# Skin Cancer Basics and How to Protect Your Skin

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DEPARTMENT OF MEDICINE
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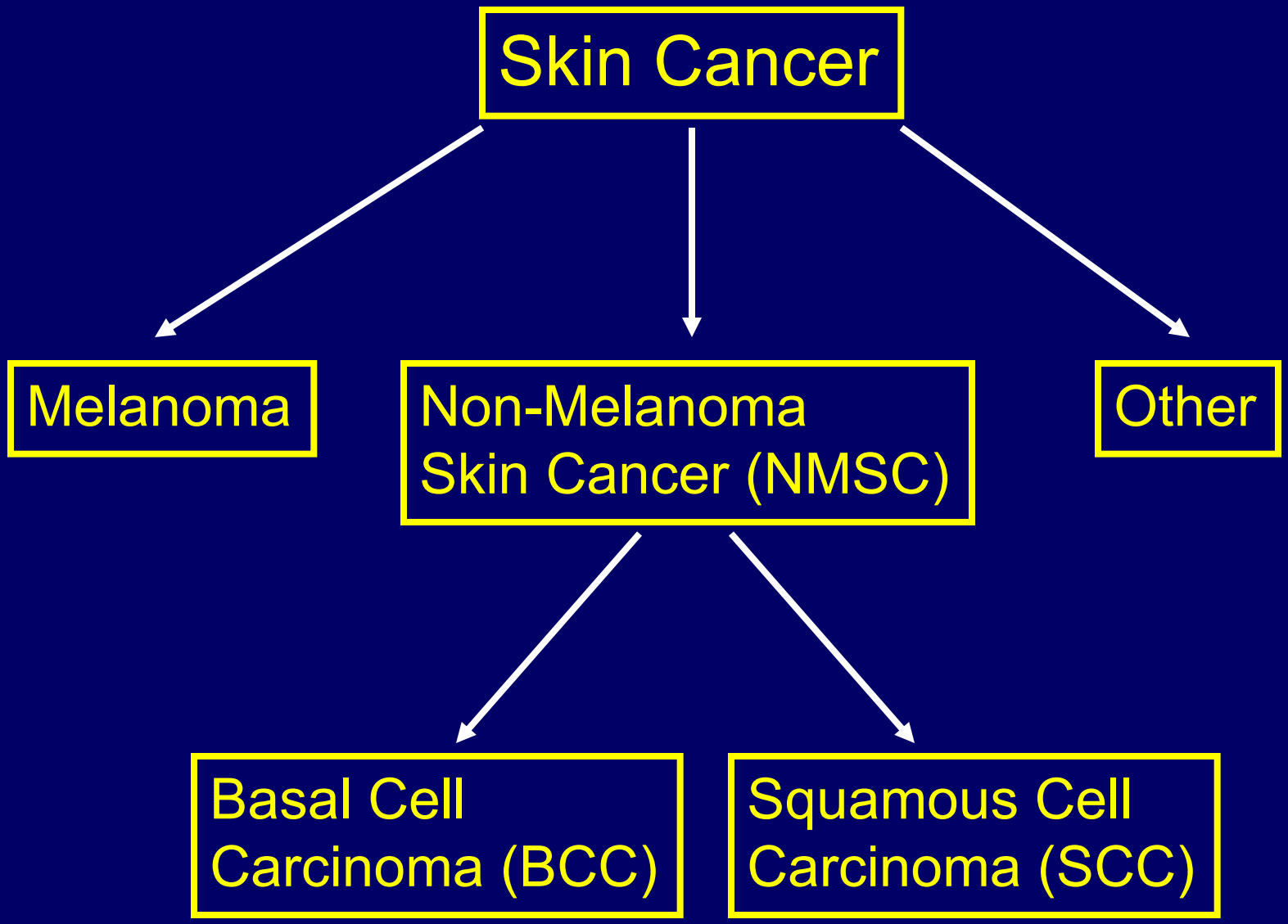
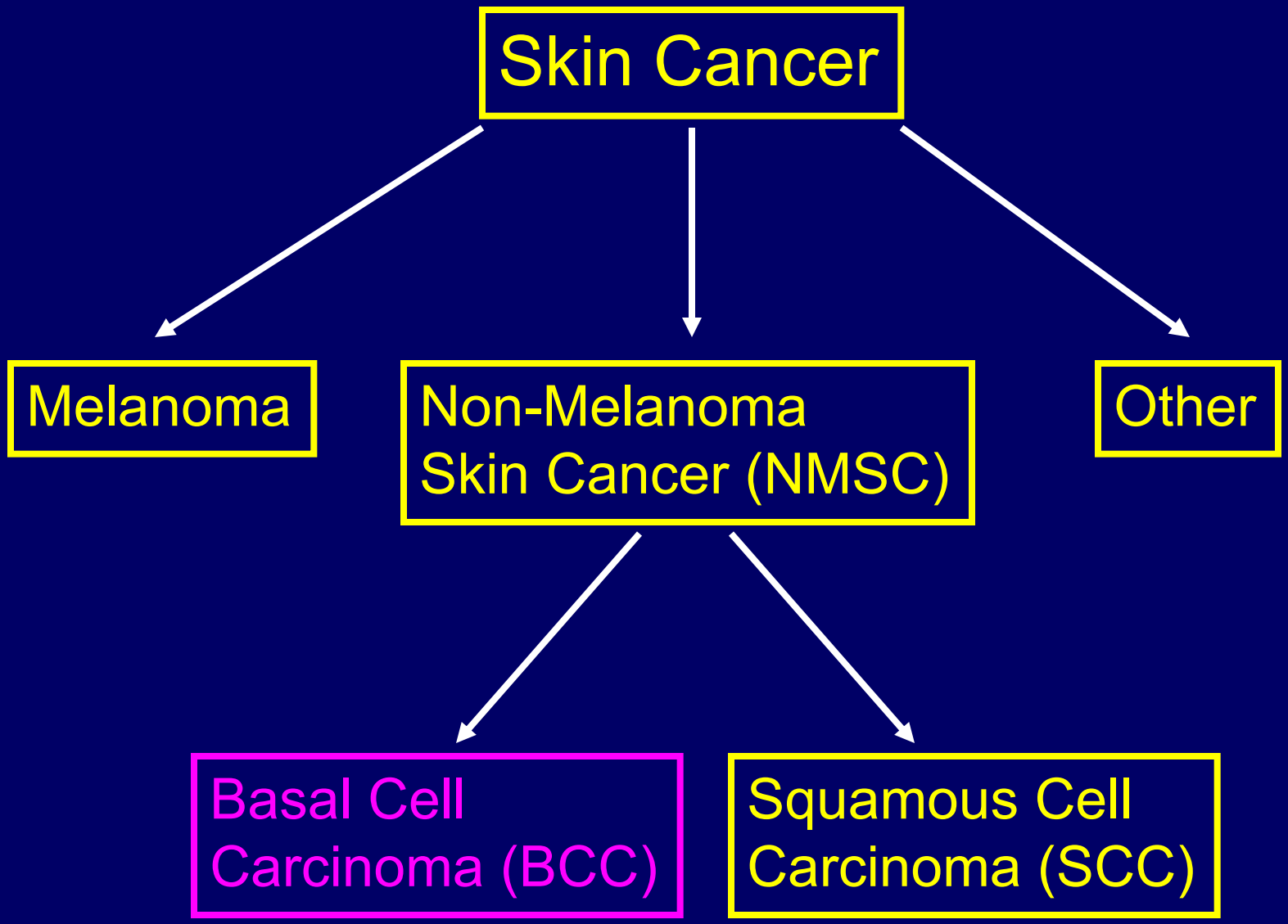
# Skin Cancer

- 1 in 5 Americans will get skin cancer in their lifetime
- Incidence of epidermal-derived skin cancer:
  - 40% in white people
  - 5% in Latinx people
  - 4% in Asian people
  - 2% in African Americans

  *Less common in skin of color but associated with higher morbidity and mortality – likely due to delay in diagnosis*


Skin Cancer
Melanoma
Non-Melanoma
Skin Cancer (NMSC)
Other
Basal Cell
Carcinoma (BCC)
Squamous Cell
Carcinoma (SCC)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# Basal cell carcinoma: Epidemiology

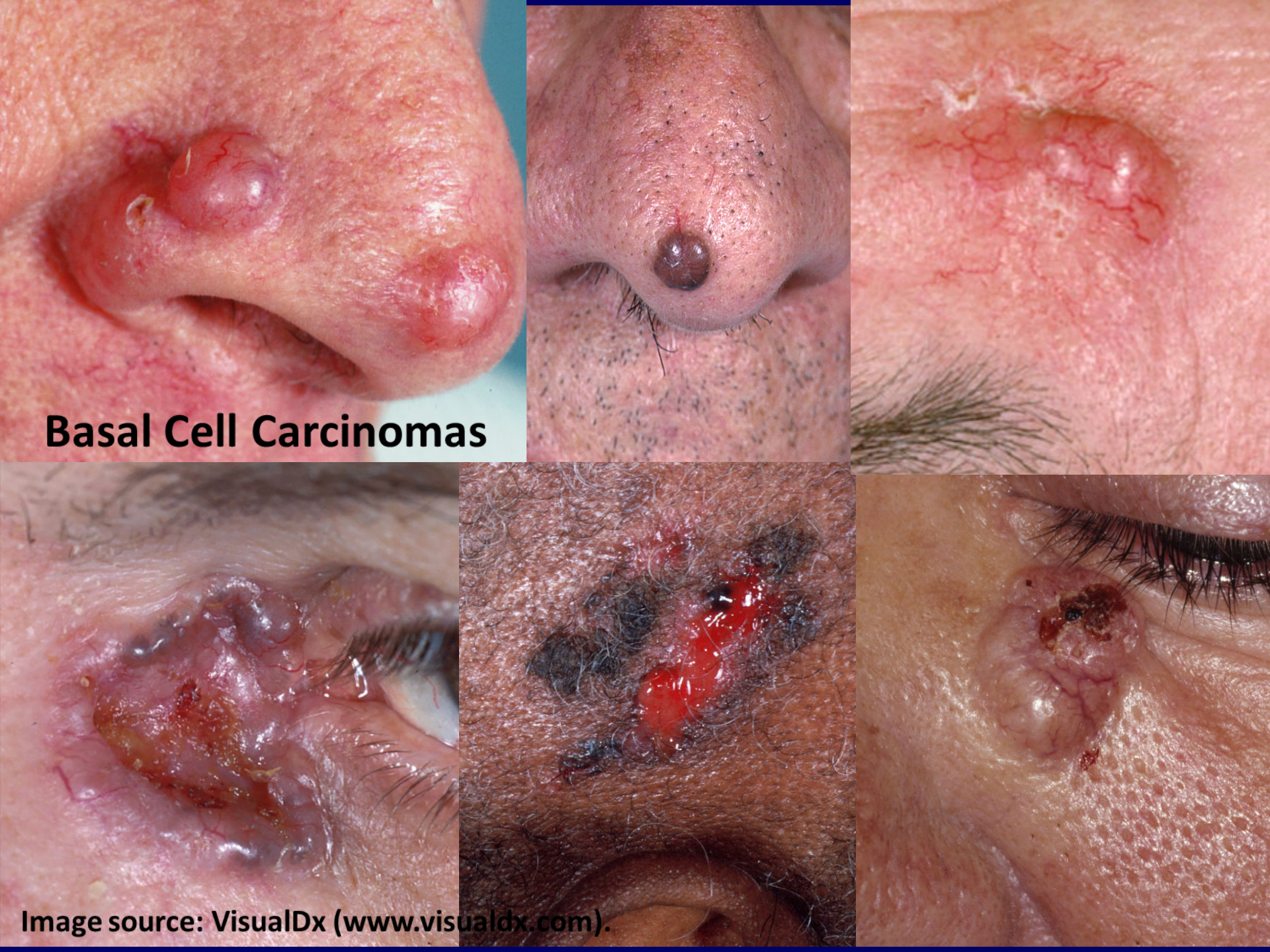
- Most common cutaneous cancer*
- 75-80% of NMSC (BCC:SCC ~4:1)
  - Transplant patients have 10x higher risk
- Incidence is increasing!
  - Younger women
  - 21-26 per 100,000 in those < 40 years old

# Basal cell carcinoma: Pathogenesis / Risk factors

- UV radiation
- Skin-type
- Ionizing radiation
- Immunosuppression

# Subtypes (>26!)

- Nodular
- Superficial
- Pigmented
- Morpheaform/Infiltrative


Basal Cell Carcinomas
Image source: VisualDx (www.visualdx.com).

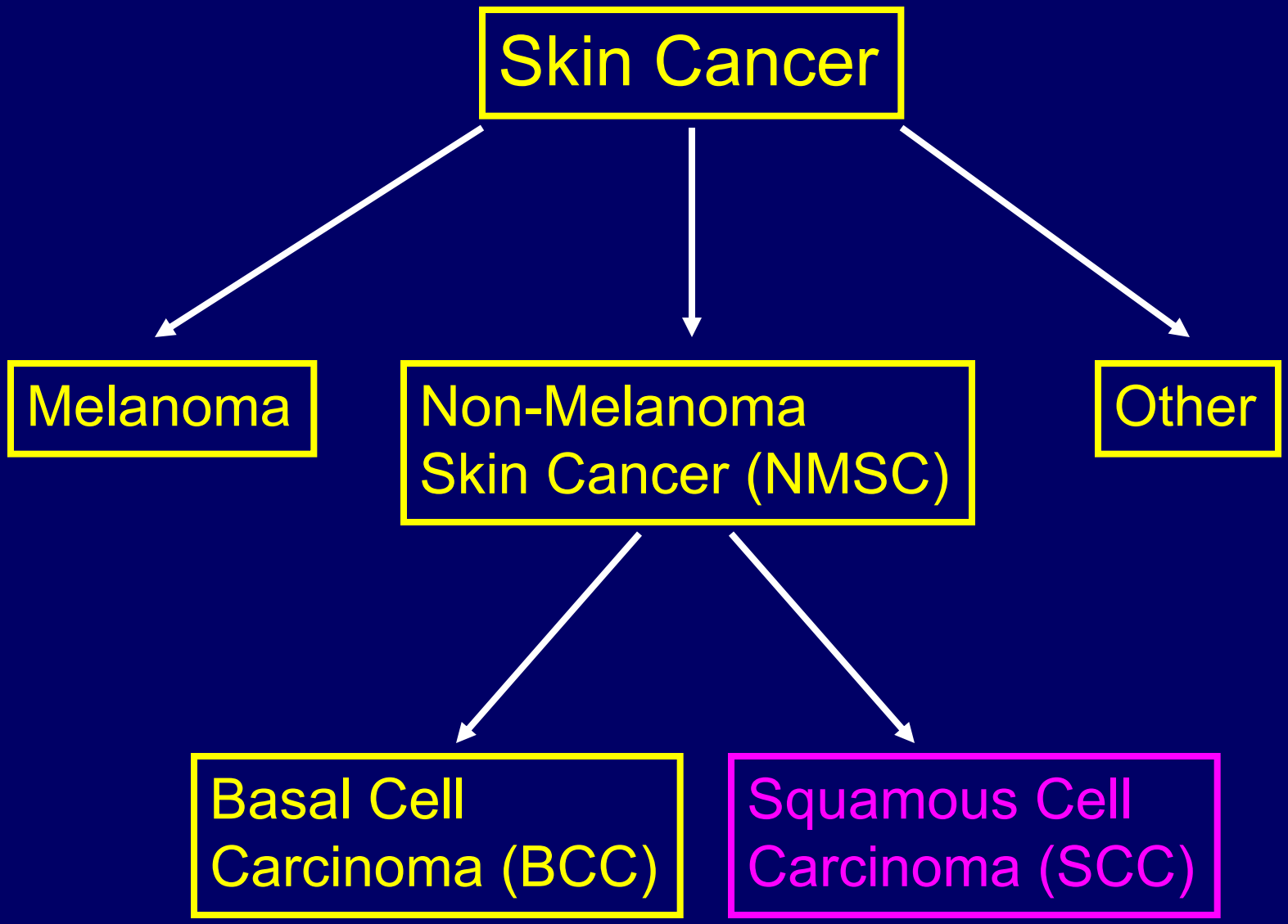
# Basal cell carcinoma: Prognosis

- Rarely metastatic (< 0.1%)
- Locally destructive
- High-risk subtypes
  - Morpheaform
  - Infiltrating
  - “Peri-neural invasion”

# Basal cell carcinoma: Treatment

- Destruction
  - Electro-desiccation and curettage (ED&C) to lesions in non-terminal hair bearing areas
  - Topical 5-FU (Efudex)
  - Imiquimod (Aldara)

  Superficial BCC
  - Primary XRT for large lesions
- Surgical
  - excision with 3-4mm margins
  - Mohs micrographic surgery
    - morpheaform/infiltrative, recurrent lesions, high risk H zone, size > 2 cm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# Squamous cell carcinoma: Epidemiology

- Second most common type of skin cancer
  - Most common skin cancer in African Americans and Asians
  - * Most common type in immunosuppressed (BCC:SCC ratio is reversed at ~1:4)
    - Risk is increased 65x in transplant patients
- Men > women (~2:1)
- Incidence is increasing (aging population)
- 2500 deaths per year in the United States, ~ 1/3 the number of Americans who die from melanoma annually

# Squamous cell carcinoma: Pathogenesis / Risk factors

- UV radiation
- Skin type, geography
- Ionizing radiation
- Chemical carcinogens (e.g. arsenic)
- Immunosuppression
- Chronic inflammation / scarring
- HPV infection - periungual, genital


Squamous Cell Carcinomas
Image source: VisualDx (www.visualdx.com).
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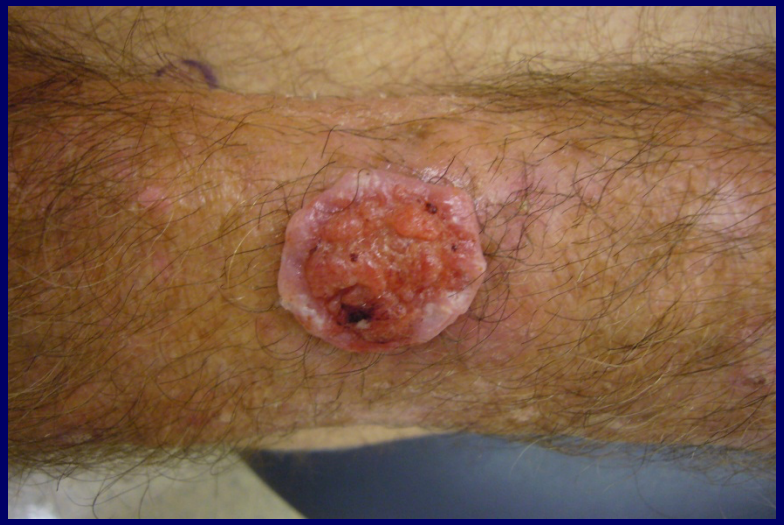
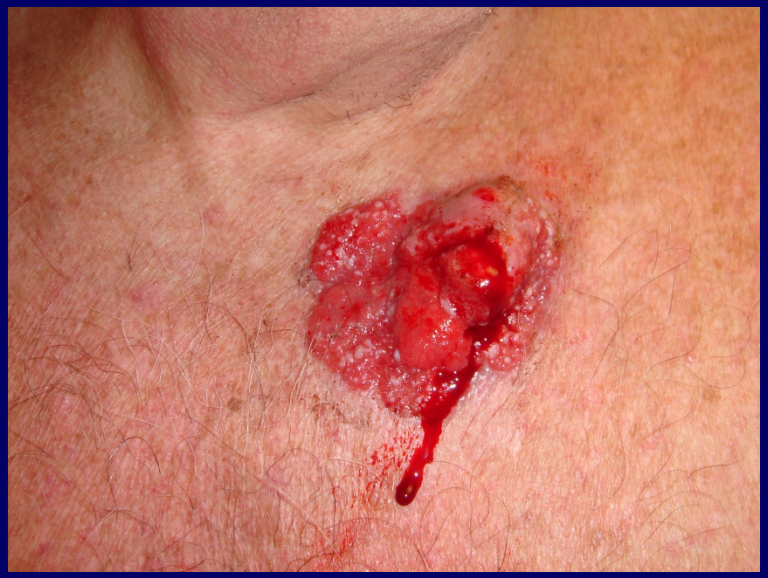
# Invasive SCC





- Sun-exposed skin
  - 70% head and neck
- Pink or flesh-colored plaque, keratotic papule, or nodule
- +/- scale, crust, erosion, ulceration

# High Risk

- HR anatomic sites
  - Ear
  - Lips
  - Mucosal sites
    - vulva
    - penis
- Recurrent SCC
- Arising within scar or chronic ulcer
- Perineural invasion

# SCC Treatment

- Destructive
  - XRT
- Surgical
  - Standard excision
  - Mohs micrographic surgery
- Adjuvant
  - XRT
  - Decrease the dose of immunosuppressive drug
  - Systemic retinoids (prophylaxis only)

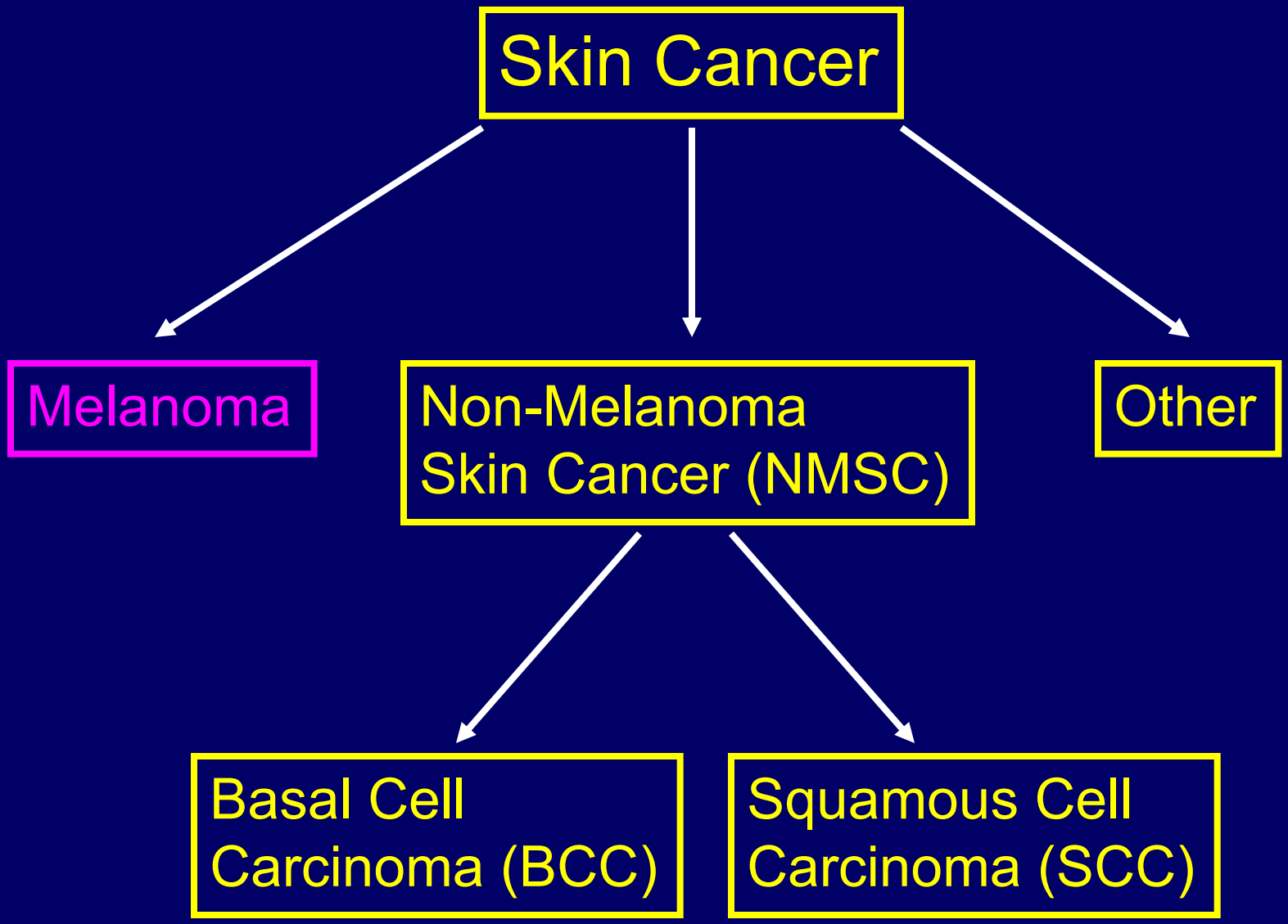
# SCC Prognosis

- 2-6% rate of metastasis (increases to 10-20% in HR tumors)
  - Lymph node metastasis = 25-35% survival at 5 years
  - Visceral metastasis < 5% survival at 5 years

# 5 Year Recurrence Rates

| Clinical features | |
|---|---|
| Size≥2cm | 15.2 |
| Location: Ear | 18.7 |
| Locations: Lip | 10.5 |
| Locally recurrent | 23.3 |
| **Pathologic factors** | |
| Depth ≥4mm | 17.2 |
| Poorly differentiated | 28.6 |
| Perineural invasion | 47.2 |

Rowe et al J Am Acad Derm 1992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# Melanoma: Epidemiology

- Lifetime risk of developing invasive MM (USA)
  - 1930 = 1 in 1500
  - 1980 = 1 in 250
  - 1993 = 1 in 100
  - 2004 = 1 in 65
  - 2010 = 1 in 50
- 4% of all skin cancer, 80% of deaths
- Earlier detection
  - Increased patient education
  - Prognosis for late stage unchanged

# Melanoma: Pathogenesis / Risk factors

- UV radiation
  - High-dose intermittent exposure (i.e. “blistering burns”)
- Nevi
  - >50 banal nevi
  - Dysplastic nevi
  - Giant congenital nevi (> 20 cm)
- Personal or family history of MM
  - CDKN2A mutation (encodes p16)- familial melanoma
- Immunosuppression
  - 3-4x fold higher risk

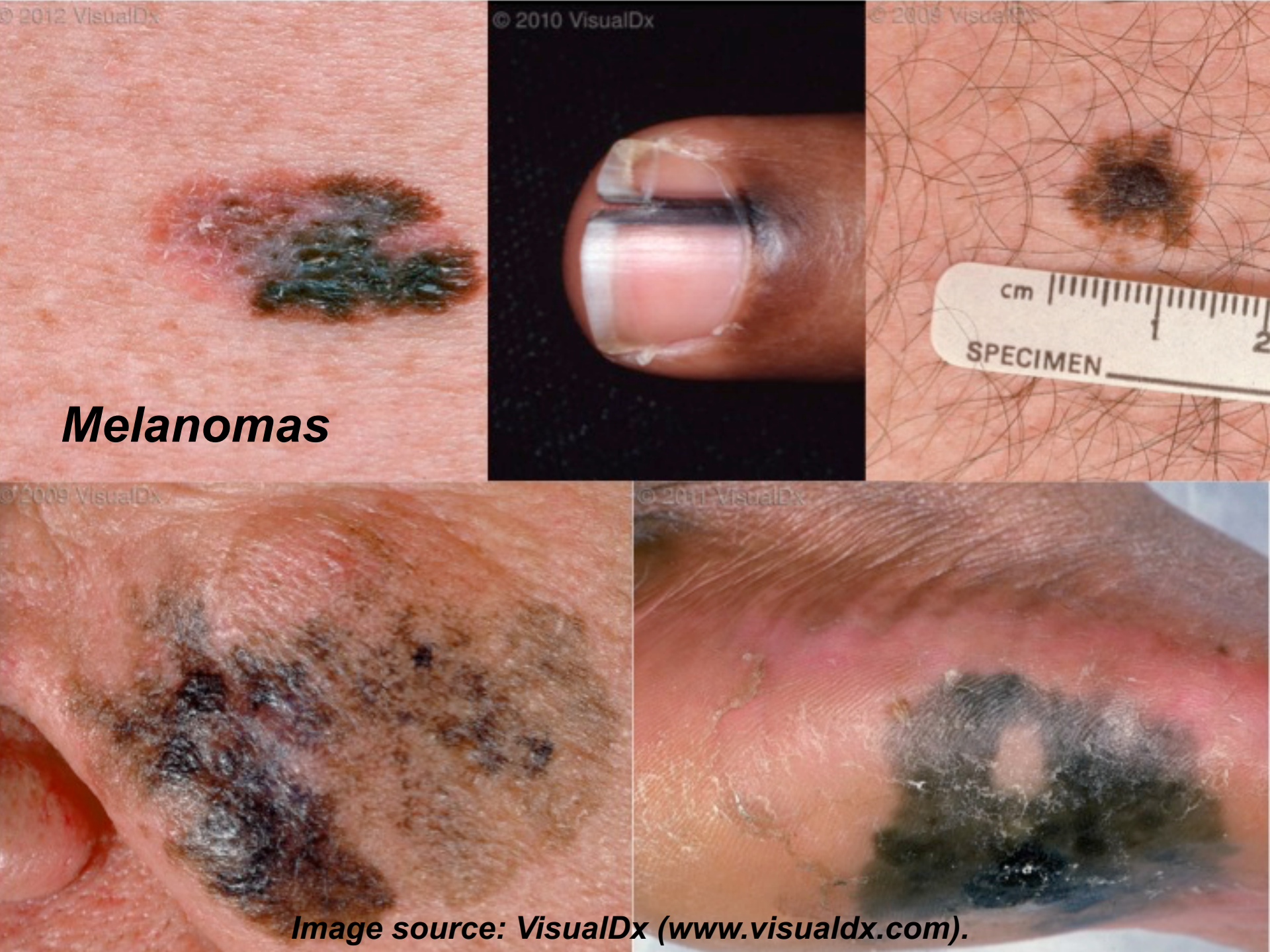
# Clinical signs of Melanoma

- “ABCDE criteria” for melanoma

A = Asymmetry
B = Border irregularity
C = Color variegation
D = Diameter > 6 mm
E* = Evolution (i.e. change over time)

# Melanoma Sub-types

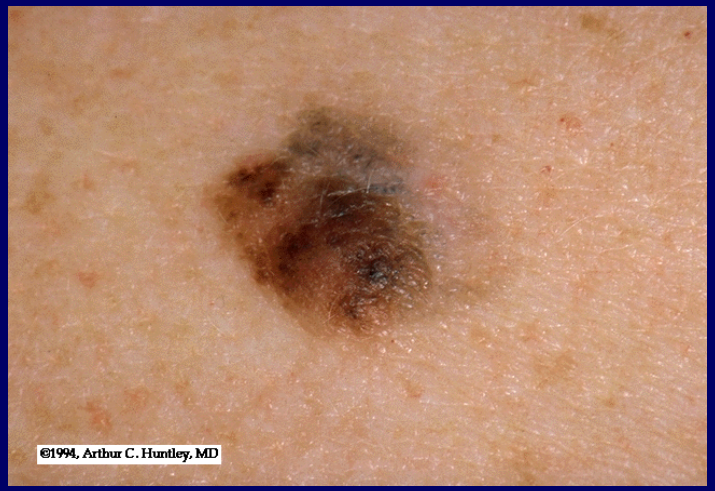
- Superficial spreading melanoma
- Nodular melanoma
- Lentigo maligna melanoma
- Acral lentiginous melanoma
- Amelanotic melanoma

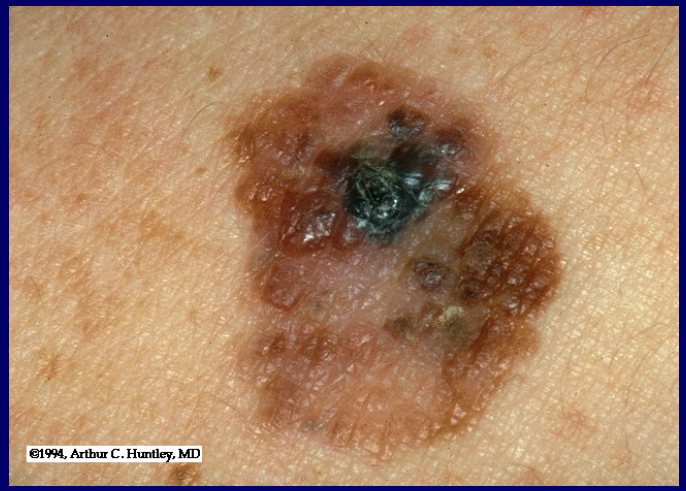



***Melanomas***

***Image source: VisualDx (www.visualdx.com).***

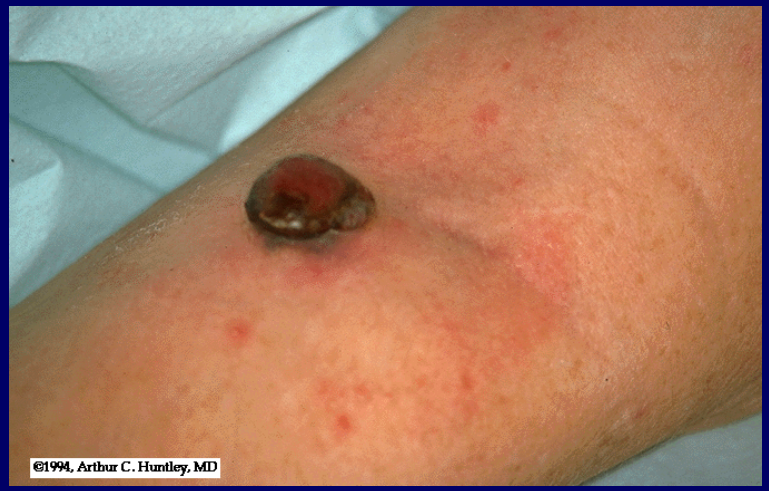
# Superficial spreading melanoma (SSM)

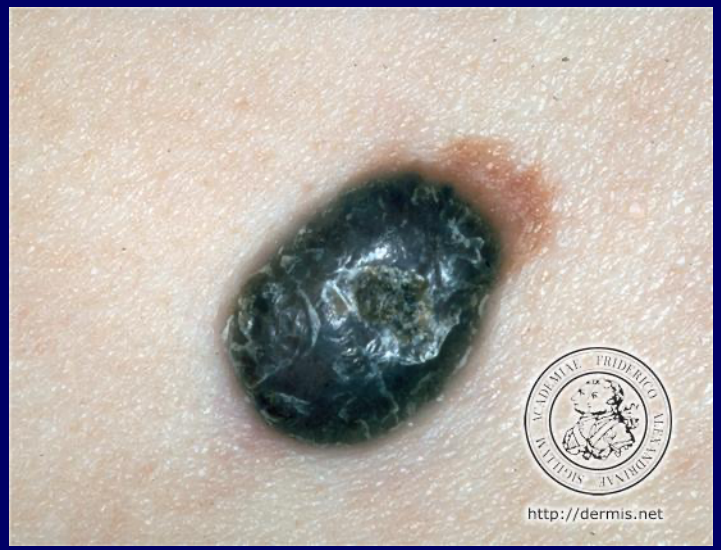



- Middle age
- Sun-exposed or non-exposed
- Upper back (men) or legs (women)
- **Arises *de novo* > from existing nevus**
- "ABCDE" criteria usually fulfilled

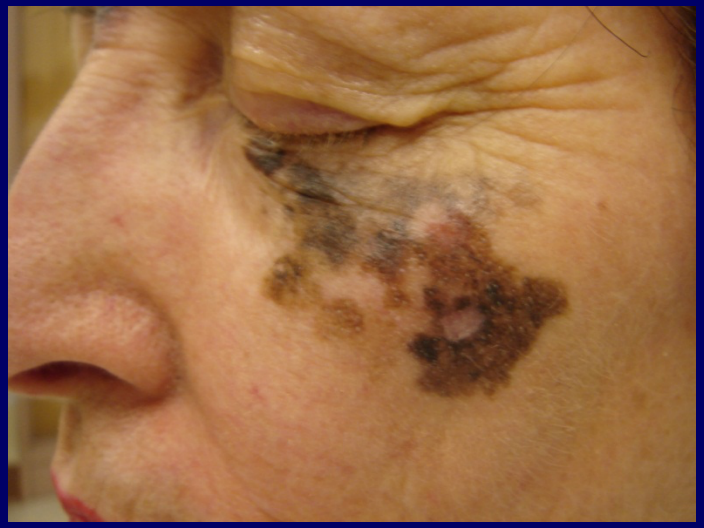
# Nodular Melanoma (NM)

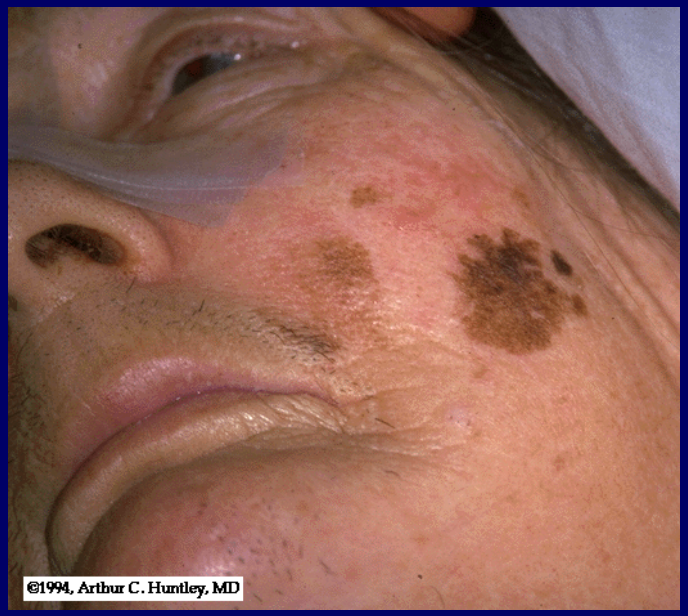



- Often young adult
- Sun-exposed skin (head, neck, trunk)
- Men > women
- Arises *de novo*
- **ABCD criteria <u>not</u> fulfilled, but lesion Evolves rapidly**

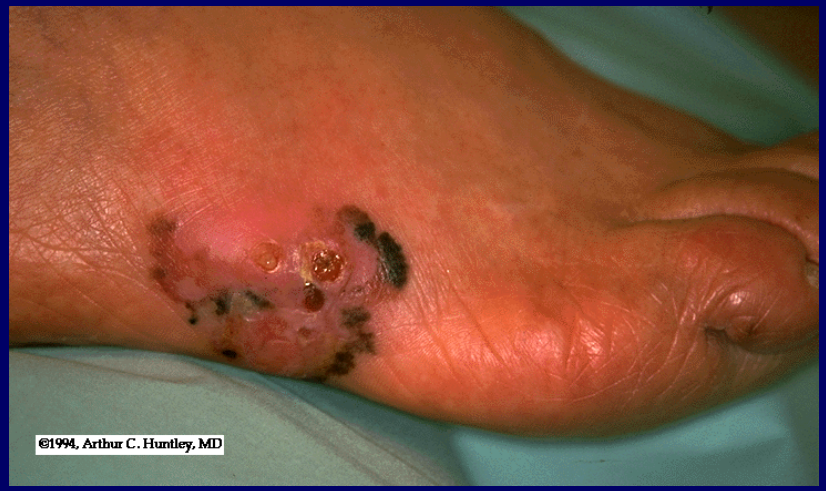
# Lentigo maligna melanoma(LMM)

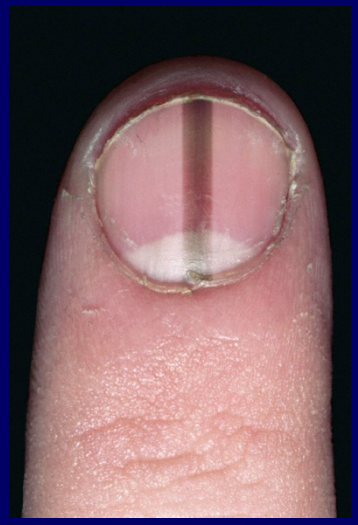


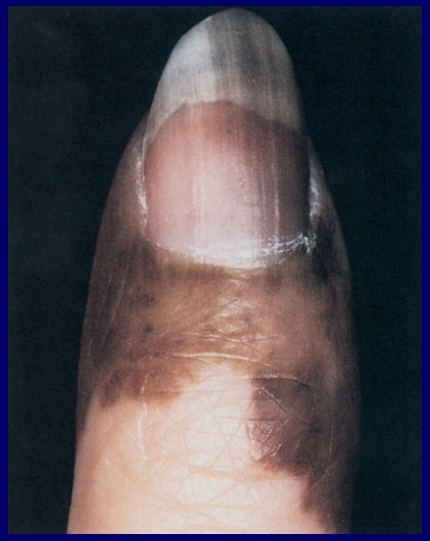



- Elderly person
- Sun-damaged skin (face, scalp, arms)
- Tan macule that slowly enlarges and develops uneven pigmentation

# Acral lentiginous melanoma (ALM)

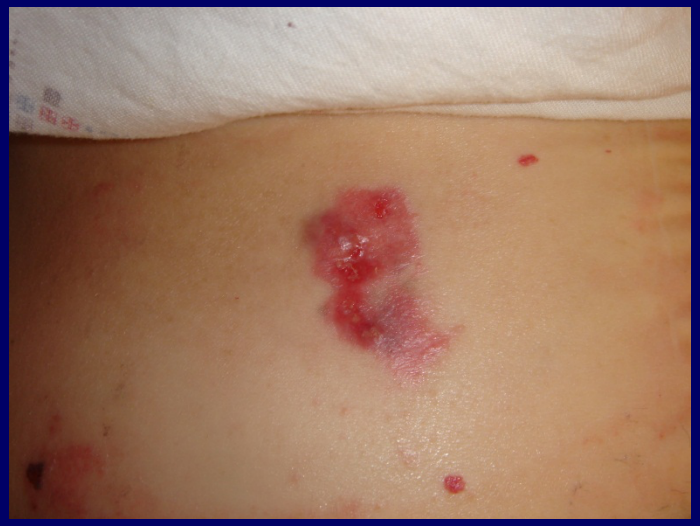


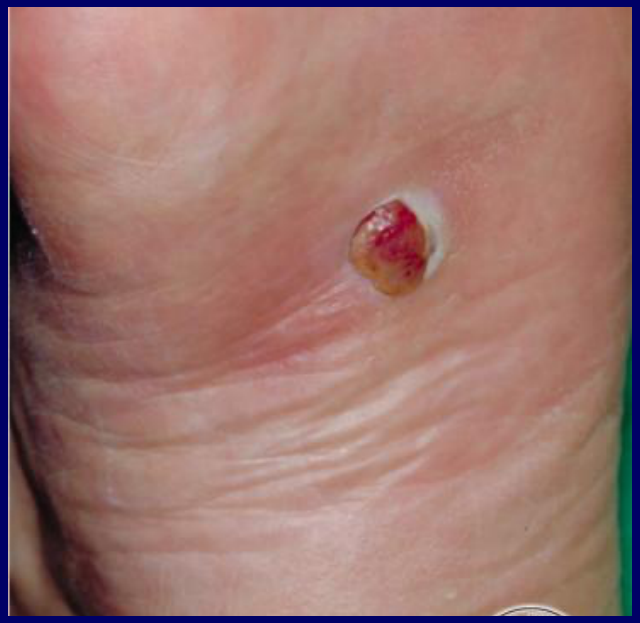





- Most common subtype in African Americans and Asians
- Middle age, M = F
- Foot > hand
- Diagnosis often delayed

# Amelanotic melanoma





- Lack of pigment
- Flesh-colored or pink
- Simulates
  - BCC
  - Pyogenic granuloma

# Important Pathology Report Characteristics

- Depth*
- Ulceration*
- Mitosis*
- Regression
- Vertical Growth Phase
- Radial Growth Phase
- Tumor infiltrating lymphocytes (TILS)
- Melanoma subtype

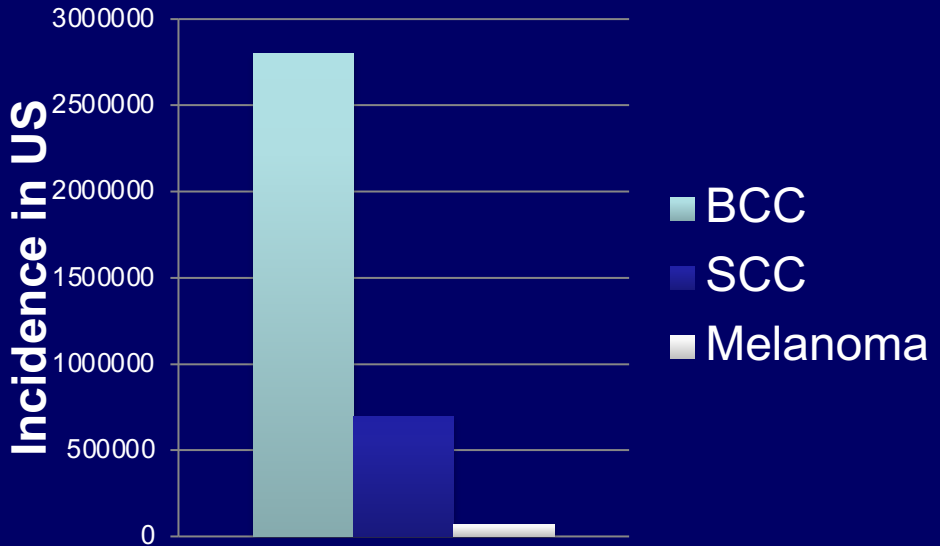
# Melanoma Workup

- Full history & physical to look for satellite lesions, lymph node metastasis
- Sentinel lymph node biopsy if tumor depth >1mm, regression or mitoses on histopathology*
- Baseline CXR, CBC, LFT's, and LDH*
- Consider PET/CT scan if there is concern about metastatic disease (e.g. palpable lymph nodes on exam)

# Poor Prognostic Factors

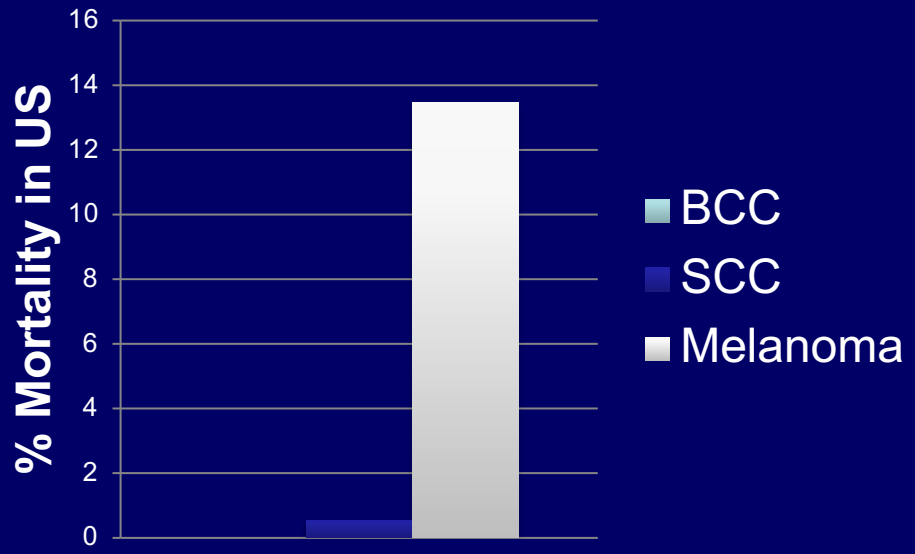
- Male gender
- Increasing age
- Increased tumor thickness
- Ulceration
- Head/neck/trunk/axial (vs. extremities)

# *Incidence of skin cancer in the US*




*How would the numbers look different for chronically immunosuppressed individuals such as from organ transplant?*

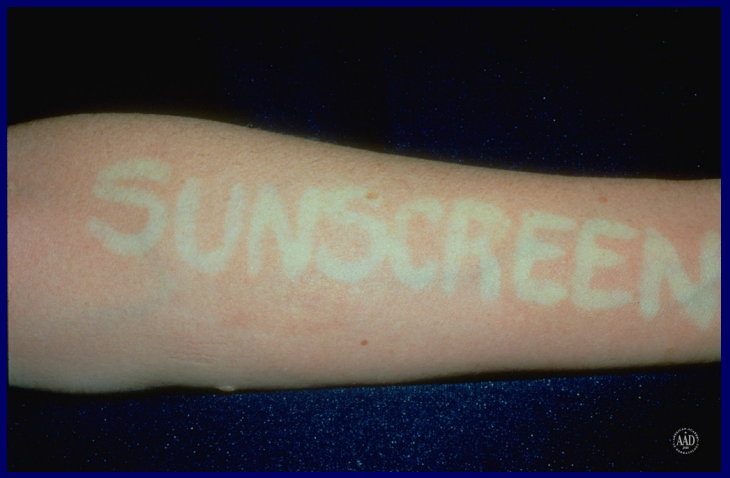
# *Mortality from skin cancer in the US*




*http://www.skincancer.org/skin-cancer-information/skin-cancer-facts#general*

# PROTECT YOURSELF!

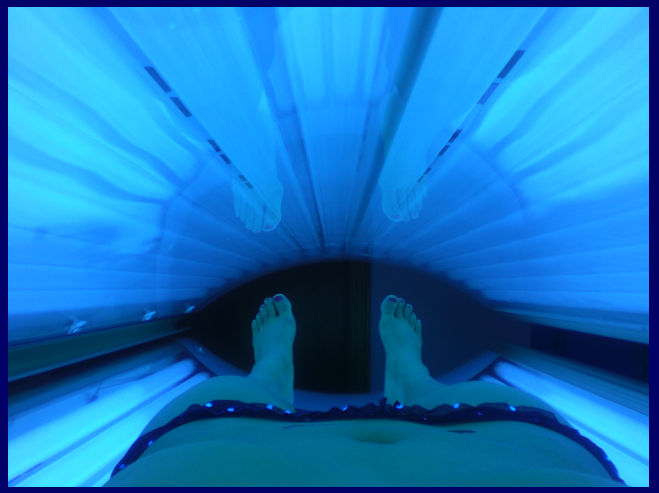
# Sun Protection




- Sunscreen
  - SPF 30 or higher
  - Higher IS better
  - Frequent application
  - Broad spectrum
    - Combo chemical UVA/UVB blockers
  - Physical blockers
- Sun protective clothing/hats

# UPF Clothing


# Base Tan?



- Indoor Tanning is bad
  - Like smoking for your skin
- Mostly UVA light
  - UVA—immediate skin darkening
    - Transient bronze “glow” to the skin
  - UVB triggers more long term protection
- Only affords very modest protection
  - SPF 1.5-3
- Causes DNA damage, collagen damage etc.
  - It is estimated that indoor tanning causes 419,000 cases of skin cancer each year
    - Increases risk of melanoma

# MYELOMA AND THE SKIN

European Journal of Haematology

European Journal of Haematology 97 (439–444)

ORIGINAL ARTICLE

# Risk of skin cancer in multiple myeloma patients: a retrospective cohort study

Austin A. Robinson[1], James Wang[2], Suzie Vardanyan[3], Erik K. Madden[4], Frank Hebroni[4], Kyle A. Udd[2], Tanya M. Spektor[5], Jason D. Nosrati[3], Alex Z. Kitto[3], Michael Zahab[3], Simrin Cheema[6], Darron H. Fors[4], Adam Norberg[4], Joseph Diehl[4], Gabriel N. Waterman[7], Regina A. Swift[2], John Crowley[8], James R. Berenson[2,3,5]

**Table 3** Cumulative incidence and SIRs of types of skin cancers

| Type | Patients | Controls | SIR (95% CI, *P*-value) |
|---|---|---|---|
| Any skin cancer | 110 | 60 | 1.72 (1.43–2.07, $P < 0.001$) |
| BCC | 52 | 37 | 1.32 (1.00–1.72, $P = 0.043$) |
| SCC | 44 | 17 | 2.44 (1.78–3.24, $P < 0.001$) |
| NMSC | 96 | 54 | 1.67 (1.36–2.03, $P < 0.001$) |
| Melanomas | 9 | 5 | 1.69 (0.83–3.11, $P = 0.109$) |
| Unknown | 5 | 1 | – |

Brief report

# A review of second primary malignancy in patients with relapsed or refractory multiple myeloma treated with lenalidomide

Meletios A. Dimopoulos,[1] Paul G. Richardson,[2] Nancy Brandenburg,[3] Zhinuan Yu,[3] Donna M. Weber,[4] Ruben Niesvizky,[5] and Gareth J. Morgan[6]

**In a retrospective pooled analysis of 11 clinical trials of lenalidomide-based therapy for relapsed/refractory multiple myeloma (MM; N = 3846), the overall incidence rate (IR, events per 100 patient-years) of second primary malignancies (SPMs) was 3.62. IR of invasive (hematologic and solid tumor) SPMs was 2.08, consistent with the background incidence of developing cancer. In a separate analysis of pooled data from pivotal phase 3 trials of relapsed or refractory MM (N = 703), the overall IR of SPMs was 3.98 (95% confidence interval [CI], 2.51-6.31) with lenalidomide/dexamethasone and 1.38 (95% CI, 0.44-4.27) with placebo/dexamethasone; IRs of nonmelanoma skin cancers were 2.40 (95% CI, 1.33-4.33) and 0.91 (95% CI, 0.23-3.66), respectively; IRs of invasive SPMs were 1.71 (95% CI, 0.86-3.43) and 0.91 (95% CI, 0.23-3.66), respectively. The risk of SPMs must be taken into account before initiating lenalidomide treatment. In the context of the observed survival benefit in relapsed or refractory MM patients, the benefit/risk profile of lenalidomide/dexamethasone remains positive. (*Blood*. 2012;119(12): 2764-2767)**

Brief report

# A review of second primary malignancy in patients with relapsed or refractory multiple myeloma treated with lenalidomide

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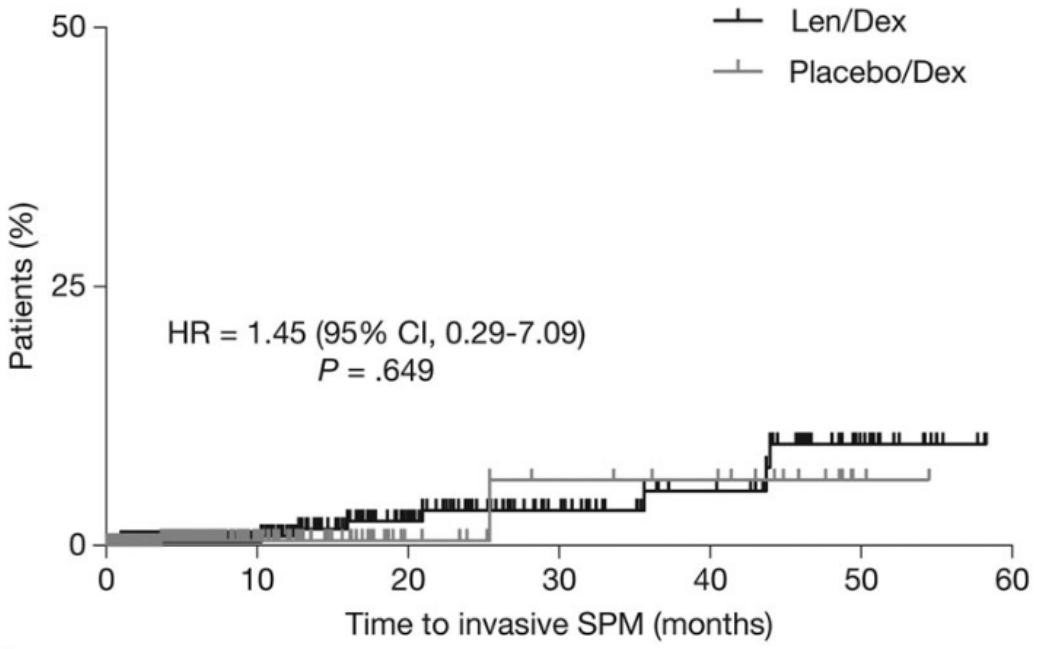


| No. at risk | | | | | | | |
|---|---|---|---|---|---|---|---|
| Len/Dex | 353 | 171 | 103 | 64 | 47 | 18 | 0 |
| Placebo/Dex | 350 | 62 | 22 | 15 | 13 | 2 | 0 |

**Figure 1. Kaplan-Meier analysis of time to invasive SPM in studies MM-009 and MM-010.** Analyses are based on the safety population (n = 703). HR indicates hazard ratio.

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journal homepage: www.elsevier.com/locate/ysonc

# Cutaneous manifestations of multiple myeloma and other plasma cell proliferative disorders

Manisha Bhutani[a], Zainab Shahid[a], Alicia Schnebelen[b], Daisy Alapat[b], Saad Z. Usmani[a,*]

**Table 1**
Spectrum of well-recognized cutaneous manifestations associated with multiple myeloma and other plasma cell disorders.

| Principal mechanism | Disorder |
|---|---|
| Malignant plasma cells infiltration | Plasmacytomas |
| Amyloid fibrils deposition | AL amyloidosis |
| Paraprotein deposition | Cryoglobulinemia |
| | Schnitzler's syndrome |
| Fibrosing dermopathies | Scleromyxedema |
| | Scleredema adultorum |
| Biologic activity of paraprotein, with anti-LDL activity | Necrobiotica xanthogranuloma Xanthomas |
| Abnormal cytokine secretion | POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, and Skin changes) |
| | AESOP (Adenopathy and Extensive Skin patch Overlying a Plasmacytoma) |
| Unknown mechanisms | Acquired cutis laxa |
| Treatment-related | Infections |
| | Drug reactions |

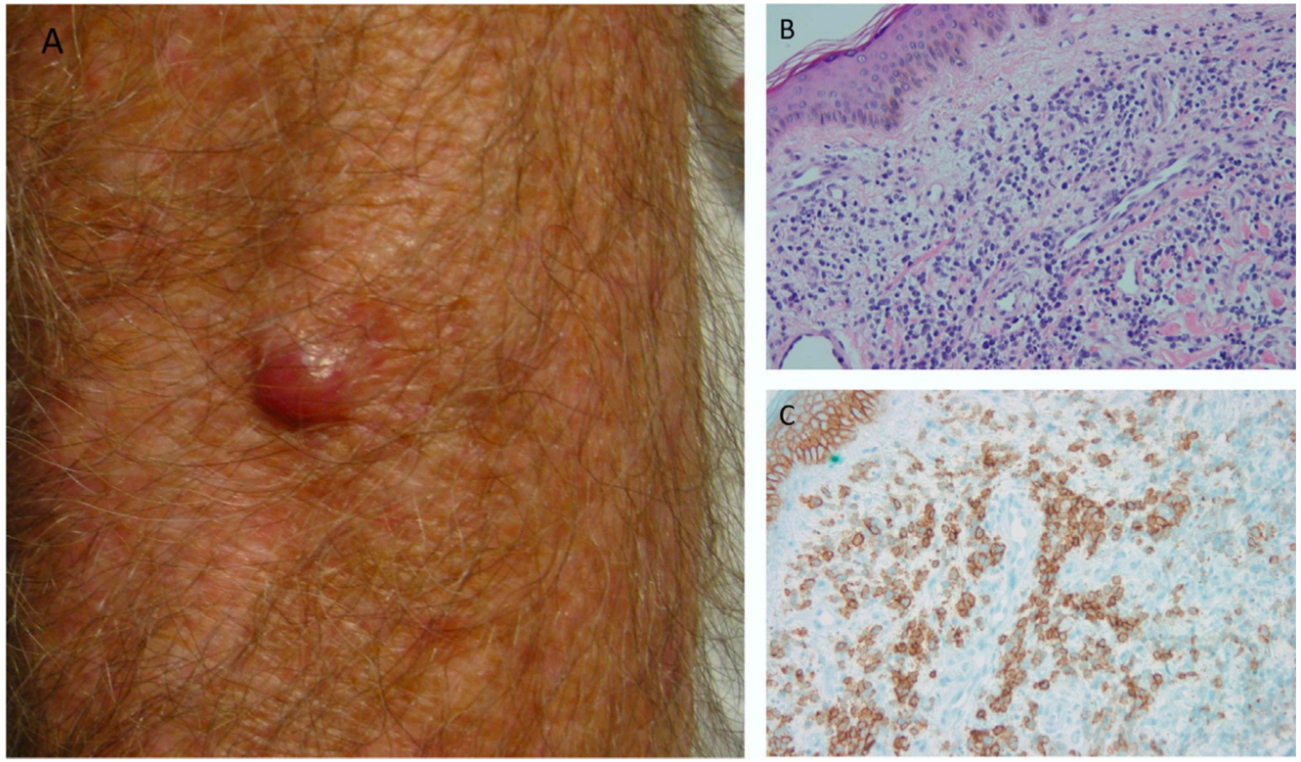


**Fig. 1.** Cutaneous plasmacytoma. (A) A pink firm papule in a patient with systemic myeloma. (B) Dermal infiltration of malignant plasma cells, which show strong immunohistochemical staining for CD138 (C).

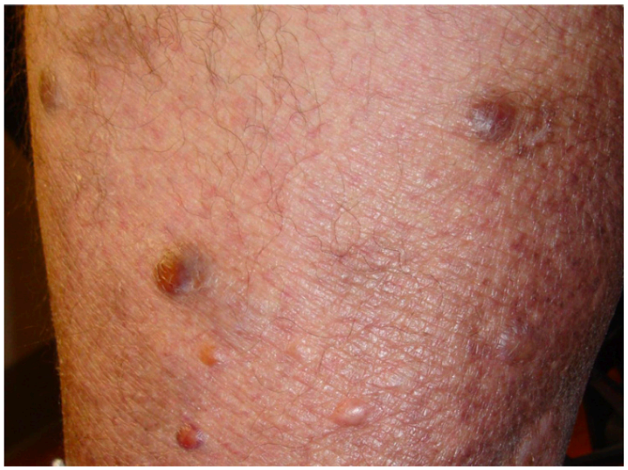

**Fig. 2.** Nodular amyloidosis with reddish brown and skin-colored firm papules and nodules on the leg.

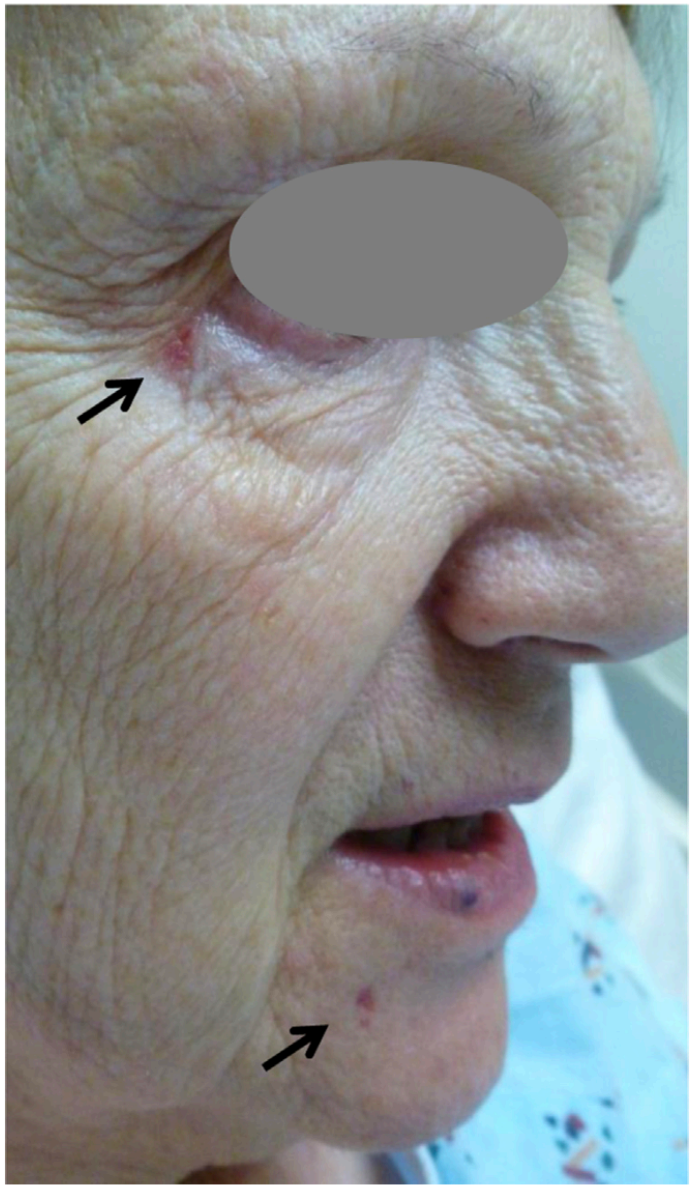

**Fig. 3.** Pinch purpura in a patient with AL amyloidosis. Black arrows indicate purpuric macules.