage
  - can track down hair follicle
  - can become an invasive SCC
  - can be difficult to completely clear



SCC: low risk (Keratoacanthoma)

Incidence

- commonly in fair skinned middle-aged to elderly
- fair skin, exposure to UVR or chemical carcinogens, genetic abnormalities, certain medications



Pathogenesis

- poorly understood
- potential contributing factors that influence epidermal cell proliferation, cell adhesion, cell survival, apoptosis

Presentation

- 1 - 2 cm nodule with central keratin on sun-exposed skin
- 3 phases: proliferative (weeks), maturation (months), regression

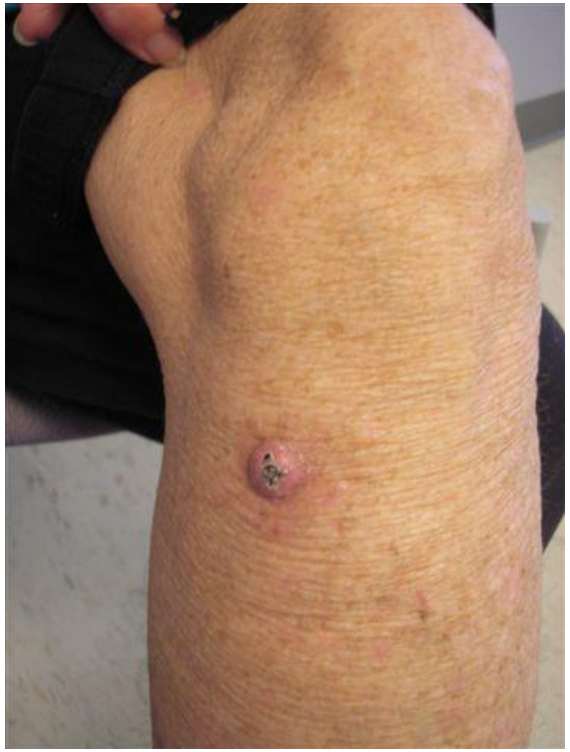
SCC: low risk (Invasive)

Presentation

- commonly at the head, neck, hands, mucosa
- dull red, firm, poorly defined plaque or domed nodule
  with central yellow keratin scale

Prognosis

- usually successfully treated, however persistent/ recurrent tumors can penetrate underlying tissues and spread to lymph nodes, distant organs



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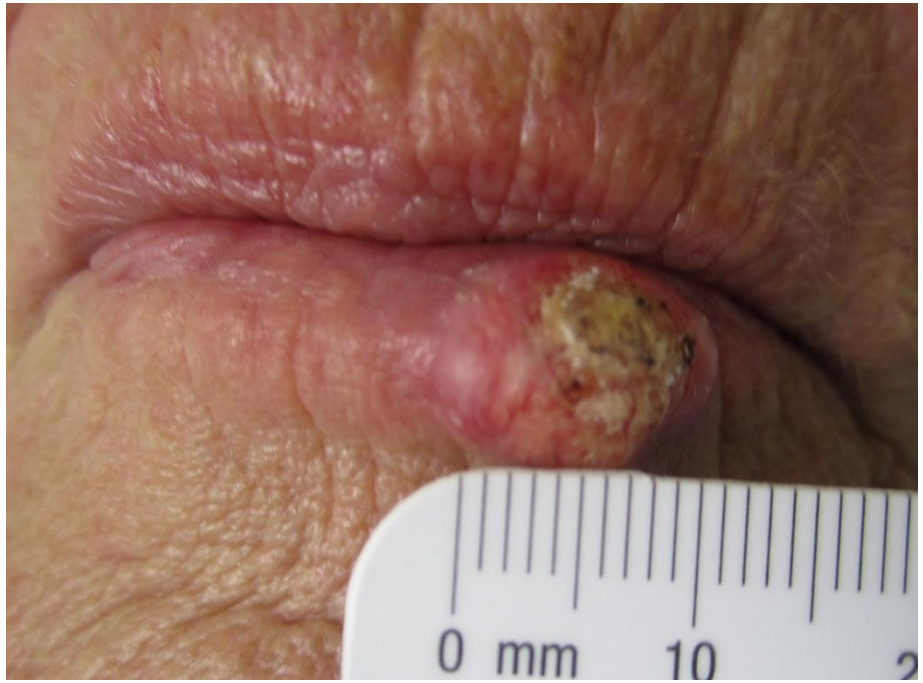
SCC: high risk

Incidence

- 9,000 – 12,000 annual deaths in U.S.
- 3-4% overall metastatic rate of SCC
- high risk SCC >20% risk of metastasis

Immune suppressed

- pts with 2-9 SCCs have
  - double the risk of local recurrence
  - triple the likelihood of nodal invasion



Work Group; Invited Reviewers; Kim JYS, Kozlow JH, Mittal B, Moyer J, Olenecki T, Rodgers P. Guidelines of care for the management of cutaneous squamous cell carcinoma. J Am Acad Dermatol. 2018 Mar;78(3):560-578.

SCC: high risk

Location: mucosal lip constitute high risk tumor independent of size

- scalp vertex, central face, eyelids, eyebrows, periorbital skin, nose, lips, chin, mandible, pre-postauricular, temple, ear, genitalia, hands, feet, digits, mucosa
- site of scar, chronic inflammation, prior radiation, PUVA

Size: >1 cm head & neck,

>2 cm trunk-exts: 3x metastatic rate of smaller tumors

Depth: of invasion >2 mm

History: older, male, immunocompromised

Histology: inflammation and infiltrative strands, single cells, small nests

- moderately-poorly differentiated, peri-neural, peri-vascular, Single Cell, recurrent
- adenoid/acantholytic, adenosquamous, desmoplastic, metaplastic

SCC: management

- low-risk SCC
  - EDC: small, superficial, in situ lesions in low-risk, in non hair-bearing sites
  - Excision: 4-6 mm surgical margin; cure rates generally > 95%

- high-risk SCC
  - Mohs Micrographic Surgery
    - 100% assessment of surgical margin
    - cure rates generally > 97%
  - XRT: for pts who are not surgical candidates

The risk of local, regional, or distant recurrence is the most important factor to consider

SCC: Mohs Micrographic Surgery

High Risk Lesions

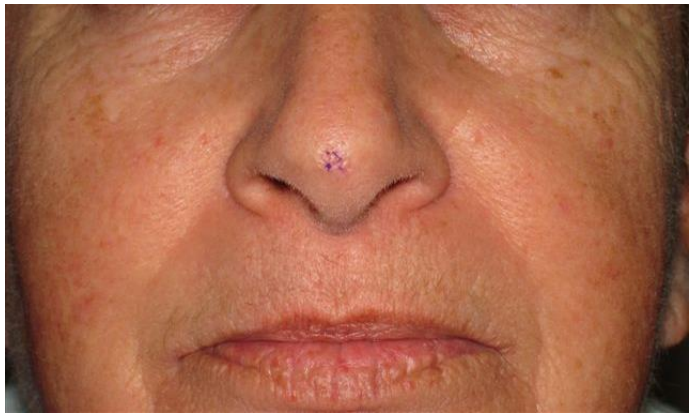
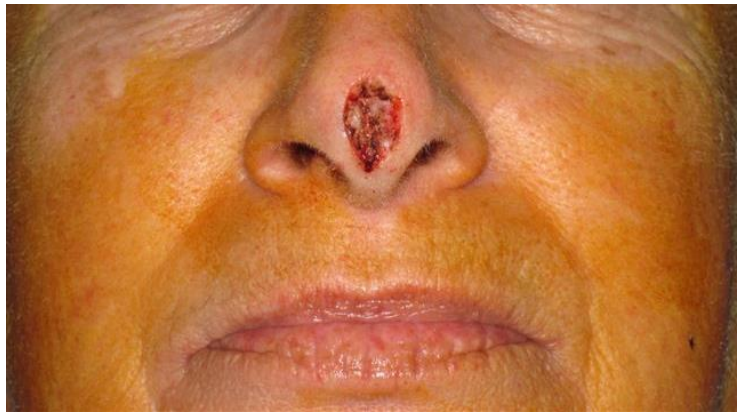
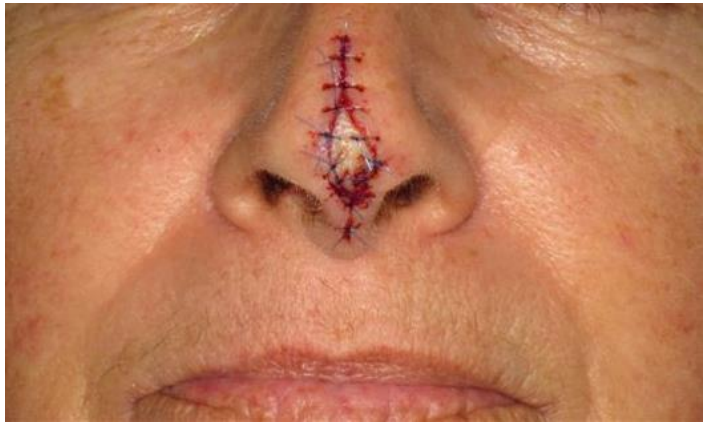
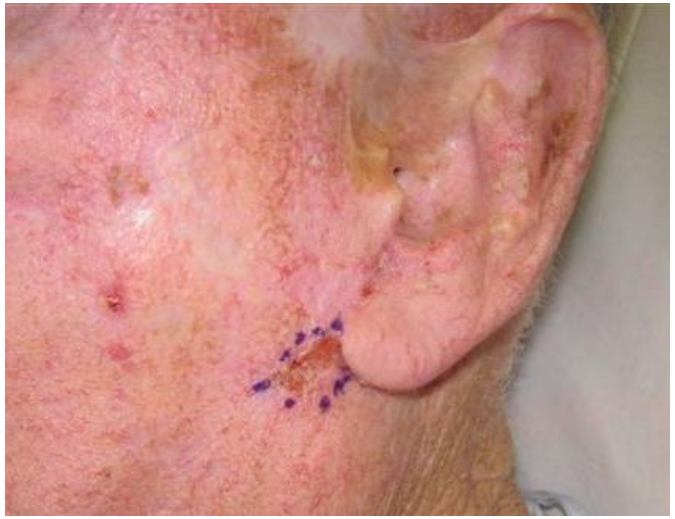
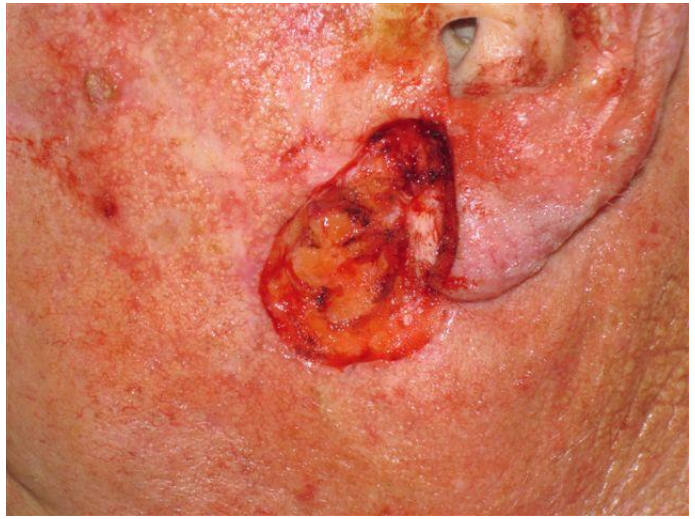
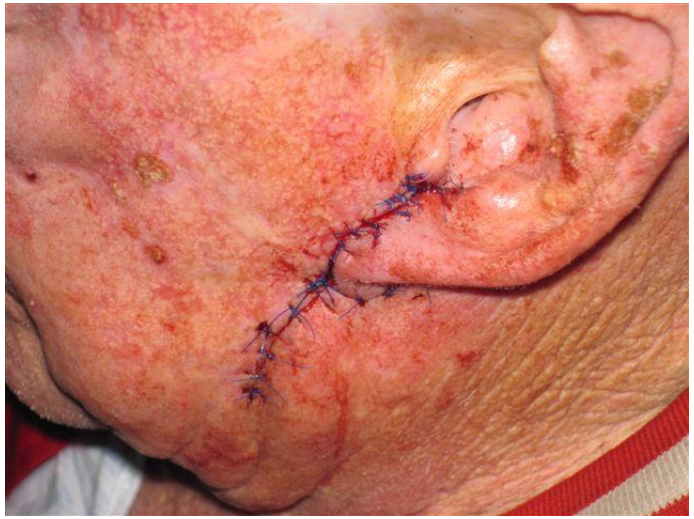
- out-pt surgical procedure performed by Dermatologist with advanced training
- pathology performed during the procedure to assess for tumor-free margins
- to provide the highest cure rate for high-risk tumors
  - 97% Mohs cure rates for primary SCC
- to spare greatest amount of healthy tissue
- to provide adjuvant therapy for (+) margins, recurrent tumors

Mohs "Appropriate Use Criteria"

- 270 different scenarios based on pt or tumor characteristics for which MMS would be appropriate, equivocal or inappropriate

AAD/ ACMS/ ASDSA, ASMS 2012 appropriate use criteria for Mohs micrographic surgery: A report of the American Academy of Dermatology, American College of Mohs Surgery, American Society for Dermatologic Surgery Association and the American Society for Mohs Surgery. *J Am Acad Dermatol* 2012; 67:531-50.

Mohs

Pre-op	Tumor Clearance	Repair
		
		

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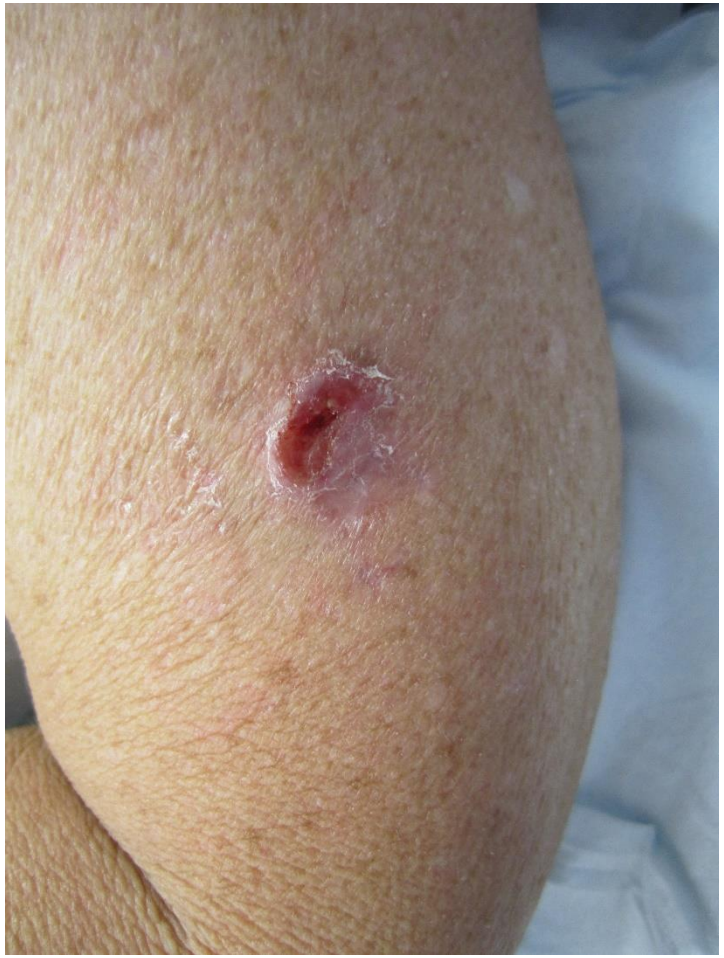
Case #2

64 yr F

PCP prescribed triamcinolone cream for psoriasis but the lesion isn't healing



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Basal Cell Carcinoma (BCC)

- most common human malignancy affecting >3 million pts/yr
- develop from basal cell layer of epidermal keratinocytes
- result from exposure to cumulative or intensive UVR or heavy metals
- lead to DNA mutations which inactivate patched (PTCH) tumor suppressor gene
- most successfully treated with surgical excision
- some lesions may be treated with topical therapy or radiotherapy
- ~40% of pts will develop another BCC within 5 yrs of the 1st

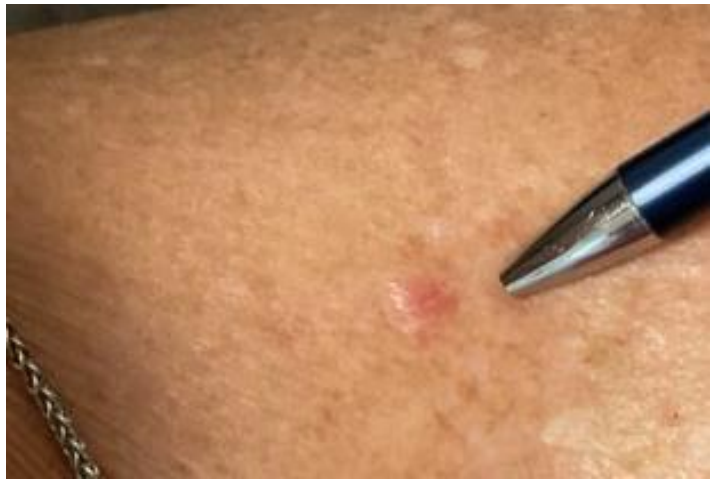
Question 2

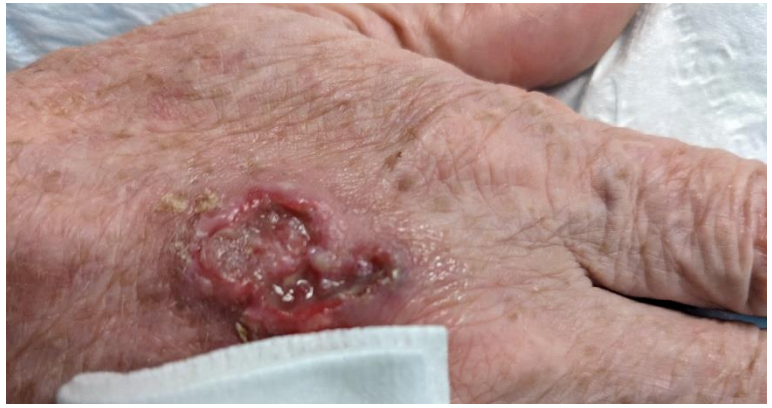
Which sub-type of Basal Cell Skin Cancer presents a high risk for recurrence?

A. Superficial
B. Nodular
C. Micronodular
D. Pigmented

Basal Cell Carcinoma

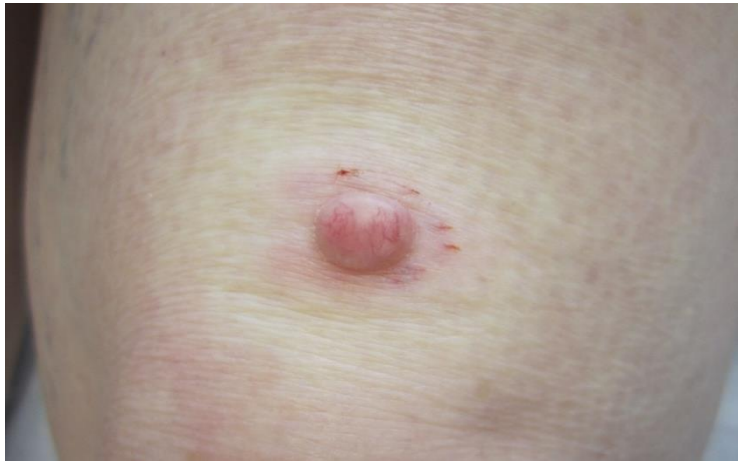
- grows slowly; common sub-types
  - nodular (nBCC)
  - pigmented (pBCC)
  - superficial (sBCC)
- rare metastatic spread however; certain BCC subtypes are aggressive & locally destructive
  - micronodular (mnBCC)
  - morpheaform/Sclerosing





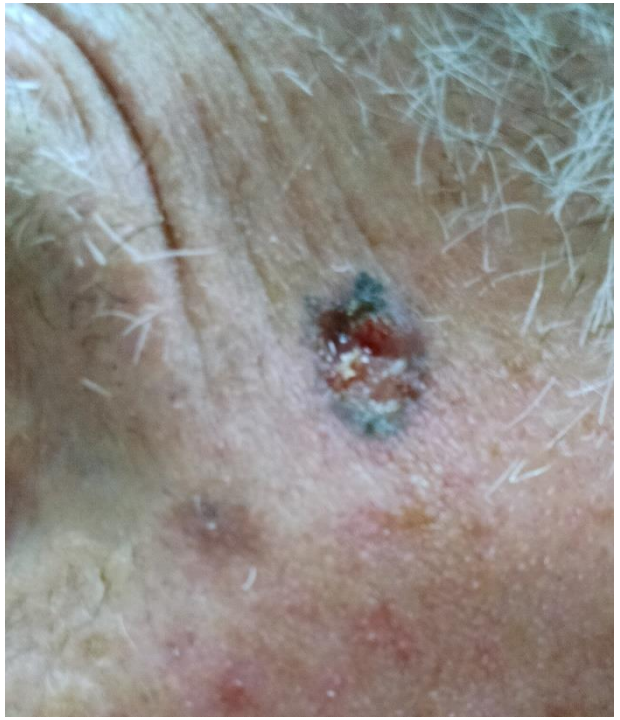
BCC: low risk

small, primary, well-defined borders, no nerve involvement, immunocompetent pts



Nodular BCC

- smooth, pearly, translucent, pink, lesions with telangiectasias



Pigmented BCC

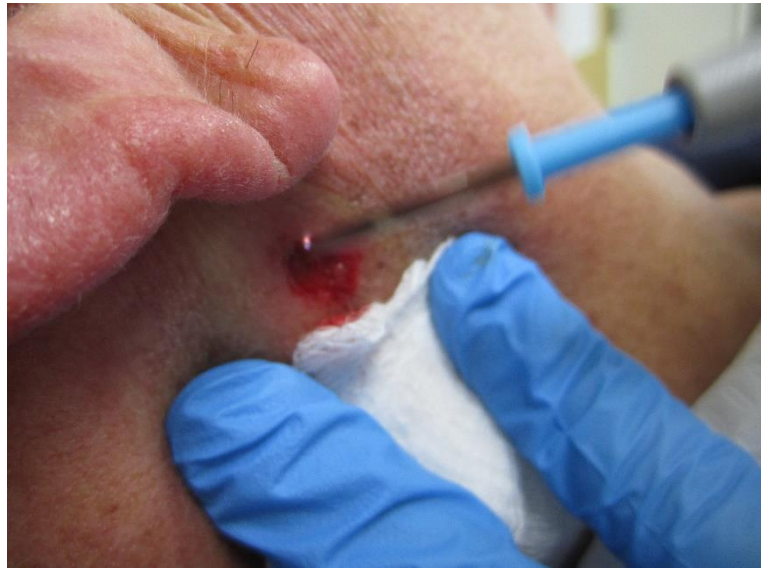
- speckled, brown, blue, black melanin in lesions; darker skin types
- bleeding & ulceration →rolled border

Personal Photo(s) V.Lazareth NP

low risk BCC: management

Electrodesiccation and Cautery

- FDA approved for small BCC's at low-risk sites
- 95% cure rate for primary lesions
- 1st line treatment for primary superficial BCCs
  - <2 cm on the trunk or extremities



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low risk BCC: management

Excision

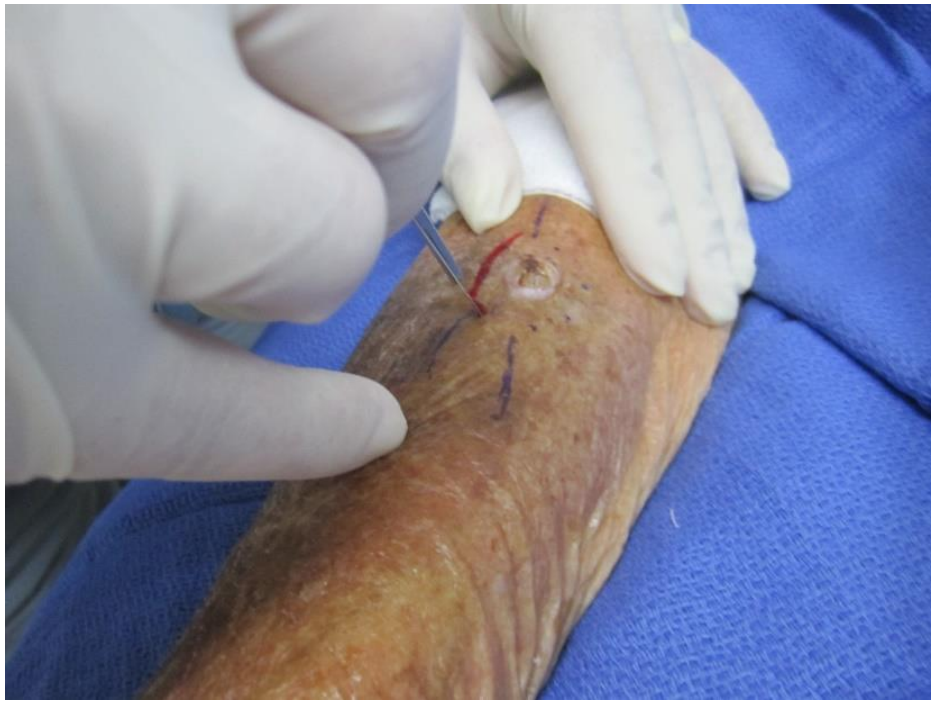
- 3 - 5 mm surgical margins
- treatment of choice for low-risk BCCs
- Mohs for incompletely excised tumors

Cure rates for low-risk tumors

- 95%

Cure rates for larger and high-risk tumors

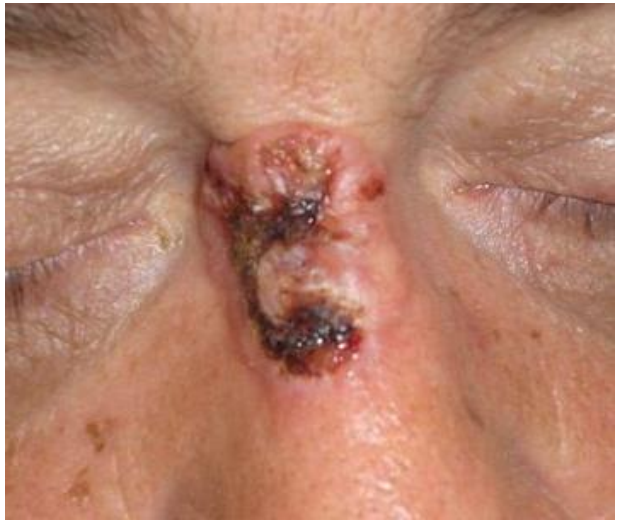
- 88% ≥ 10mm tumor
- 83% recurrent tumor
- 82% ≥ 20mm tumor

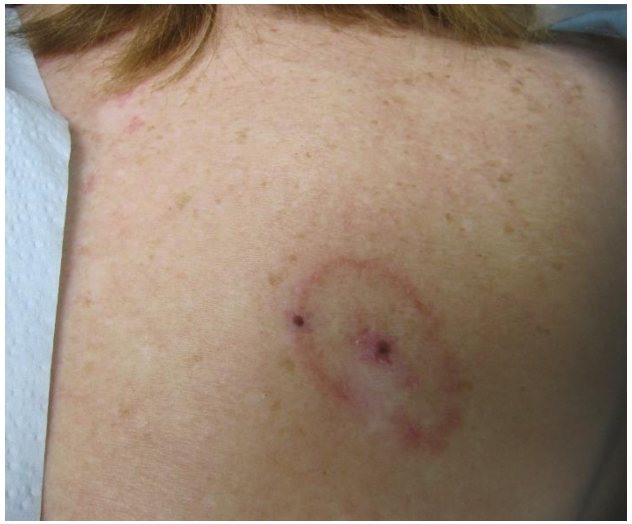


BCC: high risk

High risk characteristics

- >6 mm, scalp, ears, eyes, nose, lips, fingers, toes, genitalia
- perineural invasion, perivascular invasion
- Recurrent, poorly-defined clinical borders
- history of radiation therapy at site, Immunocompromised pt
- Micronodular / Infiltrative
- microscopic islands of tumor cells beyond the clinical margins
- Morpheaform / Sclerosing
- pale, waxy plaques; extends far beyond clinical margins

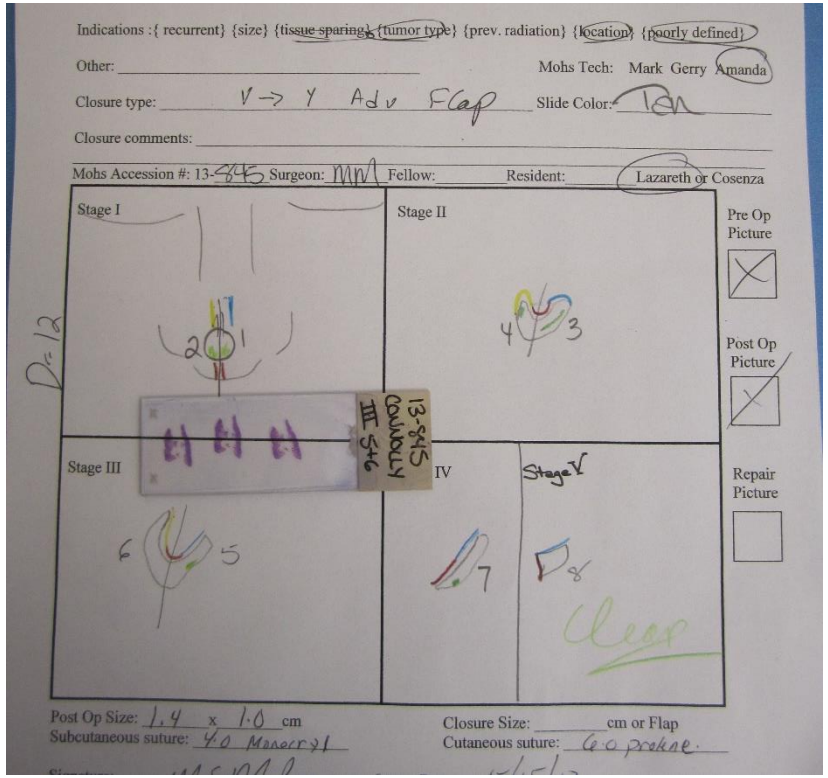




high risk BCC: management

Mohs Micrographic Surgery

- gold standard of care
- 99% cure rate for primary lesions
- high-risk histology
  - morphea, infiltrative
  - high-risk locations
    -scalp, ears, eyes, nose, lips, genitalia, digits
  - recurrent lesions



Ablative modalities like Mohs and excisional surgery have the advantage of examining tissue under the microscope to determine how completely the tumor was removed

Uncommon Non-Melanoma Skin Cancers

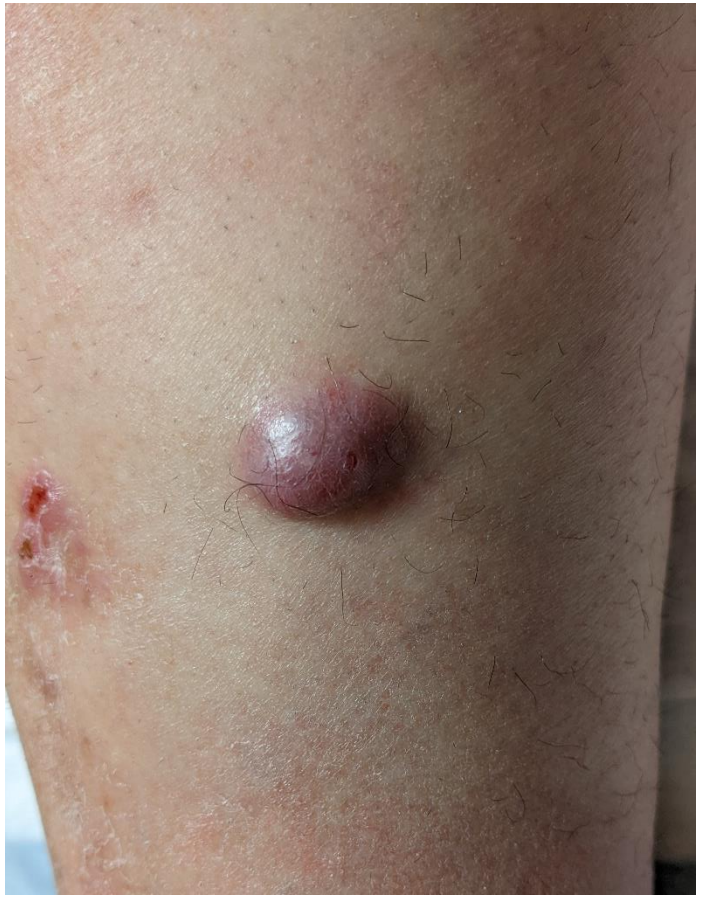
Question 3

Which skin cancer has a recurrence rate even more aggressive than melanoma?

A. Merkel Cell Carcinoma
B. Cutaneous B-cell Lymphomas
C. Cutaneous T-cell Lymphoma
D. Dermatofibromasarcoma Protuberans

Merkel Cell Carcinoma

- aggressive tumor associated with a high rate of recurrence and poor prognosis
- disease-recurrence data are not captured in national databases, but recurrence rates range from 27%-77%
- prospective cohort study included 618 MCC pts enrolled in a Seattle-based data repository 2003-2019 showed 223 experienced disease recurrence
- MCC recurrence rate (38%) was notably > melanoma (19%), SCC (5%-9%), BCC (1%-2%) following definitive treatment
- >90% of MCC recurrences occur within 3 years



McEvoy AM, Lachance K, Hippe DS, Cahill K, Moshiri Y, Lewis CW, Singh N, Park SY, Thuesmunn Z, Cook MM, Alexander NA, Zawacki L, Thomas H, Paulson KG, Nghiem P. Recurrence and Mortality Risk of Merkel Cell Carcinoma by Cancer Stage and Time From Diagnosis. JAMA Dermatol. 2022 Apr 1;158(4):382-389. doi: 10.1001/jamadermatol.2021.6096. PMID: 35195657; PMCID: PMC8867389.

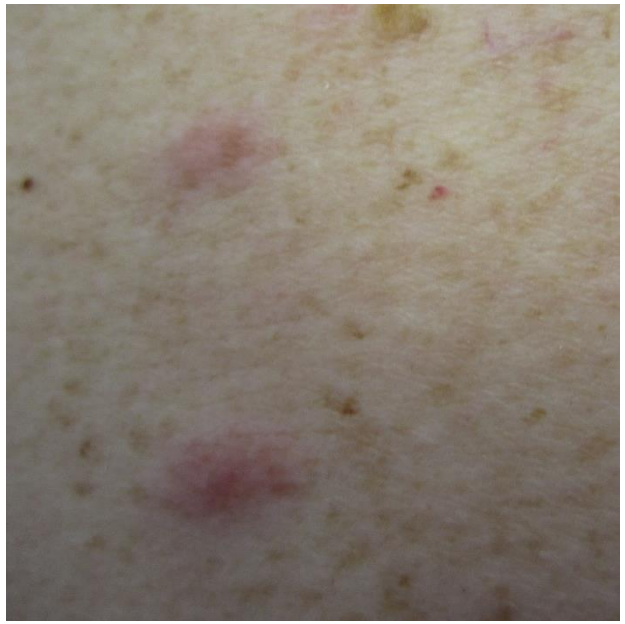
Cutaneous B-cell Lymphomas

2 main types of lymphocytes can develop into lymphomas:

- B lymphocytes (B cells) & T lymphocytes (T cells)

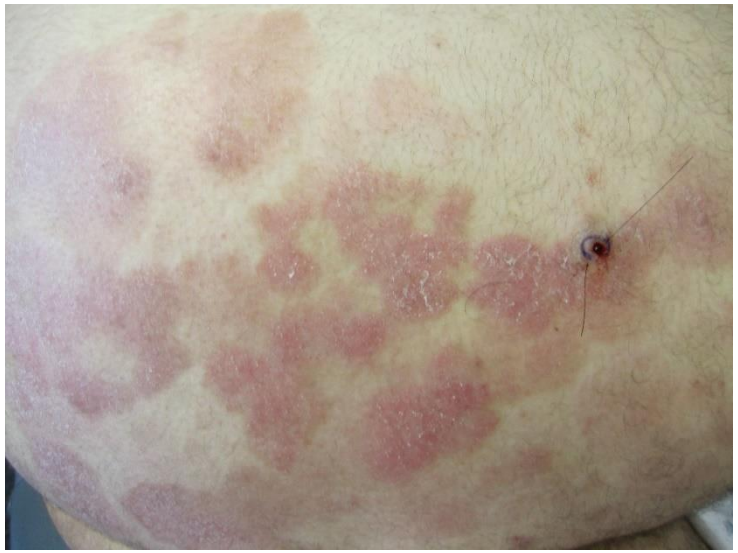
Cutaneous B-cell Lymphomas (CBCL)

- constitute 85% of all Non-Hodgkin Lymphoma (NHL)
- hyper-reactive inflammatory response
  - due to immunodeficiency disorder, viral or bacterial infection
- slow-growing subtypes
  - Primary Cutaneous Follicle Center Lymphoma
  - Primary Cutaneous Marginal Zone B-Cell Lymphoma
- uncommon subtypes
  - Primary Cutaneous Diffuse Large B-Cell Lymphoma, Leg-Type
  - Primary Cutaneous Diffuse Large B-Cell Lymphoma, Other



Cutaneous T-cell Lymphoma

- class of non-Hodgkin's lymphoma, > 50 yr, male, Black
- malignant helper T-cells migrate to the skin
- rare, unclear cause, can metastasize



Sub-types

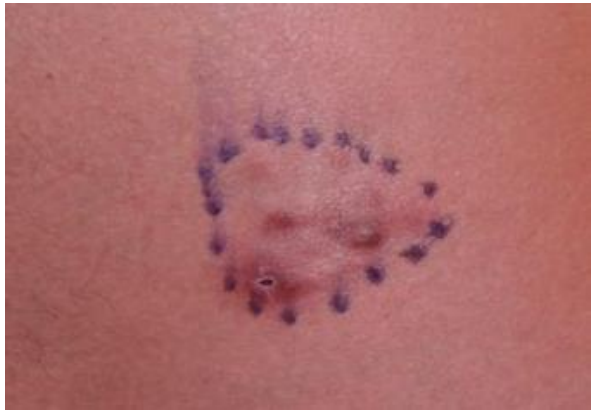
- Mycosis Fungoides (MF)
- Sezary Syndrome (SS): rare, aggressive

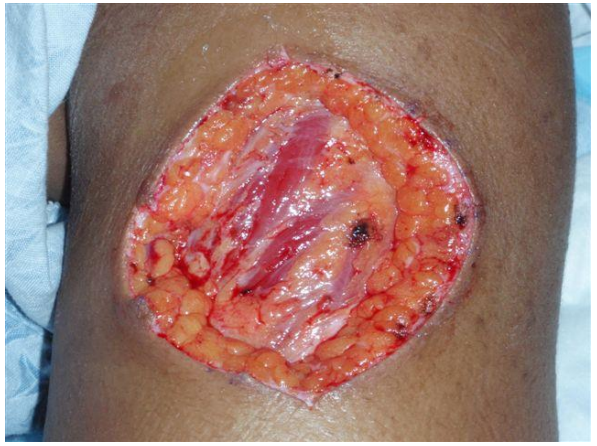
Presentation (may have 1 stage or a combination)

- *Early:* localized or widespread, ill defined, scaly, pink-red plaques
- *Patch:* sharply demarcated, red-pink, scaly atrophic, mottled, telangiectatic
- *Plaque:* dusky red-brown, patches, plaques buttocks, hips, thighs, flexural ext
- *Tumor:* red-brown expanding nodules which may ulcerate

Dermatofibromasarcoma Protuberans

- uncommon locally aggressive cutaneous sarcoma
- can attain massive "protuberant" dimensions
- may ulcerate, bleed, become painful
- becomes fixed to deeper structures in late disease
- M=F, Blacks > Whites, 30-50 yr, 6% in children
- trunk, proximal extremities, scar or tattoo
- MRI: deep extent of the tumor
- CT scan: possible bone involvement or lung metastases





Pigmented Lesions

Question 1

Which nevus may herald the development of vitiligo or melanoma?

a. Compound Nevus

b. Nevus Spilus

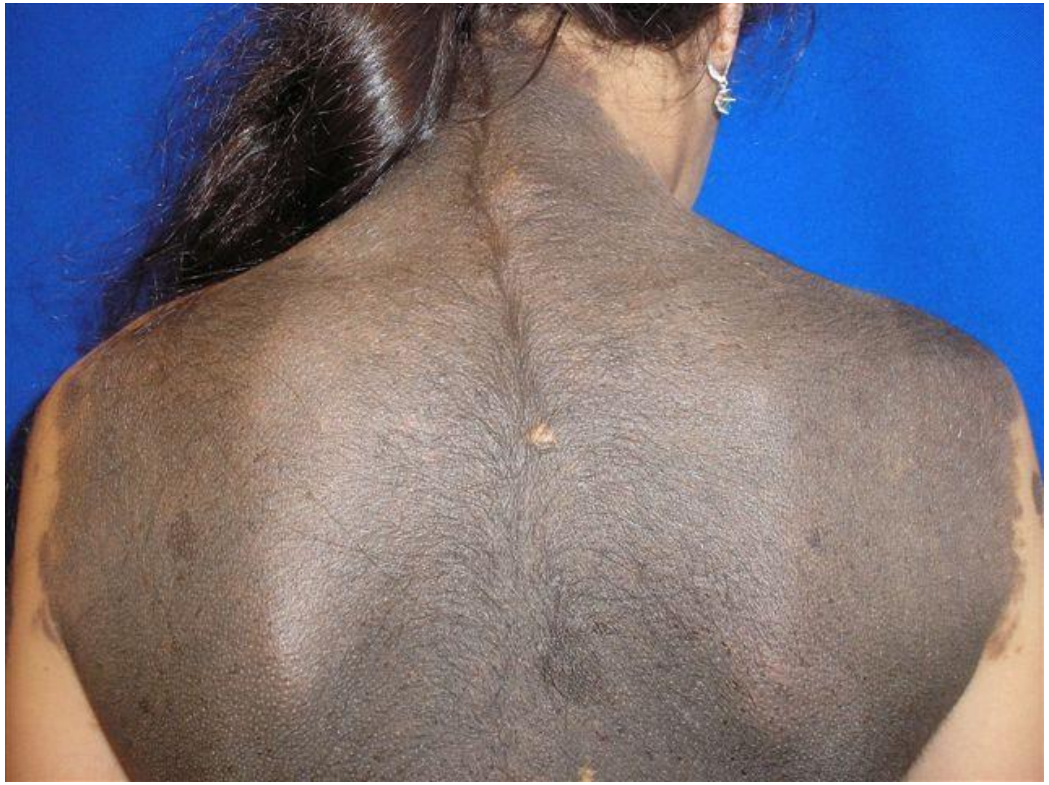
c. Halo (Sutton's) nevus

d. Spitz (Spindle cell) nevus

Congenital Melanocytic Nevi

Congenital Melanocytic Nevi (CMN)

- categorized by the largest diameter
  - Small CMN < 1.5 cm
  - Medium CMN 1.5–20 cm
  - Large CMN 20 – 40 cm
  - Giant CMN 40 – 60+ cm



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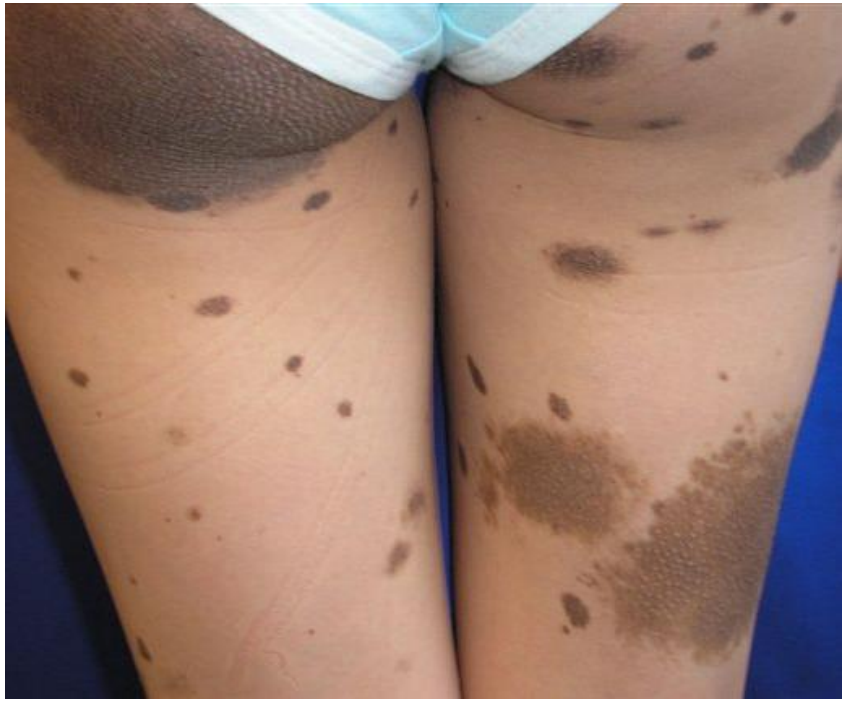
Congenital Melanocytic Nevi

Risk for malignancy of CMN increases with size

- Small-Medium CMN
  - <1% lifetime melanoma risk -*after puberty*
- Large-Giant CMN
  - 2-5% lifetime melanoma risk
  - 50% of which develop by age 5



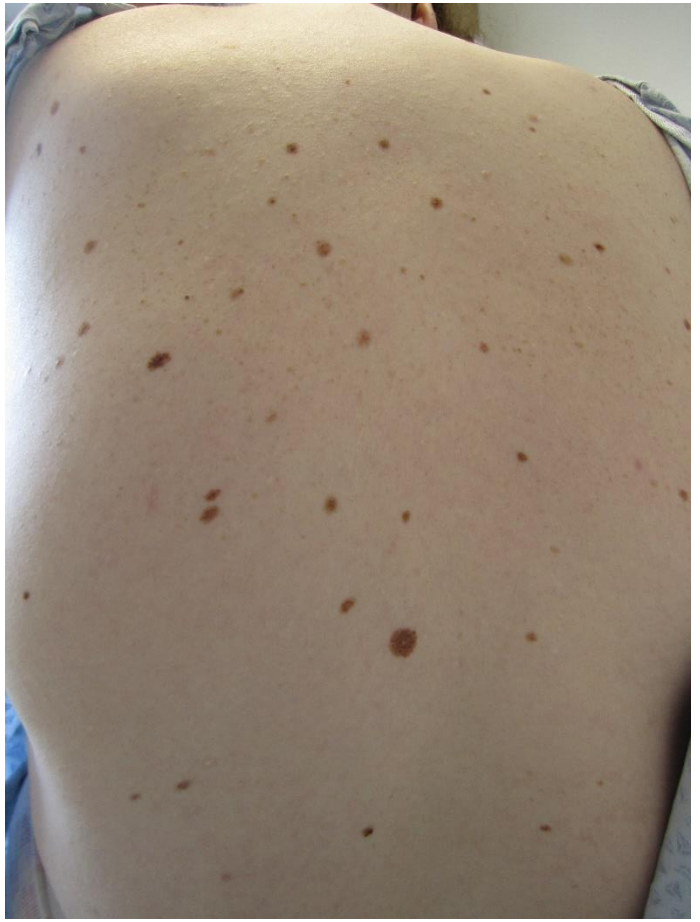
Risk for malignancy also increases with

- number of CMN, number of satellite nevi by 1 yr
- location (large lesions at back, buttocks)
- heterogeneity, rugosity, hypertricosis, nodularity, ulceration

Personal Photo(s) V.Lazareth NP

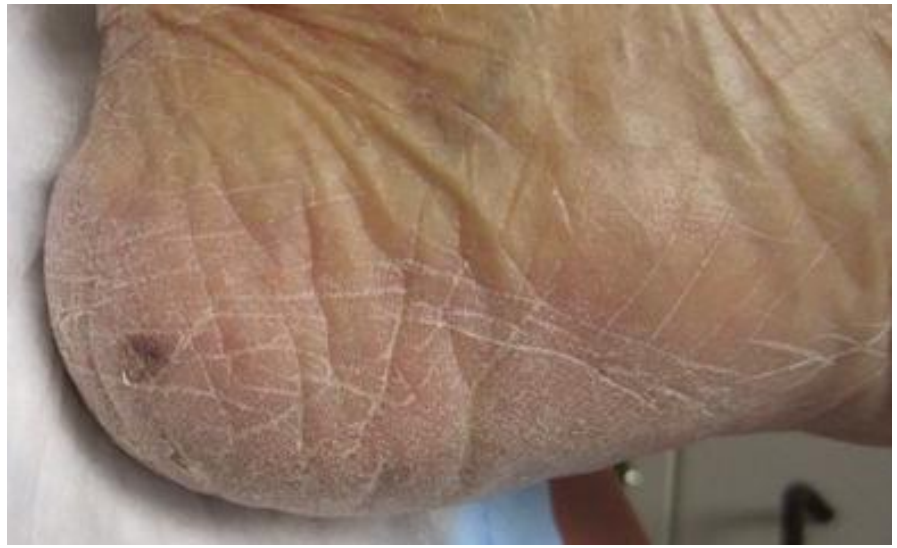
Benign Acquired Nevi

- benign proliferations of "nevus cell" melanocytes
- most remain benign needing only longitudinal observation
- increased risk of melanoma in pts with >50 acquired nevi
- regular Mole Check exams:
- Asymmetry, Border irregularity, Color discrepancy, Diameter >6 mm, Evolution
- Counseling: UVR protection



Benign Nevi: Junctional

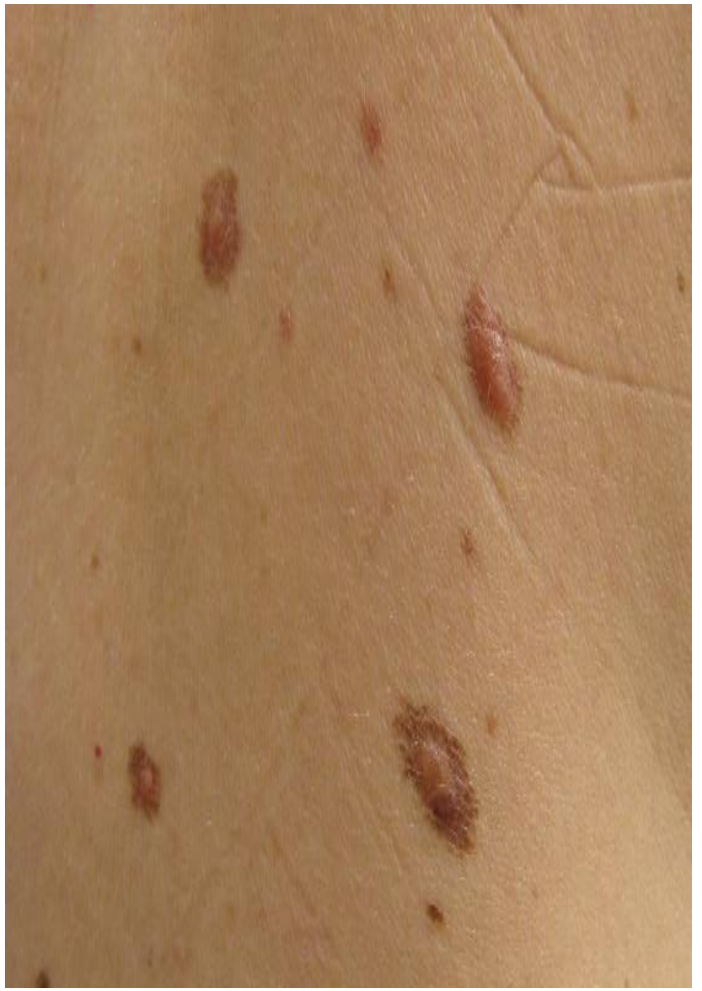
- junctional nevus has nests of nevus cells at the junction of the epidermis and the dermis
- brown-black macules with preserved relaxed skin tension lines
- most are seen in children; represent a transient phase in the development of compound nevi
- may be seen on the palms, soles, and genitalia in adults



Personal Photo(s) V.Lazareth NP

Benign Nevi: Compound

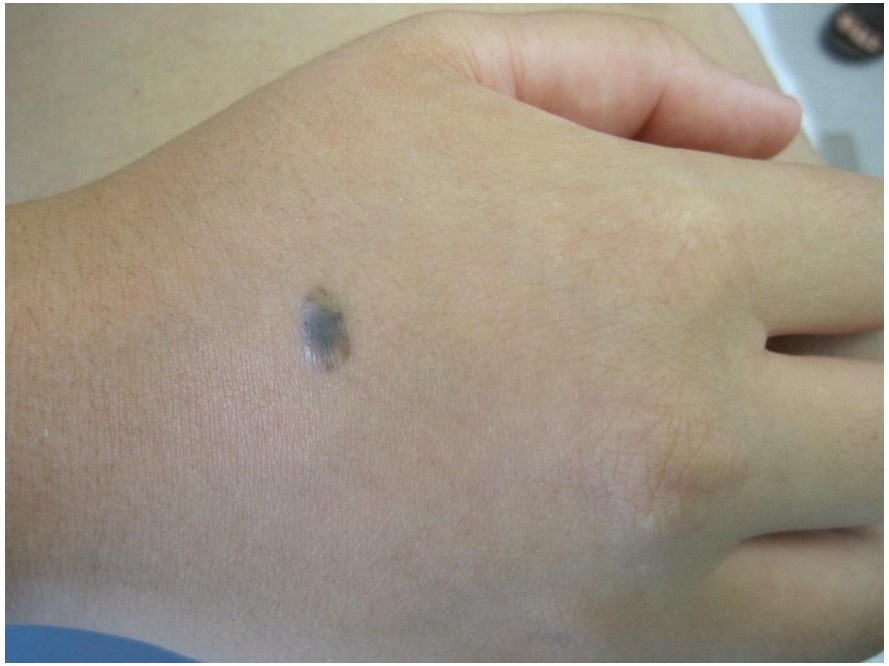
- compound nevus has nests of nevus cells at the epidermal-dermal junction as well as within the dermis
- central raised papule surrounded by a tan-brown macule
- increase in thickness & pigmentation: late childhood & adolescence
- “combined nevus” has two distinct types of mole within the same lesion; usually blue nevus + compound nevus



Personal photo, Victoria Lazareth

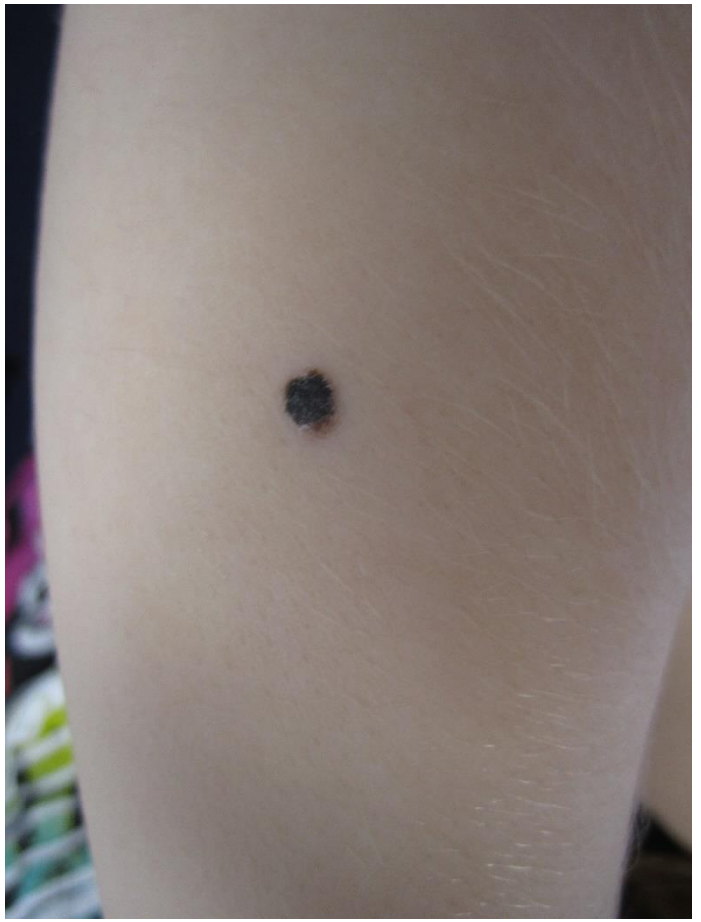
Benign Nevi: Blue

- deeply pigmented type of dermal nevus
- congenital or acquired -*adolescence*
- dorsal hands & feet <1 cm solitary, uniformly blue-black, dome-shaped papule
- ddx: traumatic tattoo, nodular melanoma, dermal melanoma metastases
- biopsy if atypical
- “cellular blue nevus” congenital, >1 cm smooth nodule; scalp, face, sacrum, buttocks



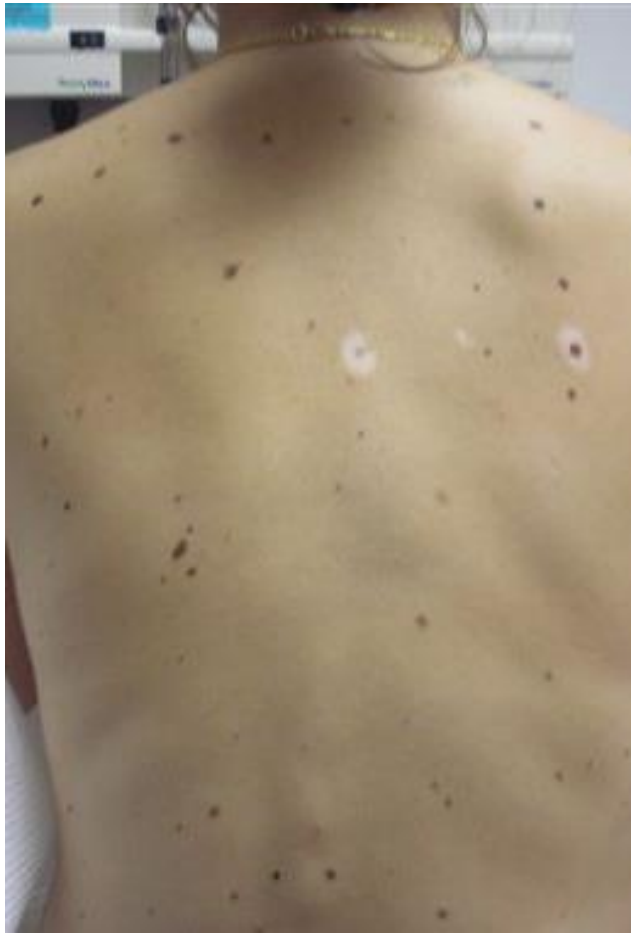
Benign Nevi: Spitz

- benign, acquired lesions with abnormal melanocytes which resemble those of melanoma
- arise in children and young adults at the scalp, face, legs with rapid initial growth phase
- <1 cm uniformly pink, tan, red, brown, symmetric, well-circumscribed, dome-shaped, smooth or verrucous papules
- classic Spitz nevi can be monitored; tend to undergo involution over time
- atypical lesions (>1 cm, asymmetrical, very dark, ulcerated) should be excised



Benign Nevi: Halo

- adolescents, young adults
- melanocytic nevus surrounded by halo of depigmentation; back most common
- heralds spontaneous regression of central nevus
- 50% have multiple lesions
- ~20% have vitiligo
- rare: middle-aged-older adults; may represent immune reaction to cutaneous or ocular melanoma
- biopsy if *central nevus* appears atypical



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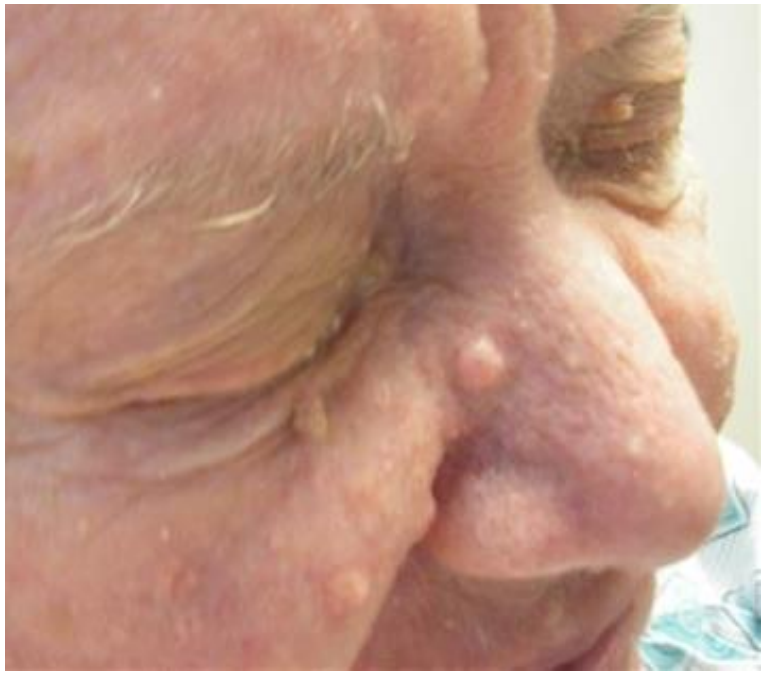
Benign Nevi: Intradermal

- dermal or intradermal nevi have nevus cell nests in the dermis
- develop after adolescence
- skin-colored - tan papules
- “Unna” papillomatous or pedunculated
- “Miescher” dome-shaped papule often found on the face



Question 2

By age 70, a patient with FAMMM syndrome will have a ___% lifetime risk of developing a melanoma.

a. 1%

b. 6%

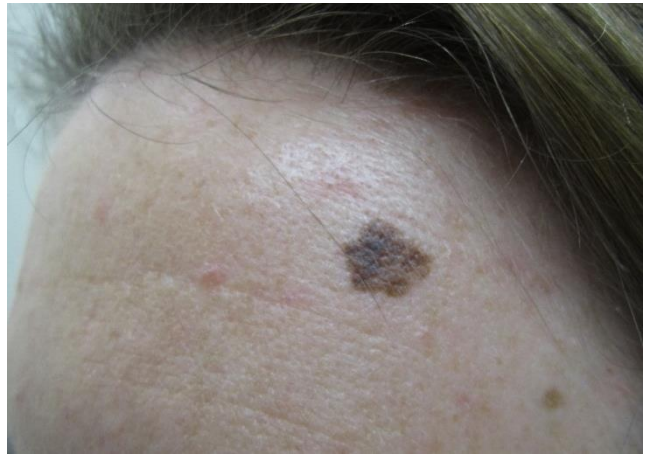
c. 15%

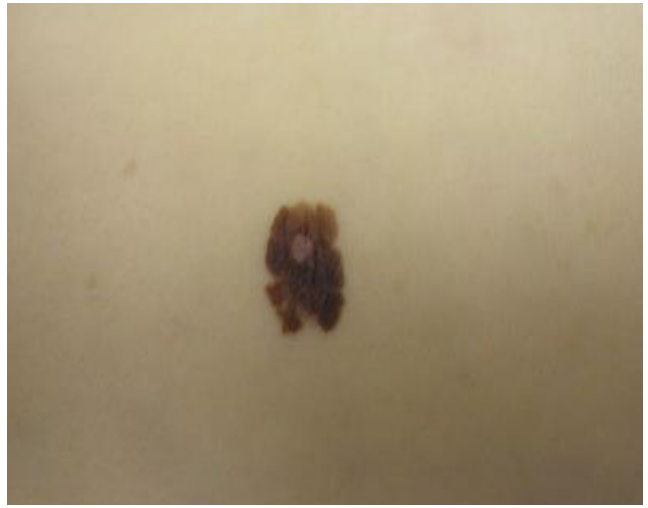
d. 100%

Atypical Nevi

- acquired melanocytic neoplasms that share some clinical features of melanoma
- trunk & extremities
- UVR history of tanning, sunburns
- Personal history of ATN/melanoma
- Family history of ATN/melanoma

"ABCDEs"
Asymmetrical, ill-defined Borders, variegated Color, Diameter >6 mm, Evolution: changes or symptoms





Atypical Nevi : dermoscopy

Dermatoscope

- handheld, noninvasive, tool used to examine skin lesions
- allows visualization of skin structures not visible to naked eye
- dermoscopic images may be photographed or recorded digitally

transilluminating light source and 10-fold magnifying optics
Non-Polarized dermoscopy
-superficial (epidermal) structures -*blue-white veil*
Polarized dermoscopy
-deeper (dermal) structures -*blood vessels*
several algorithms and scoring systems help clinician to
-differentiate nevus from melanoma
-decide to biopsy or monitor

Atypical Nevi: management

- Biopsy changing, symptomatic or suspicious moles
- pts with ATN have a 3 to 20-fold higher risk of developing melanoma
- Dysplastic Nevi are described by pathologists as "nevus with architectural disorder" with specification of the degree of melanocytic atypia present
- mildly and moderately DN with clear histologic margins
  - do *not* need re-excision
- mildly DN with positive histologic margins but no clinically residual pigmentation
  - do *not* need re-excision
- moderate-severe and severely DN with positive margins
  - may benefit from re-excision to confirm the diagnosis and exclude melanoma
- severely DN with or without residual pigment in the initial excision specimen
  - may benefit from conservative re-excision with 2-3 mm margins

Familial Atypical Multiple Mole Melanoma (FAMMM) Syndrome

- greatest risk for melanoma in pts with:
  - PMH or FMH of melanoma
  - multiple nevi
  - familial atypical multiple mole and melanoma (FAMMM) syndrome
- FAMMM: pts with >50 melanocytic nevi and FMH of melanoma
- potential precursor for melanoma (*superficial spreading*)
  - 1.3% lifetime risk of melanoma in general population
  - 6% lifetime risk of melanoma (also ocular melanoma) in pts with ATN
  - 15% lifetime risk of melanoma in pts with ATN + FMH of melanoma
  - 100% lifetime risk of melanoma by age 70 in pts with FAMMM

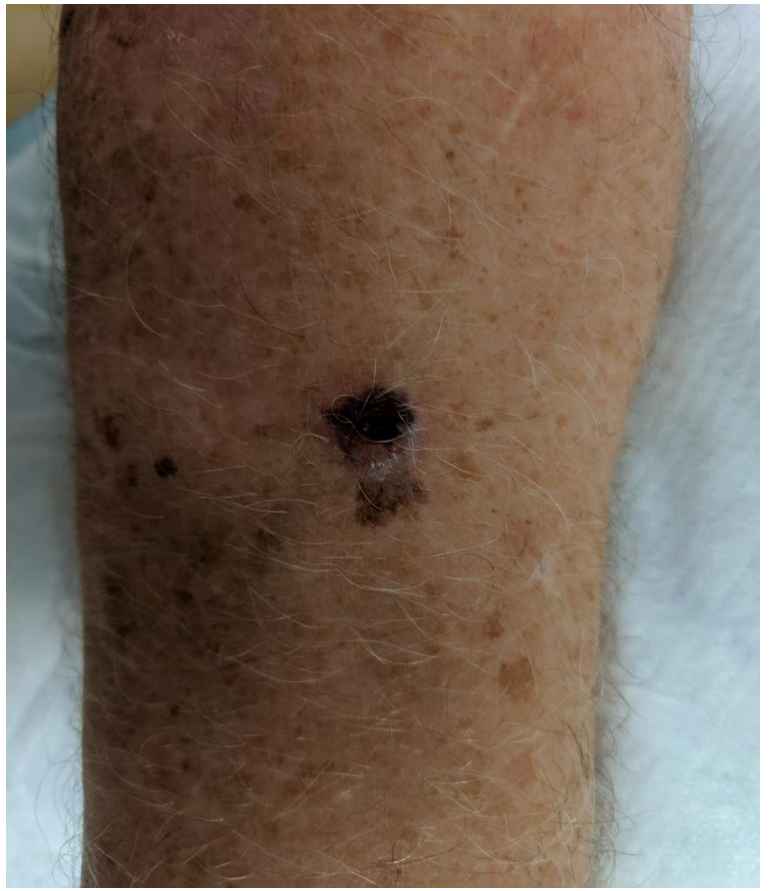
Pt Education for FAMMM pts

- UVR protection: shade, clothing, sunglasses, broad-spectrum sunscreen
  - fewer nevi in children who use sunscreen
  - 50% reduction of primary melanoma with regular application of sunscreen
  - increased risk of melanoma with tanning bed use
- regular skin self-examination
  - ABCDEs
  - 50% of melanomas are first detected by pts
  - may increase early detection, reduce incidence, reduce advanced disease
- lifelong melanoma follow-up
  - routine ophthalmologic and gynecologic examination
  - screening of family members
  - genetic counseling (FAMMM/melanoma)

Case #3

71 yr M

- dark lesion at rt forearm
- delayed access to Derm due to Covid closures
- bubbling with hydrogen peroxide but not healing



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Question 3

Which of the following is the most significant risk factor for the lifetime development of cutaneous melanoma?

a. Skin type I (fair skin)

b. History of > 6 atypical nevi

c. History of blistering sunburns

d. Family history of melanoma

Melanoma: predisposing factors

History

- new, changing lesion
- PMH / FMH of melanoma
- excessive sun exposure and/or tanning bed use
- severe sunburns in youth
- FAMMM, xeroderma pigmentosum
- hx of PUVA, Immunosuppression

Physical

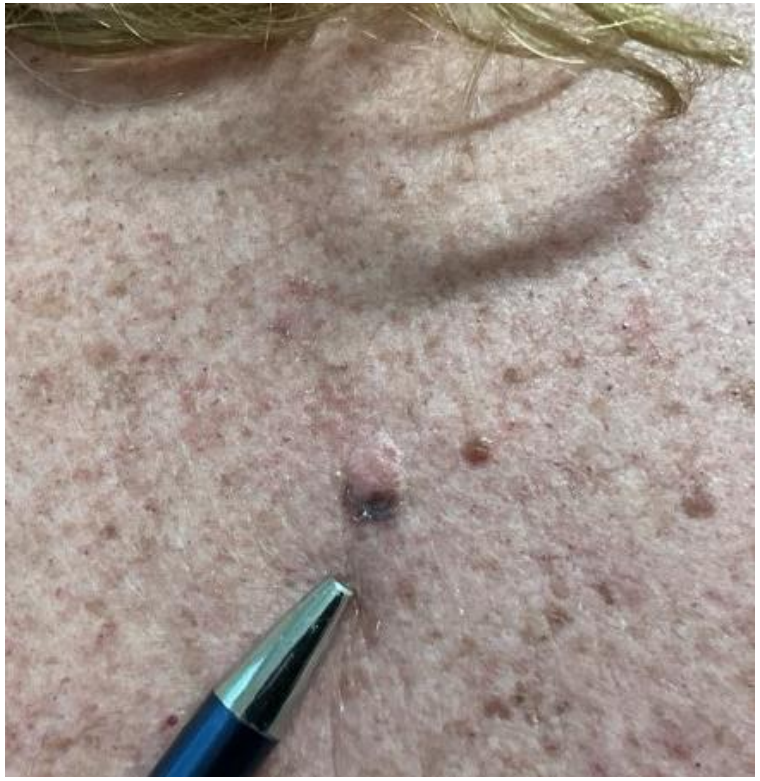
- light-complexioned phototype
- red or blond hair
- light eye color
- presence of a large number of melanocytic nevi
- atypical melanocytic nevi

Melanoma: introduction

- incidence increases with age
- early diagnosis improves outcome & survival rates
  - most are detected by pts themselves however, melanomas detected by clinicians tend to be thinner, more curable tumors
  - thin melanomas confined to the epidermis are associated with prolonged disease-free survival
  - ideally surgically excised before/during horizontal "radial" growth phase
- dermal invasion during "vertical" growth phase has metastatic potential
  - increased tumor thickness “Breslow depth” increases risk of metastases
  - Breslow depth >1 mm is associated with limited survival

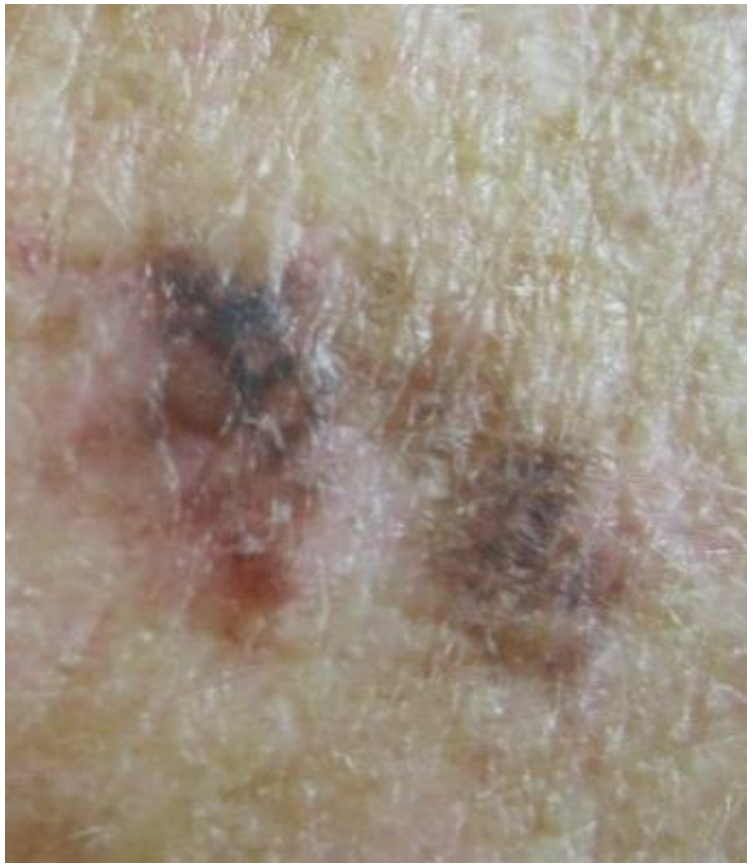
Melanoma: clinical

- 70% arise de novo
- 30% arise within an existing nevus
  - present with focal area of color change
- early S&S:
  - flat during horizontal growth phase
  - increase in size, change of color or shape, itching
- late S&S
  - thickened, raised during vertical phase
  - tender, bleeding, crusting, ulceration
- not all melanomas follow the ABCDEs (i.e., amelanotic)



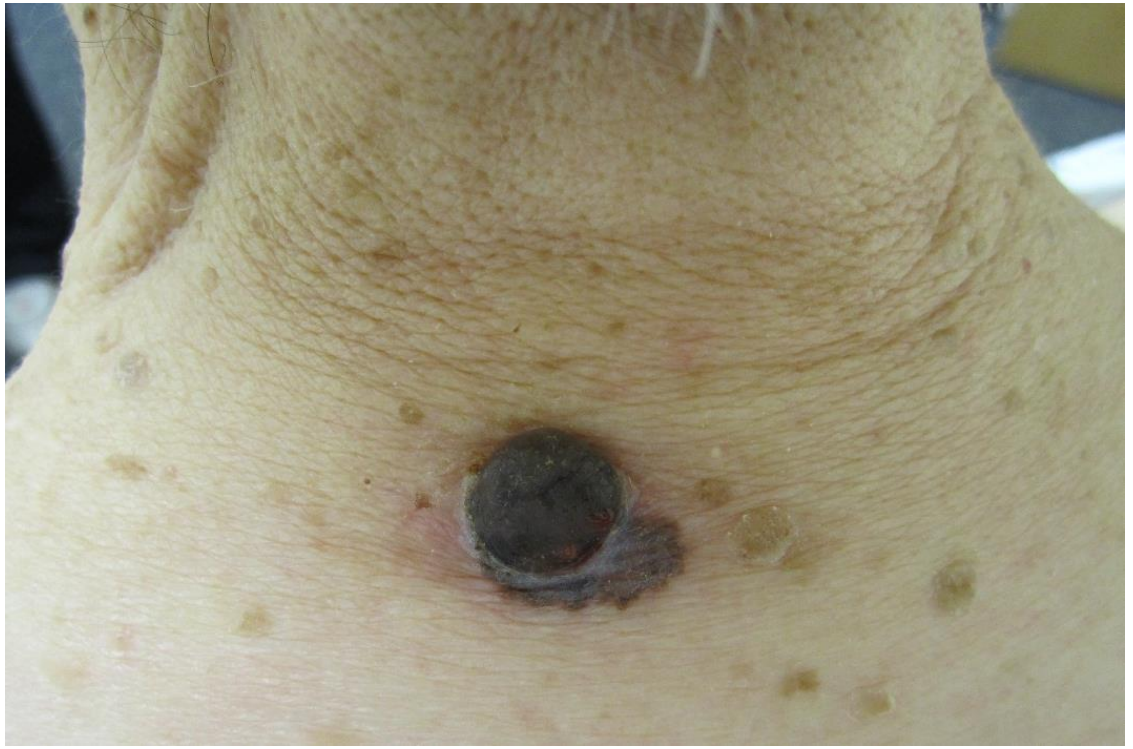
Melanoma: superficial spreading

- most common histologic subtype, ~70%
- >60% diagnosed as thin, highly curable tumors
- subtype most likely to be associated with a pre-existing nevus
- predilection: back, lower extremities (women)
- variably pigmented macule or thin plaque with an irregular border
- size ranges from a few mms to several cms
- multiple shades of red, blue, black, gray, white



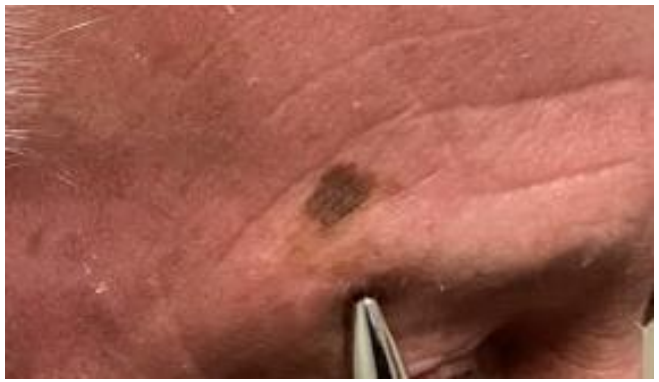
Melanoma : nodular

- 2nd most common subtype; 15-30%
- darkly pigmented, symmetrical papules or nodules
- often uniform blue-black color, may have pink hue,
- no identifiable radial growth phase
- appear to enter the vertical growth phase from their inception, resulting in thicker tumors (>2 mm) at diagnosis



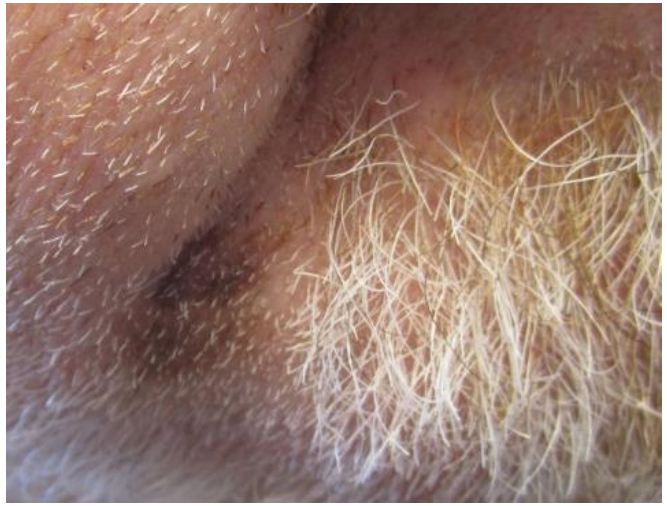
Lentigo Maligna & Lentigo Maligna Melanoma

- tan-brown macule in chronically sun-damaged skin
- enlarge over years with darker, asymmetric foci of pigmentation, color variegation, and raised areas



Lentigo Maligna

- in situ melanoma
- changes in LM signify vertical growth



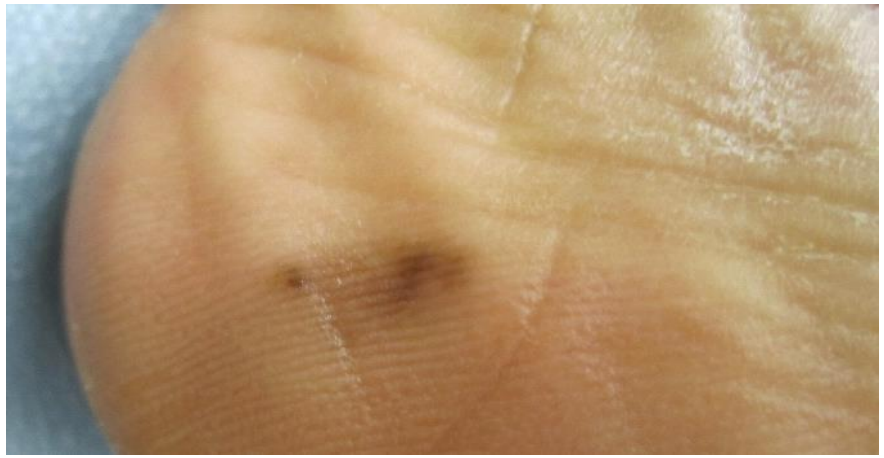
Lentigo Maligna Melanoma

- 10-15% of all melanomas
- rising incidence particularly in older pts

Personal Photo(s) V.Lazareth NP

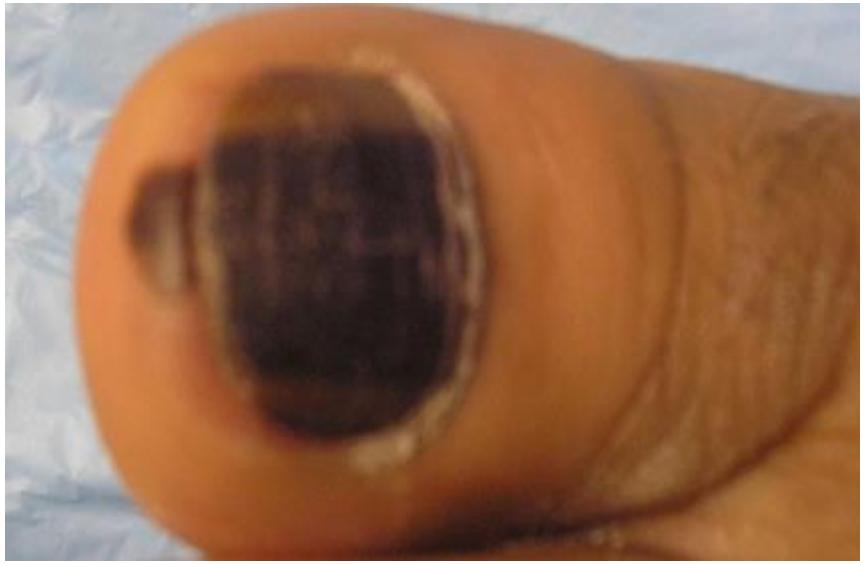
Melanoma: acral lentiginous

- <5 % of all melanomas
- most common subtype in pts with skin of color
  - 60-72% in African Americans
  - 29-46% in Asian Americans
- 5 yr relative survival
  - 93% Whites : 69% AA
  - reduced access to care, perceived lower risk, atypical sites
  - later diagnosis, timing of detection
- palmar, plantar, subungual
- dark brown-black, irregularly pigmented macules
- dermal invasion: larger lesions, raised areas, ulceration, bleeding



Melanoma : acral subungual

- arises from the nail matrix
- longitudinal, brown/black band in the nail
- with/without nail dystrophy
- may present as a mass below the nail plate with ulceration and nail plate destruction
- can mimic benign conditions: onychomycosis, paronychia, warts, calluses

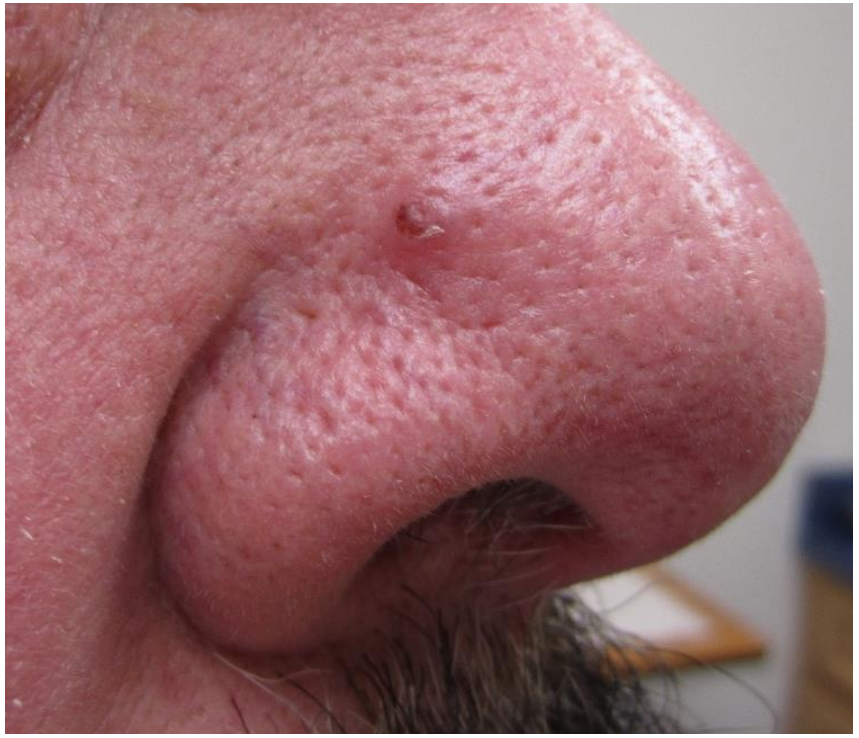


"Hutchinson sign" longitudinal pigmentation extending to the proximal nail fold or distal digit

Personal Photo(s) V.Lazareth NP

Melanoma: amelanotic

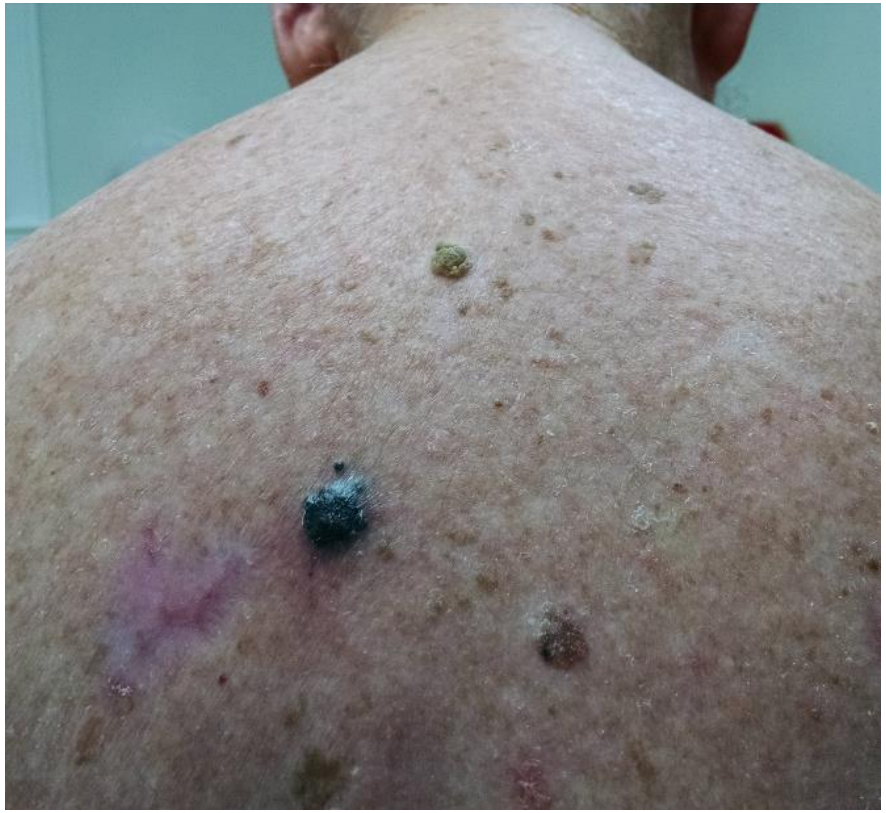
- ~2-10% of all melanomas
- *all* subtypes can present as amelanotic or hypomelanotic
- most commonly seen in nodular and desmoplastic melanomas
- pink/red macules, papules, or nodules, often well-defined borders
- benign appearance challenges and delays diagnosis



Personal Photo(s) V.Lazareth NP

Melanoma: Spitzoid

- resemble Spitz nevi, both clinically and histologically
- red (amelanotic), brown, black, blue papules or nodules
- often round in shape and uniform in color
- may be crusted and ulcerated
- head or extremities



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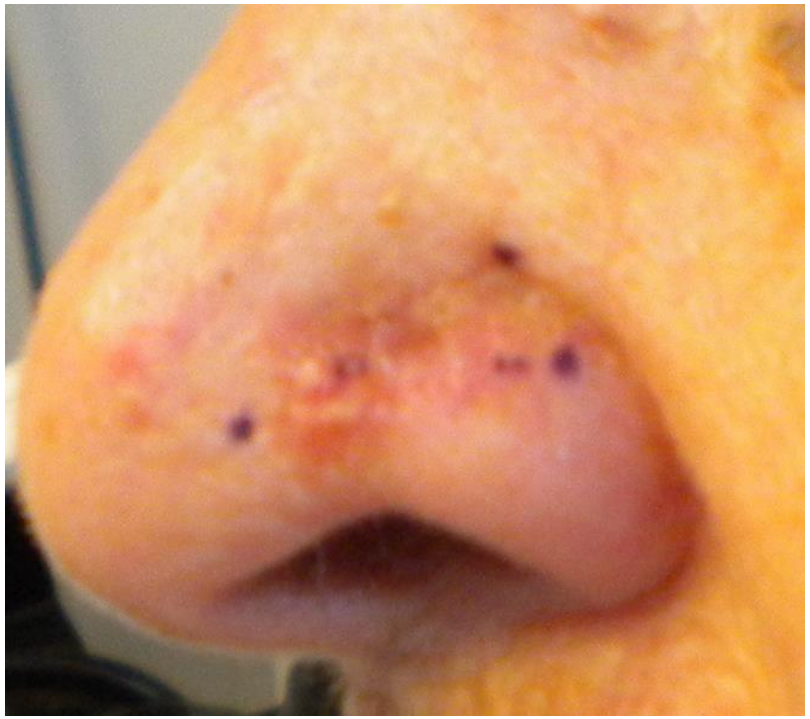
Melanoma: desmoplastic

- rare but histologically and clinically distinct variant
- slowly growing plaque, nodule
- usually amelanotic in chronically sun-exposed areas of older pts
- may resemble NMSC



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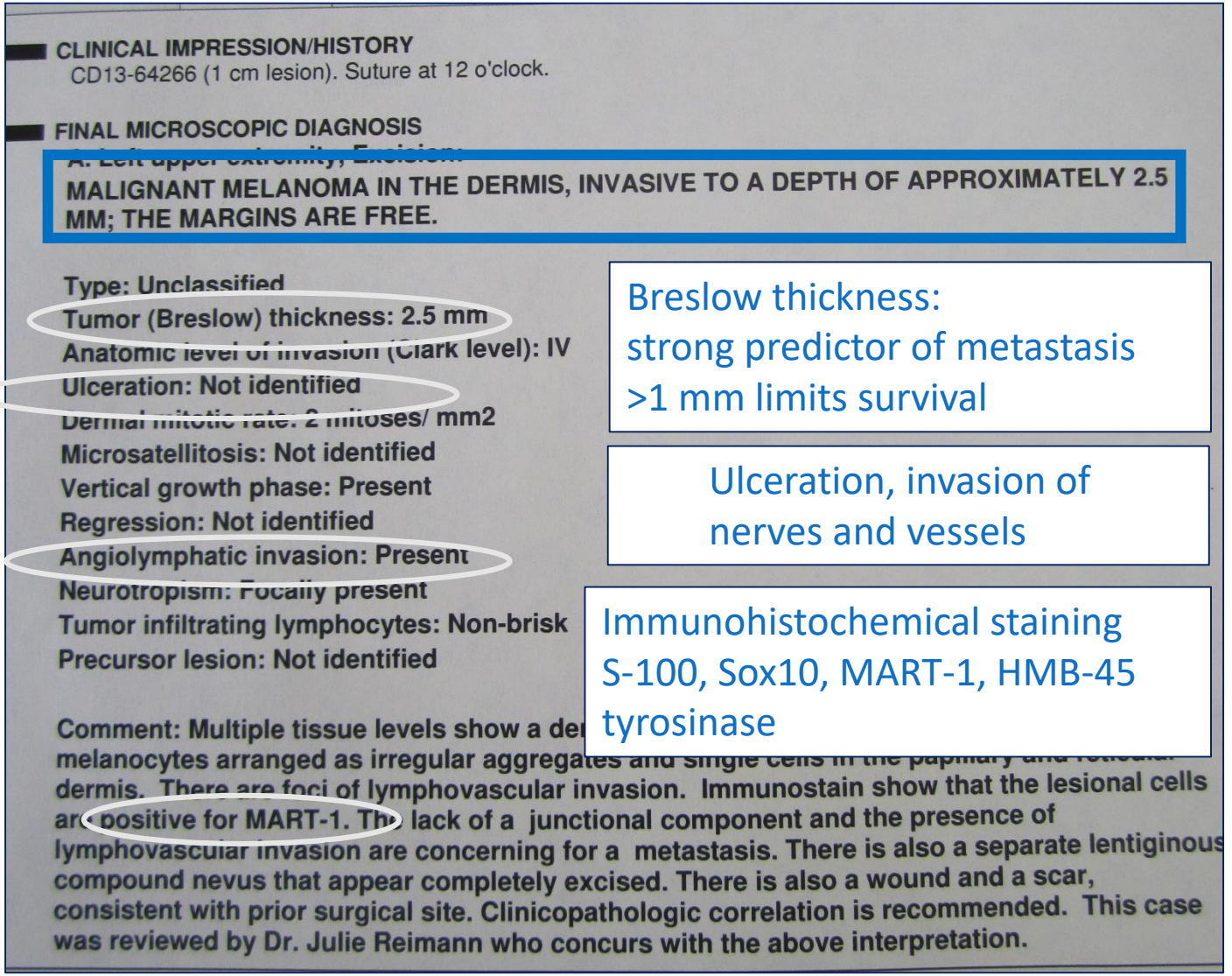
Melanoma: histology

Prior to any intervention

- document location, color, size, pattern
- photograph lesion and local landmarks
- carefully palpate local lymph nodes



CLINICAL IMPRESSION/HISTORY
CD13-64266 (1 cm lesion). Suture at 12 o'clock.

FINAL MICROSCOPIC DIAGNOSIS
MALIGNANT MELANOMA IN THE DERMIS, INVASIVE TO A DEPTH OF APPROXIMATELY 2.5 MM; THE MARGINS ARE FREE.

Type: Unclassified
Tumor (Breslow) thickness: 2.5 mm
Anatomic level of invasion (Clark level): IV
Ulceration: Not identified
Dermal mitotic rate: 2 mitoses/ mm2
Microsatellitosis: Not identified
Vertical growth phase: Present
Regression: Not identified
Angiolymphatic invasion: Present
Neurotropism: Focally present
Tumor infiltrating lymphocytes: Non-brisk
Precursor lesion: Not identified

Comment: Multiple tissue levels show a der
melanocytes arranged as irregular aggregates and single cells in the papillary and reticular
dermis. There are foci of lymphovascular invasion. Immunostain show that the lesional cells
are positive for MART-1. The lack of a junctional component and the presence of
lymphovascular invasion are concerning for a metastasis. There is also a separate lentiginous
compound nevus that appear completely excised. There is also a wound and a scar,
consistent with prior surgical site. Clinicopathologic correlation is recommended. This case
was reviewed by Dr. Julie Reimann who concurs with the above interpretation.

Breslow thickness:
strong predictor of metastasis
>1 mm limits survival

Ulceration, invasion of nerves and vessels

Immunohistochemical staining
S-100, Sox10, MART-1, HMB-45
tyrosinase

Melanoma: diagnostics

Sentinel Lymph Node Biopsy (SLNB)

- determines presence of micrometastasis which helps to stage cancer
- indicated for Breslow ≥0.8 mm
- positive lymph nodes: non-tender, firm-hard, increase in size quickly

Gene Expression Profiling (GEP)

- melanoma prognosis identifies the risk of recurrence or metastasis in pts with Stage I, II, and III melanoma
- based on the biologic profile of genes within their tumor tissue
- *CDKN2A* & BRAF genes implicated in development of melanoma

- Objective: Identify factors associated with differences in melanoma survival in 2 age groups: adolescents and young adults (AYAs; ages 15-39) and older adults (ages 40-64)
- Methods: This population-based registry study included all cases (n=81,597) of cutaneous melanoma diagnosed at ages 15-64 from 2004-2015 in CA
- Results: AYA pts with Stage IV melanoma, thicker tumors and public insurance had worse survival than was observed among older adults
- Conclusions:
- Survival was much worse for AYAs with stage IV melanoma than observed among older adults
- Greater awareness, suspicion and screening is critical to improve early melanoma detection and survival in adolescents and young adults

Melanoma Survival by Age Group: Population-Based Disparities for Adolescent and Young Adult Patients by Stage, Tumor Thickness, and Insurance Type. KY Wojcik, M Hawkins, A Anderson-Mellies, et al. Published: JAAD, January 04, 2023. DOI: https://doi.org/10.1016/j.jaad.2022.10.063

Melanoma: management

Wide Surgical Excision

- Dermatology Surgeon, Surgical Oncologist, Plastic Surgeon, General Surgeon

Wide Surgical Excision
0.5-1 cm margin: melanoma in situ
1 cm margin: Breslow </= 1 mm
1-2 cm margin: Breslow >1–2 mm
2 cm margin: Breslow > 2 mm

- worse prognosis: subungual, plantar, palmar, mucosal lesions
- adjuvant XRT: may be indicated if location precludes adequate resection or if particularly high risk of recurrence

Consultation/Collaboration

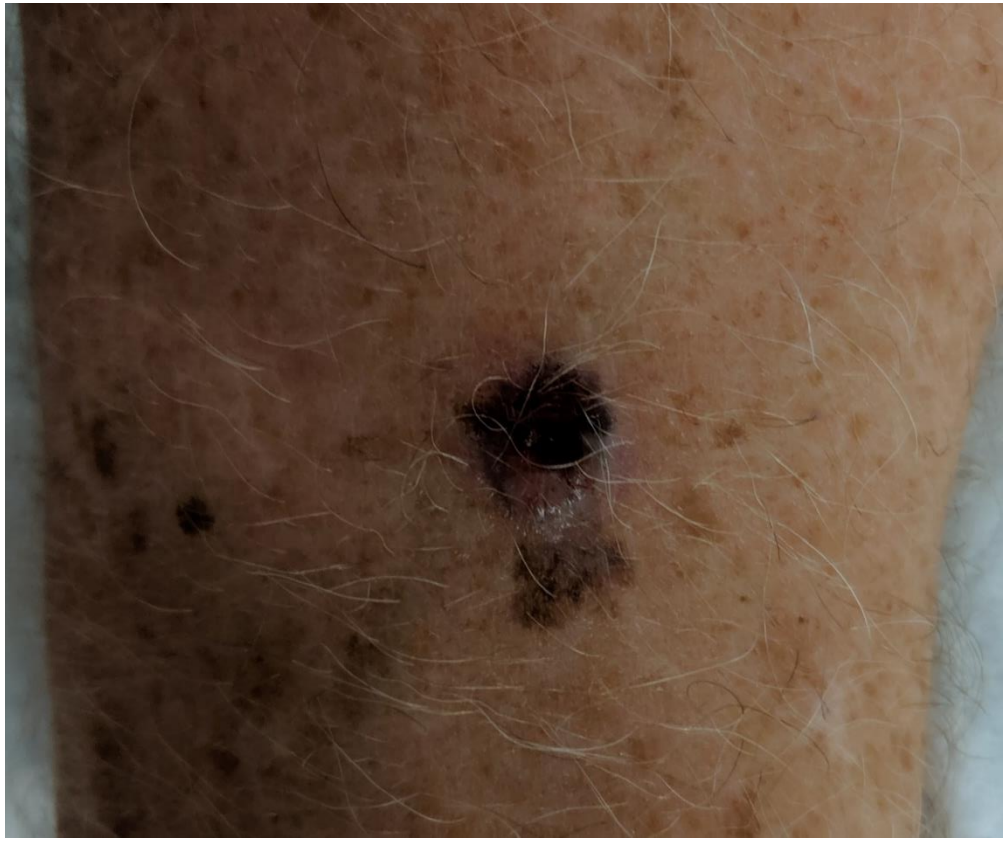
- Dermatology, Pathology, Surgical – Medical - Radiation Oncology, and/or Tumor Board

Melanoma: oncology

- most cases of melanoma are diagnosed at an early stage when surgical excision can be curative however,
- pts may present with metastatic disease or may develop metastases after initial treatment
- Chemotherapy: Stage IIIB-IIIC
  - interleukin-2
  - interferon alfa 2b
- Immunotherapy:
  - checkpoint inhibitors
  - [CTLA-4] inhibitors
  - cytotoxic T lymphocyte-associated protein 4
  - LAG-3 inhibitors
  - [BRAF plus MEK] inhibitors targeted therapy

Melanoma: pt education

- Monitoring
  - baseline TBSE then q3 mo yr 1; q 4 mo yr 2; q6 mo yr 3+
  - includes lymph node and liver palpation
  - CT Scan of head, chest, abdomen
  - annual TBSE for 1st degree relatives
- >20% of melanoma pts: develop a new melanoma in situ
  - 5–10% of melanoma pts: develop a 2nd invasive melanoma
  - Self Skin Exam, ophthalmologic examination
  - Annual screening of family members



Personal Photo(s) V.Lazareth NP

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