Skin Cancer: An Introduction for Organ Transplant Recipients

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This information is for educational purposes only, and is not intended to replace the advice of your doctor or health care provider. We encourage you to discuss with your doctor any questions or concerns you may have.

What is skin cancer? Skin cancer is a condition where abnormal skin cells grow in a disorganized fashion, invade the surrounding tissue, and disrupt normal tissue function. This pamphlet is divided into three parts: in Part I, we will describe the most common types of skin cancer. In Part II we will teach you strategies to reduce your risk for developing skin cancer. In Part III we will describe how you can work with your dermatologist to detect and treat skin cancer.

Part I:
What Transplant Patients Need to Know About Skin Cancer

- Organ transplant recipients are at high risk for developing skin cancer.
- Your risk for skin cancer increases each year following transplantation.
- Skin cancer in transplant patients can be life threatening and affect quality of life.

Remember, skin cancer is highly treatable if detected early.

Skin cancer is the most common form of cancer diagnosed today and occurs more often than all other malignancies combined. More than one million cases of skin cancer will be diagnosed in the United States this year. About 80% of these new skin cancer cases will be basal cell carcinoma (BCC), 16% will be squamous cell carcinoma (SCC), and 4% will be melanoma.

The incidence of skin cancer has increased dramatically in the United States. Each year in the United States, approximately 5 million people are treated for skin cancer; in fact, 1 in 5 people in the United States developed skin cancer at some point in their lives. About 9,940 people died of melanoma in 2015 and 2,000 people with carcinoma of keratinocyte die each year. This type of cancer is highly treatable when diagnosed early, and is usually relatively easy to diagnose.

There are three main groups of skin cancer:

1) **Keratinocyte carcinoma (basal cell carcinoma and squamous cell carcinoma)**
2) **Melanoma**
3) **Other nonmelanoma skin cancer (such as hair follicle cancer or sarcoma)**

Keratinocyte Carcinoma
Keratinocyte carcinoma (basal cell or squamous cell carcinoma) is the most common form of skin cancer. There are more than 2 million cases each year in the United States. Basal cell carcinoma is more common than squamous cell carcinoma in the general population, but squamous cell carcinoma is more common in organ transplant recipients.

Melanoma
Melanoma is less common, but it is the most aggressive type of skin cancer. Melanoma comes from the melanocytic cells of the skin that produce pigment or melanin. By 2015, there will be approximately 73,870 new cases of melanoma diagnosed in the United States. Although this amount represents approximately 2% of all cancers diagnosed in the skin, represents approximately 77% of the deaths due to skin cancer. According to the American Cancer Society, approximately one person dies from melanoma every hour.

Other Nonmelanoma Skin Cancer
Other nonmelanoma skin cancers are very rare, accounting for less than 1% of nonmelanoma skin cancers, according to the American Cancer Society. These less common skin cancers include:

- Kaposi's sarcoma, which usually starts within the deeper layers of the skin but can also form in internal organs. The tumors consist of bluish-red or purple lesions. This cancer occurs in people with compromised immune systems, such as those with HIV infection or AIDS, as well as transplant recipients who are on immune-suppressing drugs.
- Cutaneous lymphoma, a type of lymphoma that begins in the skin.
- Skin adnexal tumors, rare tumors that start in the hair follicles or sweat glands, and are usually benign.
- Sarcomas, which usually start in tissues deep beneath the skin, but can develop in the skin as well.
- Merkel cell carcinoma, a rare cancer of neuroendocrine origin that develops on or just beneath the skin and in hair follicles. These cancers usually appear as firm, reddish/purple shiny skin lumps.

What Do Skin Cancers Look Like?

Precancerous skin changes and skin cancer have characteristic appearances and are often curable when detected and treated early. Health care professionals are able to evaluate many skin abnormalities. A primary care physician may be the first health care professional you go to if you notice something suspicious on your skin. Dermatologists are physicians with extensive training in skin care and skin disorders, particularly skin cancer. Your primary care doctor may refer you for an initial assessment with a dermatologist if your condition needs further evaluation and/or treatment.

The first step in detecting abnormalities that may be skin cancer begins with you. The single most important feature that may signal the presence of a skin cancer is a new,

changing, enlarging skin growth that persists. Look for changes in color, size, thickness, and surface texture of a mole or other suspicious skin lesions. Sores that won't heal may also indicate cancerous or precancerous conditions of the skin that need attention. Examine your skin once a month for any suspicious changes. Not all skin cancers are symptomatic; many are painless. Early treatment is critical.

Actinic Keratoses: Precursors to Squamous Cell Carcinoma

An early warning sign of skin cancer is the development of an actinic keratosis. Actinic keratoses are precancerous skin lesions that result from chronic sun exposure. They are typically < 0.5 cm in diameter, pink or red in color, and rough or scaly to the touch (Figure 1). They occur on sun-exposed areas of the skin (face, scalp, ears, backs of hands or forearms). Actinic keratoses may start as small, red, flat spots but grow larger and become scaly or thick, if untreated. Sometimes they are easier to feel than to see. There may be multiple lesions next to each other (Figure 2).

Early treatment of actinic keratoses may prevent their change to cancer. These precancerous lesions affect more than 10 million Americans. People with one actinic keratosis usually develop more. Up to 1% of these lesions can develop into a squamous cell cancer.

Actinic keratoses are most common in people older than 40, but can also appear in younger individuals with extensive sun exposure. Because they can turn cancerous, affected areas should be regularly examined and treated by a primary care physician or dermatologist.

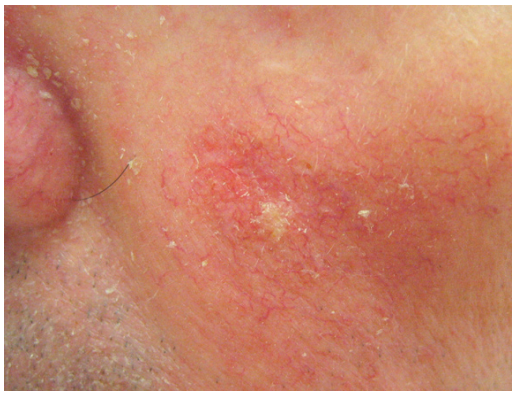


Figure 1. Actinic keratosis. A pink, scaly skin lesion on a sun-damaged cheek.

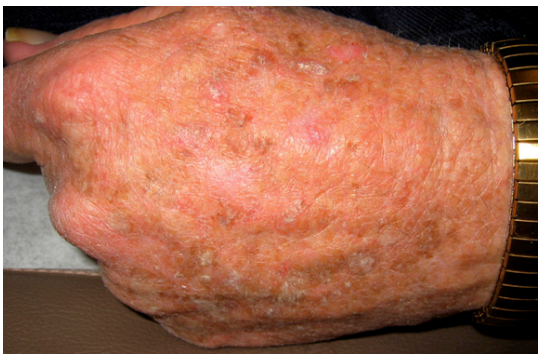


Figure 2. Actinic keratosis. Multiple skin lesions on the back of a hand.

Basal Cell Carcinoma

Basal cell carcinoma is the most common type of non-melanoma skin cancer. This type of cancer often looks like a pink waxy bump that may bleed following minor injury. There may be irregular blood vessels on its surface and its center may be sunken in (Figure 3). Large basal cell carcinomas may have oozing or crusted areas.

Basal cell carcinomas typically occur on sun-exposed skin of the face, ears, neck, and trunk, but may also occur on the arms or legs. Basal cell carcinomas grow slowly and rarely spread to other parts of the body (metastasize). However, if left untreated, they can become locally invasive and destroy surrounding muscle, bone, and nerves causing significant disfigurement and functional problems.

here are several subtypes of basal cell carcinoma. Some are more aggressive than others. The subtype of basal cell carcinoma is identified by skin biopsy and examination under a microscope.

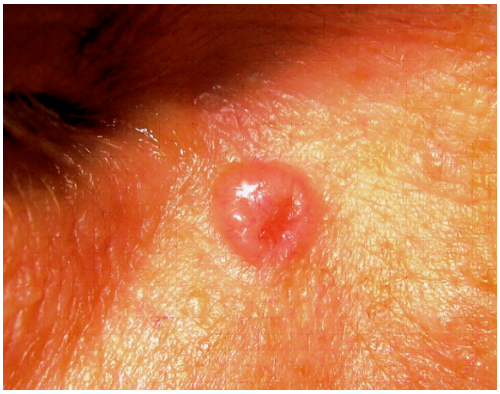


Figure 3. Basal cell carcinoma. Translucent pearly papule near the right eye.

What Causes Basal Cell Carcinoma?

The most common cause of basal cell carcinoma is ultraviolet light (UV), specifically ultraviolet B (UVB, 290-320 nm). Indoor tanning, fair-skinned complexion, prior radiation exposure, and inherited genetic conditions such as nevoid basal cell carcinoma syndrome (Gorlin's syndrome) or Bazex's syndrome are other important risks factors.

Squamous Cell Carcinoma

Squamous cell carcinoma is the second most common skin cancer after basal cell carcinoma. However, squamous cell carcinoma is the most common skin cancer in organ transplant recipients. Squamous cell carcinomas are often described as enlarging red bumps, sometimes with a rough, scaly, or crusted surface (Figure 4). They may also look like flat reddish patches in the skin that grow slowly (Figure 5). If untreated, they can become ulcerated (open sores). Most squamous cell carcinomas grow slowly. Occasionally, they may occur quite rapidly, particularly in patients who are

immunosuppressed.

Squamous cell carcinomas occur most frequently on sun-exposed areas such as the head, neck, ears, lips, back of the hands and forearms. This cancer rarely metastasizes (spreads to lymph nodes or other organs), although distant spread happens more frequently than in basal cell carcinoma. When squamous cell carcinoma does metastasize, it most commonly travels to the local lymph nodes. The squamous cell carcinoma that has metastasized is typically greater than 2 cm in diameter or greater than 4 mm in depth, or in a site previously exposed to radiation.

Organ transplant recipients have a higher rate of metastasis than other patients. While the metastatic rate of squamous cell carcinoma is 2% in the general population, it is 5-7% in adult organ transplant recipients and 13% in pediatric transplant recipients. Early detection and treatment is key in preventing metastasis.

What Causes Squamous Cell Carcinoma?

The most common cause of squamous cell carcinoma is ultraviolet (UV) light. The duration and dose of UV exposure determines your risk for squamous cell carcinoma. Although UVB (wavelength 290-320 nm) is mainly responsible, the role of UVA is also important. Indoor tanning, fair-skin complexion, prior radiation exposure, and immunosuppression are other significant risk factors.
UV light damages DNA. Normally, skin cells have ways to protect DNA or to repair DNA that is damaged by UV light. However, when these protective mechanisms fail, DNA damage can ultimately affect the genes that regulate cell division, causing tumors to form.

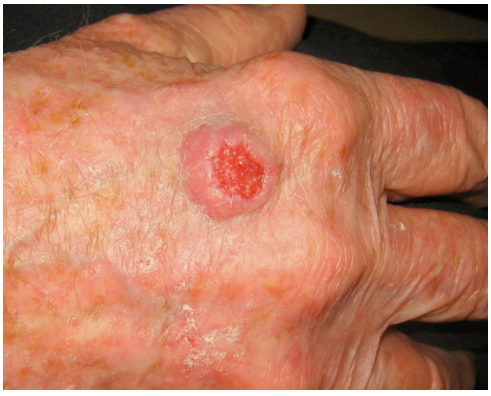


Figure 4. Squamous cell carcinoma. Firm, ulcerated nodule on the back of the hand. Notice the nearby actinic keratoses.

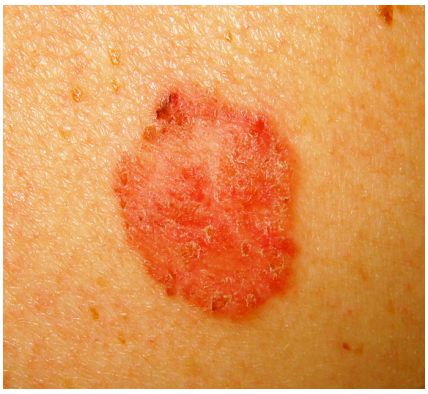


Figure 5. Squamous cell carcinoma. This broad, flat lesion measured 2 cm in diameter.

Melanoma

Melanoma is the most dangerous type of skin cancer. Although melanoma makes up only 4% of skin cancers, it causes 77% of skin cancer deaths. About 100,000 cases of melanoma are diagnosed each year. Melanoma typically presents as a brown or black spot with irregularities in symmetry, border and color (Figure 6, Figure 7). Some melanomas appear pink, with very little brown pigment. Melanoma may develop within an existing mole or on previously normal appearing skin.

Melanoma has a high fatality rate because its cells can break off and spread throughout the body (metastasize). When melanoma is caught early, your chances for successful treatment are much higher.

The "ABCDE rule" is an easy patient guide to the usual signs of melanoma. These are clues to a spot that you should show your doctor.

A) Asymmetry: One half doesn't match the other half, either in shape or color.
B) Border Irregularity: The edges are ragged, notched, blurred, or fade out without a distinct margin.
C) Color: The color is not uniform, and may contain shades of tan, brown, white, red, blue, and black.
D) Diameter: The width is greater than a pencil eraser, about six millimeters. Growth in diameter may also be of concern.
E) Evolution: Any change in an existing spot, either in size, shape, color, or other feature.

Be on the lookout and promptly notify your primary care physician or dermatologist about any spots that match the following description. Some melanomas do not fit the ABCDE rule described above, so it is important for you to notice changes in skin markings or new spots on your skin.

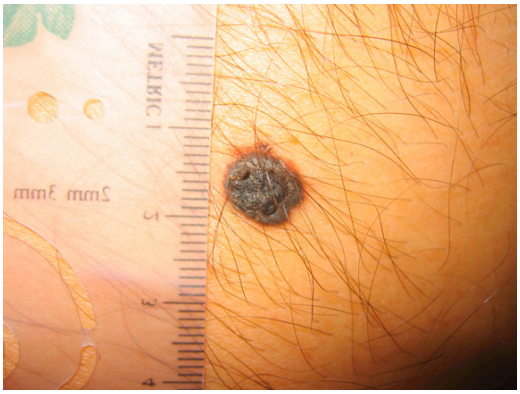


Figure 6. Melanoma. This previously flat brown spot on the back had changed, becoming larger and thicker.

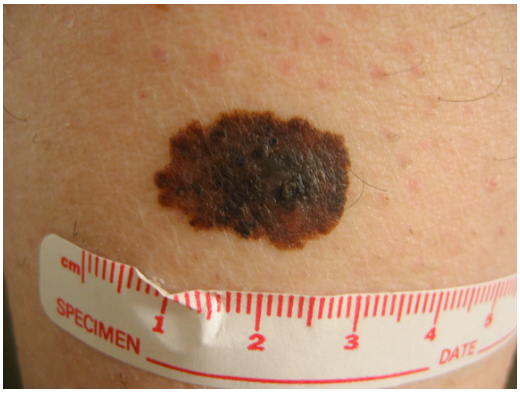


Figure 7. Melanoma. This lesion is asymmetric, has an irregular border, has mutiple colors (brown, black, and tan), and is larger than a pencil eraser.

Other warning signs are:

- A sore that does not heal
- A new growth
- Spread of pigment (color) from the border of a spot to surrounding skin
- Redness or a new swelling beyond the border
- Change in sensation – itchiness, tenderness, or pain
- Change in the surface of a mole – scaling, oozing, bleeding, or the appearance of a bump or nodule

Kaposi's Sarcoma

Kaposi's sarcoma is a rare cancer of the cells that line blood vessels (endothelial cells). They are typically brownish-red to blue colored skin lesions found most commonly on the legs and feet. Kaposi's sarcoma is caused by Human Herpes Virus 8 (HHV-8), which causes the endothelial cells to become cancerous in the setting of prolonged immunosuppression. You may have heard about Kaposi's sarcoma in the setting of HIV infection and AIDS.

There are two main forms of Kaposi's sarcoma. Cutaneous (skin) Kaposi's sarcoma is the most common form in adult organ transplant patients and typically occurs in the first 1-2 years following transplantation. Visceral (internal) Kaposi's sarcoma is the most common form in pediatric transplant patients and can affect the gastrointestinal system, the lungs, and the lymph nodes.

Anogenital Carcinoma

Anogenital carcinoma include tumors of the vulva, scrotum, penis, perianal skin, and anus. They occur at 30-100 fold higher incidence in transplant patients than in the general population. They can be multiple and extensive, and may resemble genital warts. Pediatric transplant patients are particularly at risk. Risk factors also include multiple sexual partners, Human Papillomavirus (HPV) infection, history of genital herpes, heavy smoking, and a high level of immunosuppression.

Post-adolescent female transplant recipients should have regular gynecologic exams of the anogenital region. Both male and female transplant recipients may also have anal Pap smears, a simple swab test of the area which can screen for precancerous or cancerous changes.

Risk Factors: Who's at Risk?

Anyone can develop skin cancer, not just organ transplant recipients. Other risk factors for skin cancer include:

- Personal history of skin cancer or precancerous skin lesions (actinic keratoses)
- Tendency to freckle or burn easily
- Lots of sun exposure throughout your life
- Many sunburns as a child or adolescent
- Family history of skin cancer (such as melanoma) or conditions that are more likely to develop into skin cancer (such as dysplastic nevus syndrome or numerous atypical moles)
- Chronic, non-healing wounds or burn injuries
- History of radiation therapy
- Exposure to toxic materials, such as arsenic
- Exposure to certain subtypes of human papilloma virus (HPV).
- Organ transplantation or other immunosuppression

Since the effects of sun exposure add up, the risk of developing skin cancer increases as you get older. The majority of lifetime sun exposure occurs before age 18 and skin cancer can take 20 years or more to develop. Therefore, you need to be concerned about skin cancer whether you protect yourself from the sun or continue to tan. According to the American Cancer Society, very young children who experience as few as two to three sunburns may have an increased risk of developing skin cancer later in life. It has been estimated that regular application of sunscreen with sun protection factor of 15 or greater for the first 18 years of life would reduce the lifetime incidence of

non-melanoma skin cancers by 78%.

People with a large number of moles may have a higher risk of developing skin cancer, particularly if there is a family history of melanoma. Patients with many moles should be evaluated by their primary care physician or by a dermatologist for a baseline screening exam. If any of your moles meet the ABCDE criteria or have been changing, have these moles evaluated in a timely manner.

Skin cancer risk factors can be additive. Those individuals with multiple risk factors are at highest risk for developing skin cancer. Anyone in a high-risk group should take extra precautions against skin cancer and talk with their primary care physician or dermatologist about regular full body screening exams.

Organ transplant recipients are at high risk for developing skin cancer

As people with transplants survive longer, the long-term effects and complications are becoming more apparent. One complication is skin cancer.
Transplant patients have up to a 100-fold higher risk for developing skin cancer compared to the general population. Transplant patients tend to develop a skin cancer called squamous cell carcinoma (SCC), although many patients will also develop a different type of skin cancer called basal cell carcinoma (BCC).

The frequency at which SCC occurs in transplant patients is 65-fold higher than the general population. Transplant patients also develop other skin cancers.

Skin Cancer	Increase in Incidence
SCC	65-fold
SCC of lip	20-fold
BCC	10-fold
Melanoma	3.4-fold
Kaposi's sarcoma	84-fold

Your risk for skin cancer increases each year following transplantation.

All transplant patients have a greater chance of developing skin cancer compared to the general population. This risk increases with each subsequent year following your transplant. At 5 years after transplant, some studies suggest that approximately 5% of transplant patients will develop skin cancer. At 10 years, approximately 10% of transplant patients develop skin cancer. The risk for skin cancer may vary with the type of transplant. Cardiac and kidney transplant patients seem to develop skin cancer more frequently than liver or lung transplant patients. However, all transplant patients are at higher risk for skin cancer compared to the general population.

Skin cancer in transplant patients can be life threatening and affect quality of life.

Untreated skin cancer invades and destroys tissue. It can lead to disfigurement and loss of function. In rare cases, skin cancer can metastasize. The metastasis rate in transplant patients is 3-4 fold higher than that of the general population and can be life threatening. The keys to successfully treating skin cancer while minimizing any side effects are early detection and treatment.

The main skin cancer that occurs in transplant patients is squamous cell carcinoma (SCC). SCC that occurs in transplant patients can behave differently than SCCs that occur in the general population, even though they may look the same. SCC that occur in transplant patients tend to:

- Develop at a younger age
- Develop more quickly
- Occur in greater numbers
- Be more invasive and locally destructive
- Have a greater risk for recurrence (regrowth of tumor at a previously treated area)
- Have a greater risk for metastasis (tumor breaks off and travels to lymph nodes or other distant sites of the body)

Overexposure to sunlight is a major risk factor. The more sunlight your skin has been exposed to during your lifetime, the higher your risk for developing skin cancer. Because UV radiation in linked to skin cancer, transplant patients tend to get skin cancer on sun-exposed areas (face, ears, scalp, neck, backs of hands, and backs of forearms).

Some sites where skin cancer occurs that may be associated with an increased chance of recurrence or metastasis include the ear, lip, perioral region, periorbital region, nose, and genitalia. The majority of sun damage occurs before the age of 30. However, good sun protection at any age may be beneficial at preventing future skin cancers.

Immunosuppression and Cancer

Immunosuppressive medications are essential to prevent graft rejection and to optimize graft survival. However, because these medications suppress the immune system, whose main function is to fight off infection and prevent the development of cancer, transplant recipients are at elevated risk for infection and certain cancers.

The exact mechanism by which immunosuppressive medications promote tumor growth is currently being studied. However, several lines of evidence suggest the duration, intensity, and type of immunosuppressant may be related to the development of skin cancer.

Other Medications and Cancer

There are several medications that can cause photosensitivity, which makes the skin more sensitive to sunlight. These medications can make it easier to get sunburned and increase the risk of developing skin cancer.

Voriconazole (Vfend) is one example of a drug that is frequently on the list of drugs for transplant patients; it is used to prevent fungal infections. It is very important to keep your primary care physician and/or dermatologist informed of any medications you are taking. It is best to bring an up-to-date list of medications or medicine bottles to the consultation.

Part II:
How Can I Protect Myself from Sun Damage and Prevent Skin Cancer?

More than 1 million people in the US are diagnosed with skin cancer each year, making it the most common form of cancer in the United States. Skin cancer is largely preventable. Studies have shown that most skin cancers are linked to overexposure to sunlight (UV radiation). Therefore, good sun protection is an important way to prevent the development of both sun-related skin damage (freckles, fine wrinkles, etc) and sun-related skin cancers.

Everybody, regardless of race or ethnicity, is subject to the potential adverse effects of overexposure to the sun. However, some types of skin might be more vulnerable then others. Skin type affects the degree to which you burn and the time it takes you to burn. Fair-skinned individuals who tend to burn rapidly and more severely are at the highest risk for developing skin cancer. Although darker skinned individuals are less likely to develop skin cancer, they can and do get skin cancer and should also protect their skin from overexposure to the sun.

Detection: Skin Self Exam

Monthly examination of your skin, head to toe, can help detect early skin cancers. Skin cancers detected early have a higher chance for successful treatment.

How to Examine Your Skin

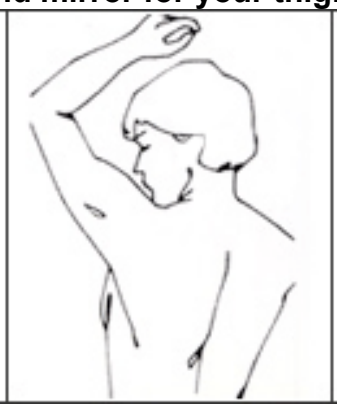
It is important to check your own skin, preferably once a month. Self-examination is best done in a well-lit room in front of a full-length mirror. A hand-held mirror can be used for areas that are hard to see. A spouse or close friend or family member may be able to help you with these exams, especially for those hard-to-see areas like the lower back or the back of your thighs.

The first time you inspect your skin, spend a fair amount of time carefully going over the entire surface of your skin. Learn the pattern of moles, blemishes, freckles, and other marks on your skin so that you will notice any changes. Any trouble spots should be

seen by a doctor. Follow these step-by-step instructions to perform your skin self-exam:

Face the mirror and have a hand mirror for your thighs, back, and scalp:

Check your face, ears, neck, chest, and belly. Women will need to lift breasts to check the skin underneath.



Check both sides of your arms, the tops and palms of your hands, and your fingernails.

Sitting down, first check one leg, then the other. Inspect the bottoms of feet, calves, and the backs of thighs.

Use a hand mirror to inspect back of neck, shoulders and upper arms.

Use a hand mirror to inspect back, buttocks and legs.

Sun Avoidance

Avoiding sunshine can help prevent most types of skin cancer. You do not have to avoid the sun altogether. Learn how to protect your skin from the sun's harmful rays and practice "sun protection" and "sun safety" whenever you can. Cover up with sunscreen and protective clothing and be sensible about how much time you spend in the sun. These steps can help greatly reduce your risk of developing skin cancer.

Tips for avoiding sun damage:

- Avoid the intense, mid-day sun between 10 a.m. and 3 p.m.
- Whenever possible, seek shade.
- Use a broad spectrum sunscreen with an SPF of at least 30.
- Reapply sunscreen at least every two hours. You should apply it more frequently if you have been swimming or sweating.
- Wear a wide-brimmed hat and if possible, tightly woven, full-length clothing.
- Wear UV-protective sunglasses.
- Wear lip balm with sunscreen with an SPF 15 or higher.
- Avoid sunlamps and tanning salons.
- Watch for the UV Index daily.
- Be aware that the sun's ultraviolet (UV) rays can reflect off water, sand, concrete, and snow, and can reach below the water's surface. Certain types of UV light penetrate fog and clouds, so it is possible to get sunburns or sun damage even on overcast days.
- If you are taking an antibiotic or other medications, ask your health care professional if it may increase your skin's sensitivity to the sun.

Sun Protective Clothing

Clothing is a simple and effective sun protection tool. It provides a physical block that doesn't wash or wear off and can shade the skin from both UVA and UVB rays. Long-sleeved shirts and pants, hats with broad brims, and sunglasses are all effective forms of sun protective clothing.

Standards

The American Society for Testing and Materials has recently developed standards for manufacture and labeling of sun protective products. The new units for UV protection are called UPF (Ultraviolet Protection Factor). UPF measures the ability of the fabric to block UV from passing through it and reaching the skin.

- Good UV Protection (UPF 15-24),
- Very Good UV protection (UPF 25-39)
- Excellent UV Protection (for UPF 40-50)

Not all fabrics block UV light to the same extent. The ultraviolet protective factor (UPF) of clothing depends on several factors including weave and chemical additives when manufactured, such as UV absorbers or UV diffusers.

UPF factors in order of importance:

- Weave: Tightly woven fabric provides greater protection than loosely woven clothing. If you can see light through a fabric, UV rays can get through, too.
- Color: Dark colors provide more protection than light colors by preventing more

UV rays from reaching your skin.
- Weight: Also called mass or cover factor - heavier is better
- Stretch: Clothing with less stretch generally has better UV protection
- Wetness: Dry fabric is generally more protective than wet fabric.

The ideal sun-protective fabrics are lightweight, comfortable, and protect against exposure even when wet. Currently, only a few companies in the U.S. manufacture clothing that is specifically designed to be UV-protective, including SunProtections, Coolibar, and SolarTex. Their products include outerwear, pants, shirts, and hats for all sizes and shapes including children.

For those who enjoy water sports, consider using UV protective swimwear including rash guards and swimsuits. Some companies even sell UV protective flotation devices and swim diapers.

Additionally, you may use sunprotective clothing additives such as Sunguard Detergent. Sunguard detergent is a UV blocking additive that can be added to your laundry to transform everyday clothing into sun protective gear with a SPF 30. The active ingredient is Tinosorb™ FD, a UV protectant that can boost the SPF protection of a white cotton T-shirt from SPF 5 to UPF 30.

Sunscreen Recommendations:
- SPF 30 or higher
- Broad spectrum UVA and UVB blocking agents
- Use daily with frequent reapplication

What SPF should I use?

Sunscreen protects your skin by absorbing and/or reflecting UVA and UVB radiation. All sunscreens have a Sun Protection Factor (SPF) rating. The SPF rating indicates how long a sunscreen remains effective on the skin. A user can determine how long their sunscreen will be effective by multiplying the SPF factor by the length of time it takes for him or her to suffer a burn without sunscreen.

For instance, if you normally develop a sunburn in 10 minutes without wearing a sunscreen, a sunscreen with an SPF of 15 will protect you for 150 minutes (10 minutes multiplied by the SPF of 15). Although sunscreen use helps minimize sun damage, no sunscreen completely blocks all wavelengths of UV light. Wearing sun protective clothing and avoiding sun exposure from 10 a.m. to 3 p.m. will also help protect your skin from overexposure and minimize sun damage.

The American Association of Dermatology (AAD) recommends that a "broad spectrum" sunscreen with an SPF of at least 15 be applied daily to all sun exposed areas, then reapplied every two hours. However, in some recent clinical trials, sunscreens with SPF 30 provided significantly better protection than sunscreens with SPF15. Therefore at UCSF, we recommend sunscreens with SPF of at least 30 with frequent reapplication.

What is the best type of sunscreen to purchase?

The best sunscreen varies from individual to individual. We recommend broad spectrum sunscreen with UVA and UVB protection, with SPF rating of at least 30, in a form that is gentle enough for daily use.

Active ingredients of sunscreen vary from manufacturer to manufacturer and can be divided into chemical versus physical agents. **Chemical sunscreens** work by absorbing the energy of UV radiation before it affects your skin. **Physical sunscreens** reflect or scatter UV radiation before it reaches your skin. Some sunscreens combine both chemical and physical sunscreens. The two types of physical sunscreens that are available are zinc oxide and titanium dioxide. Both provide broad spectrum UVA and UVB protection, and are gentle enough for everyday use. Because these are physical blocking agents and not chemicals, they are especially useful for individuals with sensitive skin, as they rarely cause skin irritation.

Most chemical sunscreens are composed of several active ingredients. This is because no single chemical ingredient blocks the entire UV spectrum (unlike physical sunscreens). Instead, most chemicals only block a narrow region of the UV spectrum. Therefore, by combining several chemicals, with each one blocking a different region of UV light, one can produce a sunscreen that provides broad spectrum protection. The majority of chemical agents used in sunscreen work in the UVB region. Only a few chemicals block the UVA region. Since UVA can also cause long-term skin injury, dermatologists at UCSF routinely recommend sunscreens that contain either a physical blocking agent (e.g. titanium dioxide or zinc oxide) or Avobenzone (also known as Parsol 1789). Two newer ingredients, Mexoryl and Helioplex, function to stabilize the UVA blockers for longer protection.

Sunscreen comes in a variety of forms. Lotions, oils, sticks, gels, sprays and creams can all be effective sunscreens. However, sunscreens are only effective if they are used. We encourage you to try several types and find the one which works and feels the best to you. All sunscreens should be applied 15-20 minutes before sun exposure to allow a protective film to develop, then reapplied after water contact and sweating. Some sunscreens can lose effectiveness after two hours, so reapply frequently.

In general, spray lotions and gels are the least oily but also the ones that wash off more easily and need to be reapplied more frequently. If you develop a rash or other type of allergic response to a sunscreen, try a different brand or form (lotion vs. oil, for example) to see if you can better tolerate it. The most common allergic reactions occur with sunscreens that contain PABA-based chemicals. If you develop a rash to a sunscreen, check the label to see if PABA is an ingredient. If so, consider avoiding sunscreens that contain this in the future. Alternatively, try a titanium dioxide or zinc oxide containing sunscreen as they rarely cause skin irritation and provide very good broad spectrum UV protection.

Water resistant sunscreens are available for active individuals or those involved in water sports. It is important to check the label to ensure they say "water-resistant" or "very water-resistant."

- **Water-Resistant sunscreen** maintains the SPF level after 40 minutes of water immersion
- **Very Water-Resistant** sunscreen maintains the SPF level after 80 minutes of water immersion

Note that water-resistant does not mean towel resistant! If you get out of the water and vigorously towel off, you are likely to rub off your sunscreen and should reapply.

Common active ingredients of sunscreen and the type of UV light blocked:

Active Ingredient	**Type of UV radiation blocked**
Aminobenzoic acid	UV-B
Avobenzone	UV-A
Cinoxate	UV-B
Dioxybenzone	UV-B, UV-A
Homosalate	UV-B
Menthyl anthranilate	UV-A
Octocrylene	UV-B
Octyl methoxycinnamate	UV-B
Octisalate	UV-B
Oxybenzone	UV-B, UV-A
Padimate O	UV-B
Phenylbenzimidazole sulfonic acid	UV-B
Sulisobenzone	UV-B, UV-A
Titanium dioxide	UV-A/B, broad spectrum
Trolamine salicylate	UV-B
Zinc oxide	UV-A/B, broad spectrum

The bottom line with sunscreen is that it only works if you are actually putting it on. If you don’t like the smell or feel of a sunscreen, it will probably sit unused in your bathroom cabinet. Find one you like and stick with it!

UV Radiation

Some exposure to sunlight can be enjoyable, but too much sunlight can be dangerous. Overexposure to the sun's ultraviolet (UV) radiation can cause immediate effects such as sunburn and long-term problems such as skin cancer and cataracts. Sunlight consists of two types of ultraviolet (UV) radiation, UVB and UVA. Both UVB and UVA radiation contribute to freckling, skin wrinkling, and the development of skin cancer.

UVB radiation (290-320 nm) has the most energy and causes the most damage. UVB is only partially blocked by clouds or fog; therefore, it is important to wear sunscreen even on cloudy days. This type of radiation intensifies during the summer and with higher

elevations. UVB can do more damage more quickly than UVA rays. Because of its damaging effect to the DNA of skin cells, UVB radiation is the main cause of sunburn and skin cancer. Over the past 25 years, the thinning ozone means more UVB penetrates the atmosphere, increasing the risk for UVB-related sun damage.

UVA radiation (320-400 nm) is less powerful than UVB, but it penetrates deeper into the skin. Small daily doses of UVA causes long-term skin injury, even without signs of sunburn. UVA light is used in tanning booths. Tanning booths not only cause the same type of skin and eye damage as natural sunlight, they may also be as much as 20 times stronger.

When the sun's ultraviolet radiation reaches the surface of the skin, the skin reacts by producing melanin, a skin pigment that has a protective effect on the skin. Therefore, tanning after sun exposure is your body's response to sun damage. Having a tan provides minimal protection against sun overexposure and is not a substitute for good sun protective measures.

What About Vitamin D?

Sun exposure is one way of obtaining vitamin D, and wearing sunscreen will decrease the skin's production of vitamin D. However, intentional sun exposure is not a recommended method for obtaining adequate vitamin D. If you are concerned that you are not getting enough vitamin D, discuss options for obtaining sufficient vitamin D from foods and/or vitamin supplements with your doctor.

Examples of individuals who are at risk for vitamin D deficiency include:

- Exclusively breast-fed infants
- Formula-fed infants and children taking less than 1 L (or 1 quart) per day of vitamin D-fortified formula or milk
- Individuals whose religious practices dictate covering the skin with veils, robes, or other coverings
- Individuals with skin conditions that dictate strict and total avoidance of the sun (such as xeroderma pigmentosum)
- Individuals with fat malabsorption (such as celiac disease, Crohn's disease, cystic fibrosis)

The UV Index: Predicting when to cover up from the sun

The UV Index, which was developed by the National Weather Service and the U.S. Environmental Protection Agency (EPA), provides important information to help you plan your outdoor activities to prevent overexposure to the sun's rays. The UV Index predicts the risk of overexposure to the sun for the following day. The Index predicts UV intensity levels on a scale of 1 to 11+, where a low number indicates a minimal risk of overexposure and a high number (e.g.11+) means an extreme risk. The UV Index takes into account the day, weather condition, time of year, elevation, latitude, amount of ozone coverage, as well as other local conditions that affect the amount of UV

radiation reaching the ground. More information on the UV index in your neighborhood can be found at: www.epa.gov/sunwise/uvindex.html.

UV Index Range	Risk for the average person	Recommendations
<2	**Low**	
3-5	**Moderate**	• sun avoidance recommended: stay in the shade from 10am-3pm • cover up by wearing sun protective clothing (hats, long-sleeved shirt, long pants, sunglasses) if you will be outside
6-7	**High**	• apply sunscreen with SPF at least 30 • cover up by wearing sun protective clothing (hats, long-sleeved shirt, long pants, sunglasses) if you will be outside • sun avoidance recommended: stay in the shade from 10am-3pm
8-10	**Very high**	• apply sunscreen frequently with SPF at least 30 • wear lip balm with sunscreen • cover up by wearing sun protective clothing (hats, long-sleeved shirt, long pants, sunglasses) if you will be outside • sun avoidance recommended: avoid being in the sun from 10am-3pm
11+	**Extreme risk**	• apply sunscreen at least every 2 hours with SPF at least 30 • wear lip balm with sunscreen • cover up by wearing sun protective clothing (hats, long-sleeved shirt, long pants, sunglasses) if you will be outside • sun avoidance recommended: avoid being in the sun from 10am-3pm

Chemoprevention

Acitretin (Soriatane) is an oral drug derived from Vitamin A that has been shown to reduce the risk of squamous cell carcinoma in transplant patients. Dermatologists may recommend this drug to transplant recipients who develop multiple squamous cell carcinomas each year, or who have these carcinomas in high-risk areas such as the ears, lips and other special circumstances.

The administration of this drug should be reviewed with your transplant team and considered carefully for its side effects. The most common side effects are: dry skin and eyes, nausea, headache, increased lipids (more often triglycerides), muscle cramps. Also, it can cause birth defects so it should not be taken by women during a pregnancy or if they plan to become pregnant.

Nicotinamide is a type of Vitamin B that has been shown to reduce the risk of keratinocyte carcinoma. Dermatologists may recommend this vitamin to transplant recipients to prevent skin cancers.

Part III:
Organ Transplant Recipients and the Dermatologist

Screening Examinations: The Skin Check

Not all transplant recipients will develop skin cancer. However, all transplant patients are encouraged to examine their skin for worrisome lesions once a month, follow up with their dermatologist for regular skin checks, and practice adequate sun protection measures.

All organ transplant recipients should talk to their doctors about having a head-to-toe skin examination by a dermatologist. Dermatologists recommend a skin check within one year following transplant, to assess your personal risk for skin cancer and answer any questions you may have. Even darker-skinned transplant recipients have increased skin cancer risk, especially if they sunburn or have sun sensitivity. Sometimes, patients will be asked to visit their dermatologist more frequently, especially if they have multiple risk factors for developing skin cancer. Some examples of risk factors that would indicate the need for more frequent skin exams are a prior history of skin cancer or a history of pre-cancerous skin lesions like actinic keratosis.

If you are a pre-transplant candidate and have a history of skin cancer, you should notify your transplant physician. Sometimes, you will be asked to have a skin examination with a dermatologist prior to your transplant. Alternatively, you should see a dermatologist within 6 months following your transplant to establish care. Any patient who has had skin cancer prior to transplant is at high risk for developing additional skin cancers in the future.
When you see the dermatologist for a skin examination, you should expect to be asked to undress and wear a patient gown to allow examination of all skin from head to toe. You should have the opportunity to show any skin spot that worries you, or injuries that you have observed on your skin.

The Skin Biopsy

If your doctor finds a lesion that is suspicious for skin cancer, a sample of skin might be removed to look at under a microscope. This is called a skin biopsy. There are several different ways to perform a skin biopsy. The choice depends on the type of skin cancer, where it is on the body, and the size of the affected area. Looking at tissue under the microscope is the most definitive method to diagnose a skin cancer.

There are three main types of skin biopsy: the shave biopsy, the punch biopsy, and the incisional or excisional biopsy. In most cases, your dermatologist will do the skin biopsy

during your visit. Shave and punch biopsies take about ten minutes. Incisional or excisional biopsies of larger lesions may take longer, and your dermatologist may have you schedule a separate appointment for the procedure.

Shave Biopsy

The skin is numbed with an injection of local anesthesia. A sharp blade is used to shave off a thin slice of skin containing the top layer of skin, the epidermis, and a portion of the bottom layer of skin, the dermis. You will wear a bandaid after the procedure.

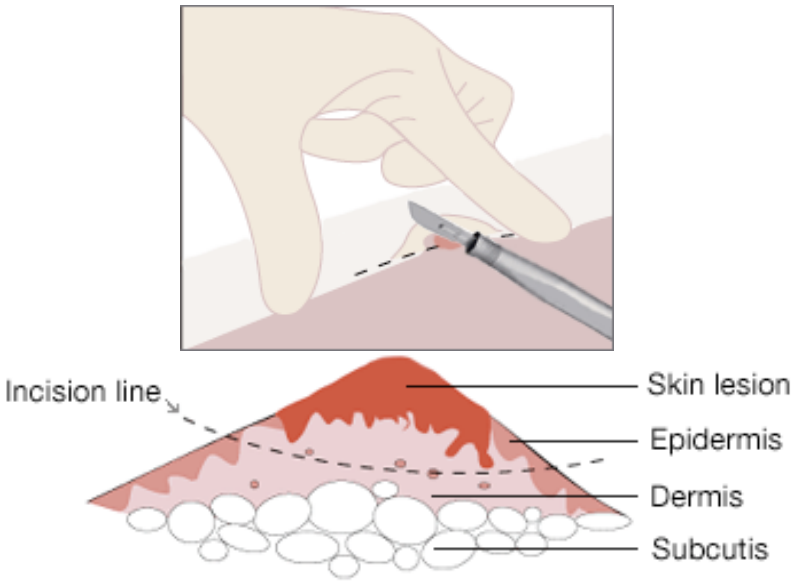


Figure 8. Schematic Representation of a shave biopsy.

Punch Biopsy

The skin is numbed with an injection of local anesthesia. A sharp, circular blade is used to remove a cylindrical core of skin and all skin layers down to the subcutaneous fat layer. The wound may be closed with stitches, which will be removed in one to two weeks.

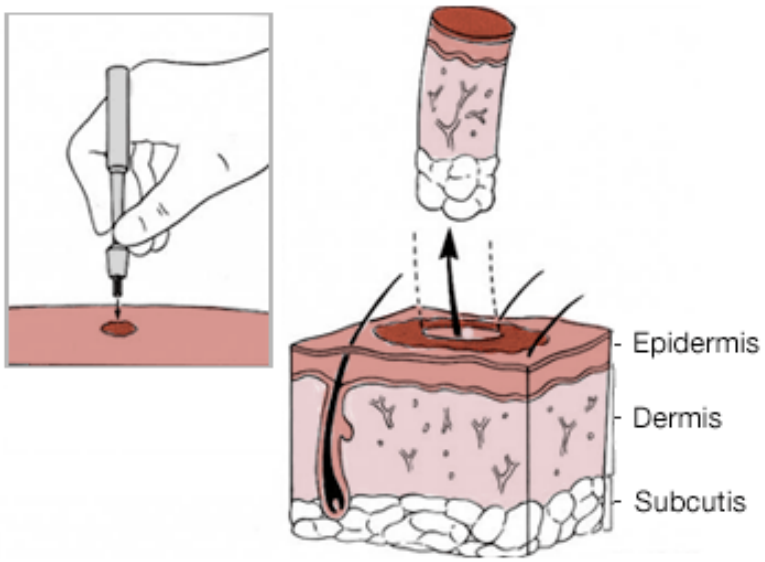


Figure 9. Schematic representation of a punch biopsy.

Incisional/Excisional Biopsy

The skin is numbed with an injection of local anesthesia. A scalpel is used to remove a portion of the lesion (incisional biopsy) or the entire lesion (excisional biopsy). The incision site is closed with stitches. You may have a pressure bandage for a day or two after the biopsy.

Treatments: What are the options?

There are multiple medical and surgical treatments for skin cancer. You and your physician should discuss the various treatment options and decide which best suits your particular diagnosis.

Actinic Keratosis

There are several treatments your health care professional may use for your actinic keratosis. Choice of treatment depends on the extent and location of the precancerous lesions. Your doctor may recommend focused treatment (if you have a few spots) or field treatment (if you have many spots). Field treatment is a way of treating an entire area, such as the scalp or the backs of the hands, at one time.

Medical Treatments for Actinic Keratoses

- **Topical chemotherapy:** Chemotherapy agents, like 5-fluorouracil (*Efudex, Carac*), are used to treat precancerous cells.
- **Topical immunomodulators:** Imiquimod (*Aldara*) is a recently FDA (Food and Drug Administration) approved topical cream that may stimulate an immune response against precancerous cells.
- **Topical anti-inflammatory agents:** Diclofenac (*Solaraze*) is another recently

FDA approved topical gel that may eliminate some actinic keratoses over a 90-day treatment period.
- **Other topical agents**: Ingenol mebutate (Picato) is a gel for topical application derived from the plant Euphorbia, which has been shown to induce cell death when treated actinic keratoses.

Your doctor will give you detailed instructions about the frequency and area of application of these drugs. The most common side effects of these topical treatments are redness, irritation and inflammation of the skin treated; This is expected and is a sign that the drug is acting in the areas damaged by the sun. Sometimes the reaction can be more severe, producing symptoms of cold, flu, or significant discomfort. If this happens please discontinue the application and contact your doctor.

Surgical Treatments for Actinic Keratoses

- **Cryotherapy:** Precancerous lesions are frozen and destroyed with liquid nitrogen.
- **Curettage and Electrodesiccation:** Precancerous lesions are scraped away with a curette, a semi-sharp, scoop-shaped instrument. The area is then cauterized with an electric needle to control bleeding and treat any remaining precancerous cells.

Laser Treatments for Actinic Keratoses

- **Photodynamic therapy (PDT):** Combines a drug (called a photosensitizer) with a specific type of light to treat precancerous cells. The photosensitizer is painted on the skin in the affected area. Then the dermatologist uses a special light box or a handheld laser light to activate the medication.
- **Resurfacing:** A laser is used to remove or destroy precancer cells.

Basal Cell and Squamous Cell Carcinoma

Medical Treatments for Basal Cell and Squamous Cell Carcinoma
- **Topical chemotherapy:** Chemotherapy agents, like 5-fluorouracil (*Efudex*), are used to treat cancerous cells. Only FDA-approved for superficial basal cell carcinoma in specific circumstances.
- **Intralesional chemotherapy:** Chemotherapy agents, like 5-fluorouracil and bleomycin, are injected into cancerous lesions. Not commonly used except for certain specific types of skin cancers.
- **Topical immunomodulators:** Creams that contain imiquimod (*Aldara*) have some success in stimulating an immune response against tumor cells. Only FDA-approved for superficial basal cell carcinoma or squamous cell carcinoma in situ in specific circumstances.

Surgical Treatments for Basal Cell and Squamous Cell Carcinoma

- **Curettage and Electrodesiccation:** Tumor cells are scraped away with a curette, a semi-sharp, scoop-shaped instrument. The area is cauterized with an electric needle to control bleeding and treat any remaining tumor cells. Only appropriate for superficial or nodular basal cell carcinoma or squamous cell carcinoma in situ in specific circumstances.
- **Surgical Excision:** Standard surgical excision cuts the cancer from the skin along with a rim of the healthy tissue around it to ensure the entire tumor is removed. Unless there are circumstances where Mohs micrographic surgery is indicated, this is the most commonly used method for excising skin cancer with 5-year cure rates of 90-95%.
- **Mohs micrographic surgery:** Mohs micrographic surgery refers to a type of highly specialized surgical technique for the removal of complex skin cancers. Mohs micrographic surgery has the highest five-year cure rates for treatment of both primary (96%) and recurrent (90%) skin cancers. The purpose of this technique is to remove all of the cancerous tissue and as little surrounding healthy tissue as possible. In addition, this method is used to remove large tumors, those in hard-to-treat places, and cancers that have recurred. The cancer is shaved off one thin layer at a time. Each layer is examined under a microscope. This process is repeated until the entire tumor is removed. This method should be used only by Mohs surgeons, dermatologists who are specially trained in this type of surgery.

Laser Treatments for Basal Cell and Squamous Cell Carcinoma

- **Photodynamic therapy (PDT):** Combines a drug (called a photosensitizer) with a specific type of light to treat cancer cells. The photosensitizer is painted on the skin in the affected area. Then the dermatologist uses a special light box or a handheld laser light to activate the medication. This is only appropriate for superficial skin cancers in specific circumstances.
- **Resurfacing:** A laser is used to remove or destroy cancer cells. Only appropriate for superficial skin cancers in specific circumstances.

Melanoma

Most melanomas are surgically removed with a layer of healthy surrounding skin. The size of the excision is based on the thickness or depth of the melanoma tumor under the microscope (determined during the biopsy).

Once a melanoma grows to a certain depth into the skin, the removal may also be done in conjunction with a diagnostic surgical technique called a sentinel lymph node biopsy. In this procedure, dye is injected into the skin at the site of the melanoma tumor, in order to identify the "sentinel" lymph nodes that "drain" that area of the skin. The sentinel lymph nodes are then removed and carefully examined for evidence of cancer. If positive, a full lymph node dissection is then usually performed. If the sentinel lymph node test is negative, there may be no need for this second, larger procedure. Typically,

patients who require a sentinel lymph node biopsy will be referred to a general surgeon for the procedure.

Treatments for more advanced melanoma are tailored to the patient, and often involve an oncologist (cancer specialist). When primary melanomas are very thick or there is lymph node involvement, a year-long treatment with an injectable agent called interferon is sometimes undertaken. For metastatic disease, orally ingested or injected chemotherapy may be used. Radiation therapy may also be used to shrink tumors.