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## Dermatologic Manifestations of Rheumatic Disease: Malignant Cutaneous Tumors

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# Malignant Cutaneous Tumors

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## Disclaimer:

This module uses terminology related to race and ethnicity in order to describe fictional patients and discuss medical conditions. We recognize that “race” (i.e. an individual’s socially-constructed phenotype, which is often viewed as biologic) and “ethnicity” (i.e. an individual’s geographic birthplace or cultural/national heritage) are imperfect terms that do not fully encapsulate the breadth of human diversity.

Additionally, we recognize that race, ethnicity, sex, and gender have traditionally been attributed as risk factors for certain health condition, when in reality, many of these risks may be more accurately explained by underlying socioeconomic and sociocultural factors.

In efforts to emphasize patient-centered care and autonomy, this module assumes that all racial-, ethnic-, sex-, and gender-related terms utilized are those specifically preferred by the patient. We are also committed to dissecting potentially biased risk factors in order to promote more equal, just, and comprehensive healthcare for all persons, regardless of their identity, beliefs, or background.

# Objectives

Upon completion of this module, participants should be able to:

- Recognize the most common types of precancerous and cancerous skin lesions in diverse skin tones
- Recall risk factors associated with skin cancers and anatomy of the skin
- Construct a differential diagnosis regarding neoplastic skin lesions based on the patient's history and physical exam findings
- Integrate histologic and laboratory results with physical exam findings to establish diagnoses
- Identify health disparities in skin cancer

# Introduction

According to the American Cancer Society, skin cancer is the most common cancer diagnosed in the United States. The three most common skin cancers are basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma. BCC and SCC are classified together as keratinocyte carcinomas (skin cancers derived from keratinocytes of the epidermis), representing ~95% of all skin cancers. These cancers have high cure rates if caught early. Melanoma, which originates from melanocytes, is less prevalent but a more fatal form of skin cancer that causes the majority of deaths from skin cancer. Skin cancers are largely preventable and curable if diagnosed early. Thus, awareness and understanding of skin cancer screening and early detection are fundamental skills for clinicians.

By the end of this module, students will be able to differentiate the most common types of skin cancer and precancerous lesions, as well as gain an awareness of cutaneous lymphomas. Throughout this module, images and clinical findings from diverse skin tones will be included to prepare students to identify cutaneous findings in a heterogeneous patient population. This module is not a comprehensive review of skin cancers but rather an introduction to understanding how skin malignancies and physical exam findings interrelate.

Background

# Actinic keratosis (AK)

**Description:** Precancerous lesions that present as rough, scaly patches on chronically sun-exposed skin (i.e. face, ears, scalp (in areas of hair loss), neck, upper chest, arms, and shins). AKs vary from flat to slightly raised patches on the top layer of skin. AKs are often pigmented pink or brown and can have white-to-yellow surface scale. They are more easily palpated than seen, described as feeling “gritty”. They have a very small potential to progress into squamous cell carcinoma (SCC).

**Risk factors:** male sex, lighter skin color, older age, underlying immunosuppression, degree of prior exposure to UV light

**Histopathology:** atypical keratinocytes involving partial thickness of the epidermis, acanthosis (thickening of epidermis and elongation of the rete ridges), hyperkeratosis (thickening of stratum corneum), parakeratosis (retained nuclei in stratum corneum)

**Presentation in skin of color:** AKs are very common in individuals with lighter skin colors and much less common in people with darker skin colors.

Image unavailable

[Actinic Keratosis](#). Visual Dx.  
Updated February 10, 2022.  
Accessed June 12, 2023.

Image unavailable

[Actinic Keratosis](#). Visual Dx.  
Updated February 10, 2022.  
Accessed June 12, 2023.

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[Actinic Keratosis](#). Visual Dx.  
Updated February 10, 2022.  
Accessed June 12, 2023.

# Basal cell carcinoma (BCC)

**Description:** BCC is the most common cancer of the skin classically presenting as a smooth, pearly papule with rolled borders and surface telangiectasias (dilated subepidermal blood vessels). Over time, lesions can expand horizontally and present with superficial changes such as ulceration. The most common subtype is nodular BCC, which is typically seen on the face.

**Risk factors:** male sex, older age, lighter skin color, sun exposure, environmental exposure (e.g. indoor tanning, arsenic, ionizing radiation), immunosuppression (e.g. solid organ transplantation), genetic syndromes (e.g. xeroderma pigmentosum)

**Histopathology:** aggregations of basaloid keratinocytes originating from epidermis with peripheral palisading (basaloid cells line up along periphery of tumor nests) and clefting (separation between tumor nests and surrounding tumor stroma)

**Presentation in skin of color:** In Black and Hispanic patients, BCCs are more commonly of the nodular and pigmented subtypes. BCC may present with foci of brown, black, or blue pigmentation within a pearly papule or nodule. The entire lesion may be pigmented. Telangiectasias may be less noticeable.

Image unavailable

[Nodular basal cell carcinoma.](#)  
Visual Dx. Updated January 29, 2023. Accessed June 12, 2023.

Image unavailable

[Nodular basal cell carcinoma.](#)  
Visual Dx. Updated January 29, 2023. Accessed June 12, 2023.

# Squamous cell carcinoma (SCC)

**Description:** SCC is the second most common skin cancer presenting as a hyperkeratotic, firm papule. Lesions may be reddish, pink, or skin colored with secondary changes such as crust and ulceration. These tumors most commonly occur on sun-exposed areas, such as the head, neck, arms, and hands, and has a higher metastatic potential than BCC.

**Risk factors:** male sex, lighter skin color, UV exposure, immunosuppression (e.g. solid organ transplantation), environmental exposure (e.g. ionizing radiation, arsenic), cigarette smoking, HPV, genetic disorders (e.g. xeroderma pigmentosum)

**Histopathology:** nests of squamous epithelial cells originating from the epidermis and extending downward into the dermis. Cells are typically brightly eosinophilic (pink) with atypical features like pleomorphism and mitoses. Keratinization, such as keratin pearls, may be seen in well-differentiated tumors.

**Presentation in skin of color:** In individuals with darker skin tones, SCC most commonly appears in sites of scars and chronic ulcers. SCC is the most common skin cancer in Black individuals. The presentation can vary from poorly demarcated rough pink patches to well-defined hyperkeratotic papules. Erythema may be more difficult to discern.

Image unavailable

[Squamous cell carcinoma in situ.](#)  
Visual Dx. Updated September 10, 2019. Accessed June 12, 2023.

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[Squamous cell carcinoma in situ.](#)  
Visual Dx. Updated September 10, 2019. Accessed June 12, 2023.

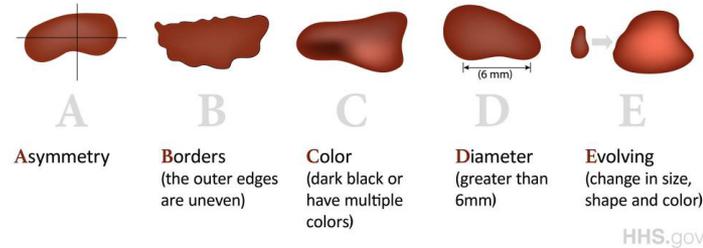
# Melanoma

## Description:

Melanoma is the most common cause of skin cancer deaths. It is an aggressive malignancy of melanocytes (pigment-producing cells). Often driven by activating mutations in the BRAF kinase. Melanoma can present with common features outlined in the **ABCDEs: Asymmetry, irregularity of Borders, variegation of Color, large Diameter (>6 mm), and Evolution**. Ulceration and bleeding are late signs.

- The most important prognostic factor of melanoma is the **depth of invasion**, which is measured histologically and called the Breslow thickness.
  - The Breslow thickness correlates strongly with outcome. Thicker melanomas are more likely to metastasize, and result in poor prognosis.
- Men are more prone to developing melanoma on the head, neck, and trunk, while women are more likely to develop melanoma on extremities.
- There are **4 main types of melanoma**: superficial spreading, nodular, lentigo maligna, and acral lentiginous

## ABCDE rule for the early detection of melanoma



HHS.gov [@HHS.gov]. (2019, July 10). Worried that a mole might be skin cancer? Remember the ABCDEs. [Tweet]. Twitter.  
<https://twitter.com/HHSGov/status/1148937165742772224>

Image unavailable

[Melanoma](#). Visual Dx. Updated June 14, 2022. Accessed June 12, 2023.

# Melanoma (cont.)

**Risk factors:** previous history of melanoma, previous history of non-melanoma skin cancer (NMSC), strong family history of melanoma (2 or more first-degree relatives affected), history of severe or blistering sunburns, older age, lighter skin tone, many melanocytic nevi, >5 atypical melanocytic nevi, and giant congenital melanocytic nevus (>20 cm)

**Presentation in skin of color:** Individuals with lighter skin tones are more likely to develop melanoma but when it does occur in people of color, diagnosis is often delayed and thus results in worse prognosis. The colors of melanoma may be more subtle and masked in darker skin tones. The most common melanoma in people of color is acral lentiginous melanoma (ALM), which occurs on acral surfaces such as palms, soles, and subungual areas.

Image unavailable

[Melanoma](#). Visual Dx. Updated June 14, 2022. Accessed June 12, 2023.

Image unavailable

[Melanoma](#). Visual Dx. Updated June 14, 2022. Accessed June 12, 2023.

# Cutaneous T-cell lymphoma (CTCL)

**Description:** Mycosis fungoides (MF) is the most common cutaneous T-cell lymphoma. Depending on the stage, it can present as erythematous patches, plaques with fine scale or tumors. It is characterized by malignant lymphocytes. The patches have epidermal atrophy that can resemble “cigarette-paper”. MF occurs most commonly on sun-protected areas such as the buttocks and posterior axillary folds. MF typically has an indolent course.

**Risk factors:** male sex, older age, African descent

**Presentation in skin of color:** Early onset (before age of 40 years) is reported in individuals of African, Hispanic and Asian descent. Erythema may be subtle or appear pink, violaceous, or grayish in darker skin colors. A hypopigmented variant of MF is seen primarily in individuals of African descent (also reported in those of Asian, Indian, and Latin American descent) as well as children.

Image unavailable

[Cutaneous T-cell lymphoma.](#)

Visual Dx. Updated October 10, 2016. Accessed June 12, 2023.

Image unavailable

[Cutaneous T-cell lymphoma.](#)

Visual Dx. Updated October 10, 2016. Accessed June 12, 2023.

# Clinical Cases

# Case #1

Image unavailable

[Nodular basal cell carcinoma.](#)  
Visual Dx. Updated January 29,  
2023. Accessed June 12, 2023.

A 40-year-old (she/her/hers) is concerned about a new mole on her cheek. She has no significant medical history. Social history is notable for living on the beach. She enjoys sunbathing on the beach and admits that she frequently forgets to apply sunscreen. Physical examination revealed a pink pearly papule on her right cheek.

## Differential diagnosis based on skin findings includes:

- Intradermal nevus
- Basal cell carcinoma
- Squamous cell carcinoma
- Molluscum contagiosum
- Amelanotic melanoma
- Adnexal tumor

# Skin biopsy results:

Histology reveals nests of basaloid cells with peripheral palisading in the dermis

Image unavailable

[Superficial Spreading Basal Cell Carcinoma](#). Jadotte, Y. T., Sarkissian, N. A., Kadire, H., & Lambert, W. C. (2010). CASE REPORT Superficial Spreading Basal Cell Carcinoma of the Face: A Surgical Challenge. *Eplasty*, 10, e46.

Case #1 Diagnosis: Basal Cell Carcinoma

# Treatment

- The treatment of choice is typically surgery with either standard surgical excision or Mohs micrographic surgery. Mohs micrographic surgery would be the preferred treatment for BCCs on the face and other high-risk sites.
- There are also topical therapies typically reserved for superficial BCCs, as well as radiation, and oral medications for inoperable BCCs.



# Keys of Case #1: Basal Cell Carcinoma

- This patient has the classic features of a **translucent, pearly nodule with telangiectasia**. BCCs can also have **rolled borders** and an **ulcerated center**.
- BCCs are the **most common type of skin cancer** that usually occur on sun-exposed areas, especially the face. They are slow-growing and rarely metastasize
- Histopathologic findings include **nests of atypical basaloid cells** with the peripheral cells arranged in parallel manner (**palisading nuclei**)

# Case #2

Image unavailable

[Cutaneous squamous cell carcinoma](#). Visual Dx. Updated April 06, 2023. Accessed June 12, 2023.

A 70-year-old (he/him/his) presents to the dermatologist's office for his annual skin exam. His past history is significant for multiple actinic keratoses, previously treated with cryotherapy. At this visit, he points to a large lesion on his nose, stating that it grew back after last year's cryotherapy. Physical exam revealed a large firm nodule with ulceration on the left nasal sidewall.

## Differential diagnosis based on skin findings includes:

- Squamous cell carcinoma
- Basal cell carcinoma
- Actinic keratosis
- Bowen's disease (i.e. SCC in situ)
- Keratoacanthoma
- Melanoma

# Skin biopsy results:

Histology reveals nodules of pleomorphic and hyperchromatic squamous cells extending into the dermis, and markers of keratin differentiation including keratin pearls

Image unavailable

[Squamous cell carcinoma](#). Web Pathology. Updated June 13, 2023. Accessed June 13, 2023.

# Case #1 Diagnosis: Squamous Cell Carcinoma

# Treatment

- The treatment of choice is surgery, which includes standard excision, Mohs micrographic surgery, and curettage and electrodesiccation (C&E). Mohs micrographic surgery would be the preferred technique for SCC of the face and other high-risk sites.
- Radiation can be utilized if surgery is not possible or contraindicated.



## Keys of Case #2: Squamous Cell Carcinoma

- SCC often presents as a **red, hyperkeratotic plaque** and can develop ulceration in advanced lesions as seen in this patient
- Our patient has a **past history of actinic keratoses**, which are premalignant lesions that have the small potential to develop into SCC, as well as markers for signs of actinic damage. They can present as brown or red papules with a **rough texture**. Most people who develop actinic keratoses have multiple lesions in sun-exposed areas like the hands and face like in this patient
- **Cellular atypia of epithelial cells** is the key histologic finding; markers of keratinization (e.g. **keratin pearls**) may also be seen in well-differentiated tumors

# Case #3

Image unavailable

[Acral lentiginous melanoma.](#)

Visual Dx. Updated December 01, 2021. Accessed June 12, 2023.

A 68-year-old (he/him/his) presents to his primary care physician concerned about a pigmented lesion on his sole. Physical examination is notable for a multi colored plaque on the plantar foot as shown.

## Differential diagnosis based on skin findings includes:

- Pigmented basal cell carcinoma
- Melanoma
- Atypical melanocytic nevus
- Lentigo

# Skin biopsy results:

Irregular proliferation of atypical melanocytes that demonstrate pleiomorphism, prominent nucleoli, and mitoses

Image unavailable

[Superficial spreading melanoma.](#)

Smoller B. R. (2006). Histologic criteria for diagnosing primary cutaneous malignant melanoma. *Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc*, 19 Suppl 2, S34–S40. doi:10.1038/modpathol.3800508

Case #3 Diagnosis: Acral lentiginous  
melanoma (ALM)

# Treatment

- The first-line treatment is surgical excision.
- Metastatic melanoma is treated by a medical oncologist using targeted therapies (e.g. with BRAF inhibitors) and immunotherapies.



# Keys of Case #3: Acral Lentiginous Melanoma (ALM)

- ALM is a rare type of melanoma that affects the **palms, soles, and underneath the nails**. Acral means peripheral and lentiginous means dark, indicating that this tumor is **pigmented** and occurs on **distal extremities**.
- ALM makes up less than 5% of all melanomas but is the **most common type of melanoma seen in darker-skinned individuals**. It can occur regardless of sun exposure. ALM has a worse prognosis compared to other types of melanomas since it tends to be diagnosed at later stages.
- The same ABCDEs used to identify melanoma can be applied to ALMs. ALM often presents as black, variegated brown, or multicolored patches that are irregularly shaped. In individuals of darker skin colors, most cases involve the foot.
- In this patient, the lesion presented as an asymmetric black, brown, and violaceous (variegated) crusted plaque on the plantar foot.

# Case #4

Image unavailable

[Cutaneous T-cell lymphoma.](#)

Visual Dx. Updated October 10, 2016. Accessed June 12, 2023.

A 55-year-old (he/him/his) presents to his dermatologist with complaints of a rash he has had for months on his flank. He states that it itches and has minimal relief with use of over-the-counter topical steroids. His flank is covered with multiple well-defined hypopigmented patches and thin scaly plaques.

## Differential diagnosis based on skin findings includes:

- Mycosis fungoides
- Psoriasis
- Atopic dermatitis
- Pityriasis or tinea versicolor

# Skin biopsy results:

- Histology reveals a lymphocytic infiltrate in the upper dermis consisting of small CD4+ cells with irregular nuclei, and intraepidermal collections of atypical cells (Pautrier microabscesses)
- Complete blood count and peripheral blood smear were unremarkable

Image unavailable

[Mycosis Fungoides: Epidermotropism](#). Web Pathology. Updated June 13, 2023. Accessed June 13, 2023.

Case #4 Diagnosis: Mycosis Fungoides (MF)

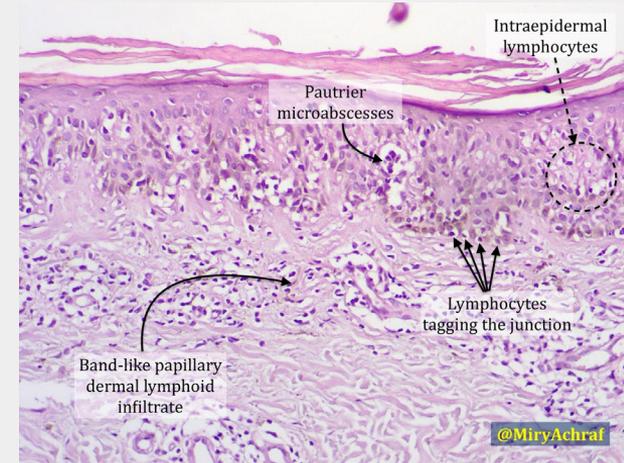
# Treatment

- Early treatment options include topical steroids and other topical agents
- Later stages of disease can be treated with phototherapy, localized radiation, electron beam therapy, extracorporeal photopheresis and systemic treatments



# Keys of Case #4: Mycosis Fungoides

- MF is the **most common cutaneous T-cell lymphoma**, occurring mostly in middle-aged or elderly patients
- MF is an indolent CD4+ cutaneous T-cell lymphoma that presents on the skin. It presents as **well-demarcated skin patches** that can progress to plaques and tumors
- A hypopigmented variant of MF is primarily seen in individuals of African descent as presented in this patient
- Histopathological findings consist of atypical lymphocytes with cerebriform nuclei in the upper dermis or aggregates within the epidermis (**Pautrier microabscesses**)



achraf miry [@MiryAchraf]. (2018, October 2). A case of mycosis fungoides in a 50 yo male [Tweet]. Twitter. <https://twitter.com/MiryAchraf/status/1047253735955730432>

# Module Summary

- Earlier diagnosis of cutaneous malignancies improves prognosis and survival rates
- UV exposure and lighter skin tones are major risk factors for skin cancers
- Different types of cutaneous malignancies can be distinguished by clinical appearance and histologic characteristics
- The presentation of malignant skin lesions can vary by different skin tones

# Resources

- [American Cancer Society - Skin Cancer](#)
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- [VisualDx](#)
- [First Aid 2022](#)
- [Web Pathology](#)