South Beach Symposium
medical + aesthetic dermatology
CELEBRATING 20 YEARS
OF PREMIER MEDICAL & AESTHETIC DERMATOLOGY EDUCATION

REIMAGINING
MEDICAL AND
AESTHETIC
DERMATOLOGY

Treatment Guidelines for Melanoma and Non-Melanoma Skin Cancer

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Melanoma

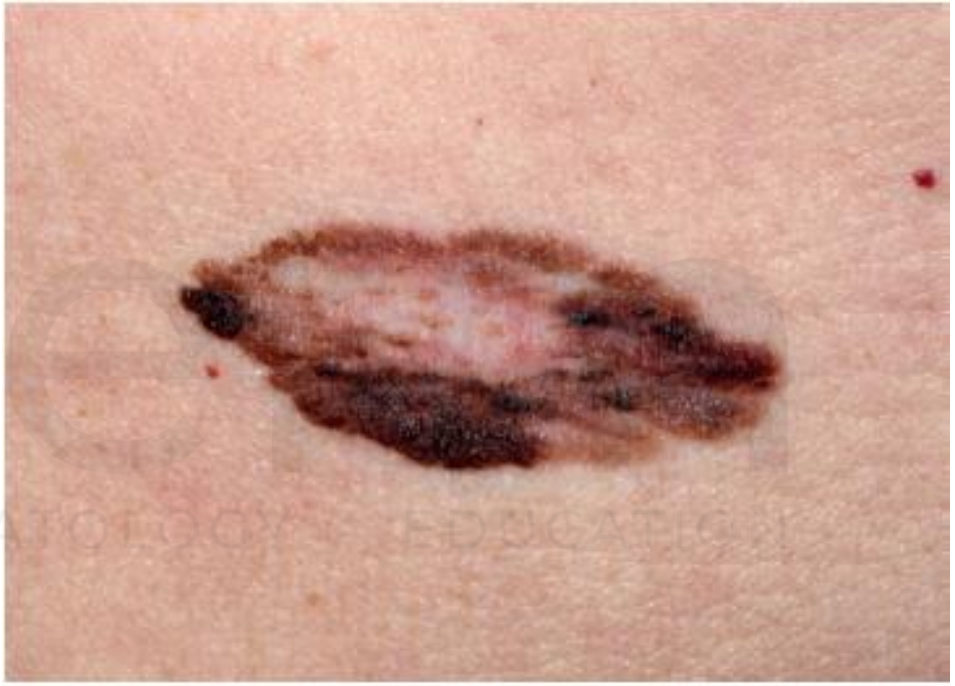
Epidemiology and Clinical Presentation

Introduction

- Melanoma represents a malignant tumor that arises from melanocytes
- Due to its metastatic potential, it leads to >75% of skin cancer deaths
- The incidence rates of melanoma have increased over the past four decades by three- to five-fold, whereas mortality rates began to stabilize in the early 1990s
- Early detection of *in situ* and early invasive cutaneous melanomas by dermoscopy has led to an improvement in diagnostic accuracy
- Early-stage melanomas are often curable by surgical excision
- For metastatic melanoma, immunotherapies (e.g. ipilimumab) and targeted therapies (e.g. vemurafenib) can be tried

Epidemiology

- Melanoma is derived from melanocytes, most commonly cutaneous
  - Can be mucosal e.g. oral, conjunctival, vaginal, uveal tract of eye and leptomeninges
- Majority are brown/black in color
  - others are pink to skin-colored or amelanotic



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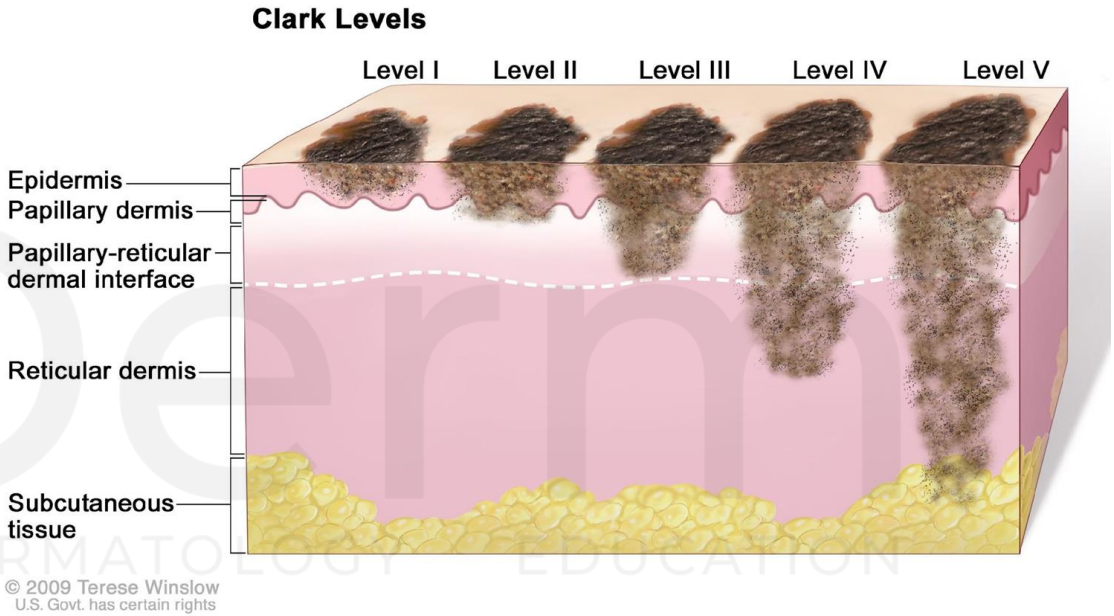
Epidemiology

- Very low prevalence in skin of color
  - Most commonly acral subtype
- Melanoma represents the most rapidly increasing cancer in white populations
- Lower rates in Mediterranean countries and higher rates in Scandanavian countries
- Highest incidence rate in Australia/New Zealand

Epidemiology

- Vertical tumor thickness (Breslow Depth) is the most important local prognostic factor in primary cutaneous melanoma
- Diagnosis of thinner tumors yields stable/decreased mortality rates, despite increasing incidence rates
- Percentage of thicker melanomas increases with age



National Cancer Institute, cancer.gov

Risk Factors For Cutaneous Melanoma: Genetics

- Germline genetic mutations/polymorphisms may predispose individuals to developing melanoma
  - Both rare high penetrance genes and very common pigmentation genes for fair-skinned individuals predispose individuals to develop melanoma
- CDKN2A is a major high-penetrance susceptibility gene locus associated with familial melanoma
  - 2% cutaneous melanoma specifically attributed to this germline mutation
  - CDKN2A linked to increased pancreatic cancer risk
- MC1R mutations associated with lighter skin phenotype
- SNPs in TYR, TRYP1, SCL45A2 associated with increased melanoma risk

Risk Factors For Cutaneous Melanoma Phenotypic Risk Factors Reflecting Gene/Environment Interactions

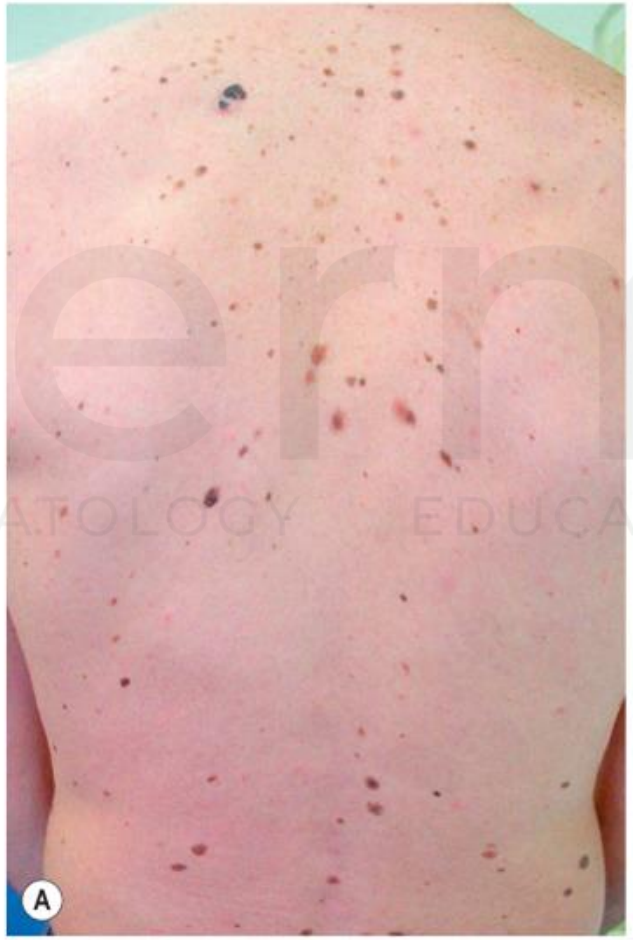
- Strongest independent risk factors for cutaneous melanoma development reflect both genetic susceptibility and environmental exposure
- Development of melanocytic nevi, atypical melanocytic nevi, and solar lentigines are independent risk factors for melanoma
  - indicate UV exposure/DNA damage
  - can serve as formal precursors of melanoma

Risk Factors For Cutaneous Melanoma: Number of nevi

- Light skinned populations have higher melanocytic nevus counts than darker-skinned populations
  - Light skinned populations have increased risk of melanoma correlating with increased number of melanocytic nevi
- Superficial spreading and nodular melanoma development has strongest association with melanocytic nevi counts
- Lentigo maligna melanoma development has strongest association with skin type and hair color

Risk Factors For Cutaneous Melanoma: Atypical Melanocytic Nevi

- Independent risk factor for sporadic melanoma
- Maximum reported relative risk for melanoma is as high as 32-fold when 10 or more atypical melanocytic nevi are found
- Five or more atypical melanocytic nevi associated with clearly higher relative risk of melanoma development



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Risk Factors For Cutaneous Melanoma: Environmental Risk Factors, UV radiation

- 80% melanomas develop in intermittently sun-exposed regions,
  - both intermittent sun exposure and sunburn history are identified as risk factors
- However, melanoma development is not all about UV radiation
  - The anatomic distribution of melanoma does not closely match sites of greatest cumulative sun exposure
  - Melanoma is most often in middle-aged adults and not elderly with most cumulative sun exposure

Risk Factors For Cutaneous Melanoma Environmental Risk Factors, UV radiation

- Sunburns in childhood and adolescence are significantly associated with melanoma development
  - duration of sun exposure stronger risk factor than the occurrence of sunburns
- Both UVB and UVA radiation are associated with the development of cutaneous melanoma, but UVB exposure serves as strongest risk factor
- However, total number of melanocytic nevi is identified as the most important risk factor for cutaneous melanoma

Risk Factors For Cutaneous Melanoma: Environmental Risk Factors, Sun Protection

- In 2009, WHO categorized tanning beds as a human carcinogen
- Tanning bed exposure before age 35 is statistically significantly associated with melanoma development
  - Suberythema doses of UVR can cause DNA mutations
  - There is a significant misunderstanding that avoidance of sunburns and use of sunscreens are sufficient to prevent skin cancer
- Encourage sun avoidance between 10 am and 4 pm, hats, non-transparent clothing (UPF)

Types of Primary Melanomas

- From most common to least common:
  - Superficial spreading melanoma
  - Nodular melanoma
  - Lentigo maligna melanoma
  - Acral lentiginous melanoma
  - Unclassifiable melanoma

DIFFERENT TYPES OF PRIMARY CUTANEOUS MELANOMA			
Clinico-histopathologic subtype	**Abbreviation**	**Percentage**	**Median age**
Superficial spreading melanoma	SSM	57.4%	51 years
Nodular melanoma	NM	21.4%	56 years
Lentigo maligna melanoma	LMM	8.8%	68 years
Acral lentiginous melanoma	ALM	4%	63 years
Unclassifiable melanoma	UCM	3.5%	54 years
Others		5%	54 years

Table 113.3 Different types of primary cutaneous melanoma. Data from the German Central Malignant Melanoma Registry (N = 30 015).

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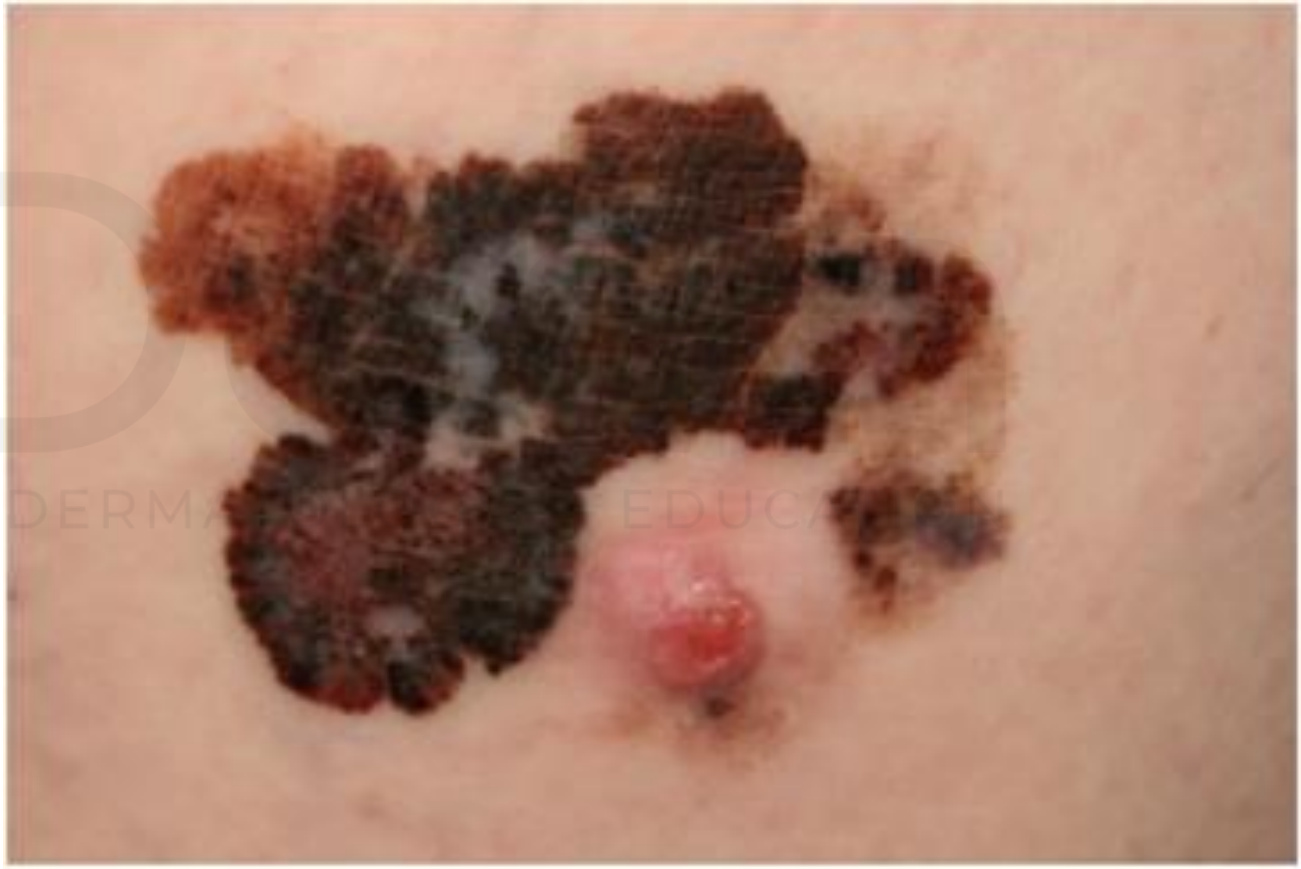
Types of Primary Melanomas: Superficial Spreading Melanoma

- Most common type in fair-skinned individuals
- Comprises 60-70% of all melanomas at any site
- Most commonly on the trunk of men, legs of women
- 2/3 present with regression, including networkless areas on dermoscopy
- Initially, characterized by horizontal growth
- ½ occur in pre-existing nevus



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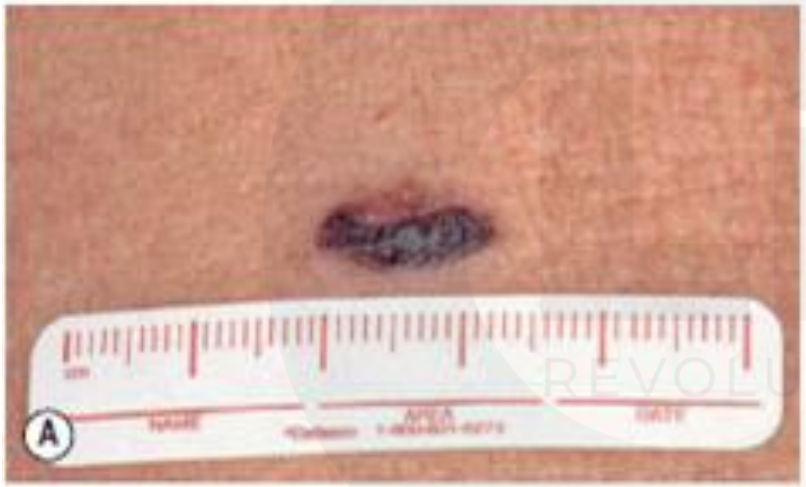
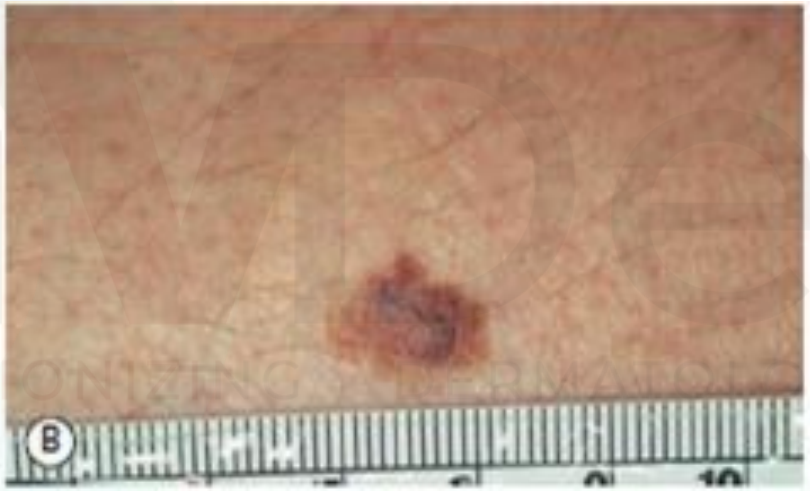
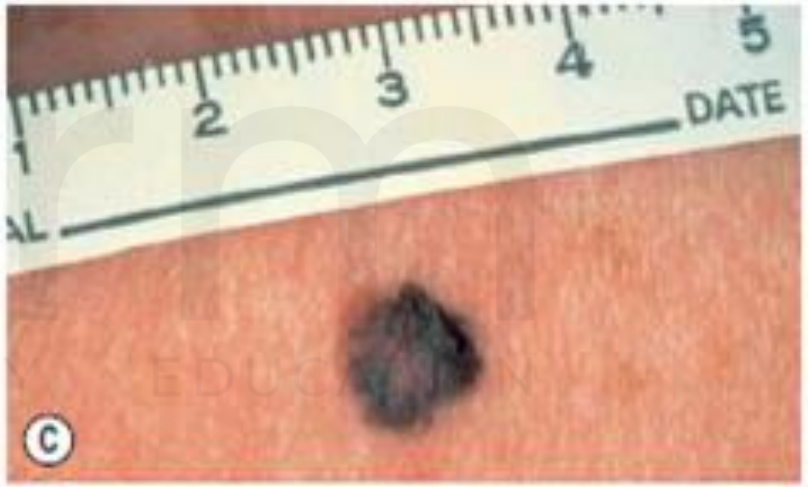
Superficial Spreading Melanoma: Clinical images







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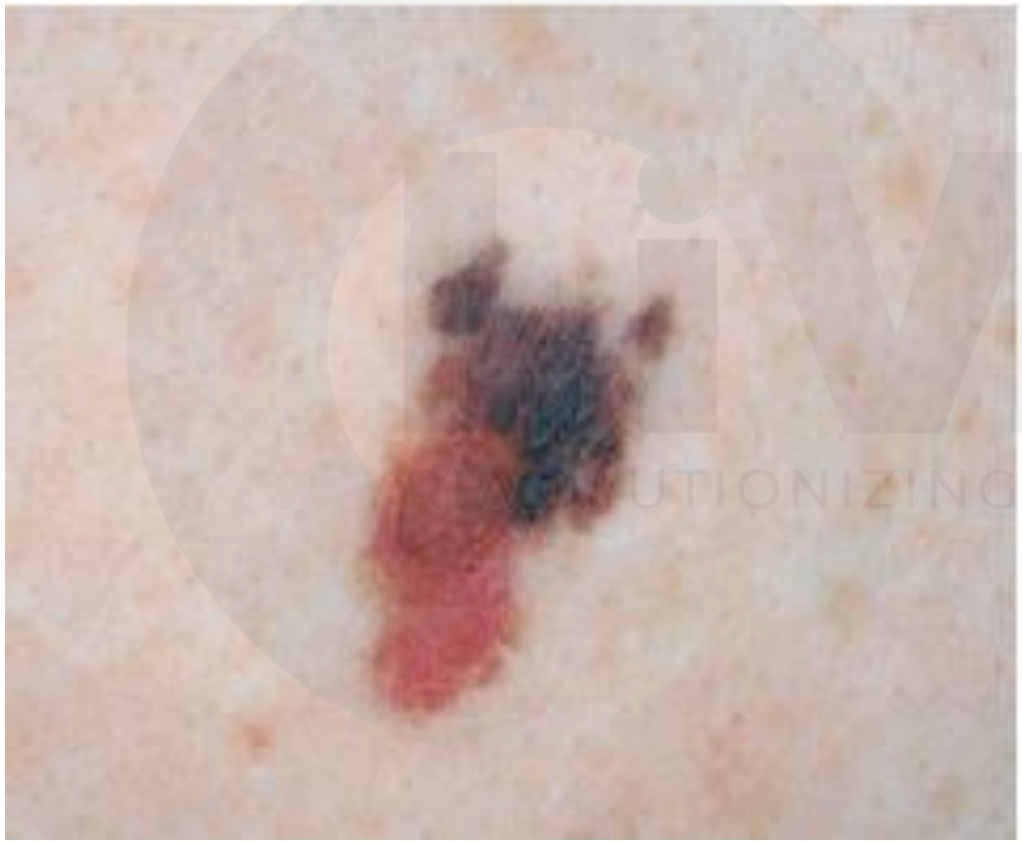
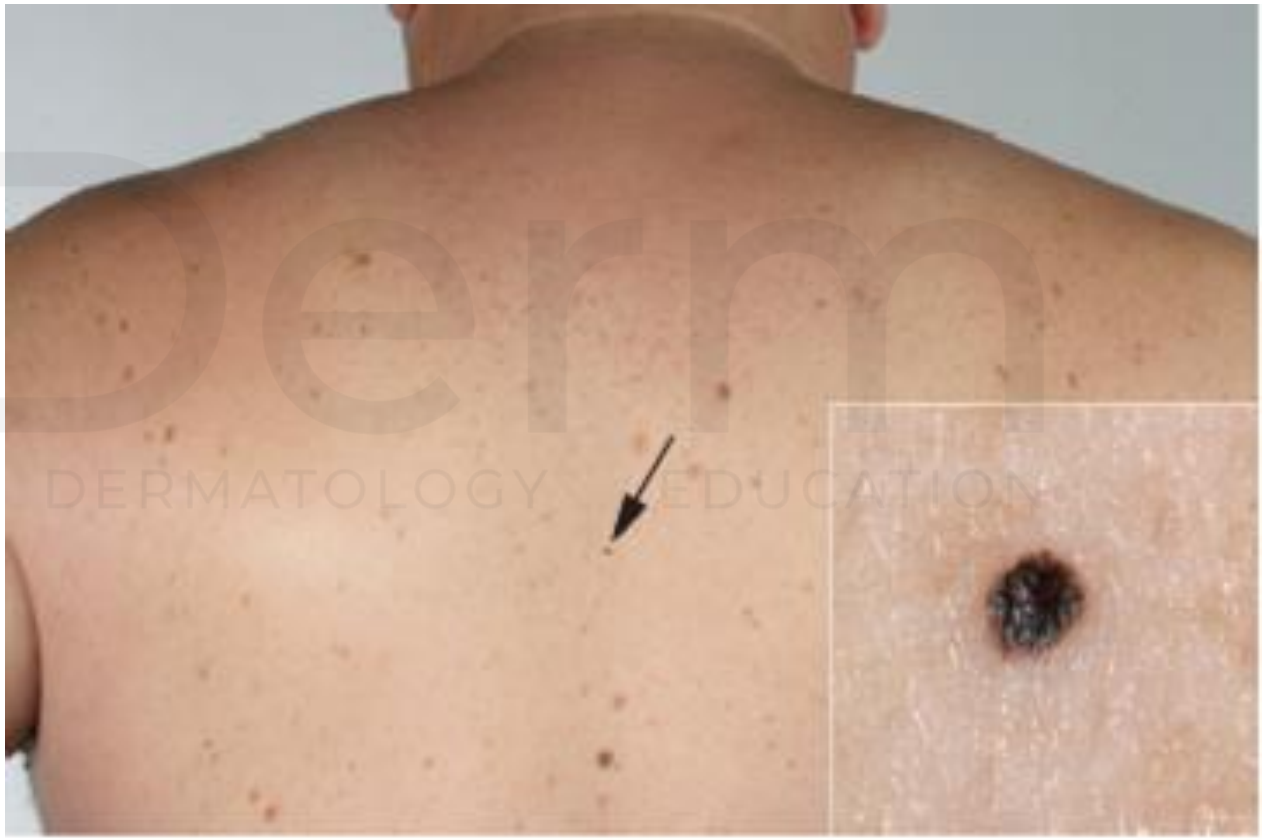
Superficial Spreading Melanoma: Clinical Images





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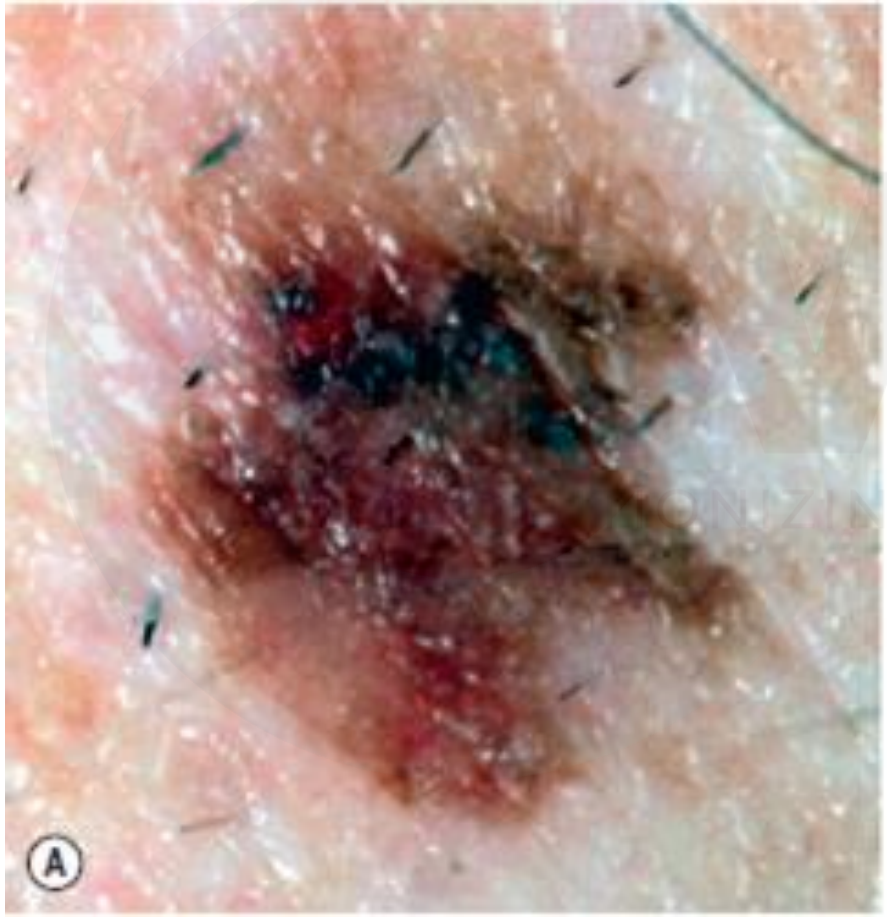
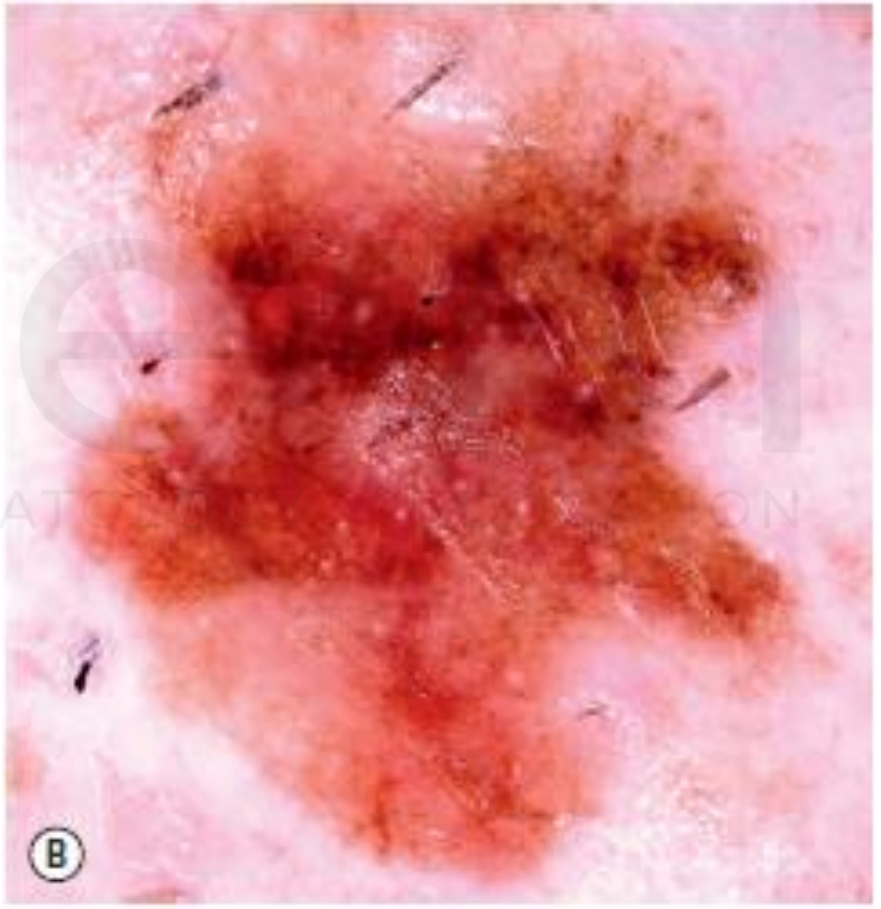
Superficial Spreading Melanoma: Clinical Images



“Little Red Riding hood sign”: erythema around melanoma



Dermoscopy of SSM

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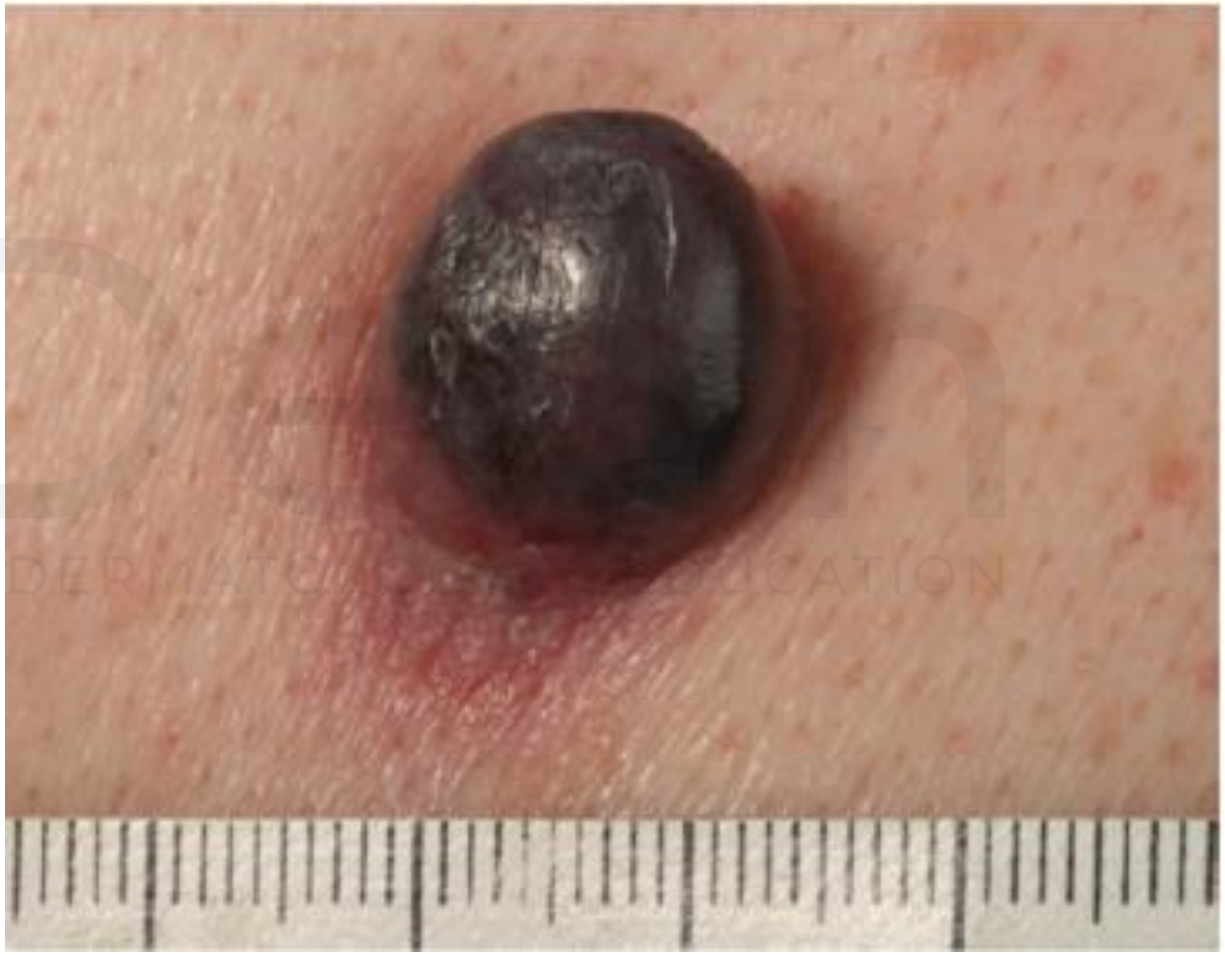
Types of Primary Melanomas
Nodular Melanoma

- 2nd most common type in fair-skinned individuals
- Most common in 6th decade of life
- 15-30% all melanomas, occurs on any body site
- Most frequently on neck, head, and trunk
- More prevalent in men
- Can be blue to black
- may ulcerate or bleed
- Rapid vertical growth phase tumor
- Thicker more advanced stage at diagnosis, poorer prognosis



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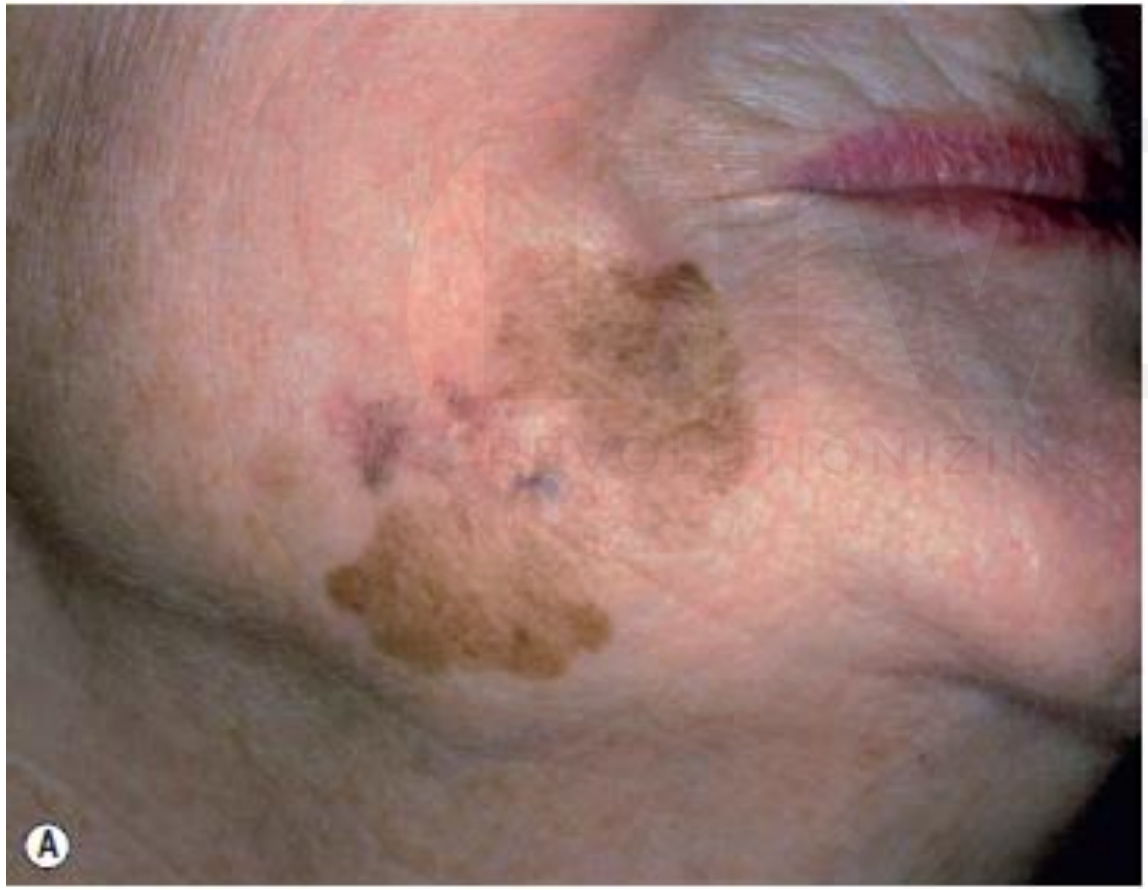
Types of Primary Melanomas
Lentigo Maligna Melanoma (LMM)

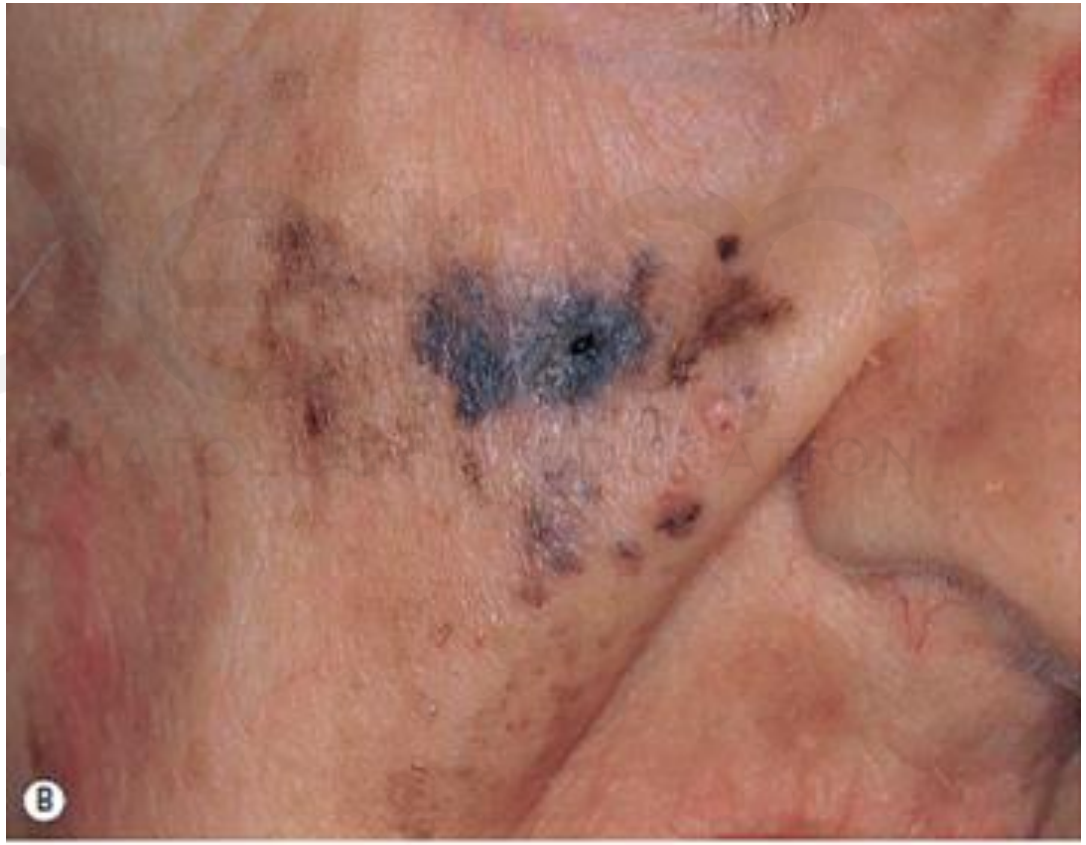
- Represents 10% of cutaneous melanomas
- Most frequently diagnosed in 7th decade of life
- Usually located on chronically sun-damaged skin, most commonly on face
  - Usually nose or cheek
- Slowly growing, asymmetric brown to black macule with color variation and irregular indented border
- Invasive LMM arises in precursor lesion termed lentigo maligna (LM)
  - LM represents an in situ melanoma in sun-damaged skin)
  - 5% of LM progresses to invasive LMM
- Dermoscopy: Hyperpigmented follicular openings on facial skin, circle in circle, irregular pigmented dots around follicles, rhomboidal structures

Types of Primary Melanomas
Lentigo Maligna Melanoma

Lentigo maligna



Lentigo maligna melanoma



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Lentigo Maligna Melanoma: Clinical Images

Lentigo maligna melanoma on nose

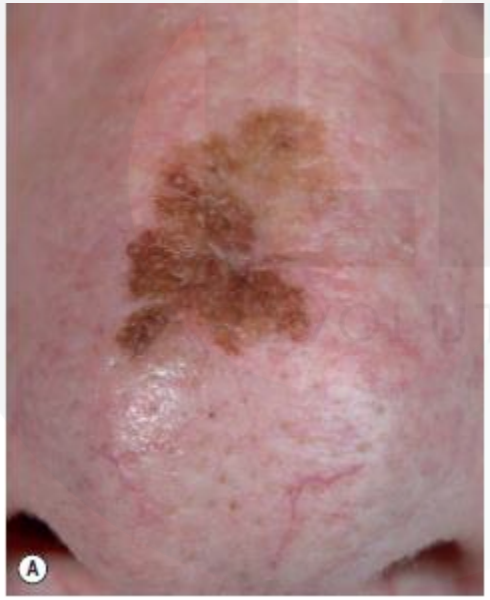
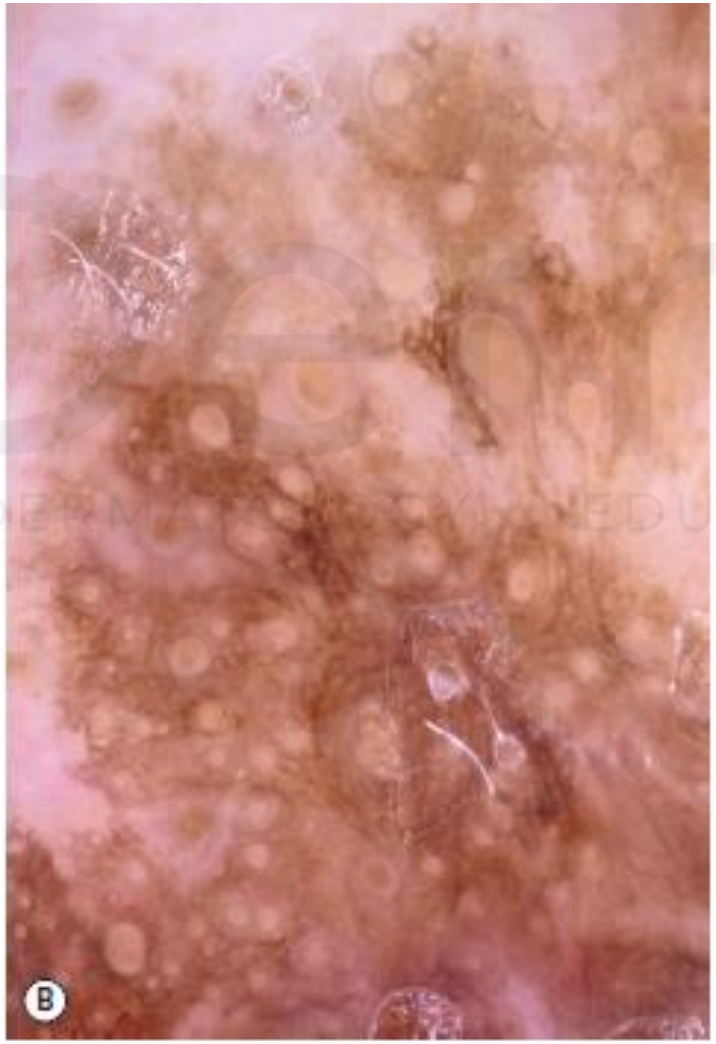


Fig. 113.16 Lentigo maligna melanoma (LMM). A A pigmented lesion on the dorsal nose, with irregular borders, light to dark brown pigmentation and marked asymmetry. **B** Dermoscopy demonstrating annular structures corresponding to follicular openings surrounded by melanoma cells ("circle in a circle").

Dermoscopy image



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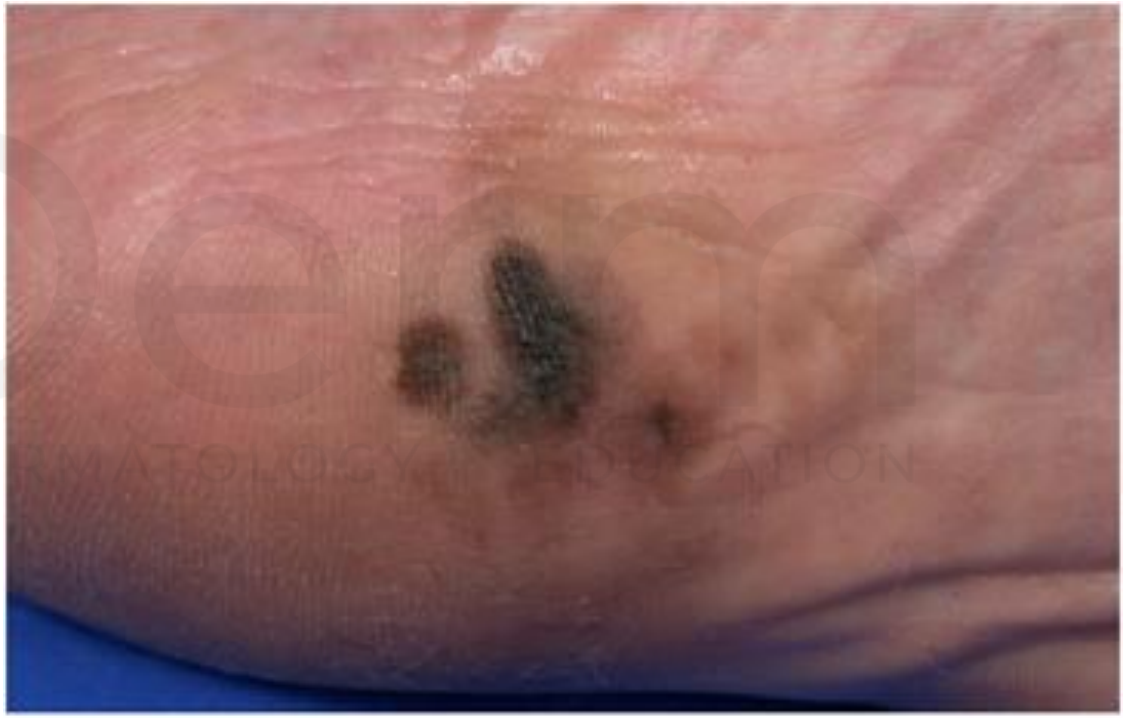
Types of Primary Melanomas
Acral Lentiginous Melanoma (ALM)

- Relatively uncommon
- Most frequently in 7th decade of life
- Located on Palms and soles and around nails
- Represents 5% of all melanomas
- Incidence is similar across all racial/ethnic groups
  - Most common melanoma subtype in darker-skin phenotypes, representing 70% of melanomas in blacks and 45% of melanomas in Asians



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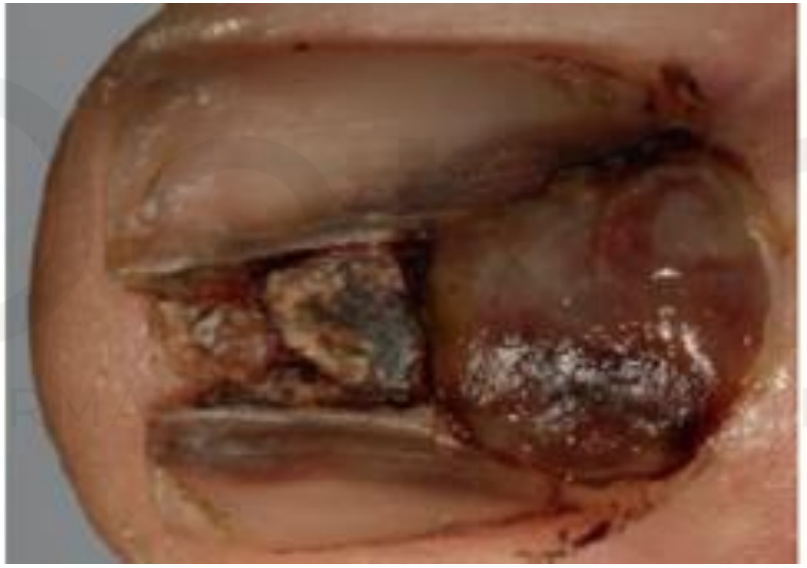
Types of Primary Melanomas
Acral Lentiginous Melanoma

- Presents as asymmetric brown to black macule with color variation and irregular borders
- Disproportionate amount diagnosed at advanced stage
- Physicians should have elevated threshold to biopsy due to increased morbidity with surgery at acral sites



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Types of Primary Melanomas
Acral Lentiginous Melanoma

- **Hutchinson sign:** pigment beyond the lateral or proximal nail fold/on hyponychium
- Longitudinal melanonychia should be biopsied if darkly pigmented, irregular, or >3 mm width
- ALM, displays KIT activating mutations, making the tumor sensitive to KIT-inhibiting drugs e.g. imatinib

Hutchinson Sign

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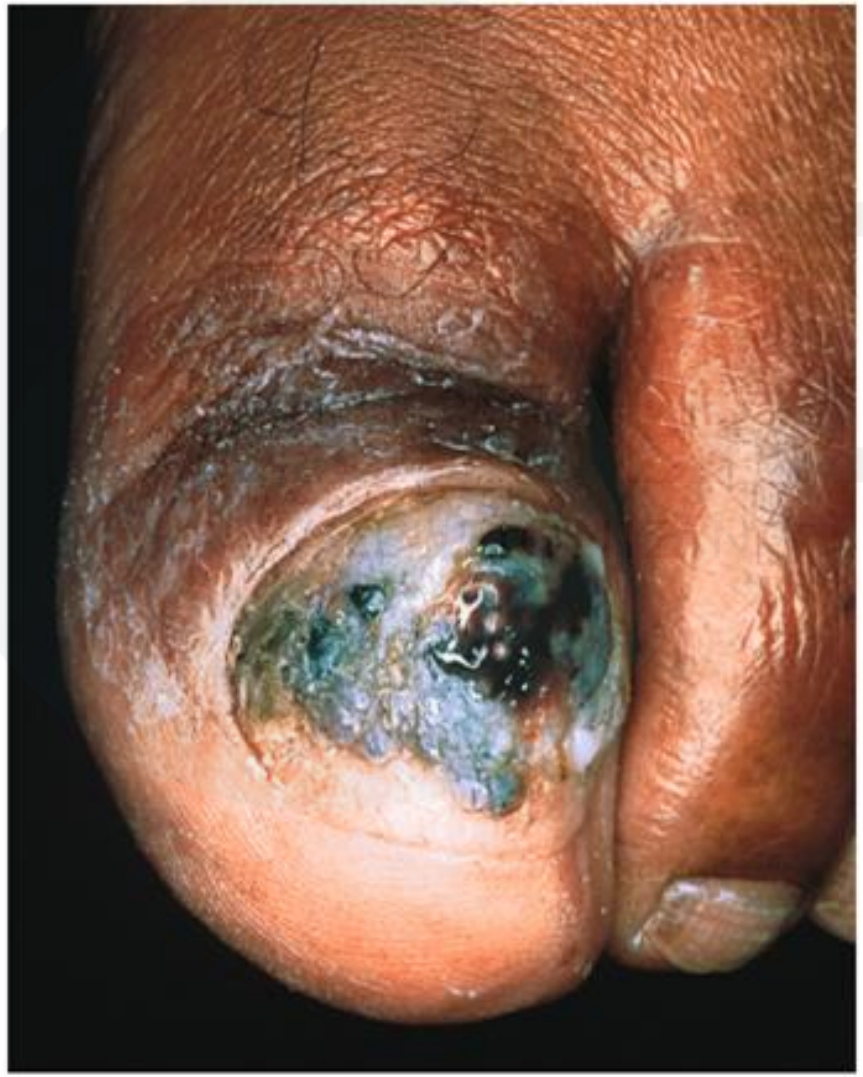
Acral melanoma: clinical images



Ulcerated and nodular component

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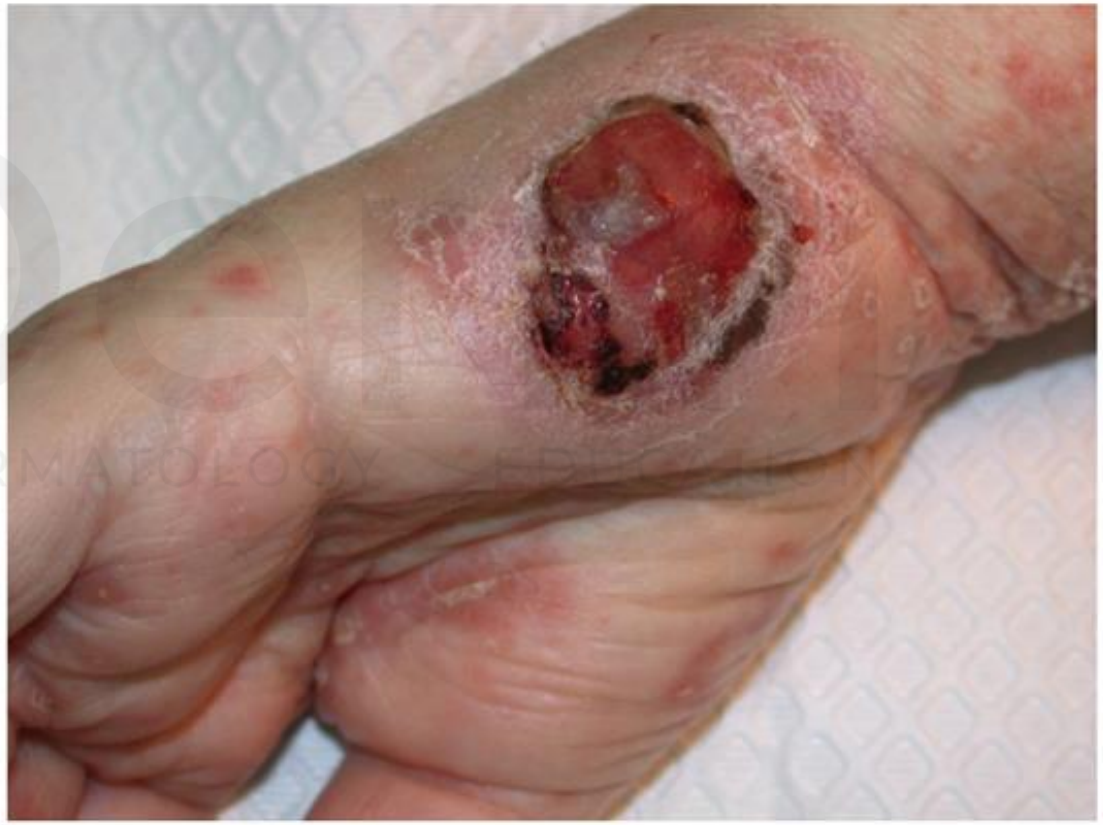
Other Melanoma Variants
Amelanotic Melanomas

- Vast majority of melanomas are pigmented
- All four histologic subtypes of melanoma can have amelanotic variants that largely defy clinical diagnosis
- Often biopsied due to suspicion of BCC
- ALMs amelanotic may be mistaken for warts or SCC
- Do not differ in prognosis or therapy



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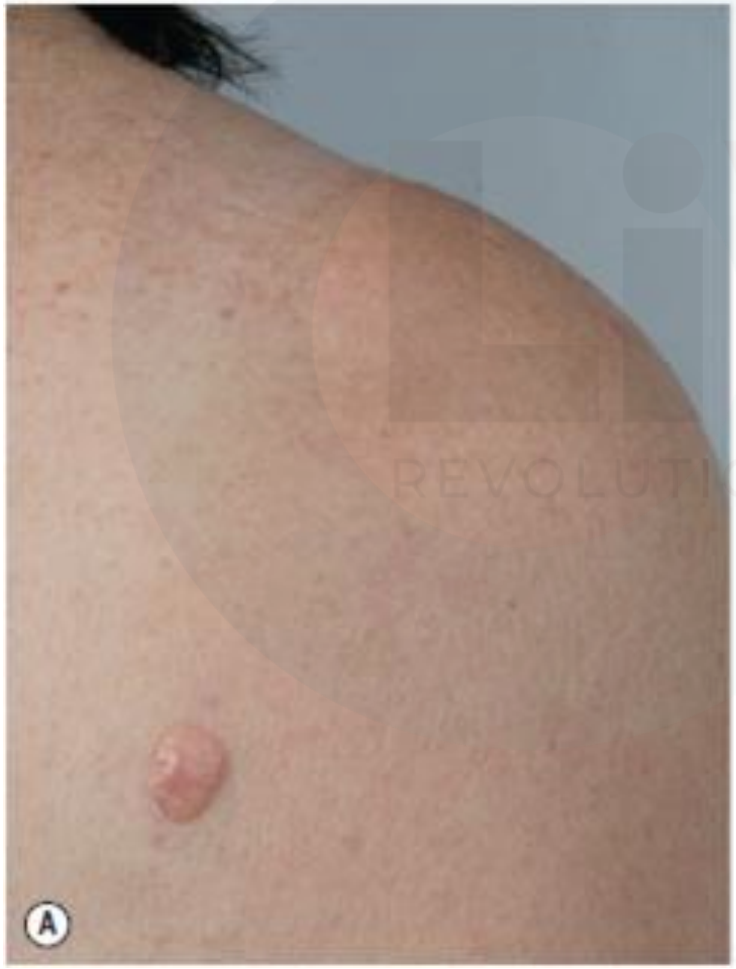
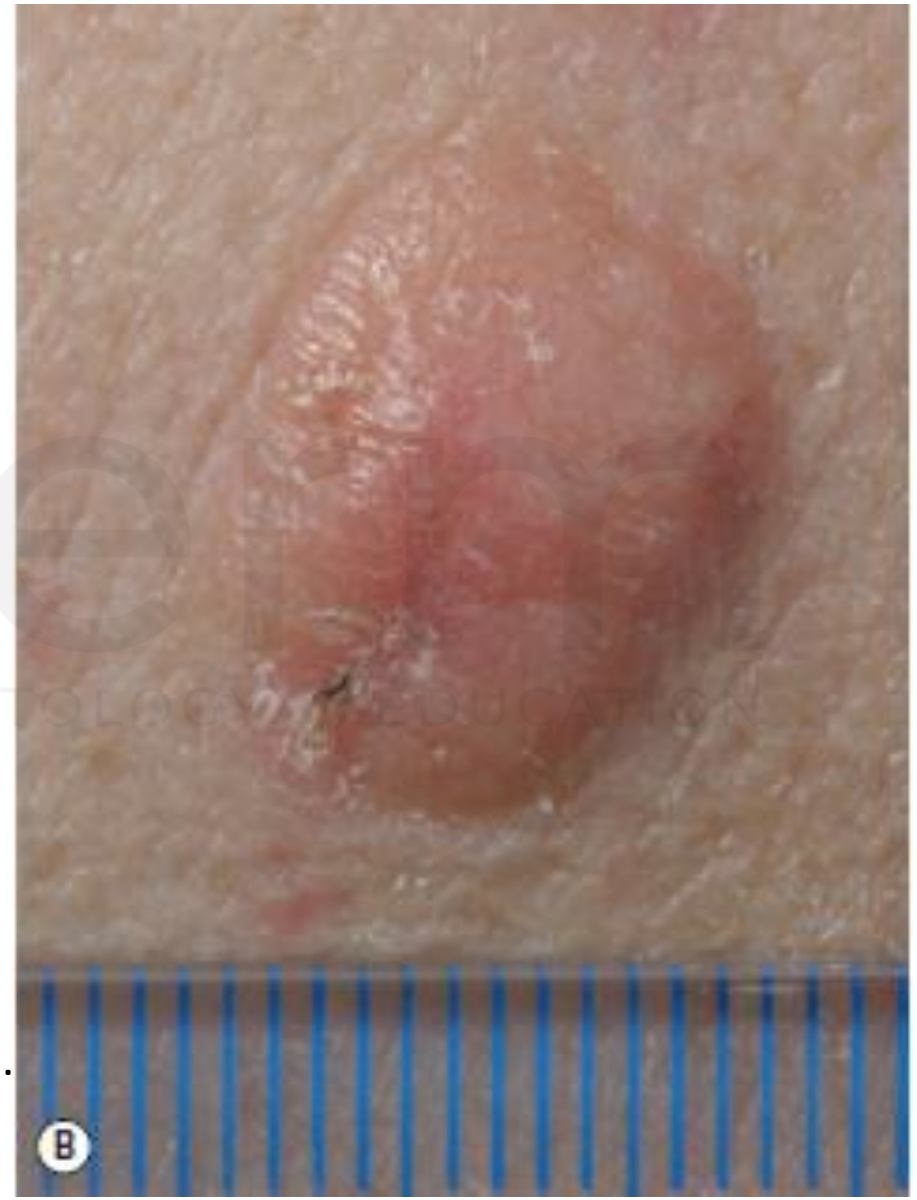
Other Melanoma Variants
Amelanotic Melanomas





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Melanoma and Pregnancy

- Hormones/growth factors stimulate melanocytes
- Yields increased pigmentation
- >10% women have darkening of melanocytic nevi in first 3 months
- However, no demonstration of development of melanoma or worsening in pregnancy
- Transplacental metastases are very rare
- Surgical excision and SLN are performed based on stage
- Ultrasound/MRI are okay but CT scans should be avoided
- Women with diagnosed high risk melanoma should wait 2 years before becoming pregnant again
  - 2/3 of recurrence occur during this window

Childhood Melanoma

- Very rare
- 2% of melanomas are present in population younger than 20 years of age
- 0.3% of melanomas are in those younger than 14 years
- Melanomas with Spitz features are more common in this age range
- Survival/prognosis is similar to adults and stage dependent

Melanoma

- Evaluation
- Surgery
- Lymph Node Dissection
- Adjuvant Therapy
- Immunotherapy

Yagerman S and Goldberg DJ
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BCC and SCC
Epidemiology and Clinical Presentation

Introduction

- Non-melanoma skin cancer (NMSC) represents the most frequently observed malignancy amongst Caucasians
- UV light exposure is the major risk factor for development
- Other risk factors include: exposure to ionizing radiation, arsenic or organic chemicals; human papillomavirus infection; immunosuppression; and genetic predisposition
- Surgery is the mainstay of treatment, but immunomodulators, photodynamic therapy, and drugs that address genetic defects show promise

Overall Epidemiology

- Caucasians most affected
- Exact incidence of NMSCs difficult to obtain due to limited reporting to state cancer registries
- Positive correlation observed with latitude and average annual UV exposure
- Under 40 years old, majority of NMSC is found in women
- However, sharp increase for men for NMSC after 60 years old, leading women in 2-3:1 ratio by age 80

Squamous cell carcinoma (SCC) Epidemiology

- Increasing age, male sex, and previous history of actinic keratoses noted as risks for developing invasive SCC
- Incidence increases significantly after 60 years old
- Majority are located on head/neck, upper extremities
- Mortality from SCC is higher in whites, older persons, and men
- Males have a 3:1 greater SCC mortality than women
- In darker skin, associated with chronic irritation, scar, or injury
- SCCs on ear, lip, genitalia associated with higher risk of death

Basal cell carcinoma (BCC) epidemiology

- BCC most common skin cancer in humans
- More common in males, with male to female ration of 1.5-2:1
- Risk factors for development: Increasing age, Caucasian race, male gender (2x than women)
- Mortality from BCC quite rare, usually in immunocompromised or with patients with basal cell nevus syndrome
- Metastatic BCC usually with aggressive histopathologic patterns, including morpheaform, infiltrative, metatypical, and basosquamous
- Perineural involvement is also sign of aggressive disease
- Metastases involve regional lymph nodes, lungs, bone and skin

Risk factors: Ultraviolet (UV) exposure

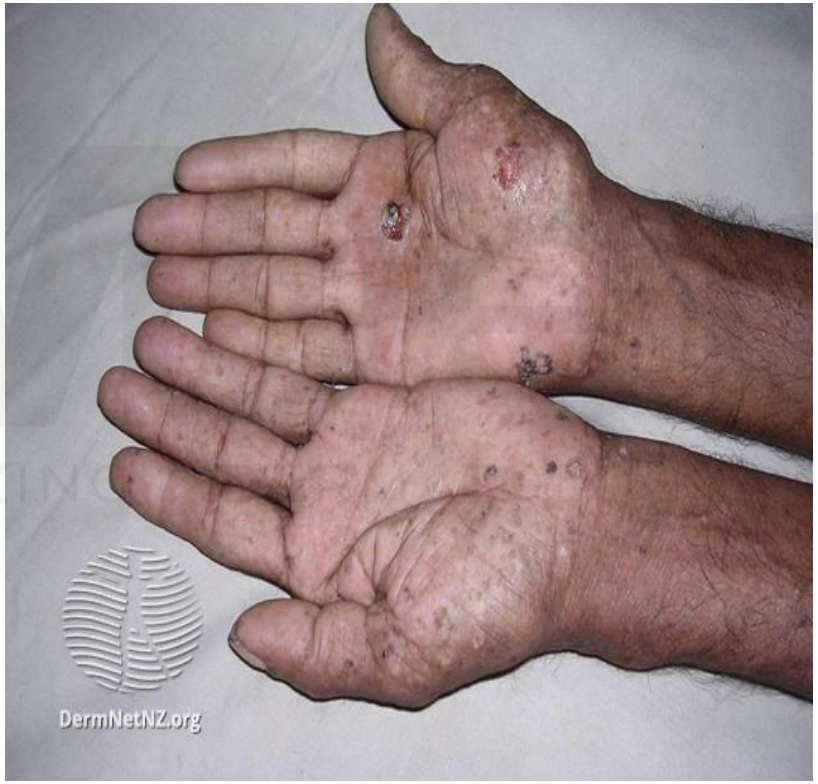
- UV exposure is the predominant cause of NMSC development
- BCC has higher risk with intermittent intense episodes of UV exposure and sunburns at any age
- SCC usually related to cumulative long-term UV exposure and childhood sunburns
- Incidence is inversely proportional to latitude
- Artificial sources of UV radiation, intentional tanning shown to increase risk of SCC and BCC development, even after adjusting for sunburn history and sun exposure
- Red hair, light skin, poor ability to tan, freckling are risk factors

Risk Factors: Medications/Work exposure

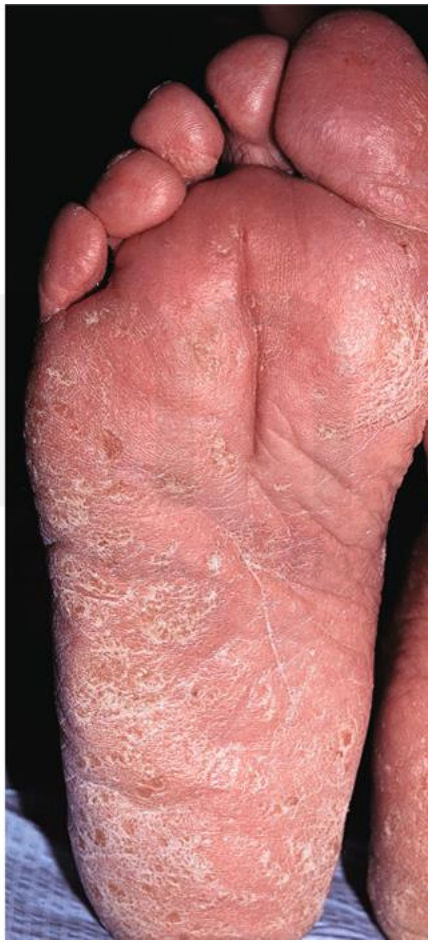
- PUVA has a significant dose related-risk of SCC and BCC after 100 treatments
  - PUVA immunosuppression may also play a role
- Exposure to ionizing radiation leads to a threefold increased risk of NMSC, risk is in proportion to radiation dose
- Pilots, sailors, locomotive engineers, agricultural workers at increased risk of NMSC development

Risk Factors- Chemical exposure

- Usually located on arms in multiples
- Pesticides, asphalt, tar, polycyclic aromatic hydrocarbons, typically result in SCC
- Arsenic exposure results in palmoplantar arsenical keratosis and BCCs with latency of 20-40 years



DermnetNZ.org



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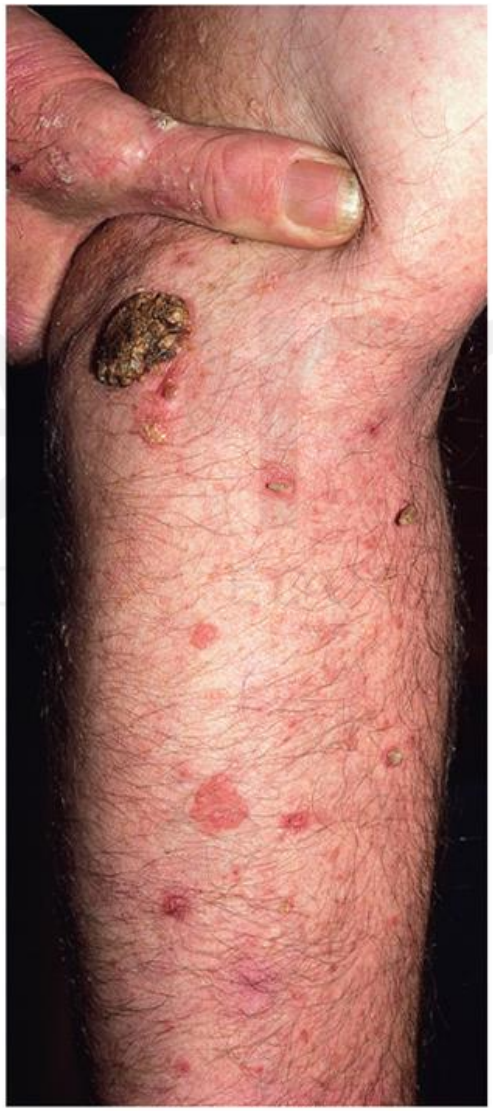
Arsenical keratoses on palms and soles

Risk Factors- Immunosuppression

- BCC risk 5-10 times higher with organ transplant recipients
- SCC risk 40-250 times higher with organ transplan recipients
- Skin type, cumulative sun exposure, age at transplant, length of immunosuppression impact NMSC development
- SCC pathogenesis: decreased immunity, direct carcinogenic effects of immunosuppressive medications, HPV, UV light
- More likely to have numerous lesions, more local/regional recurrences and metastases
- HPV DNA in 70-90% SCCs in this population



Multiple SCCs in renal transplant patient

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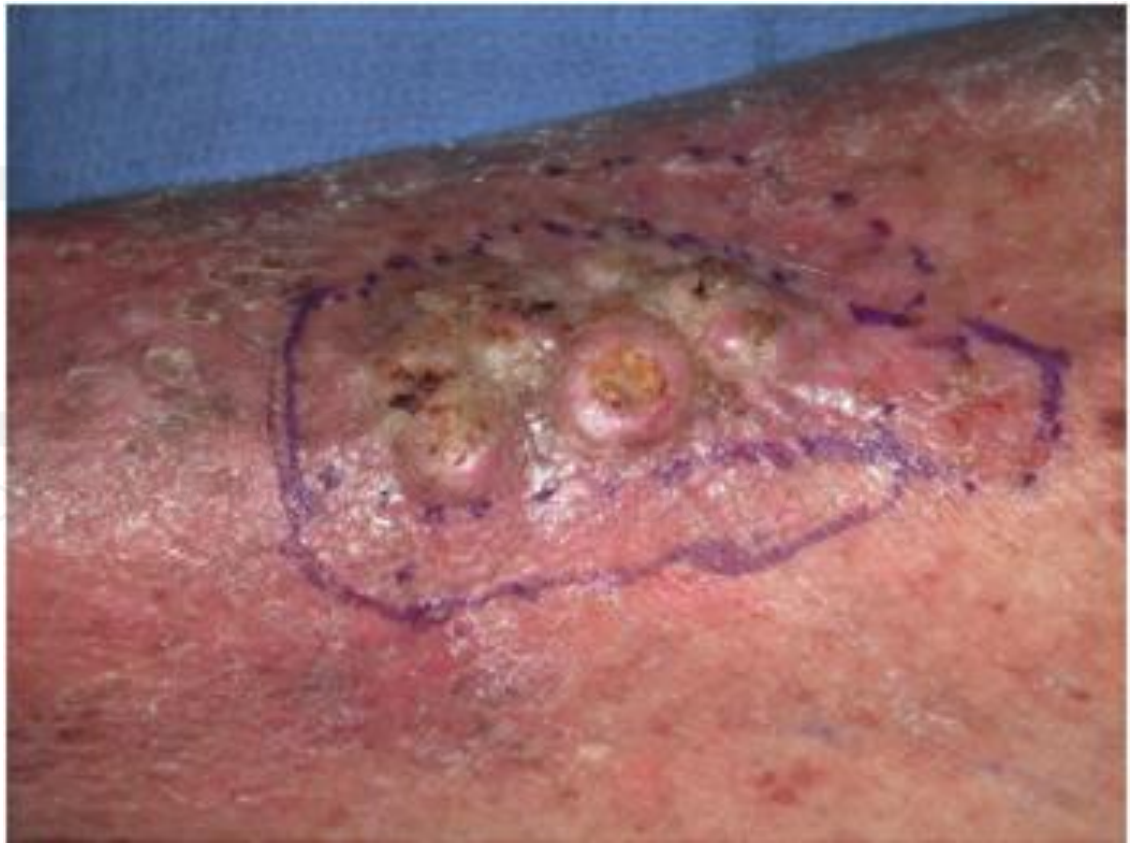
Transplant patients

- Of renal transplant patients, 5% died from skin cancer
- Of heart transplant patients, 27% died of skin cancer
- 2/3 skin cancer related deaths in transplant patients were from SCC
- Hematopoietic transplants usually do not encounter this marked increased risk of skin cancer, unless received long-term voriconazole



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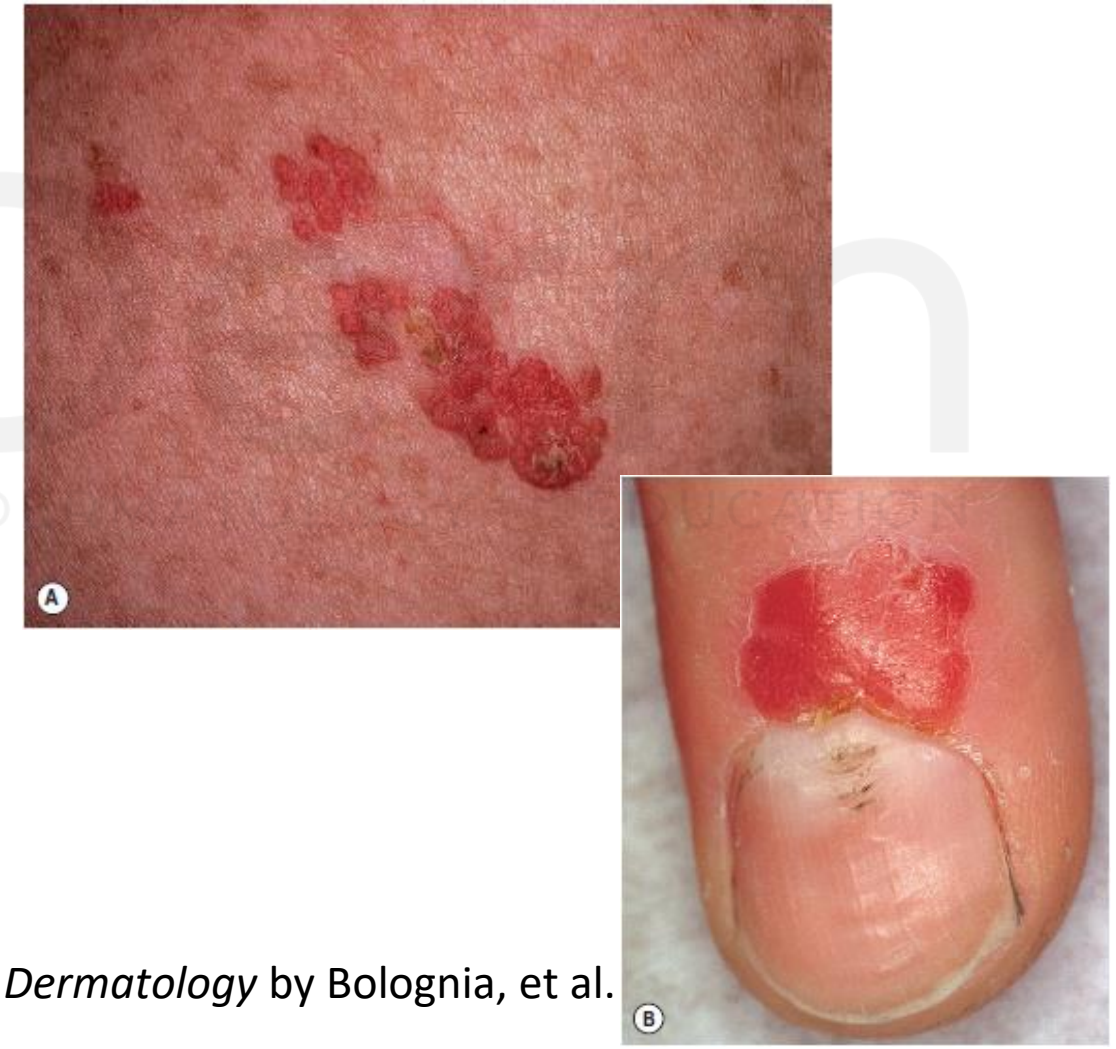
Clinical Features: SCC in situ

- Also known as Bowen's disease
- Presents as erythematous scaly patch or slightly elevated plaque on sun-exposed skin
- May arise de novo or from an existing AK
- Rarely becomes invasive
- Can be difficult to tell SCC in situ apart from AK, superficial BCC, psoriasis, or chronic eczema
- Arsenical SCC in situ: located on non-sun exposed areas; multiple lesions with hyperpigmentation
- Bowenoid papulomatosis: SCC in situ arising from genital warts with HPV 16, 18



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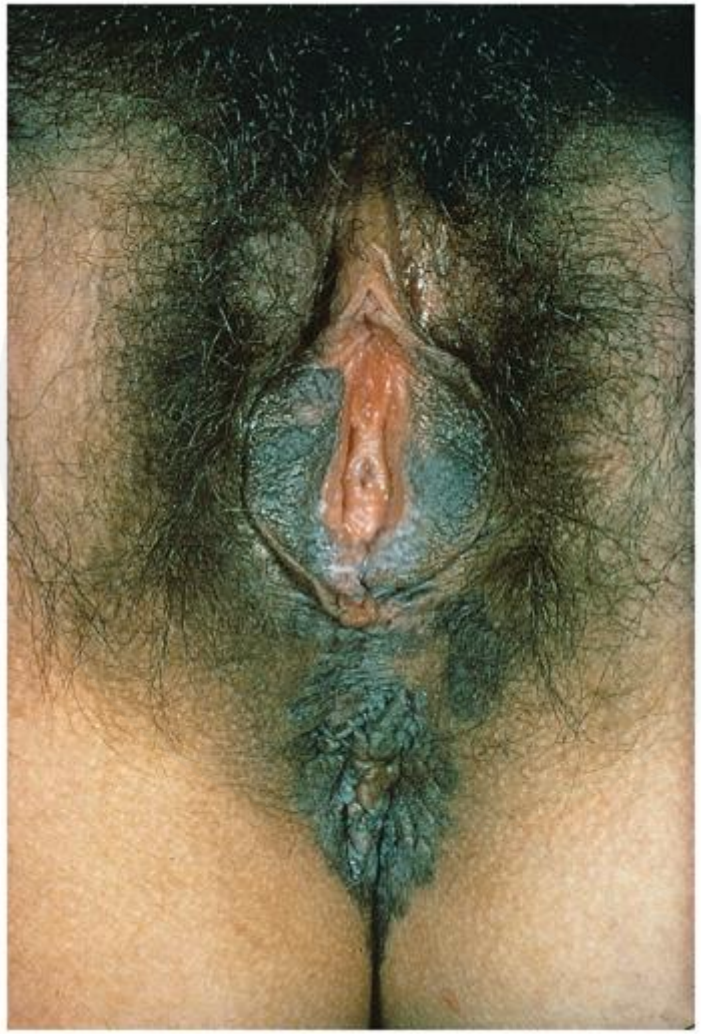
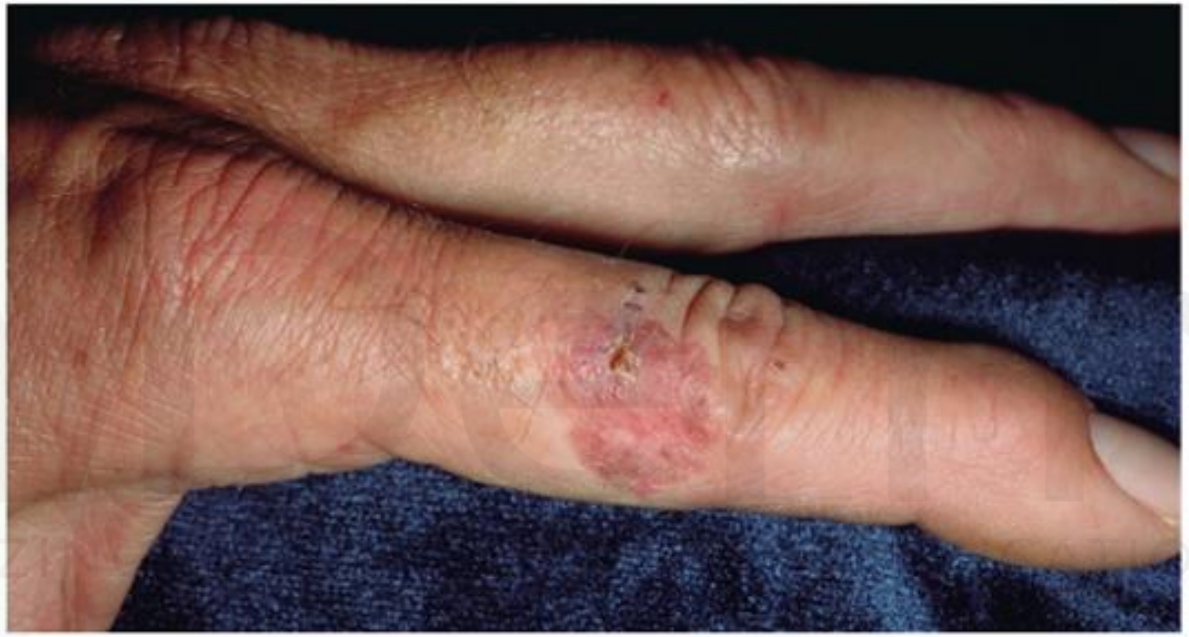
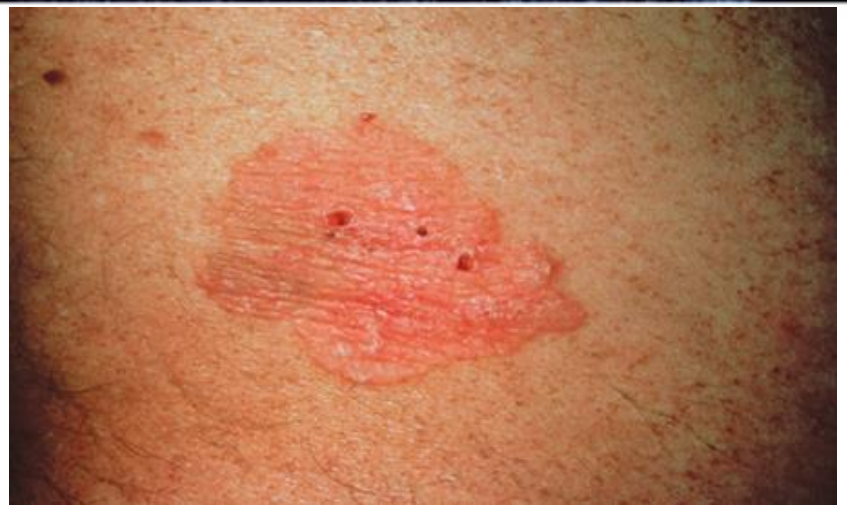
Bowen’s Disease: Clinical Images







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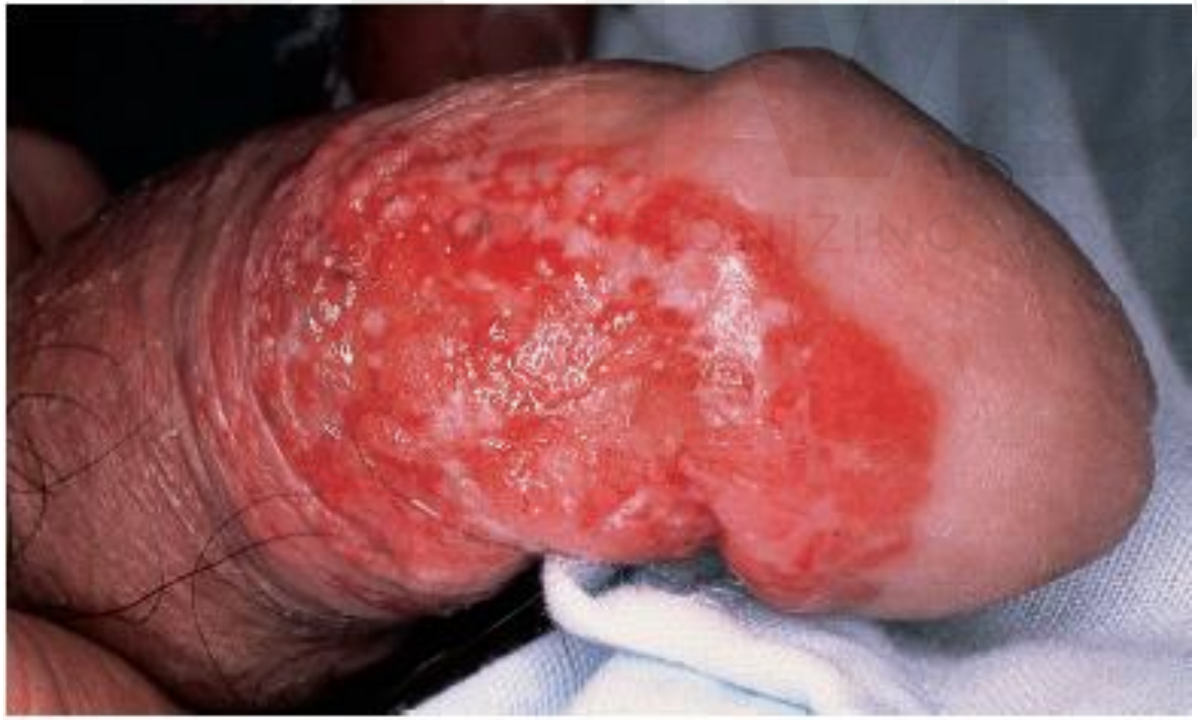
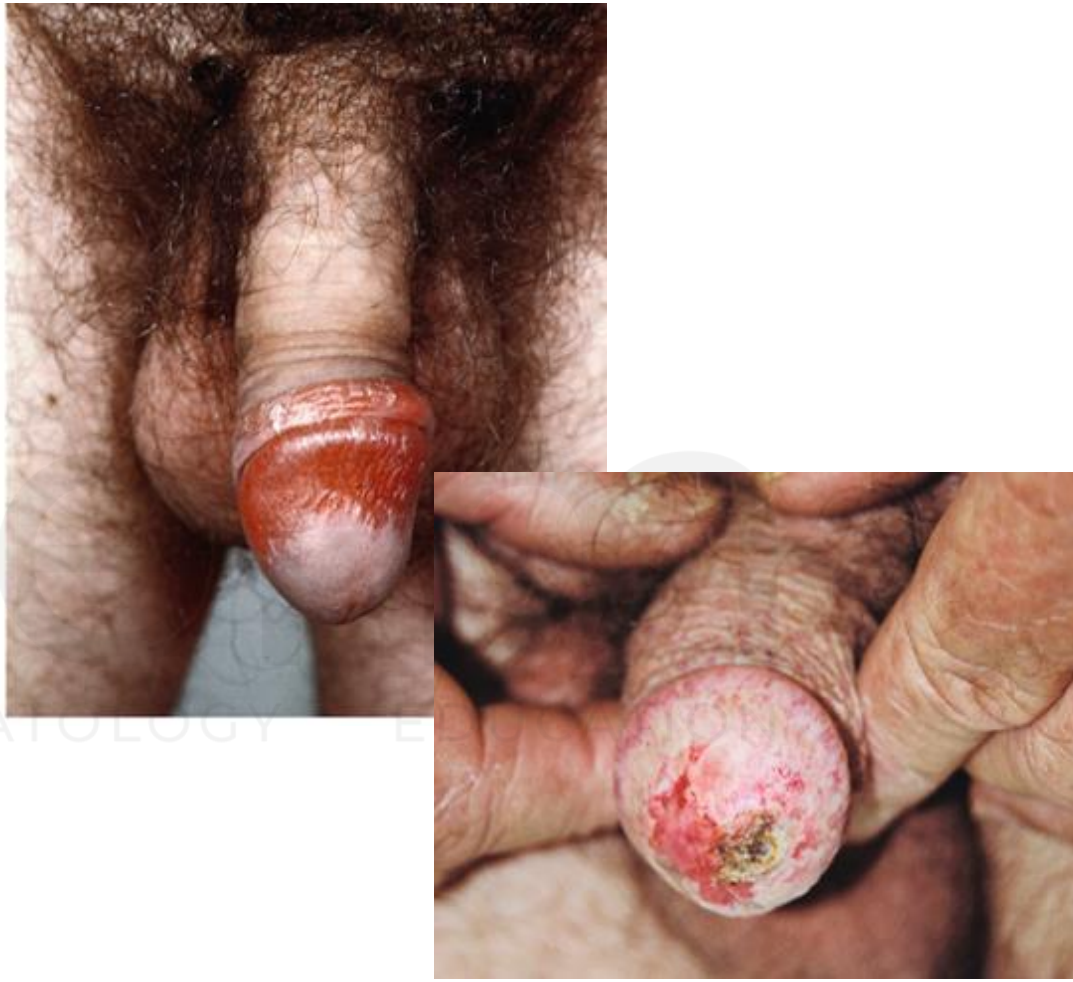
SCCIS: subtypes

- Erythroplasia of Queyrat
  - Subtype of SCCIS on penile shaft and glans



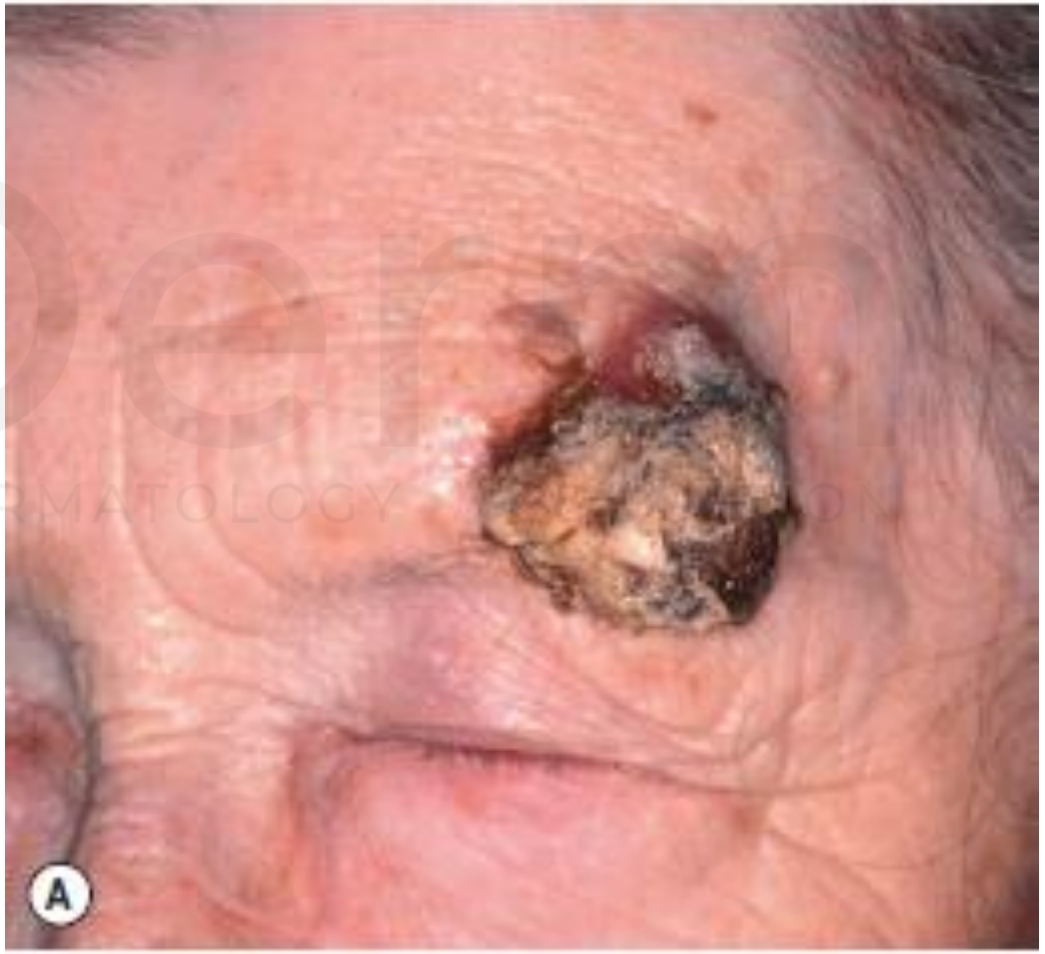
Dermatology by Bolognia, et al.



Andrews' Diseases of the Skin by James et al.

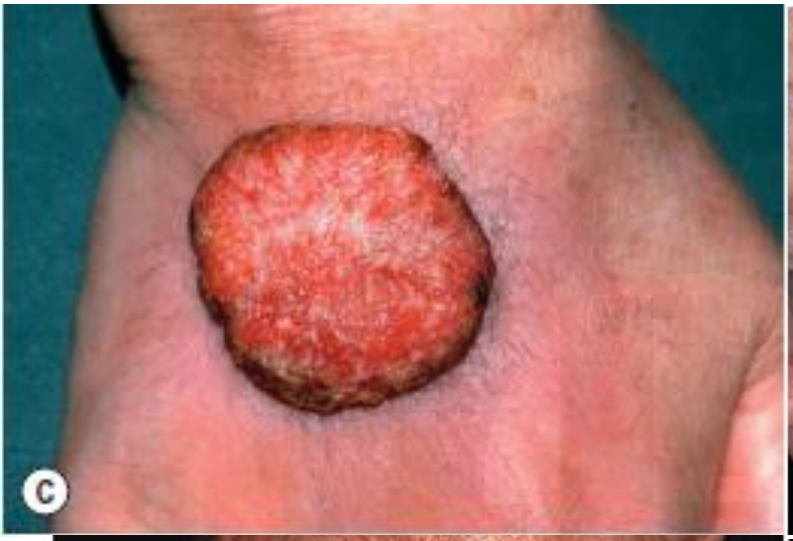
Invasive SCC
Clinical Features

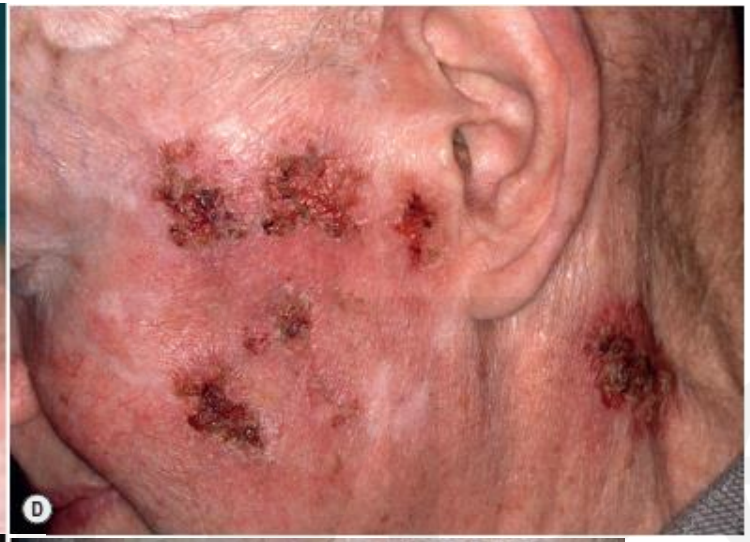
- Most common locations: bald scalp, face, neck, extensor forearms, dorsal hands and shins
- Usually papulonodular, but can often be exophytic or papillomatous
- Can have hyperkeratosis, crusting, and ulceration
- May enlarge slowly or rapidly and can be accompanied by pain



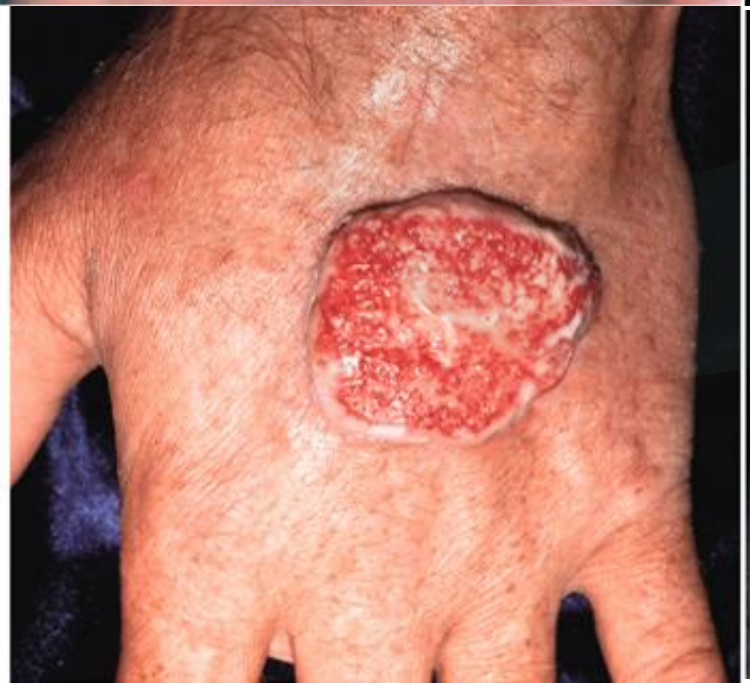
Dermatology by Bolognia, et al.

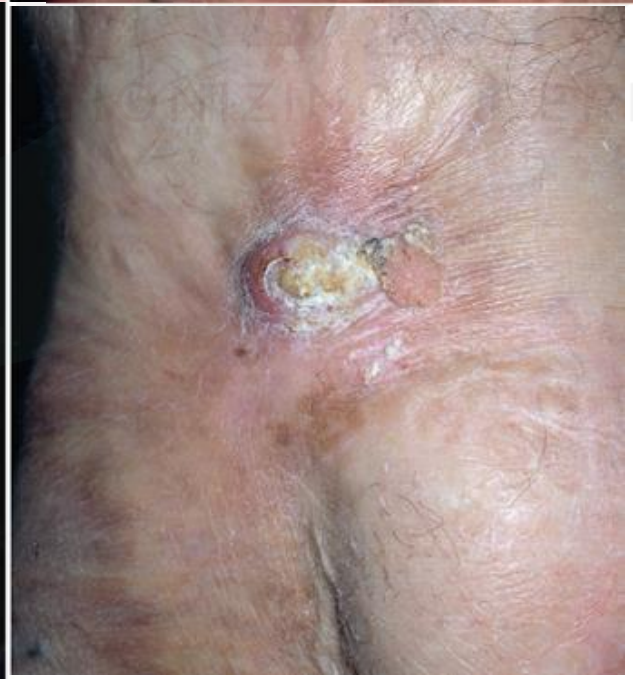
Invasive SCC: Clinical images





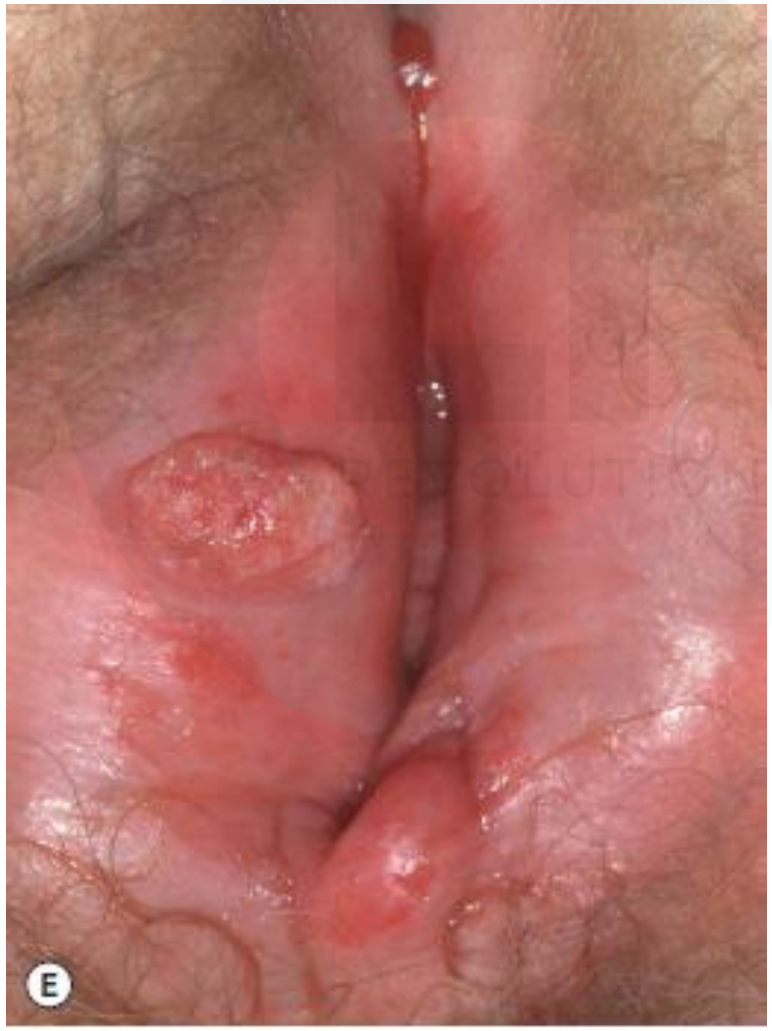
Dermatology by Bolognia, et al.

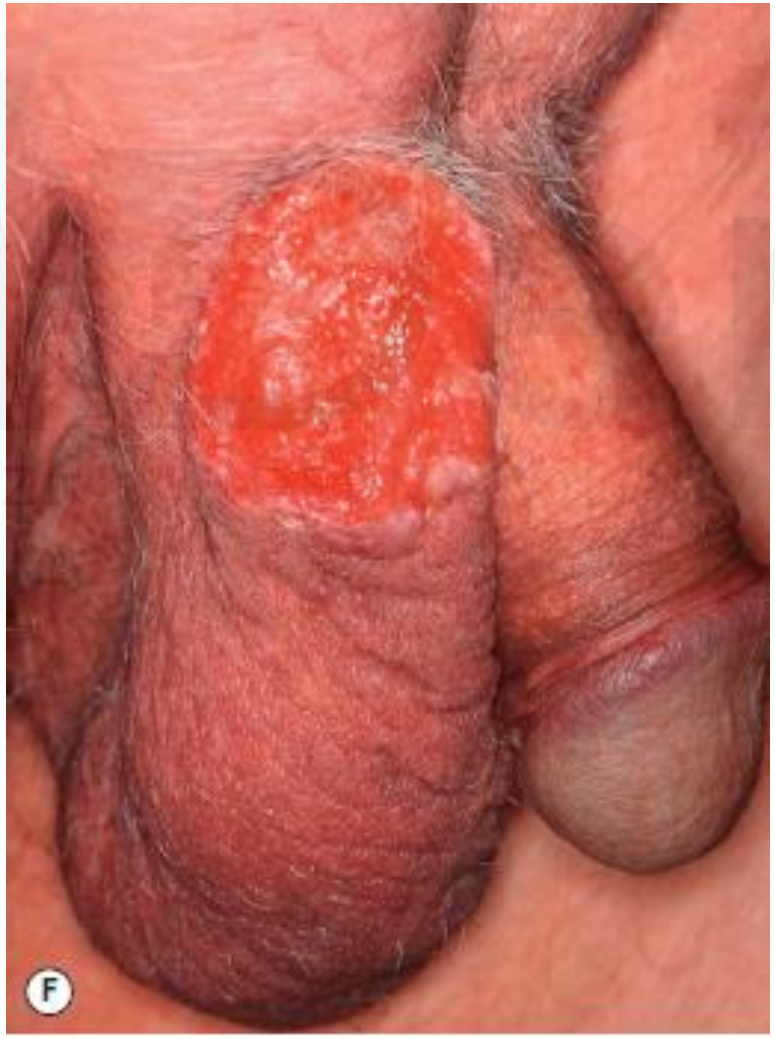




Andrews' Diseases of the Skin by James et al.

Invasive SCC: Clinical Images

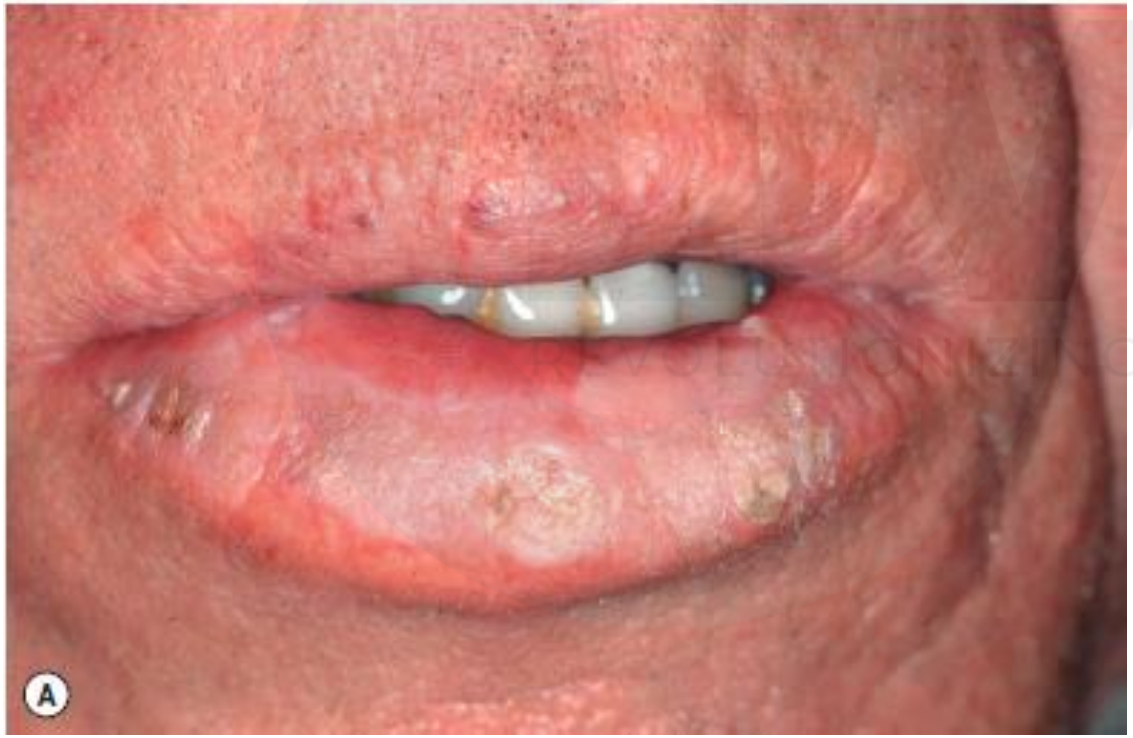


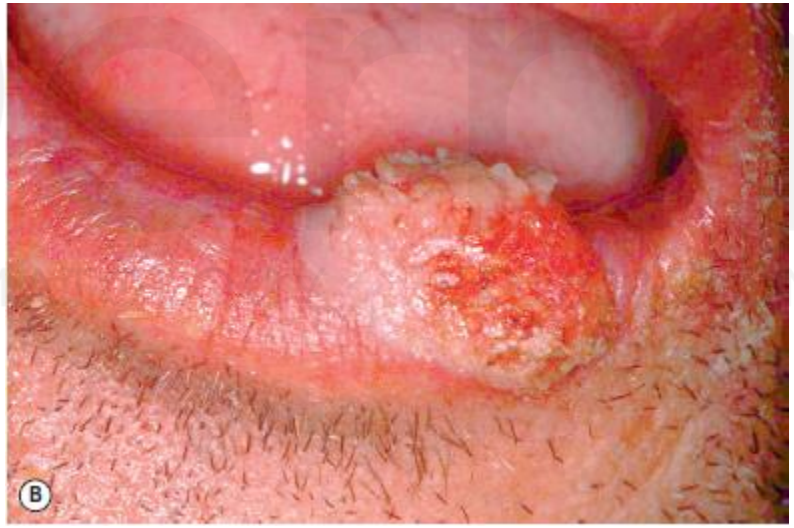


Given location, likely HPV-induced

Dermatology by Bolognia, et al.

Invasive SCC: Clinical Images

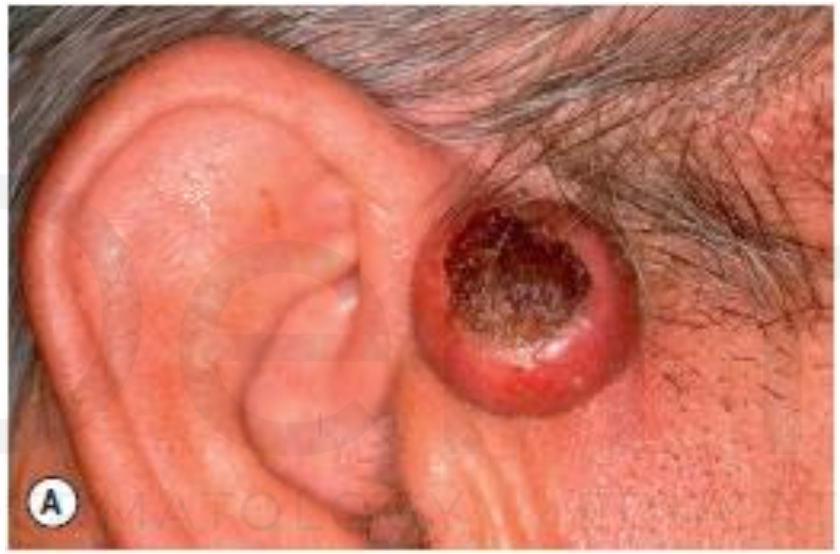




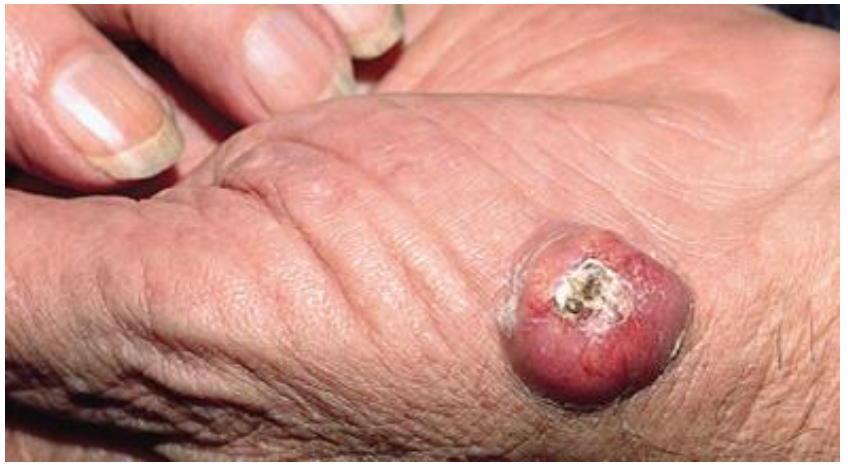
Dermatology by Bolognia, et al.

Keratoacanthomas (KAs)

- Debate if this is a benign entity vs variant of SCC
  - Largely treated as SCC
- Rapidly enlarging papule, sharply circumscribed, crateriform nodule with keratotic core over a few weeks
- May resolve slowly over months to leave an atrophic scar
- Ferguson-Smith and Gryzbowski syndromes represent inherited conditions leading to the development of multiple KAs

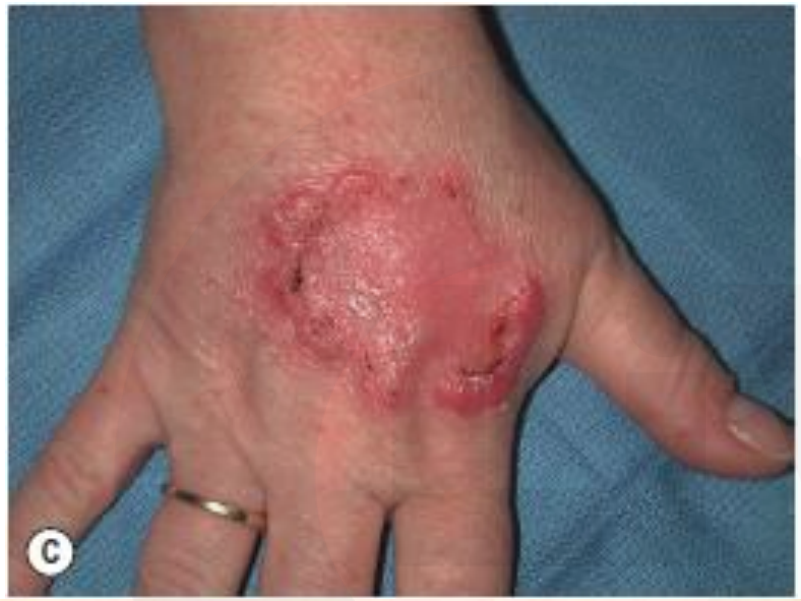


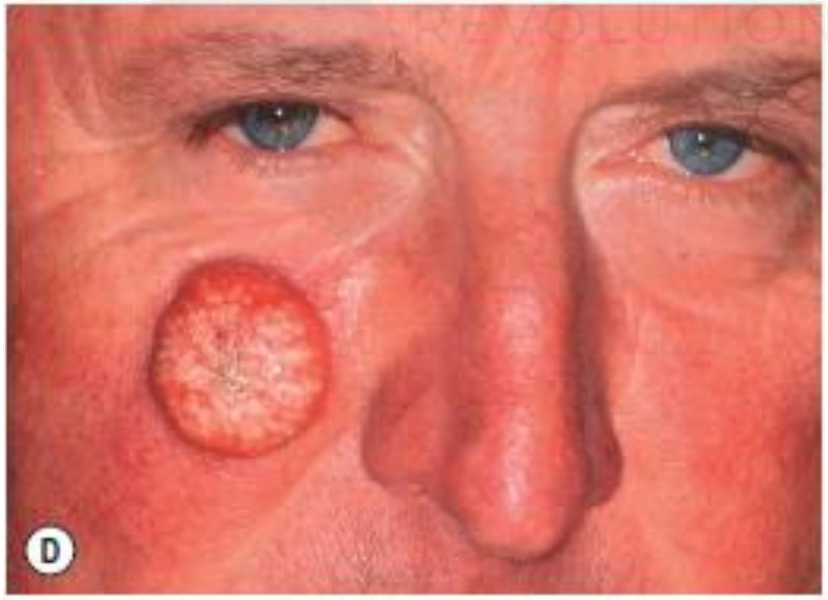
Dermatology by Bolognia, et al.



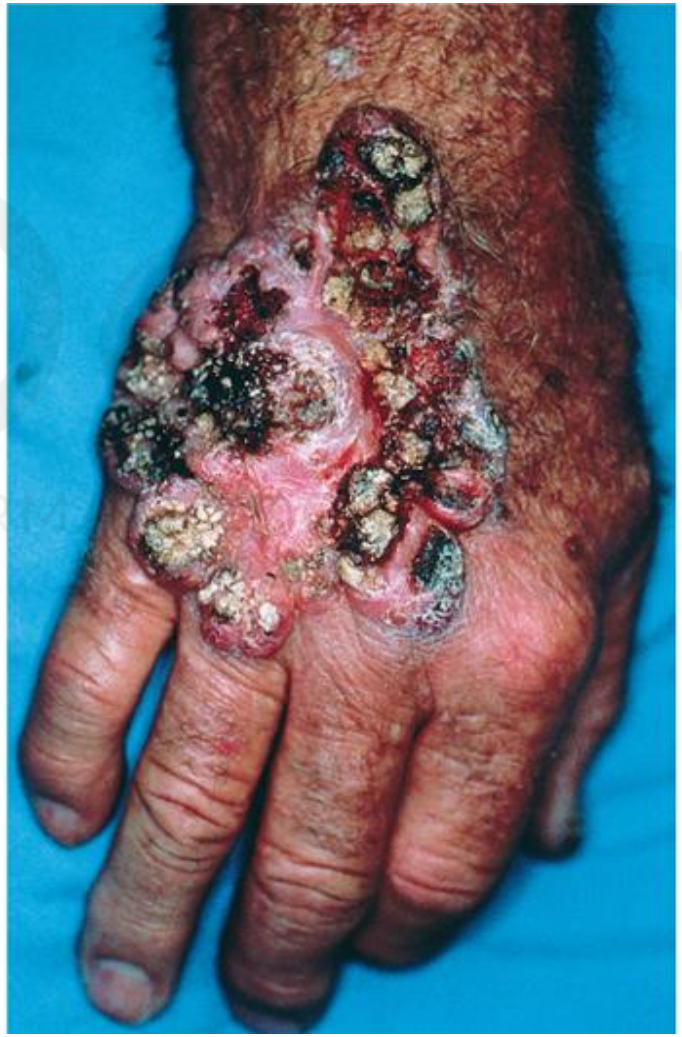
Andrews' Diseases of the Skin by James et al.

KAs: Clinical Images





Dermatology by Bolognia, et al.



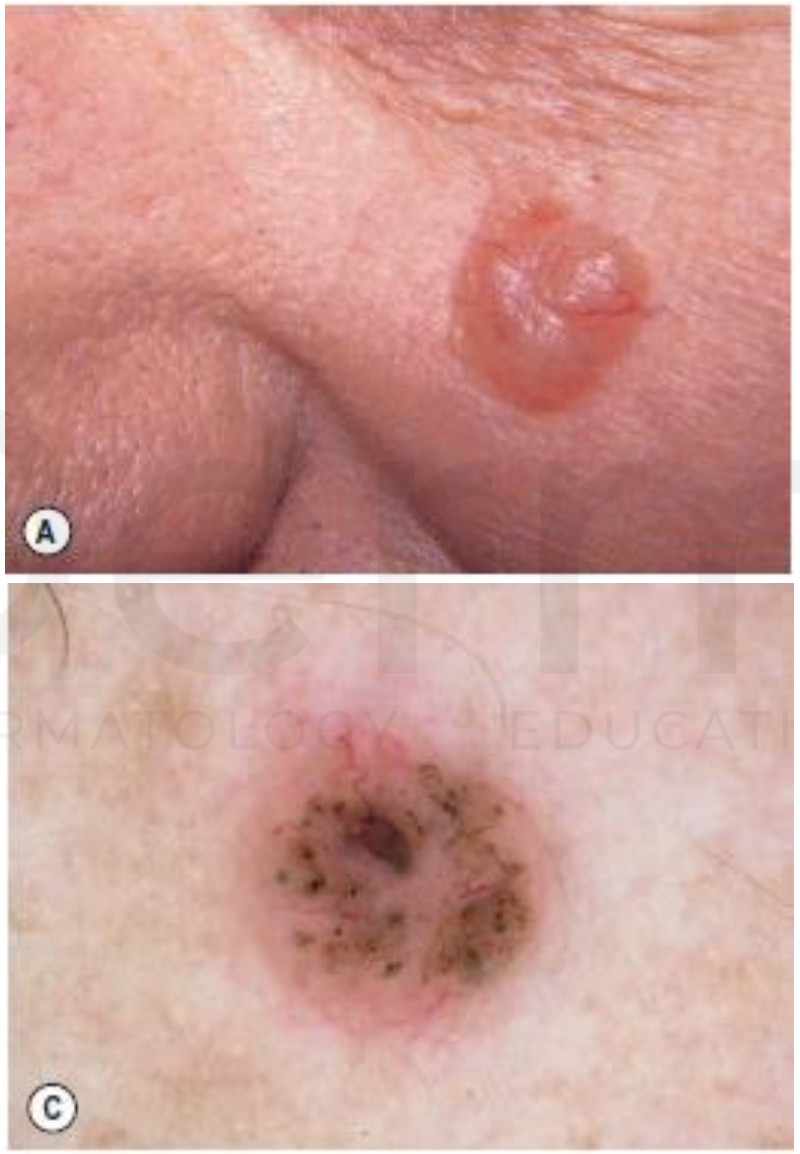
Andrews' Diseases of the Skin by James et al.

SCC: Metastasis

- SCC in chronically sun exposed areas have relatively indolent behavior with low metastatic rate <5%
- There is a strong correlation between tumor thickness and metastasis
- Secondary risk factors for metastasis include immunosuppression, location on lips or ear
- SCCs genitalia and perianal area more aggressive, higher risk of metastasis

BCC
Clinical Features

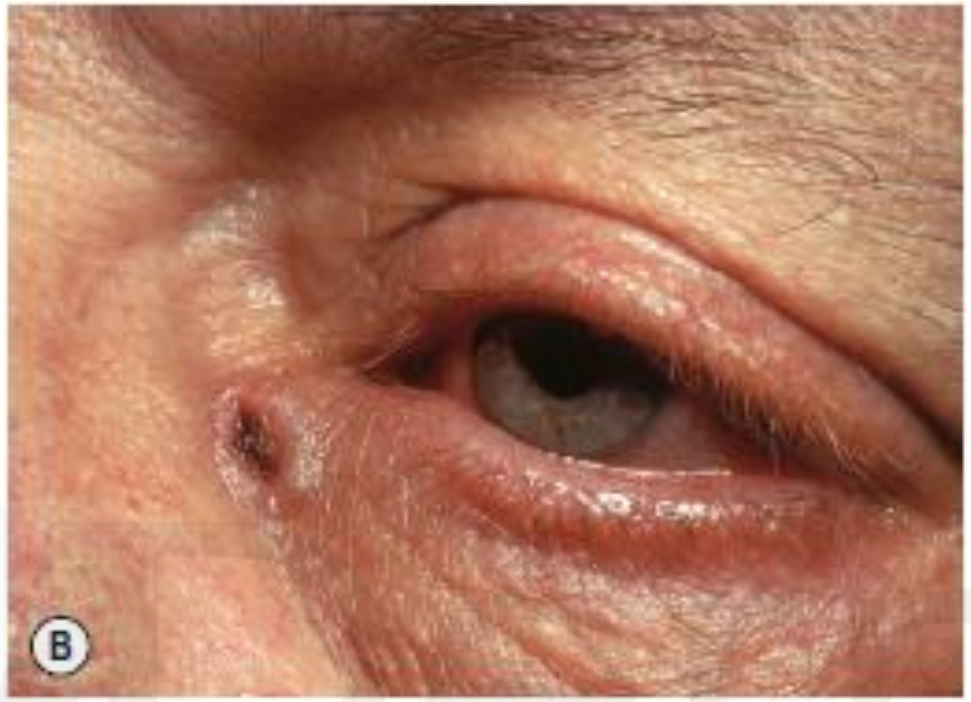
- Tumor arising in sun-damaged skin
- Rarely on palms and soles or mucous membranes
- 4 major distinctive clinicopathologic types
  - 1) Nodular
  - 2) Superficial
  - 3) Morpheaform
  - 4) Fibroepithelial
- Can be combination lesions, often ulcerate
- May have pigmented BCCs, melanin in tumors
  - More common in darker skin



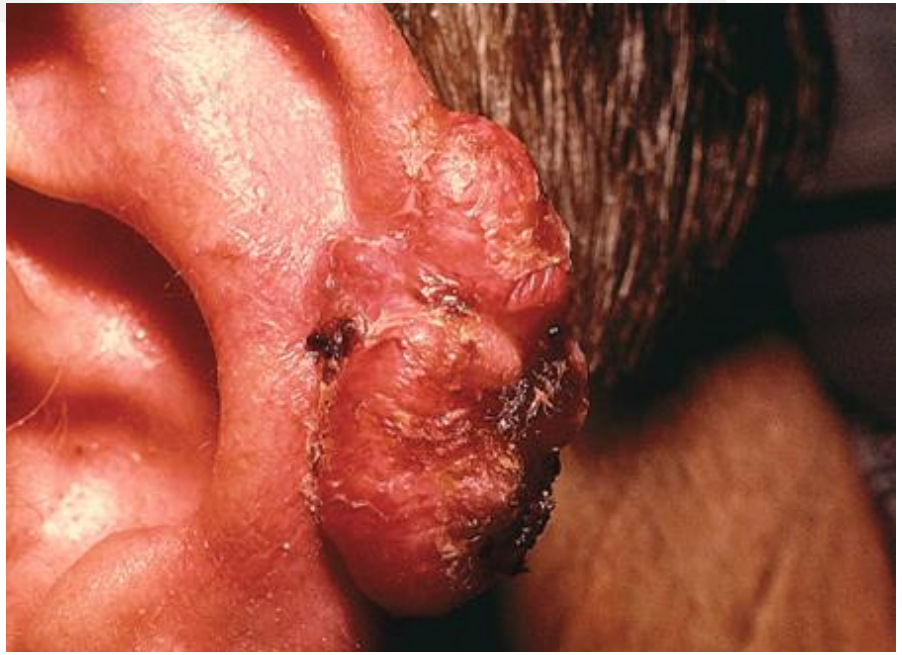
Dermatology by Bolognia, et al.

Nodular BCC

- Most common subtype
- Presents as shiny, pearly papule with arborizing telangiectasias
- Tumor can enlarge and ulcerate, often with elevated rolled borders



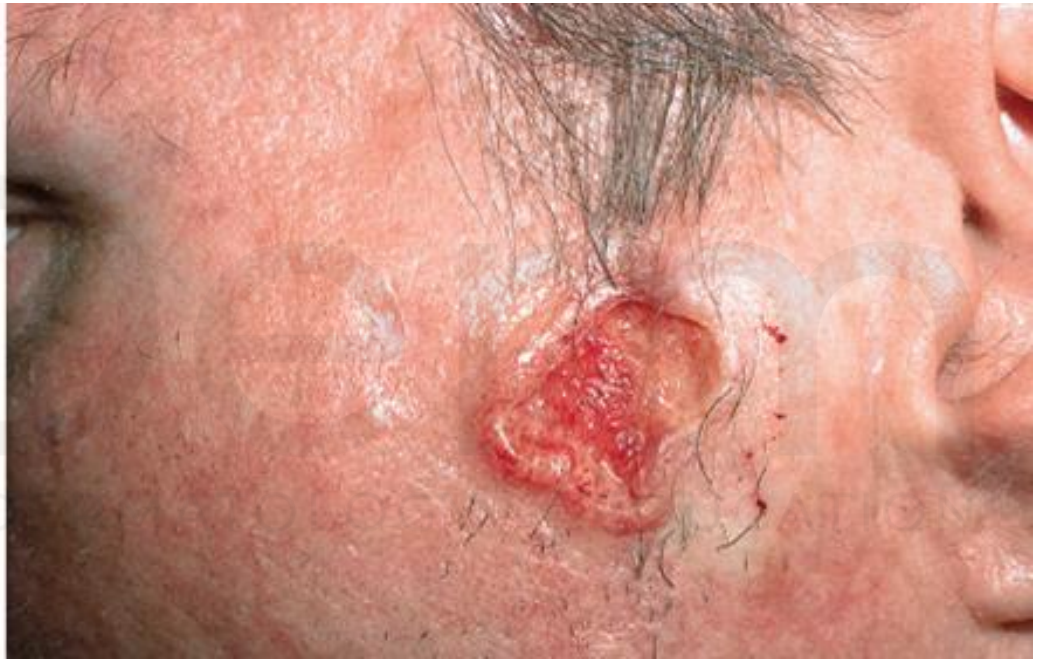
Dermatology by Bolognia, et al.



Andrews' Diseases of the Skin by James et al.

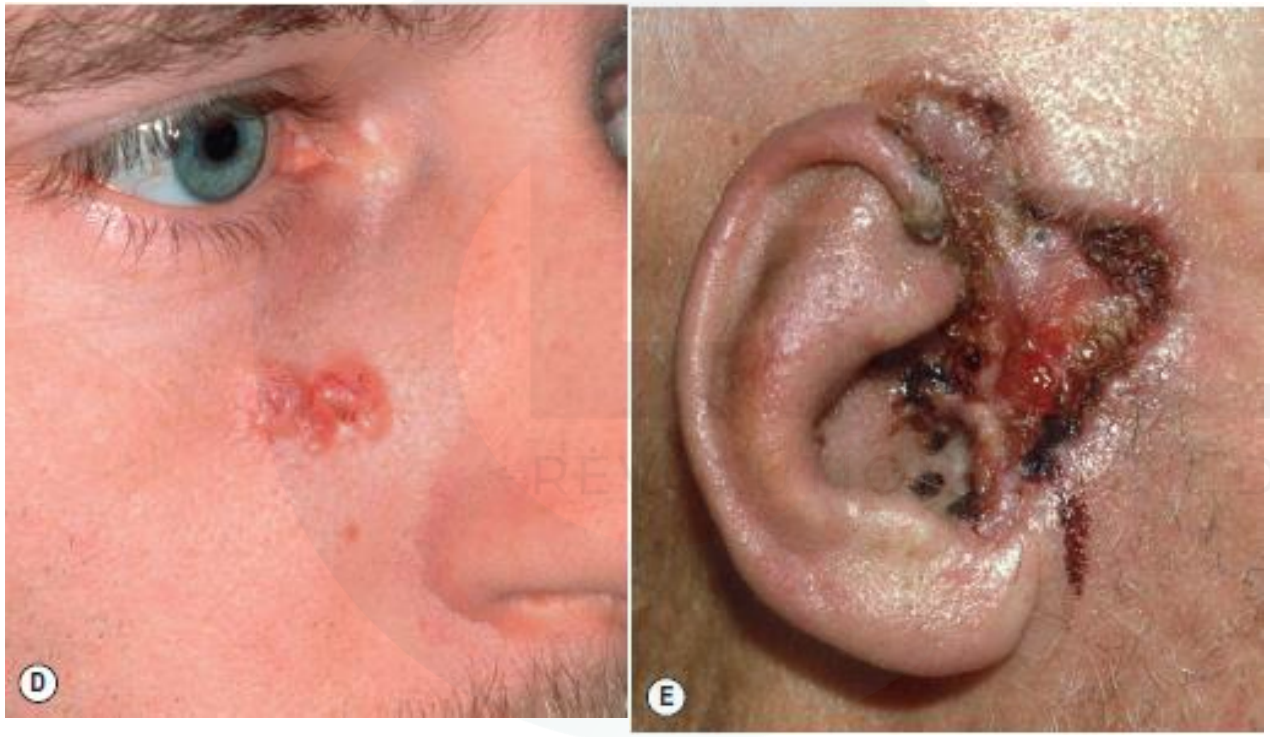
Nodular BCC subtypes

- Basosquamous Carcinoma
  - Histologic features of both BCC/SCC
  - May behave more like SCC,
    - greater likelihood of recurrence after treatment and metastasis
- Micronodular BCCs
  - Destructive behavior, subclinical spread, high rates of recurrence and potential for metastasis

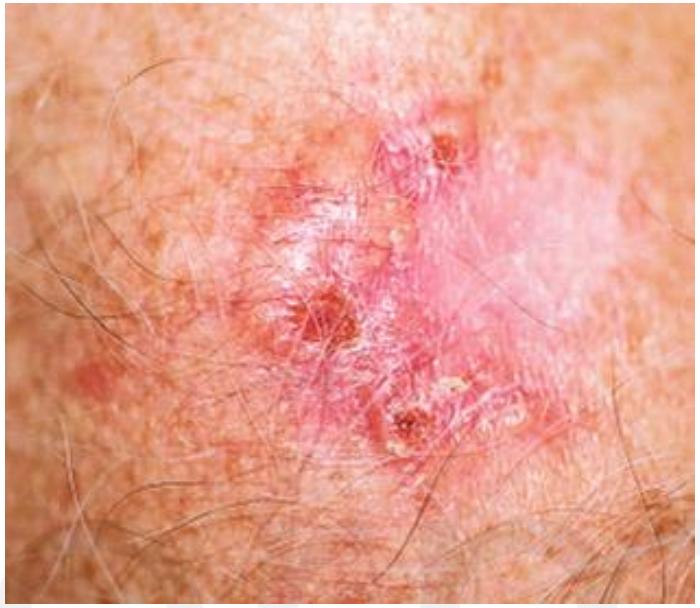


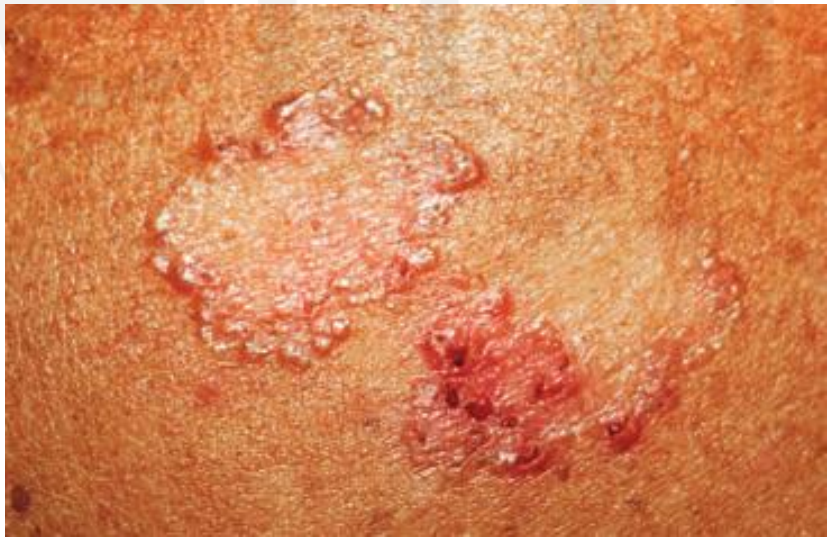
Basosquamous subtype
Andrews' Diseases of the Skin by James et al.

BCC
Clinical Images



Dermatology by Bolognia, et al.



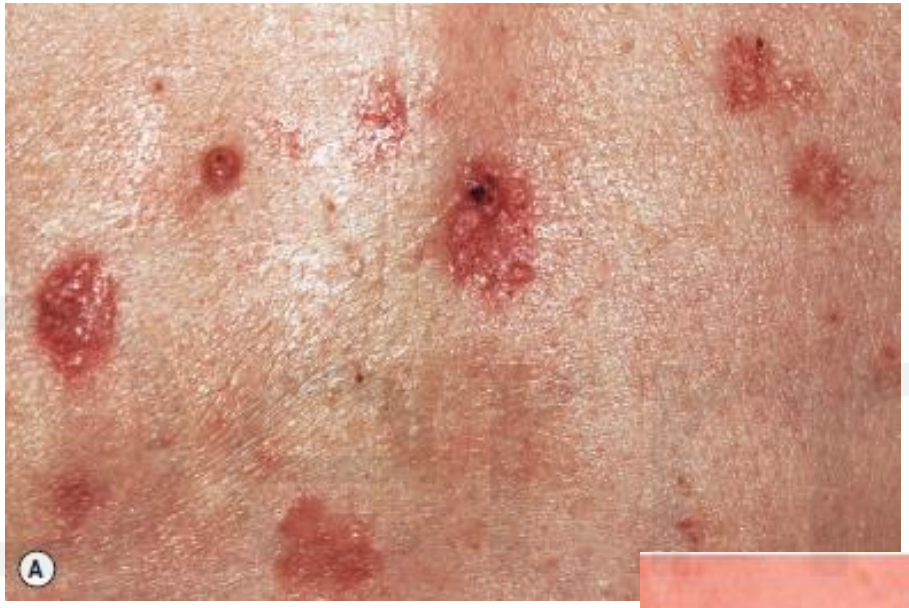


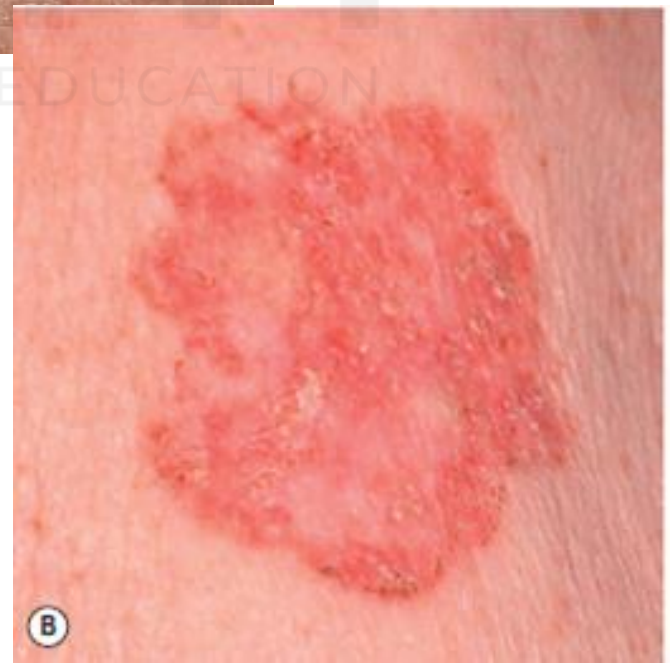
Andrews' Diseases of the Skin by James et al.

Superficial BCC

- Well-circumscribed, erythematous macule/patch or thin papule/plaque
- Usually displays focal scale/crusts, thin rolled border, atrophy and hypopigmentation
- Most common subtype in younger patients
- Trunk + extremities more common location

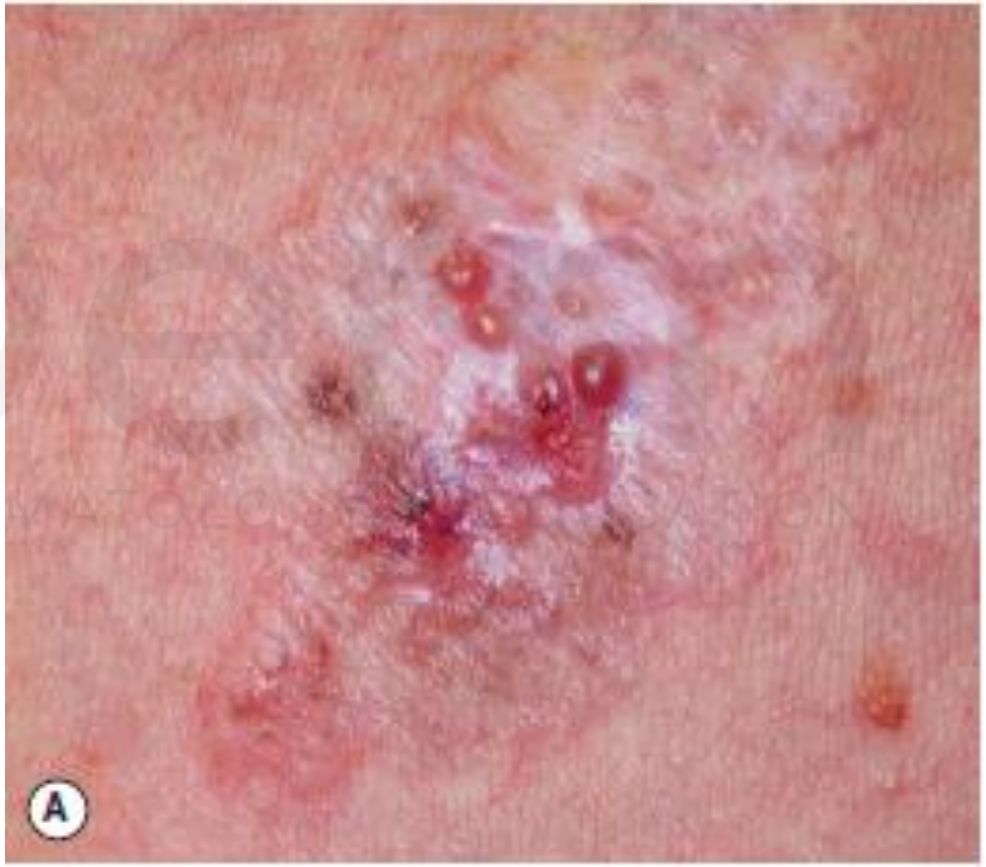
Dermatology by Bolognia, et al.





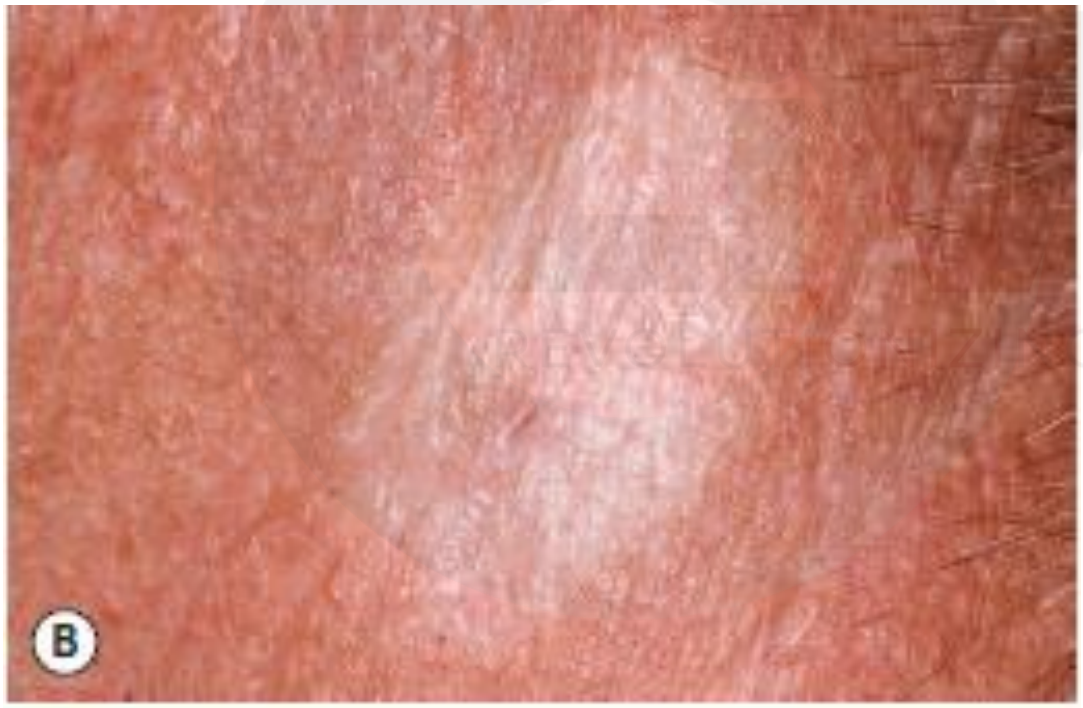
Morpheaform BCC

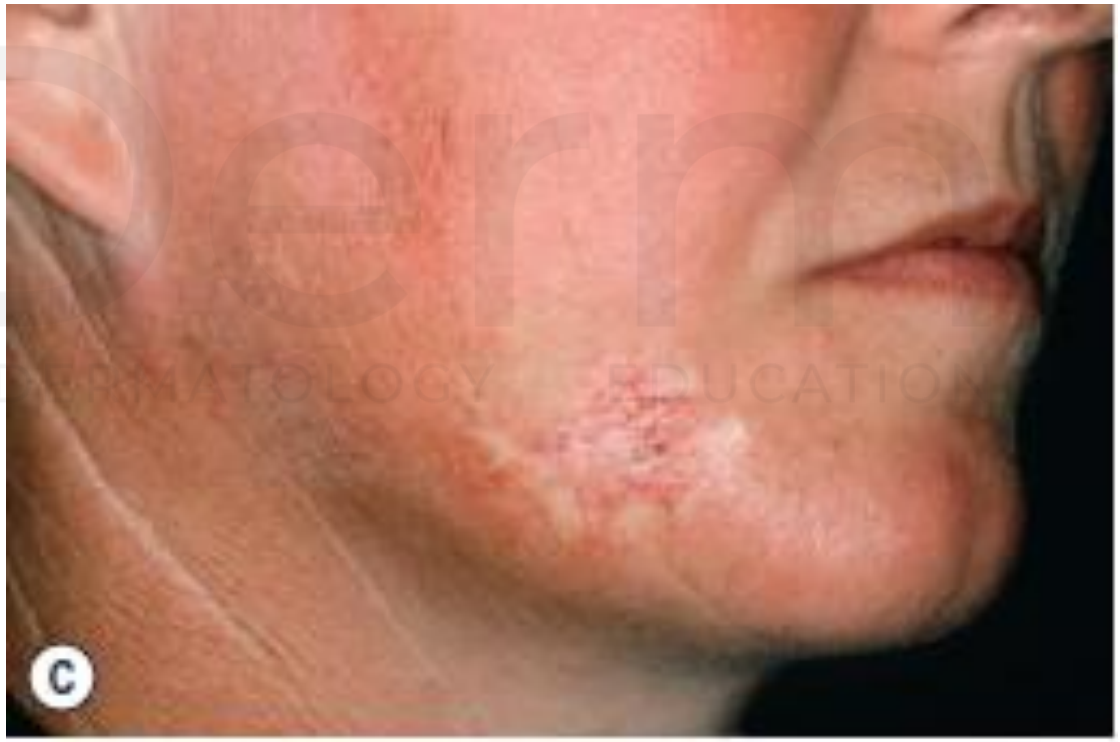
- Less common subtype
- Slightly elevated to even depressed area of induration
- Light pink to white in color with ill-defined borders
- Similar to scar or plaque of morphea
- Telangiectasias often present
- Behavior is usually more aggressive with extensive local destruction



Dermatology by Bolognia, et al.

Morpheaform BCC





Dermatology by Bolognia, et al.

BCC: Metastasis

- 1:1000 to 1:35000 rate of metastasis (exceedingly rare)
- Most common progression: Lymph node then lung and bone metastasis

NMSK: Multiple Approaches

- Mohs Micrographic Surgery (Mohs)
- Other Destructive Methods
- PD-1 Inhibitors
- Superficial Radiation Therapy (SRT)

Thank you