

<b>Title</b>	ABCs of Skin Lesions: Benign, Pre-cancerous, & Cancerous
<b>Authored By</b>	Wanda Lockwood RN, BA, MA
<b>Course No</b>	SL081707
<b>Contact Hours</b>	3

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## Purpose

The purpose of this course is to differentiate between benign, pre-cancerous and cancerous skin lesions and to explain the appearance, symptoms, and treatment for those and common lesions.

## Objectives

1. Identify at least 5 benign lesions that pose little danger of malignancy. Identify 2 common pre-cancerous lesions.
  2. Explain the difference between common and dysplastic nevi. Identify 4 types of malignant skin lesions.
  3. Explain the difference between basal cell carcinoma and squamous cell carcinoma.
  4. Identify at least 8 different treatment options for skin lesions. Outline the symptoms and treatment for malignant melanoma.
  5. Identify 3 different variants of Kaposi's sarcoma.
  6. Explain treatment options for Kaposi's sarcoma.
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## Introduction

Almost everyone will develop some type of skin lesion over the course of a lifetime, and differentiating among those that are benign, pre-cancerous, or cancerous is an important part of assessment. Many lesions are related to sun exposure, and incidence is increasing, despite warnings to avoid overexposure to ultraviolet light. Benign lesions, such as acrochordons (skin tags) and seborrheic keratoses, are those that are not clinically significant but may be a cosmetic concern. Generally, they do not spread and do not recur after they are removed. Precancerous lesions, such as dysplastic nevi and actinic keratoses, have the potential of evolving into malignancies and may be difficult to diagnose accurately without biopsy. Other lesions, such as basal cell carcinoma, squamous cell carcinoma, melanoma, and Kaposi's sarcoma are malignant, and early diagnosis and treatment can prevent metastasis, which can be life threatening.

## Benign and pre-cancerous lesions

### Acrochordons (skin tags)

Acrochordons, commonly known as skin or cutaneous tags, are benign tumors that often occur in areas of skin creases, such as the neck, eyelids, axillae, and groin. They may be a millimeter or 2 in size to 5 cm. They are often raised from the skin on a peduncle (stalk). While skin tags do not become malignant, they are often in areas of the skin that can cause irritation, so they are frequently removed although removal is not always covered by insurance.



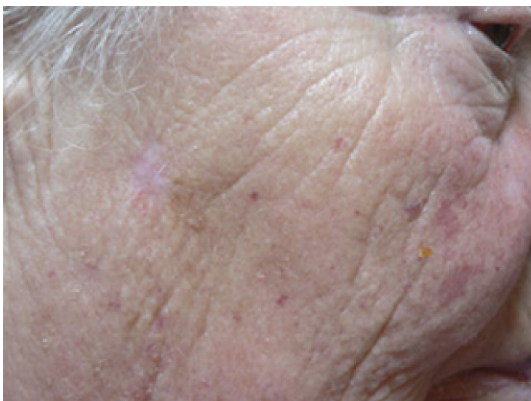
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Acrochordons are associated with age, pregnancy, and obesity and are common in those with diabetes mellitus, occurring in both males and females. Studies of those with acrochordons indicate that about 40% are type II diabetics or are insulin-resistant so those with skin tags should be tested for diabetes. Acrochordons are also a symptom of Birt-Hogg-Dube (BHD) syndrome, an autosomal dominant disorder of the skin involving a number of different types of lesions. Studies have indicated that human papillomavirus (HPV) types 6 and 11 are found in a large percentage of skin tag biopsies, suggesting that viral infections are a cause. There are 3 types of acrochordons:

- Small 1-2mm papules, usually on the neck and axillae
- Single or multiple filiform lesion 2mm x 5 mm occurring in other areas of the body.
- Large soft pedunculated fibromas, usually on lower trunk (1, 2).

### **Actinic keratosis**

Actinic keratosis (AK), also known as solar keratosis, is the most common type of pre-cancerous skin lesion. It usually presents as a very small flat or slightly raised crusty, scaly, or discolored lesions on the skin surface that may be hard to see but palpable. The base of the lesion may change color to red, pink, or tan. AK develops slowly to 2-4 mm although it can reach 2.5 cm in size. AK occurs most commonly in areas of the skin that are most sun-exposed. About 2-5% progress to squamous cell carcinoma, and 40-60% of squamous cell carcinomas presented originally as untreated AKs, so monitoring and treating AKs is an important step in preventing skin cancer (3, 4).



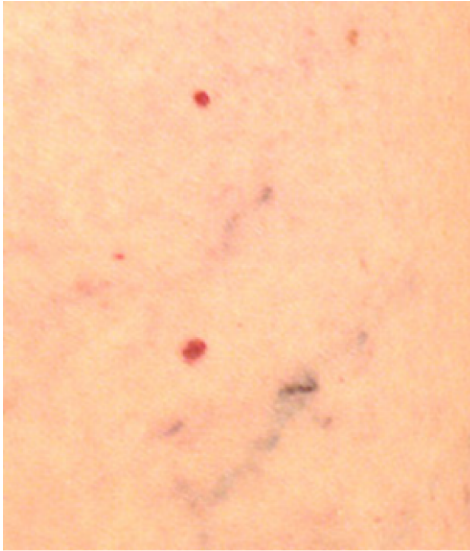
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When AKs occur on the lips, they are referred to as **actinic cheilitis**, usually affecting the lower lip and causing them to be dry and cracked, often pale in color. Treatment of AKs is usually preceded by a biopsy to determine the presence of malignancy. Risk factors include:

- Frequent exposure to the sun and sunburn
- Pale skin
- Blond or red hair
- Blue/green/hazel eyes
- Tendency to freckle
- Immunocompromised status
- (3, 4).

### **Cherry angioma/hemangioma**

Cherry angioma/hemangioma is a benign red-purple vascular lesion that is most common after age 40. It is formed from clusters of dilated capillaries at the surface of the skin.



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Cherry angiomas are the most common vascular skin lesion, occurring in both sexes. They can be found anywhere on the body, especially on the torso, and usually appear as small cherry-red macules or larger papules. While they are benign, if a large number occur suddenly, it may be an indication of an internal malignancy. Because they are vascular, even small lesions can bleed freely if traumatized, so if they are in an area, such as the axillae or legs, that a woman shaves, then the lesions may need to be removed. Sometimes people want them removed for cosmetic reasons (5).

#### **Cutaneous horn (Cornu cutaneum)**

Cutaneous horn is a benign keratotic horn-like lesion that grows out of numerous types of base lesions, such as actinic keratosis (25-35%), verruca vulgaris (15-25%) or seborrheic keratosis. Cutaneous horns vary in length from a few millimeters to a few centimeters, often growing slowly over years although they may grow more rapidly (6, 7, 8).

#### **Cutaneous horn arising from actinic keratosis:**



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Usually the base lesion is benign, but it is malignant in about 20% of cases, usually with squamous cell carcinoma, so biopsy is important. Tenderness at the base of the cutaneous horn is often associated with malignancy. However, because they protrude from the base lesion, they are prone to trauma, which can cause tenderness. Cutaneous horns are most frequently found on sun-exposed areas of the skin but can occur anywhere there is a hyperproliferative lesion, such as on the penis. Cutaneous horns are most common in the elderly, 60-70, with malignant base lesions more common >70 although they do occasionally occur in children. They are most common

in Caucasian males. Attempting to cut the horn off without treating the underlying lesion is not successful as the horn grows back. Treatment is selected according to guidelines for the underlying base lesion (6, 7, 8).

### **Dermatofibroma**

Dermatofibroma is a benign lesion of the dermal dendritic histiocyte cells. Dermatofibromas are firm pea-sized (0.5-1cm) pigmented nodules, usually yellow to dark brown, most commonly found on the arms or legs.



The lesions are anchored to the underlying fibrous tissue, so if a lesion is squeezed ("pinch test"), it will dimple as the fibrous tissue pulls it inward. The majority of the lesion is in the mid-dermal area. The cause of dermatofibromas is not clear, but some theorize they may occur at the site of old injuries, but others believe that this is unlikely. Some may be itchy or tender. They are usually singular, but may be multiple with >15 lesions, commonly associated with immunocompromised status. In rare occasions, they have evolved into basal cell carcinomas, so lesions should be monitored for changes. Dermatofibromas may occur at any age, but are 4 times more common in females than males. Dermatofibromas may be removed if they are in an area that is shaved, but because they extend into the tissue, the scar is often larger than the lesion. Cryosurgery may result in a large white scar (9, 10).

### **Lentigo (Liver spot)**

Lentigo, commonly known as a liver or age spot, is a benign lesion that appears like a large brown-black freckle, often 0.5-1 cm in size but can be as large as 2.5cm.



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Lentiginos are caused by pigment changes in the epidermis in areas that are sun-exposed, especially the hands and arms, shoulders, and forehead. Lentiginos are common in those over age 40. No treatment is necessary although some people choose to have them removed with cryotherapy or lasers or lightened with skin bleaching creams or lotions for cosmetic reasons (11).

### **Neurofibroma (dermal)**

Neurofibroma is one of the most common tumors of nerves, affecting the peripheral nerve sheath. Neurofibromas may occur anywhere along the nerve but often affect nerves close to the body surface, such as those of the skin or the tissue below the skin, so the dermal neurofibromas appear on the surface. Neurofibromas may be single or

multiple and often occur in young people 20-30. While the cause for many is not known, they are a symptom of neurofibromatosis, especially if there are multiple lesions. Neurofibromatosis (NF) is an autosomal dominant genetic disorder with two types: NF1 and NF2. NF1 is associated with multiple neurofibromas as well as other types of lesions. While NF1 may be only a cosmetic concern because of the skin lesions for some affected by the disorder, in others, neurofibromas may become malignant neurofibrosarcomas (12, 13).



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Neurofibromas are usually slow growing and may be painful or without pain. If the lesion is palpated, people may experience an electric-shock type sensation, known as the "Tinel" sign. If the neurofibroma is causing no problem, it may just be observed and not treated. In some cases, the nerve may be removed or the tumor may be excised from the nerve (12, 13).

### **Nevus (mole)**

Nevi (moles) are the most common lesions in human beings and may be present at birth or acquired, usually through adolescence. They usually begin as small freckle-like lesions that may grow and darken to brown or black and sometimes dark blue with time, also sometimes growing hairs. Nevi are composed of melanocytes, cells that carry the pigment melanin and can range in size, usually from pinpoint to about 1 centimeter although some may be larger. They may be flat or slightly elevated, rough or smooth.



Sometimes nevi develop white rings around them ("halo nevi"), commonly during adolescence. These moles often fade over time but must be differentiated from melanoma, which also sometimes have halos.

Most moles are benign, but dysplastic nevus (atypical/Clark's nevus) is an atypical mole, either single or multiple, that is acquired by about 4% of white Americans and carries a substantial risk of developing into melanomas. Dysplastic nevi usually appear during adolescence on the torso and scalp and are about 1 centimeter in size and instead of being solid in color; they may be in varying shades of brown to black with a darker center.



Congenital nevi, which affect about 1% of newborns, may be quite large and carry an increased risk of developing melanoma as well. All nevi should be examined regularly for changes, but dysplastic nevi, congenital nevi, and nevi >1cm are of special concern. Moles may be removed for biopsy or cosmetic reasons (14, 15).

### **Sebaceous hyperplasia**

Sebaceous hyperplasia is a benign condition that results in enlargement of sebaceous glands, causing them to appear on the skin surface as soft, pink-yellowish papules on the face or other areas of the body. The lesions may be 10 times the normal size but with decreased sebum production. The central opening is noticeable as a small spot. They may occur singly or in multiples. Sebaceous glands are affected by androgen, both in size and activity, and it is believed that decreasing levels of androgen with age contribute to the development of sebaceous hyperplasia.

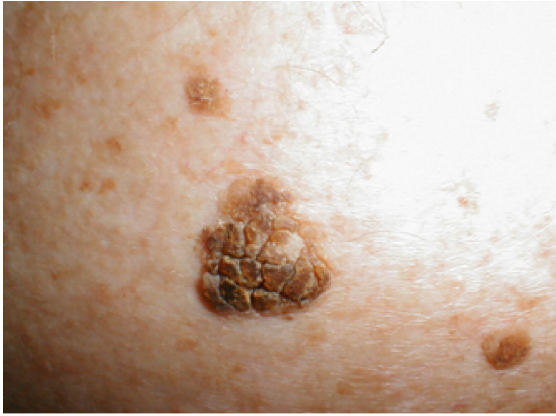


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Sebaceous hyperplasia is most common in the elderly, but in some people with a genetic disposition, they may occur during adolescence. Sebaceous hyperplasia has also been found in those who are immunocompromised and is associated with long-term cyclosporin A, with 10-15% of patients exhibiting sebaceous hyperplasia (16).

### **Seborrheic keratosis**

Seborrheic keratosis (SK) is a benign, crusty wart-like growth, usually brown or black. SKs occur most commonly on the back, chest, face, and shoulders. They are the most common skin lesions found in those who are middle-aged or elderly. SKs do not progress to malignancies and are of little clinical significance, but many people find them unsightly and prefer to have them removed (14, 17).



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They develop from the epidermis and grow on the skin surface with the edges not attached to the underlying skin. They often have a rough cauliflower-like appearance. Some have a different appearance with tiny bumps called "horn pearls" that are bits of keratin, similar to a cutaneous horn. SKs are sometimes itchy, causing people to pick at them, and this can result in bleeding. Black SKs may be mistaken for melanoma. SKs are removed if they cause discomfort from itching, if they are in an area where clothing rubs against them, causing irritation, or if people want them removed for cosmetic purposes (14, 17).

## **Cancerous lesions**

### **Basal cell carcinoma**

Basal cell carcinoma (BCC) is the most common type of cancer involving the skin, affecting about 1 million Americans each year. It is related to sun damage, so it occurs on areas of the skin exposed to the sun, such as the face, arms, and hands. The incidence increases with age. Basal cell carcinoma arises from the basilar cells at the base of the epidermis. Initially, it often appears as a small waxy-appearing nodule with translucent, rolled borders often with telangiectatic vessels on the surface.



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As it continues to grow, the central portion begins to ulcerate and may crust over.



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Some variants appear as yellow or gray plaques. While BCC rarely metastasizes, it does tend to recur and can spread through the tissue, invading cartilage and bone if neglected, resulting in the loss of the nose, ear, or part of the lip (1, 2). Signs of a BCC include:

- Chronic open bleeding sore that won't heal.
- Reddish or irritated area of skin, often on the chest, shoulders, or extremities. It may crust and is sometimes itching or painful.
- A translucent nodule, often pink, red, or white although it may be black or brown in people with dark hair.
- A pink lesion with elevated rolled border and indentation that is crusted in the middle.
- A yellow, waxy scar-like area with taut, shiny skin and irregular borders.

There are a number of different variants of BCC:

- *Basal cell nevus*: This results from a genetic condition and may involve 50-100 cancerous lesions, developing in childhood or adolescence.
- *Basosquamous*: This involves both basal and squamous cells and is more likely to metastasize.
- *Fibroepithelioma*: This is a rare type that usually occurs on the back as reddish lesions that are slightly elevated.
- *Nodular*: This is the most common type, with depression and ulceration at the center.
- *Pigmented*: This almost black lesion occurs primarily in dark-haired people and may be mistaken for melanoma.
- *Sclerosing/fibrosing*: This is a rare sometimes slow-growing but often rapidly spreading type that appears as flat shiny yellowish patches with roots extending into underlying tissue, making it hard to eradicate.
- *Superficial*: This is a slow-growing cancer with lesions appearing as patches on the torso, face, or neck, and is often mistaken for fungal infections, eczema, or psoriasis.

There are a variety of treatments available, and the choice depends upon a number of factors, including the size and location. Because many lesions occur on the face, the choice of treatment may relate to the amount of disfigurement that occurs with the treatment. Topical chemotherapy, laser therapy, cryosurgery, and excision are all common treatments (3, 14).

### **Squamous cell carcinoma**

Squamous cell carcinoma (SCC) is the second most commonly occurring skin cancer, affecting about 250,000 Americans each year. It arises from the squamous cells in the middle section of the epidermis (keratinocytes). SCC is more malignant than BCC and while 96-97% remain localized, a small number metastasize to other organs, so they should be treated promptly. Risk for metastasis increases in those who are immunocompromised. SCC is related to sun exposure, so lesions most commonly occur on sun-exposed areas of the skin, such as the face, neck, scalp, shoulders, back, and extremities. The lower lip and outer rims of the ears are also frequent sites for lesions. SCC may also occur in skin that has been previously damaged by chemicals, chronic lesions, burns, or x-rays. UV light treatments used for psoriasis may also cause development of SCC over time. Other risk factors include age (over 50), sex (male), fair skin, and history of human papilloma virus. Some precancerous lesions, such as actinic keratosis, actinic cheilitis, and leukoplakia may develop into SCC over time. There has been a significant increase in SCC over the past few decades, especially in women. Signs of an SCC include:

- Wart-like lesions that may crust over and bleed.



- Chronic scaly, red areas of skin with irregular borders that sometimes crust over and bleed.
- Chronic open lesions that crust over and bleed repeatedly.
- A lesion that is elevated with a central depression that bleeds occasionally, often growing rapidly (3, 14, 18, 19).



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There are a number of different variants:

- *Keratoacanthoma*: This is usually a single rapidly-growing nodule with a central depression. It sometimes involutes (rolls inward and decreases in size).
- *Spindle cell*: This type is typical SCC and may be aggressive.
- *Acantholytic*: This type is typical SCC and found in elderly patients and is aggressive.
- *Verrucous*: This type is oral, genital, or on the plantar foot. It is slow growing and rarely metastasizes (19).

As with other types of skin cancer, treatment depends on the area of involvement and the extent of the lesion. Lesions are usually excised, but large or aggressive lesions may require radiation therapy. Lymph node metastasis is treated with lymphadenectomy and radiation. Local recurrence is not uncommon and is associated with significant morbidity and mortality, with overall mortality rates for primary SCC at about 2-6%. If metastasis occurs to distant organs, chemotherapy may be used as with other metastatic malignancies; however, if metastasis to the lungs occurs, SCC is incurable (3, 18, 19).

### **Kaposi's sarcoma**

Kaposi's sarcoma (KS) is a type of malignancy with lesions in the tissues of the skin and mucous membranes of the mouth, nose, and anus. The lesions are usually red-purple to dark brown macules as well as papules and nodules that most commonly occur on the skin, usually beginning with the legs and feet. The lesions usually are small and painless but may increase in size or ulcerate and become painful over time, ranging from a few millimeters to several centimeters in size. Internal lesions in the gastrointestinal and respiratory tract may cause dysphagia, bleeding, and shortness of breath (20, 21, 22).



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KS is caused by proliferation of endothelial spindle cells. More than 90% of cases involve human herpes virus 8 (HHV-8), which is exacerbated by co-infection with HIV.

While historically Kaposi's sarcoma was a rare disease found primarily in elderly males or young males and children in Africa, with the onset of the AIDS epidemic it became a disease affecting primarily young homosexual males. The 3 primary types of KS include:

- *Classic*: This affects primarily elderly males of Jewish, Italian, or Mediterranean heritage and is a slowly progressing disease, over 10-15 years, resulting in circulatory impairment and edema of the lower extremities and eventually affecting other organs.
- *Immunosuppressive-treatment-related*: This develops in those who take immunosuppressive drugs, especially cyclosporin but including corticosteroid, in patients receiving organ transplants.
- *Epidemic (AIDS-related)* : This type of KS spreads more quickly than other types, affecting many organs as well as the skin.

There was a marked increase in cases of Kaposi's sarcoma through the 1980's and 1990's, but with improved treatment for AIDS, cases have fallen dramatically. However it is still the most common AIDS-related malignancy and is the AIDS-defining disease in about 15% of homosexual males with AIDS and about 2% of others with AIDS. Kaposi's sarcoma affects about 4 times more males than females. Pulmonary invasion of KS is the most common cause of death from the disease. A variety of treatment approaches may be used, including excision of lesions, chemotherapy, immunotherapy, and radiation, depending upon whether there are single or multiple lesions. Radiotherapy is frequently used for local treatment, with response in 80-90% of patients although lesions may recur. AIDS patients receiving highly active antiretroviral therapy (HAART) may have regression or slower progression of the disease. Radiotherapy (20, 21, 22).

<b>Treatment for pre- and cancerous lesions (non-melanoma)</b>	
<p><b>Chemical peeling</b></p> <p>Used for:</p> <ul style="list-style-type: none"> <li>• Actinic keratoses</li> <li>• Sebaceous hyperplasia</li> </ul>	<p>This uses a topical agent, such as trichloroacetic acid (TCA) that causes the top skin layers to slough off, replaced by new epidermis in about 7 days. This is done under local anesthetic and causes temporary red discoloration and irritation of the tissue.</p>
<p><b>Chemotherapy, systemic or intralesional</b></p> <p>Used for:</p> <ul style="list-style-type: none"> <li>• Kaposi's sarcoma</li> </ul>	<p>This treatment may be given systemically through intravenous or oral medications:</p> <ul style="list-style-type: none"> <li>• <i>Liposomal doxorubicin</i> (Doxil®).</li> <li>• <i>Liposomal daunorubin</i> (DaunoXome®)</li> <li>• <i>Paclitaxel</i> (Taxol®)</li> </ul> <p>The chemotherapeutic agent may also be injected directly into the lesion in some cases.</p> <ul style="list-style-type: none"> <li>• <i>Vinblastine</i> is used for intralesional chemotherapy.</li> </ul>
<p><b>Chemotherapy, topical</b></p> <p>Used for:</p> <ul style="list-style-type: none"> <li>• Actinic keratosis</li> <li>• Basal cell carcinoma</li> </ul>	<p>This is less effective than excision because the cancer may recur, but it is simple and results in less scarring, so even though it may require periodically repeating the treatment, this is a good option for many people. Topical chemotherapeutic agents include:</p> <ul style="list-style-type: none"> <li>• <i>Imiquimod</i> is used for lesions on the trunk, neck, and extremities and has a 75-90% cure rate. It is applied to the lesion 5 x a week for 6 weeks. It cannot be used with people who are immunocompromised.</li> </ul>

	<ul style="list-style-type: none"> <li>• <i>5-fluorouacil (5-FU) 5%</i> is applied to tumor twice daily for 3-6 weeks. Many people experience inflammation, pain, and itching and must avoid ultraviolet light during treatment.</li> </ul>
<p><b>Cryosurgery</b></p> <p>Used for:</p> <ul style="list-style-type: none"> <li>• Acrochordons</li> <li>• Actinic keratosis</li> <li>• Basal cell carcinoma</li> <li>• Cherry angioma</li> <li>• Dermatofibroma</li> <li>• Kaposi's sarcoma</li> <li>• Lentigo (liver spot)</li> <li>• Sebaceous hyperplasia</li> <li>• Seborrheic keratosis</li> <li>• Squamous cell carcinoma</li> </ul>	<p>Liquid nitrogen destroys malignant and pre-malignant tissue by freezing to <math>\geq -40^{\circ}\text{C}</math>. The lesion is sprayed with liquid nitrogen 2-3 times for 30 seconds with 2-5 minutes of thawing time in between. The tissue dies over 24 hours and then slowly sloughs off and heals in over 4-6 weeks, revealing pink healing tissue. Local anesthetic may be used during the treatment. It may result in loss of pigmentation, and hair follicles are destroyed. Cure rates and overall cosmetic results are good.</p>
<p><b>Curettage-electrodesiccation</b></p> <p>Used for:</p> <ul style="list-style-type: none"> <li>• Acrochordons</li> <li>• Actinic keratosis</li> <li>• Basal cell carcinoma</li> <li>• Cherry angioma (electrodesiccation only)</li> <li>• Kaposi's sarcoma</li> <li>• Sebaceous hyperplasia</li> <li>• Squamous cell carcinoma</li> </ul>	<p>This involves using a local anesthetic and scraping away the lesion with a curette and then using electrodesiccation to cauterize the tissue. The procedure may be repeated 2-3 times during the visit, but should destroy all the diseased tissue. This technique is often used for small or multiple lesions and has a cure rate of 85-95%. The wound usually heals in 2-4 weeks. It may scar more than excision so is often avoided for facial lesions.</p> <p>In some cases, electrodesiccation may be used by itself to eradicate small lesions.</p>
<p><b>Dermabrasion</b></p> <p>Used for:</p> <ul style="list-style-type: none"> <li>• Actinic keratosis</li> </ul>	<p>A local anesthetic is given and the outer layers of the epidermis are removed using a rapidly circulating brush.</p>
<p><b>Excision/ Shave excision</b></p> <p>Used for:</p> <ul style="list-style-type: none"> <li>• Acrochordon</li> <li>• Basal cell carcinoma</li> <li>• Dermatofibroma</li> <li>• Kaposi's sarcoma</li> <li>• Neurofibroma</li> <li>• Nevus</li> <li>• Seborrheic keratosis.</li> <li>• Sebaceous hyperplasia</li> <li>• Squamous cell carcinoma</li> </ul>	<p>This is surgical removal of the tumor and adjacent tissue. Results are very good and there is often little scarring, especially for small lesions. It is usually done under local anesthetic in the doctor's office. Small skin tags may be snipped off with no adjacent tissue removed, followed by cauterization. Shave excision is used for some lesions, such as seborrheic keratosis, which may be shaved with a flexible blade and then cauterized with silver nitrate.</p>
<p><b>Immunotherapy/biochemotherapy:</b></p> <p>Used for:</p> <ul style="list-style-type: none"> <li>• Kaposi's sarcoma</li> </ul>	<p><i>Interferon-alfa</i> may be used with some patients in conjunction with antiretroviral therapy if their immune systems are healthy enough.</p>

<p><b>Laser</b></p> <p>Used for:</p> <ul style="list-style-type: none"> <li>• Actinic keratosis</li> <li>• Basal cell carcinoma</li> <li>• Cherry angioma</li> <li>• Lentigo</li> <li>• Sebaceous hyperplasia</li> <li>• Squamous cell carcinoma</li> </ul>	<p>Carbon dioxide and argon lasers can evaporate cancerous tissue or cut it away bloodlessly, making this a good treatment for those on anticoagulants, but it is expensive and not readily available in many areas.</p>
<p><b>Ligation</b></p> <p>Used for:</p> <ul style="list-style-type: none"> <li>• Acrochordons</li> </ul>	<p>This involves tying off a lesion with a suture or copper wire to shut off circulation, causing it to fall off.</p>
<p><b>Mohs micrographic surgery</b></p> <p>Used for:</p> <ul style="list-style-type: none"> <li>• Basal cell carcinoma</li> <li>• Squamous cell carcinoma</li> </ul>	<p>This technique has the highest cure rate and is the treatment of choice for recurrent local skin cancers (95-97% cure rate). This is a very precise technique that involves removing the tissue and then excising thin layers around the tumor and examining them under a microscope for malignant cells until the tissue is tumor-free. This is especially valuable for removal of lesions on the face where saving as much normal tissue as possible is important cosmetically. The procedure is done in stage in which first tissue is removed and then slides prepared for the physician to view. This takes about an hour. Usually 2-3 stages are required, so the procedure usually takes about 2 hours. The wound may be sutured closed or left to close by secondary intention or repaired by a skin graft.</p>
<p><b>Photodynamic therapy</b></p> <p>Used for:</p> <ul style="list-style-type: none"> <li>• Actinic keratosis</li> <li>• Basal cell carcinoma</li> <li>• Sebaceous hyperplasia</li> <li>• Squamous cell carcinoma</li> </ul>	<p>This involves application of a light-sensitive agent, 5-aminolevulinic acid (5-ALA) topically or given intravenously. It is absorbed by tumor cells, which are exposed to light from a laser the following day, activating the chemical and destroying tumor cells. It is used for superficial lesions.</p>
<p><b>Radiotherapy</b></p> <p>Used for:</p> <ul style="list-style-type: none"> <li>• Basal cell carcinoma</li> <li>• Squamous cell carcinoma</li> <li>• Kaposi's sarcoma</li> </ul>	<p>Both conventional x-ray and electron beam radiotherapy may be used, usually requiring several treatments a week for a few weeks. This treatment has a high rate of cure and good cosmetic results. It is often reserved for elderly who cannot tolerate or refuse surgery or for large tumors where repair and reconstruction are difficult.</p>
<p><b>Retinoids</b></p> <p>Used for:</p> <ul style="list-style-type: none"> <li>• Actinic keratosis</li> <li>• Sebaceous hyperplasia</li> </ul>	<p>Both oral and topical retinoid drugs are effective in treating and preventing actinic keratoses. Drugs include:</p> <ul style="list-style-type: none"> <li>• Oral: Accutane® (used primarily in high-risk or severe lesions because of side effects)</li> <li>• Topical: Differin® and Vesanoid®</li> </ul>

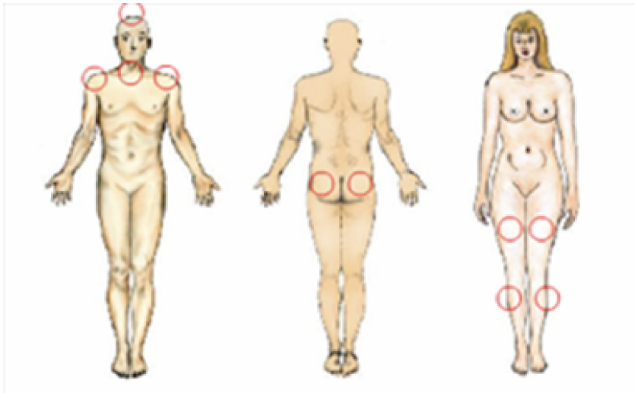
(1, 2, 3, 4, 11, 19, 20, 21).

## **Melanoma**

Malignant melanoma is one of the most serious forms of skin cancer, resulting in 2% of the deaths from cancer each year. Melanomas originate in melanocytes within the skin. In rare cases melanomas may also arise in the uvea of the eyes or the meninges, digestive tract, or lymph nodes where melanocytes are found. Melanocytes produce melanin, which is a pigment that gives color to the skin. With exposure to the sun, the skin produces more melanin, causing the skin to tan. Sometimes melanocytes group together and form moles, but in some cases they become malignant. The incidence of melanoma has increased markedly worldwide, doubling every 10 years. This increase is believed related to increased sun exposure in recreational activities, the use of tanning beds, and better detection.

Early diagnosis is important because lesions >1.5 mm in thickness or with regional lymph node involvement have a poor prognosis with only a 20-50% chance of surviving for 5 years compared to 95% chance for those with thinner lesions and no lymph node involvement. The American Cancer Society estimates >= 8000 deaths a year in the United States, with almost twice as many males as females. Melanomas can occur at any age, most after adolescence. Recent research has identified mutated genes, including BRAF and p53, which are associated with melanoma. Melanoma can occur anywhere on the body, but some sites are more common:

- *Males*: Torso, head, and neck.
- *Females*: Legs.
- *People with dark skin* : nail beds, palms, and soles of feet.



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Risk factors are similar to those of other skin cancers:

- *Exposure to ultraviolet (UVA and UVB) rays*: A history of burning, long-term frequent use of tanning beds, and cumulative exposure over many years is implicated.
- *Nevi, especially dysplastic nevi*: The greater the number of moles, the greater the change of developing melanoma. Those with >100 moles are especially at risk.
- *Skin type*: Those with the fairest skin are most prone to developing melanoma although even those with very dark skin can still get skin cancer:
  - *Type I*: Very fair with blond or red hair and blue or green eyes. Does not tan and burns easily (high risk).
  - *Type II*: Fair with blue, hazel, or brown eyes and blond, red, or brown hair. Gets a minimal tan but burns easily (high risk).
  - *Type III*: Darker hair and eyes and sometimes burns before tanning (moderate risk).
  - *Type IV*: Increasingly darker hair and eyes and does not burn but tans rapidly (moderate-low risk).
  - *Type V*: Brown skin (low risk).
  - *Type VI* : Black/ very dark brown skin (low risk).
- *Family history of melanoma*: The risk of developing melanoma increases 50% if a first-degree relative has melanoma. Children in families with melanoma history should be examined from infancy as familial melanoma can occur in children. From age 10, they should have physical examinations every 6 months and all moles should be monitored carefully, especially during adolescence when hormonal changes can activate moles.
- *Previous skin cancer*: Previous melanoma, basal cell carcinoma, and squamous cell carcinoma all increase risk of melanoma.
- *Immunocompromised status*: Impairment of the immune system from chemotherapy, organ transplants, and diseases, such as HIV/AIDS and lymphoma increase risk.

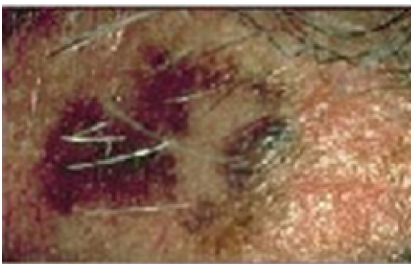
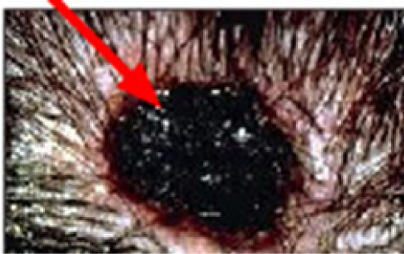
It is especially important that those with nevi inspect their skin on a regular basis and observe for the ABCDEs of melanomas.

#### The ABCDEs of Melanomas

- **A**symmetry.
- **B**orders uneven, scalloped or notched.
- **C**olor variations within a mole.
- **D**iameter is usually larger than 1/4 inch (6 mm).
- **E**volving changes in size, shape, color, or appearance.

There are 4 primary types of melanoma, and determining the type is an important part of diagnosis and follow-up treatment:

- *Superficial spreading*: These affect about 70%, especially those who are young. This spreads along the top layers of the skin for long periods before invading underlying tissue. This occurs most often on the trunk and upper back in males and the legs and upper back in females. Lesions are usually flat or slightly raised with irregular borders and may occur in a previous mole.
- *Lentigo-maligna*: These are slowly evolving lesions that progress with changes in size and color over time, often many years. They spread along the surface of the skin before invading. They are most common in the elderly on the hands, head, and neck.
- *Nodular*: This is a blue-black (occasionally red-purple) round nodule that is smooth and relatively uniform, sometimes with a dome-shape. In some individuals, it may be irregularly shaped. Nodular melanomas are the most aggressive type of melanoma and directly invade adjacent tissues and have a poor prognosis.
- *Acral-lentiginous*: These are irregularly-pigmented macules, which develop into nodules that appear in areas without hair follicles, such as the palms and soles of the feet, the mucous membranes, and nail beds of people with dark skin. These spread superficially at first but may become invasive very early. This type is the most common in African-Americans and Asians (3, 14, 23, 24).



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Staging of the melanoma is the next step after identifying the type of melanoma, but a number of factors must be evaluated in order to stage properly. One factor that is considered is the thickness of the tumor (Breslow's

thickness), which measure the distance from the upper layer of the epidermis to the deepest point of tumor invasion in millimeters:

- In situ tumors are just in the epidermis with no lower invasion of tissue.
- Very thin tumors penetrate < 1 mm. These are further classified into Clark's levels I-V, depending upon how much of the epidermis, dermis, and subcutaneous tissue is involved.
- Thin tumors penetrate 1.01-2.0 mm.
- Intermediate tumors penetrate 2.0-4.0 mm.
- Thick tumors are  $\geq 4.0$  mm.

A second factor is evaluation of the epidermis microscopically to see if it is intact. If there is ulceration, then the tumor is staged higher and requires more aggressive treatment. Another important factor is whether or not the tumor cells have spread to the sentinel nodes. Once the tumor type is identified, the thickness, ulceration, and invasion of sentinel nodes determined, then the tumor is staged:

- *Stage I*: This is further divided according to tumor thickness.
  - *Ia* with tumor <1.0 mm without ulceration and Clark level II or III.
  - *Ib* with tumor <1.0 mm with ulceration and Clark level III or IV

OR 1.01-2.0 mm with ulceration or spread to nearest lymph nodes.

- *Stage II*: This is further divided according to thickness, ulceration, and lymph node metastases.
  - *Iia* with tumor 1.01-2.0 mm with ulceration OR 2.01-4 mm without ulceration.
  - *Iib* with tumor 2.01-4.0 mm with ulceration OR > 4.0 mm without ulceration.
  - *Iic* with tumor >4.0 mm with ulceration.
- *Stage III*: This tumor has spread through the lymph system and is evident in the sentinel node biopsy. Alternately, a tumor that has spread to the skin or adjacent tissue for >2 cm but not beyond the regional lymph nodes is included.
- *Stage IV* : These tumor cells have spread to distant lymph nodes or internal organs. Most common areas of metastases are the lung, followed by the liver, brain, bone, and gastrointestinal tract.

Treatment usually follows guidelines established by the National Institutes of Health and the American Academy of Dermatology Task Force on Cutaneous Melanoma (3, 14, 23, 24). A number of clinical trials are in progress so new treatments may be developed:

<b>Treatment for melanoma</b>	
<b>Primary Excision</b>	<p>Sentinel node biopsy and excision are usually done at the same time, with the margins set (tumor and adjoining tissue) according to the extent of the tumor:</p> <ul style="list-style-type: none"> <li>• <i>In situ melanoma</i>: the tumor and 0.5cm of surrounding tissue removed along with skin layers down to fat layer.</li> <li>• <math>\leq 1\text{-mm thickness}</math>: The tumor and 1 cm of surrounding tissue are removed down to the fascia.</li> <li>• <math>\leq 2\text{-mm thickness}</math> : The tumor and 2-3 cm of surrounding tissue are removed.</li> </ul>
<b>Evaluation of lymph nodes</b>	<p><i>Palpable nodes</i> in the area of the tumor are removed for node biopsy. If this is positive, the other nodes in the same basin are removed and adjuvant treatment recommended.</p> <p><i>Non-palpable nodes</i> may be checked at regular intervals although some physicians do a radical node dissection as a preventive measure, but there is no evidence that this radical approach is necessary. A more common approach is to remove the sentinel nodes and those in the region of the primary tumor (usually done if melanomas are &gt;1 mm deep).</p>
<b>Adjuvant therapy for Stages III and IV and distant metastasis</b>	<p><b>Chemotherapy:</b></p> <ul style="list-style-type: none"> <li>• <i>Dacarbazine (DTIC)</i> is the only FDA-approved drug, but it may be combined with carmustine and tamoxifen or cisplatin and vinblastine intravenously.</li> </ul>

- Temozolomide may be given orally.

**Anti-angiogenic drugs** may be given in combination with temozolomide to cut off blood vessels that nourish tumors:

- Thalidomide
- Angiostatin and endostatin

**Immunotherapy/biochemotherapy:**

- *Vaccines* are given to stimulate the immune system of those who already have melanoma. These are currently in clinical trials.
- *Interferon alpha and tumor necrosis factor* have been shown to improve survival rates for Stage III, but they have significant side effects.
- *Lymphokines* (chemical messengers produced by lymphocytes) are being used experimentally with Stage IV.

**Gene therapy** is under investigation.

(3, 14, 23, 24)

## Summary

Skin lesions are very common, ranging from benign, to precancerous, to cancerous. Benign lesions include acrochordons (skin tags), which do not become malignant but can cause irritation because they occur in skin creases. Actinic keratoses are benign lesions that may appear as discolored or small scaly lesions, but they have the potential to progress to squamous cell carcinoma. Cherry angiomas, which can bleed, seborrheic keratoses, which may be cosmetically unsightly, are benign lesions that pose no danger of malignancy. Cutaneous horns, while themselves benign, can arise from a wide range of underlying lesions, some of which may be malignant. Dermatofibromas may, in rare cases, evolve into basal cell carcinomas. Neurofibromas, in turn, may in some cases become malignant neurofibrosarcoma. Sebaceous hyperplasia is common in the elderly and those receiving immunosuppressive drugs, such as cyclosporin A. Lentigines (age spots) are benign areas of increased pigmentation in the skin. Nevi, also caused by pigment changes, are the most common lesion in human beings, but one type—dysplastic nevi—pose a particular danger of becoming melanomas. Cancerous lesions include basal cell carcinoma, which rarely metastasizes, and squamous cell carcinoma, which poses a greater risk of metastasis. Malignant melanomas pose the greatest threat to both morbidity and mortality and require aggressive treatment. Another malignancy that causes skin lesions is Kaposi's sarcoma, most common in those with HIV/AIDS. A wide range of treatment options, including excision, cryotherapy, laser therapy, and topical and systemic chemotherapy, are available for skin lesions, depending upon the type of lesion and the degree of tissue involvement.

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### Course Exam

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1. Benign lesions are those that are not clinically significant but may be of cosmetic concern.  
 True  False
2. Precancerous lesions begin as benign lesions but always eventually become cancerous.  
 True  False
3. Acrochordons (skin tags) are benign tumors that grow in skin creases, such as neck, eyelids, axillae, and groin.  
 True  False
4. Actinic keratoses (solar keratoses) may be very small, flat or slightly raised crusty, scaly, or discolored lesions on the skin surface, and about 2-5% progress to squamous cell carcinoma.  
 True  False
5. Cherry angiomas are benign lesions that can indicate an internal malignancy.  
 True  False
6. Cutaneous horns are pre-cancerous lesions that arise from benign base lesions.  
 True  False
7. Dermatofibromas are unrelated to immunocompromised status.  
 True  False
8. Lentiginosities are caused by pigment changes in the epidermic areas that are sun-exposed, especially in those >40.  
 True  False

9. Neurofibromas, which may be single or multiple, are most common in those >60.  
 True  False
10. While nevi are usually benign, dysplastic nevi may evolve into melanoma.  
 True  False
11. Sebaceous hyperplasia may be caused by decreasing levels of androgen with age and the use of cyclosporin A.  
 True  False
12. Seborrheic keratoses may develop into basal cell carcinomas.  
 True  False
13. Basal cell carcinoma has a high occurrence of metastasis.  
 True  False
14. Basal cell carcinoma often appear first as a waxy looking nodule that later ulcerates in the center and crusts over.  
 True  False
15. There are a number of different variants of basal cell carcinoma, including, basal cell nevus, basosquamous, fibroepithelioma, nodular, pigmented, sclerosing/fibrosing, and superficial.  
 True  False
16. Squamous cell carcinoma is less malignant than basal cell carcinoma.  
 True  False
17. Squamous cell carcinoma may develop from some precancerous lesions, such as actinic keratosis, actinic cheilitis, and leukoplakia.  
 True  False
18. Squamous cell carcinoma lesions may vary from wart-like lesions to open or scaly lesions but all have a tendency to bleed.  
 True  False
19. Verrucous squamous cell carcinoma is a fast-growing type of lesion that frequently metastasizes.  
 True  False
20. Kaposi's sarcoma is a type of malignancy with red-purple to brown lesions in the tissues of the skin and mucous membranes of the mouth, nose, and anus.  
 True  False
21. More than 90% of Kaposi's sarcoma involve human herpes virus 8 (HHV-8), which is exacerbated by co-infection with HIV.  
 True  False
22. Kaposi's sarcoma cases related to the AIDS epidemic continue to rise.  
 True  False
23. Imiquimod and 5-fluorouacil are two commonly used topical chemotherapeutic agents for treatment of squamous cell carcinoma.  
 True  False
24. Cryosurgery uses liquid nitrogen to destroy malignant and pre-malignant tissue by freezing to  $\geq -40^{\circ}\text{C}$ .  
 True  False
25. Mohs micrographic surgery has the highest cure rate for basal cell and squamous cell carcinoma and is the treatment of choice for recurrent local skin cancers.

True  False

26. Melanomas originate in the melanocytes, which produce melanin, within the skin.

True  False

27. The incidence of melanoma has remained stable over the past 20 years.

True  False

28. Melanoma lesions >1.5 mm in thickness with regional lymph node involvement have a poor prognosis with a 20-50% survival rate at 5 years.

True  False

29. Malignant melanoma is more common in females than males.

True  False

30. Common signs of a melanoma include asymmetry, uneven borders, color variations, diameter >6 mm, and evolving change in size, shape, color, or appearance.

True  False