Melanoma Skin Cancer

What is melanoma skin cancer?

Cancer starts when cells in the body begin to grow out of control. Cells in nearly any part of the body can become cancer, and can spread to other areas of the body. To learn more about how cancers start and spread, see *What Is Cancer?*

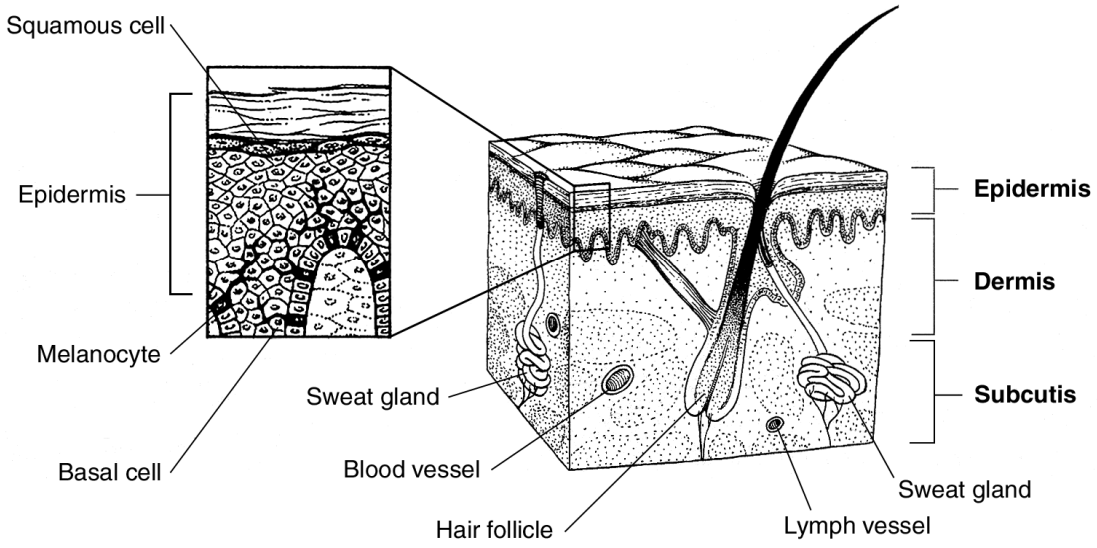
Melanoma is a cancer that starts in a certain type of skin cell. To understand melanoma, it helps to know about the normal structure and function of the skin.

Normal skin

The skin is the largest organ in your body. It does many different things, such as:

- Covering the internal organs and helping protect them from injury
- Serving as a barrier to germs such as bacteria
- Preventing the loss of too much water and other fluids
- Helping control body temperature
- Protecting the rest of the body from ultraviolet (UV) rays
- Helping the body make vitamin D

The skin has 3 layers: the epidermis, the dermis, and the subcutis (see picture).



Epidermis

This top layer of skin is very thin, averaging only about 1/100 of an inch thick. It protects the deeper layers of skin and the organs of the body from the environment.

The main types of cells in the epidermis include:

- **Squamous cells:** These are flat cells in the outer part of the epidermis that are constantly shed as new ones form.
- **Basal cells:** These cells are in the lower part of the epidermis, called the *basal cell layer*. These cells constantly divide to form new cells to replace the squamous cells that wear off the skin's surface. As these cells move up in the epidermis, they get flatter, eventually becoming squamous cells.
- **Melanocytes:** These are the cells that can become melanoma. They make a brown pigment called *melanin*, which gives the skin its tan or brown color. Melanin protects the deeper layers of the skin from some of the harmful effects of the sun. For most people, when skin is exposed to the sun, melanocytes make more of the pigment, causing the skin to tan or darken.

The epidermis is separated from the deeper layers of skin by the basement membrane. When a skin cancer becomes more advanced, it generally grows through this barrier and into the deeper layers.

Dermis

This middle layer of the skin is much thicker than the epidermis. It contains hair follicles, sweat glands, blood vessels, and nerves that are held in place by a protein called *collagen*, which gives the skin its elasticity and strength.

Subcutis

The deepest layer of the skin (the subcutis) and the lowest part of the dermis form a network of collagen and fat cells. The subcutis helps the body conserve heat and has a shock-absorbing effect that helps protect the body's organs from injury.

Benign skin tumors

Many types of benign (non-cancerous) tumors can develop from different types of skin cells.

Benign tumors that start in melanocytes

A **mole** (nevus) is a benign skin tumor that develops from melanocytes. Almost everyone has some moles. Nearly all moles (nevi) are harmless, but having some types can raise your risk of melanoma. See the section "What are the risk factors for melanoma skin cancer?" for more information about moles.

A **Spitz nevus** is a kind of mole that sometimes looks like melanoma. It is more common in children and teens, but it can also be seen in adults. These tumors are generally benign and don't spread. But sometimes doctors have trouble telling Spitz nevi from true melanomas, even when looking at them under a microscope. Therefore, they are often removed, just to be safe.

Benign tumors that develop from other types of skin cells

- **Seborrheic keratoses:** Tan, brown, or black raised spots with a "waxy" texture
- **Hemangiomas:** Benign blood vessel growths, often called strawberry spots
- **Lipomas:** Soft growths made up of fat cells
- **Warts:** Rough-surfaced growths caused by some types of human papilloma virus (HPV)

Most of these tumors rarely, if ever, turn into cancers. There are many other kinds of benign skin tumors, but most are not very common.

Melanoma skin cancers

Melanoma is a cancer that begins in the melanocytes. Other names for this cancer include *malignant melanoma* and *cutaneous melanoma*. Most melanoma cells still make melanin, so melanoma tumors are usually brown or black. But some melanomas do not make melanin and can appear pink, tan, or even white.

Melanomas can develop anywhere on the skin, but they are more likely to start on the trunk (chest and back) in men and on the legs in women. The neck and face are other common sites.

Having darkly pigmented skin lowers your risk of melanoma at these more common sites, but anyone can develop this cancer on the palms of the hands, soles of the feet, and under the nails. Melanomas in these areas account for more than half of all melanomas in African Americans but fewer than 1 in 10 melanomas in whites.

Melanomas can also form in other parts of your body such as the eyes, mouth, genitals, and anal area, but these are much less common than melanoma of the skin.

Melanoma is much less common than basal cell and squamous cell skin cancers, but it is far more dangerous. Like basal cell and squamous cell cancers, melanoma is almost always curable in its early stages. But it is much more likely than basal or squamous cell cancer to spread to other parts of the body if not caught early.

Other skin cancers

Skin cancers that are not melanomas are sometimes grouped as *non-melanoma skin cancers* because they develop from skin cells other than melanocytes. They tend to behave very differently from melanomas and are often treated with different methods.

Basal and squamous cell skin cancers

Most non-melanoma skin cancers are basal cell or squamous cell cancers. They are by far the most common skin cancers, and actually are more common than any other form of cancer. Because they rarely spread (metastasize) to other parts of the body, basal cell and squamous cell skin cancers are usually less concerning and are treated differently from melanoma. These cancers are discussed in *Skin Cancer: Basal and Squamous Cell*.

Less common skin cancers

Other types of non-melanoma skin cancer are much less common than basal and squamous cell cancers and are treated differently. They include:

- **Merkel cell carcinoma**
- **Kaposi sarcoma**
- **Cutaneous (skin) lymphoma**

- **Skin adnexal tumors** (tumors that start in hair follicles or skin glands)
- **Various types of sarcomas**

Together, these types account for less than 1% of all skin cancers.

What are the key statistics about melanoma skin cancer?

Cancer of the skin is by far the most common of all cancers. Melanoma accounts for only 1% of skin cancer cases but causes a large majority of skin cancer deaths.

Here are the American Cancer Society's estimates for melanoma in the United States for 2016:

- About 76,380 new melanomas will be diagnosed (about 46,870 in men and 29,510 in women).
- About 10,130 people are expected to die of melanoma (about 6,750 men and 3,380 women).

The rates of melanoma have been rising for at least 30 years.

Melanoma is more than 20 times more common in whites than in African Americans. Overall, the lifetime risk of getting melanoma is about 2.4% (1 in 40) for whites, 0.1% (1 in 1,000) for blacks, and 0.5% (1 in 200) for Hispanics. The risk for each person can be affected by a number of different factors, which are described in the section "What are the risk factors for melanoma skin cancer?"

The risk of melanoma increases as people age. The average age at the time it is found is 62. But melanoma is not uncommon even among those younger than 30. In fact, it is one of the most common cancers in young adults (especially young women).

For melanoma survival statistics, see the section "What are the survival rates for melanoma skin cancer, by stage?"

Visit the American Cancer Society's Cancer Statistics Center for more key statistics.

What are the risk factors for melanoma skin cancer?

A risk factor is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. Some risk factors, like smoking and excess sun exposure, can be changed. Others, like a person's age or family history, can't be changed.

But having a risk factor, or even many risk factors, does not mean that you will get the disease. And some people who get the disease may have few or no known risk factors.

Several risk factors can make a person more likely to develop melanoma.

Ultraviolet (UV) light exposure

Exposure to ultraviolet (UV) rays is a major risk factor for most melanomas. Sunlight is the main source of UV rays. Tanning beds and sun lamps are also sources of UV rays.

While UV rays make up only a very small portion of the sun's rays, they are the main cause of the damaging effects of the sun on the skin. UV rays damage the DNA of skin cells. Skin cancers begin when this damage affects the DNA of genes that control skin cell growth.

The nature of the UV exposure may play a role in melanoma development. For example, the development of melanoma on the trunk (chest and back) and legs has been linked to frequent sunburns (especially in childhood). This might also have something to do with the fact that these areas are not constantly exposed to UV light. Some experts think that melanomas that start in these areas are different from those on the face, neck, and arms, where the sun exposure is more constant. And different from either of these are melanomas that develop on the palms of the hands, soles of the feet, under the nails, or on internal surfaces such as the mouth and vagina, where there has been little or no sun exposure.

To learn more about the effects of UV rays on the skin and what you can do to protect yourself and your loved ones, see *Skin Cancer Prevention and Early Detection*.

Moles

A mole (also known as a *nevus*) is a benign (non-cancerous) pigmented tumor. Babies are not usually born with moles; they often begin to appear in children and young adults. Most moles will never cause any problems, but a person who has many moles is more likely to develop melanoma.

Atypical moles (dysplastic nevi): These moles look a little like normal moles but also have some features of melanoma. They are often larger than other moles and have an abnormal shape or color. (See the section "Signs and symptoms of melanoma skin cancer" for descriptions of how moles and melanomas look.) They can appear on skin that is exposed to the sun as well as skin that is usually covered, such as on the buttocks or scalp.

Dysplastic nevi often run in families. A small number of dysplastic nevi may develop into melanomas. But most dysplastic nevi never become cancer, and many melanomas seem to arise without a pre-existing dysplastic nevus.

Dysplastic nevus syndrome (also known as *familial atypical multiple mole melanoma syndrome*, or FAMMM): People with this inherited condition have many dysplastic nevi and at least one close relative who has had melanoma.

People with this condition have a very high lifetime risk of developing melanoma, so they need to have very thorough, regular skin exams by a dermatologist (a doctor who specializes in skin problems). In some cases, full body photos are taken to help the doctor recognize if moles are changing and growing. Many doctors recommend that these patients be taught to do monthly skin self-exams as well.

Congenital melanocytic nevi: Moles present at birth are called *congenital melanocytic nevi*. The lifetime risk of melanoma developing in congenital melanocytic nevi is estimated to be between 0 and 10%, depending on the size of the nevus. People with very large congenital nevi have a greater risk, while the risk is less for those with small nevi. For example, the risk for melanoma in congenital nevi smaller than the palm of your hand is very low, while those that cover large portions of back and buttocks ("bathing trunk nevi") have significantly higher risks.

Congenital nevi are sometimes removed by surgery so that they don't have a chance to become cancer. Whether doctors advise removing a congenital nevus depends on several factors including its size, location, and color. Many doctors recommend that congenital nevi that are not removed should be examined regularly by a dermatologist and that the patient should be taught how to do monthly skin self-exams.

Again, the chance of any single mole turning into cancer is very low. However, anyone with lots of irregular or large moles has an increased risk for melanoma.

Fair skin, freckling, and light hair

The risk of melanoma is much higher for whites than for African Americans. Whites with red or blond hair, blue or green eyes, or fair skin that freckles or burns easily are at increased risk.

Family history of melanoma

Your risk of melanoma is greater if one or more first-degree relatives (parent, brother, sister, or child) has had melanoma. Around 10% of all people with melanoma have a family history of the disease.

The increased risk might be because of a shared family lifestyle of frequent sun exposure, a family tendency to have fair skin, certain gene changes (mutations) that run in a family, or a combination of factors.

Most experts do not recommend that people with a family history of melanoma have genetic testing to look for mutations, as it's not yet clear how helpful this is. Rather, experts advise that they do the following:

- Have regular skin exams by a dermatologist
- Thoroughly examine their own skin once a month
- Be particularly careful about sun protection and avoiding artificial UV rays (such as those from tanning booths)

(For more information on genetic testing, see “Can melanoma skin cancer be prevented?”)

Personal history of melanoma or other skin cancers

A person who has already had melanoma has a higher risk of getting melanoma again. About 5% of people with melanoma will develop a second one at some point. People who have had basal or squamous cell skin cancers are also at increased risk of getting melanoma.

Weakened immune system

A person’s immune system helps fight cancers of the skin and other organs. People with weakened immune systems (from certain diseases or medical treatments) are more likely to develop many types of skin cancer, including melanoma.

For example, people who get organ transplants are usually given medicines that weaken their immune system to help prevent them from rejecting the new organ. This increases their risk of developing melanoma.

People infected with HIV, the virus that causes AIDS, often have weakened immune systems and are also at increased risk for melanoma.

Older age

Melanoma is more likely to occur in older people, but it is also found in younger people. In fact, melanoma is one of the most common cancers in people younger than 30 (especially younger women). Melanoma that runs in families may occur at a younger age.

Male gender

In the United States, men have a higher rate of melanoma than women, although this varies by age. Before age 45, the risk is higher for women; after age 45 the risk is higher in men.

Xeroderma pigmentosum

Xeroderma pigmentosum (XP) is a rare, inherited condition that affects skin cells’ ability to repair damage to their DNA. People with XP have a high risk of developing melanoma and other skin cancers when they are young, especially on sun-exposed areas of their skin.

Do we know what causes melanoma skin cancer?

Although researchers have found some things that can raise a person's risk of melanoma (see "What are the risk factors for melanoma skin cancer?"), it's not yet clear exactly how these factors cause melanoma.

For example, while most moles never turn into a melanoma, some do. Researchers have found some gene changes inside mole cells that may cause them to become melanoma cells. But it is still not known exactly why some moles become cancerous or why having many moles or atypical (dysplastic) moles increases your risk of developing melanoma.

Researchers have learned a great deal in recent years about how certain changes in DNA can make normal cells become cancerous. DNA is the chemical in each of our cells that makes up our genes – the instructions for how our cells function. We usually look like our parents because they are the source of our DNA. But DNA affects more than just how we look.

Some genes control when our cells grow, divide into new cells, and die. Certain genes that help cells grow, divide, and stay alive are called *oncogenes*. Genes that keep cell growth in check or cause cells to die at the right time are called *tumor suppressor genes*. Cancers can be caused by DNA changes that turn on oncogenes or turn off tumor suppressor genes. Changes in several different genes are usually needed for a cell to become cancerous.

Ultraviolet (UV) rays are clearly a major cause of many melanomas. UV rays can damage the DNA in skin cells. Sometimes this damage affects certain genes that control how skin cells grow and divide. If these genes no longer work properly, the affected cells may form a cancer.

Most UV rays come from sunlight, but some can come from man-made sources such as tanning beds. Usually it's not clear exactly when UV exposure causes DNA damage that might eventually lead to cancer. Some of the damage may take place in the few years before the start of the cancer. But much of it may be from exposures that happened many years earlier. Children and young adults often get a lot of intense sun exposure that might not result in cancer until many years or even decades later.

Most of the gene changes commonly seen in melanoma cells are not inherited. They are more likely the result of damage caused by sunlight. In some people, such as those with xeroderma pigmentosum (XP), the skin cells are not as able to repair damaged DNA. These people are more likely to develop melanoma.

Some melanomas occur in parts of the body that are rarely exposed to sunlight. These melanomas often have different gene changes than those in melanomas that develop in sun-exposed areas.

When melanomas run in families, gene mutations that greatly increase the risk of melanoma are often passed from one generation to the next. Familial (inherited)

melanomas most often have changes in tumor suppressor genes such as *CDKN2A* (also known as *p16*) and *CDK4* that prevent them from doing their normal job of controlling cell growth. Scientists reason that this could eventually lead to cancer.

Many other gene changes have been found in melanoma cells as well. Some of these have proven to be good targets for drugs to help treat this disease. For example, about half of all melanomas have a change (mutation) in the *BRAF* oncogene that helps drive their growth. This change is not inherited. It seems to occur during the development of the melanoma. Several drugs that specifically target cells with this gene change are now used to treat these melanomas (see the section "Targeted therapy for melanoma skin cancer").

Can melanoma skin cancer be prevented?

Not all melanomas can be prevented, but there are things you can do that could reduce your risk of getting melanoma and other skin cancers.

Limit your exposure to ultraviolet (UV) rays

The most important way to lower your risk of melanoma is to protect yourself from exposure to UV rays. Practice sun safety when you are outdoors.

Seek shade

Simply staying in the shade is one of the best ways to limit your UV exposure.

"Slip! Slop! Slap!®… and Wrap"

If you are going to be in the sun, this catchphrase can help you remember some of the key steps you can take to protect yourself from UV rays:

- Slip on a shirt.
- Slop on sunscreen.
- Slap on a hat.
- Wrap on sunglasses to protect the eyes and sensitive skin around them.

Avoid tanning beds and sunlamps

Many people believe the UV rays of tanning beds are harmless. This is not true. Tanning lamps give out UV rays, which can cause long-term skin damage and can contribute to skin cancer. Tanning bed use has been linked with an increased risk of melanoma, especially if it is started before a person is 30. Most dermatologists (skin doctors) and health organizations recommend not using tanning beds and sun lamps.

Protect children from the sun

Children need special attention, since they tend to spend more time outdoors and can burn more easily. Parents and other caregivers should protect children from excess sun exposure by using the steps above. Children need to be taught about the dangers of too much sun exposure as they become more independent.

To learn more about sun safety

For more information on how to protect yourself and your family from UV exposure, see our document *Skin Cancer: Prevention and Early Detection*.

Watch for abnormal moles

Checking your skin regularly may help you spot any new or abnormal moles or other growths and show them to your doctor before they even have a chance to turn into skin cancer.

Certain types of moles are more likely to develop into melanoma (see the section “What are the risk factors for melanoma skin cancer?”). If you have moles, depending on how they look, your doctor may want to watch them closely with regular exams or may remove some of them if they have certain features that suggest they might change into a melanoma.

Routine removal of many moles is not usually recommended as a way to prevent melanoma. Some melanomas may develop from moles, but most do not. If you have many moles, getting careful, routine exams by a dermatologist, along with doing monthly skin self-exams, might be recommended.

If you find a new, unusual, or changing mole, you should have it checked by a doctor experienced in recognizing skin cancers. See the section “Signs and symptoms of melanoma skin cancer” for descriptions of what to look for.

Genetic counseling and testing for people at high risk

Gene mutations (changes) that increase melanoma risk can be passed down through families, but they account for only a small portion of melanomas. You *might* have inherited a gene mutation that increases your risk of melanoma if any of the following apply:

- Several members of one side of your family have had melanoma
- A family member has had more than one melanoma
- A family member has had both melanoma and pancreatic cancer
- You have had more than one melanoma

Some families with high rates of melanoma have mutations in genes such as *CDKN2A* (also known as *p16*). Tests for these gene changes are now available, although they are not widely recommended by doctors at this time. People interested in learning whether they carry gene changes linked to melanoma may want to think about taking part in genetic research that will advance progress in this field.

It is very important to meet with a genetic counselor before deciding if you should have testing. The counselor can describe the tests to you and explain what the results may or may not tell you about your risk. Genetic testing is not perfect, and in some cases the tests may not provide solid answers. To learn more about genetic testing in general, see *Genetic Testing: What You Need to Know*.

At this time, because it's not clear how useful the test results might be, most melanoma experts don't recommend genetic testing for people with a personal or family history of melanoma. Still, some people may choose to get tested. In any event, people with a family history of melanoma should ask their doctor about getting regular skin exams, learning to do skin self-exams, and being particularly careful about sun safety.

Can melanoma skin cancer be found early?

Melanoma can often be found early. Everyone can play an important role in finding skin cancer early, when it is most likely to be cured.

Skin self-exam

It's important to check your own skin, preferably once a month. You should know the pattern of moles, blemishes, freckles, and other marks on your skin so that you'll notice any new moles or changes in existing moles.

Self-exam is best done in a well-lit room in front of a full-length mirror. Use a hand-held mirror to help look at areas that are hard to see, such as the backs of your thighs. Examine all areas, including your palms and soles, scalp, ears, nails, and your back (in men, about 1 of every 3 melanomas occurs on the back). Friends and family members can also help you with these exams, especially for those hard-to-see areas, such as your scalp and back.

For a more thorough description of how to do a skin self-exam, see *Skin Cancer Prevention and Early Detection* and *Why You Should Know About Melanoma*, or visit our Skin Self-exam Image Gallery.

See the section "Signs and symptoms of melanoma skin cancer" to know what to look for when examining your skin.

Be sure to show your doctor any areas that concern you, and ask your doctor to look at areas that may be hard for you to see.

Exam by a health care professional

As part of a routine cancer-related checkup, your doctor or other health care professional should check your skin carefully. He or she should be willing to discuss any concerns you might have about this exam.

If your primary doctor finds any unusual moles or other suspicious areas, he or she may refer you to a dermatologist, a doctor who specializes in skin problems. Dermatologists can also do regular skin exams. Many dermatologists use a technique called *dermatoscopy* (also known as *dermoscopy*, *epiluminescence microscopy [ELM], or surface microscopy*) to look at spots on the skin more clearly. A digital or photographic image of the spot may be taken. (See the section “How is melanoma skin cancer diagnosed?” for more information.)

Regular skin exams are especially important for people who are at higher risk of melanoma, such as people with dysplastic nevus syndrome, people with a strong family history of melanoma, and people who have had melanoma before. If you have many moles, your doctor might advise taking full-body photos so your moles can be tracked over time and new ones can be seen more readily. (This is sometimes called *total body photography* or *mole mapping*.) Talk to your doctor about how often you should have your skin examined.

Signs and symptoms of melanoma skin cancer

Unusual moles, sores, lumps, blemishes, markings, or changes in the way an area of the skin looks or feels may be a sign of melanoma or another type of skin cancer, or a warning that it might occur.

Normal moles

A normal mole is usually an evenly colored brown, tan, or black spot on the skin. It can be either flat or raised. It can be round or oval. Moles are generally less than 6 millimeters (about ¼ inch) across (about the width of a pencil eraser). Some moles can be present at birth, but most appear during childhood or young adulthood. New moles that appear later in life should be checked by a doctor.

Once a mole has developed, it will usually stay the same size, shape, and color for many years. Some moles may eventually fade away.

Most people have moles, and almost all moles are harmless. But it is important to recognize changes in a mole – such as in its size, shape, or color – that can suggest a melanoma may be developing.

Possible signs and symptoms of melanoma

The most important warning sign for melanoma is a new spot on the skin or a spot that is changing in size, shape, or color. Another important sign is a spot that looks different from all of the other spots on your skin (known as the *ugly duckling sign*). If you have any of these warning signs, have your skin checked by a doctor.

The **ABCDE** rule is another guide to the usual signs of melanoma. Be on the lookout and tell your doctor about spots that have any of the following features:

- **A is for Asymmetry:** One half of a mole or birthmark does not match the other.
- **B is for Border:** The edges are irregular, ragged, notched, or blurred.
- **C is for Color:** The color is not the same all over and may include shades of brown or black, or sometimes with patches of pink, red, white, or blue.
- **D is for Diameter:** The spot is larger than 6 millimeters across (about ¼ inch – the size of a pencil eraser), although melanomas can sometimes be smaller than this.
- **E is for Evolving:** The mole is changing in size, shape, or color.

Some melanomas do not fit the rules described above. It is important to tell your doctor about any changes or new spots on the skin, or growths that look different from the rest of your moles.

Other warning signs are:

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

Be sure to show your doctor any areas that concern you and ask your doctor to look at areas that may be hard for you to see. It is sometimes hard to tell the difference between melanoma and an ordinary mole, even for doctors, so it’s important to show your doctor any mole that you are unsure of.

To see examples of normal moles and melanomas, visit our Skin Cancer Image Gallery.

How is melanoma skin cancer diagnosed?

Most melanomas are brought to a doctor’s attention because of signs or symptoms a person is having.

If an abnormal area of skin raises the suspicion of skin cancer, your doctor will do exams and tests to find out if it is melanoma, non-melanoma skin cancer, or some other skin condition. If melanoma is found, other tests may be done to determine if it has spread to other areas of the body.

Medical history and physical exam

Usually the first step your doctor takes is to get your medical history. The doctor will probably ask when the change on the skin first appeared, if it has changed in size or appearance, and if it is causing any symptoms (pain, itching, bleeding, etc.). You may also be asked about possible risk factors for skin cancer, such as your history of tanning and sunburns, and if you or anyone in your family has had skin cancer.

During the physical exam, your doctor will note the size, shape, color, and texture of the area(s) in question, and whether they are bleeding, oozing, or crusting. The rest of your body may be checked for moles and other spots that could be related to skin cancer.

The doctor may also feel the lymph nodes (small, bean-sized collections of immune cells) under the skin in the neck, underarm, or groin near the abnormal area. When melanoma spreads, it often goes to nearby lymph nodes first, making them larger. Enlarged lymph nodes might suggest that melanoma could have spread there.

If your primary doctor suspects melanoma, you may be referred to a dermatologist, a doctor who specializes in skin diseases, who will look at the area more closely.

Along with a standard physical exam, many dermatologists use a technique called *dermatoscopy* (also known as *dermoscopy, epiluminescence microscopy [ELM], or surface microscopy*) to see spots on the skin more clearly. The doctor uses a dermatoscope, which is a special magnifying lens and light source held near the skin. Sometimes a thin layer of alcohol or oil is used with this instrument. The doctor may take a digital photo of the spot.

When used by an experienced dermatologist, this test can improve the accuracy of finding skin cancers early. It can also often help reassure you that a spot on the skin is probably benign (non-cancerous) and doesn’t need a biopsy.

Skin biopsy

If the doctor thinks a spot might be a melanoma, a sample of skin will be removed from the suspicious area and sent to a lab to be looked at under a microscope. This is called a *skin biopsy*.

There are many ways to do a skin biopsy. The doctor will choose one based on the size of the affected area, where it is on your body, and other factors. Any biopsy is likely to leave at least a small scar. Different methods can result in different types of scars, so ask your doctor about scarring before the biopsy. No matter which type of biopsy is done, it should remove as much of the suspected area as possible so that an accurate diagnosis can be made.

Skin biopsies are done using a local anesthetic (numbing medicine), which is injected into the area with a very small needle. You will likely feel a small prick and a little stinging as the medicine is injected, but you should not feel any pain during the biopsy.

Shave (tangential) biopsy

For this type of biopsy, the doctor shaves off the top layers of the skin with a small surgical blade. Usually just the epidermis and the outer part of the dermis are removed, although deeper layers can be taken as well if needed. Bleeding from the biopsy site is stopped by applying an ointment, a chemical that stops bleeding, or a small electrical current to cauterize the wound.

A shave biopsy is useful in diagnosing many types of skin diseases and in sampling moles when the risk of melanoma is very low. This type of biopsy is not generally recommended if a melanoma is strongly suspected unless the biopsy blade will go deep enough to get below the suspicious area. Otherwise, if it is a melanoma, the biopsy sample may not be thick enough to measure how deeply the cancer has invaded the skin.

Punch biopsy

For a punch biopsy, the doctor uses a tool that looks like a tiny round cookie cutter to remove a deeper sample of skin. The doctor rotates the punch biopsy tool on the skin until it cuts through all the layers, including the dermis, epidermis, and the upper parts of the subcutis. The sample is removed and the edges of the biopsy site are often stitched together.

Incisional and excisional biopsies

To examine a tumor that might have grown into deeper layers of the skin, the doctor may use an incisional or excisional biopsy. For these types of biopsies, a surgical knife is used to cut through the full thickness of skin. A wedge or sliver of skin is removed for examination, and the edges of the cut are usually stitched together.

An incisional biopsy removes only a portion of the tumor. An excisional biopsy removes the entire tumor, and is usually the preferred method of biopsy for suspected melanomas if it can be done. But it is not always possible, so other types of biopsies may be needed.

Biopsies of melanoma that may have spread

Biopsies of areas other than the skin may be needed in some cases. For example, if melanoma has already been diagnosed on the skin, nearby lymph nodes may be biopsied to see if the cancer has spread to them.

Rarely, biopsies may be needed to figure out what type of cancer someone has. For example, some melanomas can spread so quickly that they reach the lymph nodes, lungs, brain, or other areas while the original skin melanoma is still very small. Sometimes these tumors are found with imaging tests (such as CT scans) or other exams even before the

melanoma on the skin is discovered. In other cases they may be found long after a skin melanoma has been removed, so it's not clear if it's the same cancer.

In still other cases, melanoma may be found somewhere in the body without ever finding a spot on the skin. This may be because some skin lesions go away on their own (without any treatment) after some of their cells have spread to other parts of the body. Melanoma can also start in internal organs, but this is very rare, and if melanoma has spread widely throughout the body, it may not be possible to tell exactly where it started.

When melanoma has spread to other organs, it can sometimes be confused with a cancer starting in that organ. For example, melanoma that has spread to the lung might be confused with a primary lung cancer (cancer that starts in the lung).

Special lab tests can be done on the biopsy samples that can tell whether it is a melanoma or some other kind of cancer. This is important because different types of cancer are treated differently.

Biopsies of suspicious areas inside the body often are more involved than those used to sample the skin.

Fine needle aspiration biopsy

A fine needle aspiration (FNA) biopsy is not used on suspicious moles. But it may be used, for example, to biopsy large lymph nodes near a melanoma to find out if the melanoma has spread to them. For this type of biopsy, the doctor uses a syringe with a thin, hollow needle to remove very small pieces of a lymph node or tumor. The needle is smaller than the needle used for a blood test. A local anesthetic is sometimes used to numb the area first. This test rarely causes much discomfort and does not leave a scar.

If the lymph node is just under the skin, the doctor can often feel it well enough to guide the needle into it. For a suspicious lymph node deeper in the body or a tumor in an organ such as the lung or liver, an imaging test such as ultrasound or a CT scan is often used to help guide the needle into place.

FNA biopsies are not as invasive as some other types of biopsies, but they may not always collect enough of a sample to tell if a suspicious area is melanoma. In these cases, a more invasive type of biopsy may be needed.

Surgical (excisional) lymph node biopsy

This procedure can be used to remove an enlarged lymph node through a small incision (cut) in the skin. A local anesthetic (numbing medicine) is generally used if the lymph node is near the surface of the body, but the person may need to be sedated or even asleep (using general anesthesia) if the lymph node is deeper in the body.

This type of biopsy is often done if a lymph node's size suggests the melanoma has spread but an FNA biopsy of the node was not done or did not find any melanoma cells.

Sentinel lymph node biopsy

If melanoma has been diagnosed and has any concerning features (such as being at least a certain thickness), a sentinel lymph node biopsy is often done to see if it has spread to nearby lymph nodes, which in turn might affect treatment options. This test can be used to find the lymph nodes that are likely to be the first place the melanoma would go if it has spread. These lymph nodes are called *sentinel nodes* (they stand sentinel, or watch, over the tumor, so to speak).

To find the sentinel lymph node (or nodes), a nuclear medicine doctor injects a small amount of a radioactive substance into the area of the melanoma. After the substance has travelled to the lymph node areas near the tumor, a special camera is used to see if the radioactive substance collects in one or more sentinel lymph nodes. Once the radioactive area has been marked, the patient is taken to where the surgery will be done and a blue dye is injected in the same place as the radioactive substance. A small incision is then made where the nuclear medicine doctor has marked, and the lymph nodes are then checked to find which one(s) became radioactive and turned blue. These sentinel nodes are removed and looked at under a microscope.

If there are no melanoma cells in the sentinel nodes, no more lymph node surgery is needed because it is very unlikely the melanoma would have spread beyond this point. If melanoma cells are found in the sentinel node, the remaining lymph nodes in this area are removed and looked at as well. This is known as a *lymph node dissection* (see “Surgery for melanoma skin cancer”).

If a lymph node near a melanoma is abnormally large, a sentinel node biopsy probably won’t be needed. The enlarged node is simply biopsied.

Lab tests of biopsy samples

Samples from any biopsies will be sent to a lab, where a doctor called a *pathologist* will look at them under a microscope for melanoma cells. Often, skin samples are sent to a dermatopathologist, a doctor who has special training in making diagnoses from skin samples.

If the doctor can’t tell for sure if melanoma cells are in the sample just by looking at it, special tests will be done on the cells to try to confirm the diagnosis. These tests have names such as *immunohistochemistry* (IHC), *fluorescence in situ hybridization* (FISH), and *comparative genomic hybridization* (CGH).

If the samples do contain melanoma, the pathologist will look at certain important features such as the tumor thickness and mitotic rate (the portion of cells that are actively dividing). These features help determine the stage of the melanoma (see the section “How is melanoma of the skin staged?”), which in turn affects treatment options and prognosis (outlook).

For people who have advanced melanoma, biopsy samples may be tested to see if the cells have mutations in certain genes, such as the *BRAF* gene. About half of melanomas

have *BRAF* mutations. Some newer drugs used to treat advanced melanomas are only likely to work if the cells have *BRAF* mutations (see "Targeted therapy for melanoma skin cancer"), so this test is important in helping to determine treatment options.

Imaging tests

Imaging tests use x-rays, magnetic fields, or radioactive substances to create pictures of the inside of the body. They are used mainly to look for the possible spread of melanoma to lymph nodes or other organs in the body. They are not needed for people with very early-stage melanoma, which is very unlikely to have spread.

Imaging tests can also be done to help determine how well treatment is working or to look for possible signs of cancer coming back (recurring) after treatment.

Chest x-ray

This test may be done to help determine whether melanoma has spread to the lungs.

Computed tomography (CT) scan

The CT scan uses x-rays to make detailed, cross-sectional images of your body. Unlike a regular x-ray, CT scans can show the detail in soft tissues (such as internal organs). This test can help tell if any lymph nodes are enlarged or if organs such as the lungs or liver have suspicious spots, which might be due to the spread of melanoma. It can also help show spread to the lungs better than a standard chest x-ray.

Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around you while you lie on a table. A computer then combines these pictures into detailed images of the part of your body that is being studied.

Before the scan, you may be asked to drink a contrast solution and/or get an intravenous (IV) injection of a contrast dye that helps better outline normal and abnormal areas in the body. You may need an IV line through which the contrast dye is injected. The injection can cause some flushing (a feeling of warmth, especially in the face). Some people are allergic and get hives or, rarely, more serious reactions like trouble breathing and low blood pressure. Be sure to tell the doctor if you have any allergies (especially to iodine or shellfish) or have ever had a reaction to any contrast material used for x-rays.

A CT scanner has been described as a large donut, with a narrow table that slides in and out of the middle opening. You need to lie still on the table while the scan is being done. CT scans take longer than regular x-rays, and you might feel a bit confined by the ring while the pictures are being taken.

CT-guided needle biopsy: CT scans can also be used to help guide a biopsy needle into a suspicious area within the body. For this procedure, you stay on the CT scanning table while the doctor moves a biopsy needle through the skin and toward the suspicious area. CT scans are repeated until the needle is in the mass. A needle biopsy sample is then removed and looked at under a microscope.

Magnetic resonance imaging (MRI) scan

Like CT scans, MRI scans give detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of x-rays to create pictures. A contrast material might be injected, just as with CT scans, but is used less often.

MRI scans are very helpful in looking at the brain and spinal cord.

MRI scans take longer than CT scans – often up to an hour – and are a little more uncomfortable. You may have to lie inside a narrow tube, which is confining and can upset people with a fear of enclosed spaces. Newer, more open MRI machines can sometimes be used instead, but the images might not be as sharp in some cases. The MRI machine also makes loud buzzing noises, so some places provide earplugs to help block this noise out.

Positron emission tomography (PET) scan

A PET scan can help show if the cancer has spread to lymph nodes or other parts of the body. It is most useful in people with more advanced stages of melanoma – it is not usually done in people with early-stage melanoma.

For this test, you are injected with a radioactive substance (usually a type of sugar related to glucose, known as *FDG*). The amount of radioactivity used is very low and will pass out of the body over the next day or so. Because cancer cells in the body are growing quickly, they absorb more of the radioactive sugar. After about an hour, you are moved onto a table in the PET scanner. You lie on the table for about 30 minutes while a special camera creates a picture of areas of radioactivity in the body. The picture is not detailed like a CT or MRI scan, but it can provide helpful information about your whole body.

Many centers have special machines that can do both a PET and CT scan at the same time (PET/CT scan). This lets the doctor compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT scan.

For more information on these imaging tests, see our document *Imaging (Radiology) Tests*.

Blood tests

Blood tests aren’t used to diagnose melanoma, but some tests may be done before or during treatment, especially for more advanced melanomas.

Doctors often test blood for levels of a substance called lactate dehydrogenase (LDH) before treatment. If the melanoma has spread to distant parts of the body, a high LDH level is a sign that the cancer may be harder to treat. This affects the stage of the cancer (see “How is melanoma skin cancer staged?”).

Other tests of blood cell counts and blood chemistry levels may be done in a person who has advanced melanoma to see how well the bone marrow (where new blood cells are made), liver, and kidneys are working during treatment.

How is melanoma skin cancer staged?

The stage of a cancer is a description of how widespread it is. For melanoma, this includes its thickness in the skin, whether it has spread to nearby lymph nodes or any other organs, and certain other factors. The stage is based on the results of physical exams, biopsies, and any imaging tests (CT or MRI scan, etc.) or other tests that have been done. These tests are described in the section "How is melanoma skin cancer diagnosed?"

The stage of the melanoma is very important in planning your treatment and estimating your prognosis (outlook).

The American Joint Committee on Cancer (AJCC) TNM staging system

A staging system is a standard way to describe how far a cancer has spread. The system most often used to stage melanoma is the American Joint Commission on Cancer (AJCC) TNM system. It can be complicated, so ask your doctor if you have any questions about the stage of your cancer. The TNM system is based on 3 key pieces of information:

- **T** stands for **tumor** (how far it has grown within the skin and other factors). The T category is assigned a number (from 0 to 4) based on the tumor's thickness (how far down it has grown). It may also be assigned a small letter a or b based on ulceration and mitotic rate, which are explained below.

- **N** stands for spread to nearby **lymph nodes** (bean-sized collections of immune system cells, to which cancers often spread first). The N category is assigned a number (from 0 to 3) based on whether the melanoma cells have spread to lymph nodes or are found in the lymphatic channels connecting the lymph nodes. It may also be assigned a small letter a, b, or c, as described below.

- The **M** category is based on whether the melanoma has **metastasized** (spread) to distant organs, which organs it has reached, and on blood levels of a substance called LDH.

There are 2 types of staging for melanoma:

- *Clinical staging* is based on what is found on physical exams, biopsy/removal of the main melanoma, and any imaging tests that are done.

- *Pathologic staging* uses all of this information, plus what is found during biopsies of lymph nodes or other organs if they are done.

The pathologic stage (determined after the lymph node biopsy) may actually be higher than the clinical stage (determined before the lymph node biopsy) if the biopsy finds cancer in new areas. Doctors use the pathologic stage if it is available, as it gives a more accurate picture of the extent of the cancer, but in many cases lymph node biopsies are not needed.

T categories

The T category is based on the thickness of the melanoma and other key factors seen in the skin biopsy.

Tumor thickness: The pathologist looking at the skin biopsy measures the thickness of the melanoma under the microscope. This is called the *Breslow measurement*. In general, melanomas less than 1 millimeter (mm) thick (about 1/25 of an inch) have a very small chance of spreading. As the melanoma becomes thicker, it has a greater chance of spreading.

Mitotic rate: To measure the mitotic rate, the pathologist counts the number of cells in the process of dividing (mitosis) in a certain amount of melanoma tissue. A higher mitotic rate (having more cells that are dividing) means that the cancer is more likely to grow and spread. The mitotic rate is used to help stage thin melanomas (T1; see below).

Ulceration: Ulceration is a breakdown of the skin over the melanoma. Melanomas that are ulcerated tend to have a worse prognosis.

The possible values for T are:

TX: Primary (main) tumor cannot be assessed.

T0: No evidence of primary tumor.

Tis: Melanoma in situ. (The tumor remains in the epidermis, the outermost layer of skin.)

T1a: The melanoma is less than or equal to 1.0 mm thick (1.0 mm = 1/25 of an inch), without ulceration and with a mitotic rate of less than $1/mm^2$.

T1b: The melanoma is less than or equal to 1.0 mm thick. It is ulcerated and/or the mitotic rate is equal to or greater than $1/mm^2$.

T2a: The melanoma is between 1.01 and 2.0 mm thick without ulceration.

T2b: The melanoma is between 1.01 and 2.0 mm thick with ulceration.

T3a: The melanoma is between 2.01 and 4.0 mm thick without ulceration.

T3b: The melanoma is between 2.01 and 4.0 mm thick with ulceration.

T4a: The melanoma is thicker than 4.0 mm without ulceration.

T4b: The melanoma is thicker than 4.0 mm with ulceration.

N categories

The possible values for N depend on whether or not a sentinel lymph node biopsy was done.

The *clinical staging* of the lymph nodes, which is done without the sentinel node biopsy, is listed below.

NX: Nearby (regional) lymph nodes cannot be assessed.

N0: No spread to nearby lymph nodes.

N1: Spread to 1 nearby lymph node.

N2: Spread to 2 or 3 nearby lymph nodes, OR spread of melanoma to nearby skin (known as *satellite tumors*) or toward a nearby lymph node area (known as *in-transit tumors*) without reaching the lymph nodes.

N3: Spread to 4 or more lymph nodes, OR spread to lymph nodes that are clumped together, OR spread of melanoma to nearby skin (satellite tumors) or toward a lymph node area and into the lymph node(s).

Following a lymph node biopsy, the *pathologic stage* can be determined, in which small letters may be added in some cases:

- Any Na (N1a or N2a) means that the melanoma is in the lymph node(s), but it is so small that it is only seen under the microscope (also known as *microscopic* spread).
- Any Nb (N1b or N2b) means that the melanoma is in the lymph node(s) and was large enough to be visible on imaging tests or felt by the doctor before it was removed (also known as *macroscopic* spread).
- N2c means the melanoma has spread to very small areas of nearby skin (satellite tumors) or has spread to skin lymphatic channels around the tumor (without reaching the lymph nodes).

M categories

The M values are:

M0: No distant metastasis.

M1a: Metastasis to skin, subcutaneous (below the skin) tissue, or lymph nodes in distant parts of the body, with a normal blood LDH level.

M1b: Metastasis to the lungs, with a normal blood LDH level.

M1c: Metastasis to any other organs, OR distant spread to any site along with an elevated blood LDH level.

Stage grouping

Once the T, N, and M groups have been determined, they are combined to give an overall stage, using Roman numerals I to IV (1 to 4) and sometimes subdivided using capital letters. This process is called *stage grouping*. In general, patients with lower stage cancers have a better outlook for a cure or long-term survival.

Stage 0

Tis, N0, M0: The melanoma is in situ, meaning that it is in the epidermis but has not spread to the dermis (lower layer).

Stage IA

T1a, N0, M0: The melanoma is less than 1.0 mm in thickness. It is not ulcerated and has a mitotic rate of less than 1/mm^2. It has not been found in lymph nodes or distant organs.

Stage IB

T1b or T2a, N0, M0: The melanoma is less than 1.0 mm in thickness and is ulcerated or has a mitotic rate of at least 1/mm^2, OR it is between 1.01 and 2.0 mm and is not ulcerated. It has not been found in lymph nodes or distant organs.

Stage IIA

T2b or T3a, N0, M0: The melanoma is between 1.01 mm and 2.0 mm in thickness and is ulcerated, OR it is between 2.01 and 4.0 mm and is not ulcerated. It has not been found in lymph nodes or distant organs.

Stage IIB

T3b or T4a, N0, M0: The melanoma is between 2.01 mm and 4.0 mm in thickness and is ulcerated, OR it is thicker than 4.0 mm and is not ulcerated. It has not been found in lymph nodes or distant organs.

Stage IIC

T4b, N0, M0: The melanoma is thicker than 4.0 mm and is ulcerated. It has not been found in lymph nodes or distant organs.

Stage IIIA

T1a to T4a, N1a or N2a, M0: The melanoma can be any thickness, but it is not ulcerated. It has spread to 1 to 3 lymph nodes near the affected skin area, but the nodes are not enlarged and the melanoma is found only when they are viewed under the microscope. There is no distant spread.

Stage IIIB

One of the following applies:

T1b to T4b, N1a or N2a, M0: The melanoma can be any thickness and is ulcerated. It has spread to 1 to 3 lymph nodes near the affected skin area, but the nodes are not enlarged and the melanoma is found only when they are viewed under the microscope. There is no distant spread.

T1a to T4a, N1b or N2b, M0: The melanoma can be any thickness, but it is not ulcerated. It has spread to 1 to 3 lymph nodes near the affected skin area. The nodes are enlarged because of the melanoma. There is no distant spread.

T1a to T4a, N2c, M0: The melanoma can be any thickness, but it is not ulcerated. It has spread to small areas of nearby skin (satellite tumors) or lymphatic channels (in-transit tumors) around the original tumor, but the nodes do not contain melanoma. There is no distant spread.

Stage IIIC

One of the following applies:

T1b to T4b, N1b or N2b, M0: The melanoma can be any thickness and is ulcerated. It has spread to 1 to 3 lymph nodes near the affected skin area. The nodes are enlarged because of the melanoma. There is no distant spread.

T1b to T4b, N2c, M0: The melanoma can be any thickness and is ulcerated. It has spread to small areas of nearby skin (satellite tumors) or lymphatic channels (in-transit tumors) around the original tumor, but the nodes do not contain melanoma. There is no distant spread.

Any T, N3, M0: The melanoma can be any thickness and may or may not be ulcerated. It has spread to 4 or more nearby lymph nodes, OR to nearby lymph nodes that are clumped together, OR it has spread to nearby skin (satellite tumors) or lymphatic channels (in transit tumors) around the original tumor and to nearby lymph nodes. The nodes are enlarged because of the melanoma. There is no distant spread.

Stage IV

Any T, any N, M1(a, b, or c): The melanoma has spread beyond the original area of skin and nearby lymph nodes to other organs such as the lung, liver, or brain, or to distant areas of the skin, subcutaneous tissue, or distant lymph nodes. Neither spread to nearby lymph nodes nor thickness is considered in this stage, but typically the melanoma is thick and has also spread to the lymph nodes.

What are the survival rates for melanoma skin cancer, by stage?

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some people may want to know the survival statistics for people in similar situations, while others may not find the numbers helpful, or may even not want to know them. If you don't want to know them, stop reading here and skip to the next section.

The 5-year and 10-year survival rates refer to the percentage of patients who live *at least* this long after their cancer is diagnosed. Of course, many people live much longer than 5 or 10 years (and many are cured).

To get 5- and 10-year survival rates, doctors have to look at people who were treated at least 5 or 10 years ago. Improvements in treatment since then may result in a better outlook for people being diagnosed with melanoma now.

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they can't predict what will happen in any person's case. Many factors other than the stage of the melanoma can also affect a person's outlook, such as the genetic changes in the cancer cells and how well the cancer responds to treatment. Even when taking these other factors into account, survival rates are at best rough estimates. Your doctor can tell you how the numbers below apply to you, as he or she knows your situation best.

The following survival rates are based on nearly 60,000 patients who were part of the 2008 AJCC Melanoma Staging Database. These are *observed* survival rates. They include some people diagnosed with melanoma who may have later died from other causes, such as heart disease. Therefore, the percentage of people surviving the melanoma itself may be higher.

Stage IA: The 5-year survival rate is around 97%. The 10-year survival is around 95%.

Stage IB: The 5-year survival rate is around 92%. The 10-year survival is around 86%.

Stage IIA: The 5-year survival rate is around 81%. The 10-year survival is around 67%.

Stage IIB: The 5-year survival rate is around 70%. The 10-year survival is around 57%.

Stage IIC: The 5-year survival rate is around 53%. The 10-year survival is around 40%.

Stage IIIA: The 5-year survival rate is around 78%. The 10-year survival is around 68%.*

Stage IIIB: The 5-year survival rate is around 59%. The 10-year survival is around 43%.

Stage IIIC: The 5-year survival rate is around 40%. The 10-year survival is around 24%.

Stage IV: The 5-year survival rate is about 15% to 20%. The 10-year survival is about 10% to 15%. The outlook is better if the spread is only to distant parts of the skin or distant lymph nodes rather than to other organs, and if the blood level of lactate dehydrogenase (LDH) is normal.

**The survival rate is higher for stage IIIA cancers than for some stage II cancers. This is likely because the main (primary) tumor is often less advanced for IIIA cancers, although this is not clear.*

Other factors affecting survival

Other factors aside from stage can also affect survival. For example:

- Older people generally have shorter survival times, regardless of stage. The biggest drop in survival begins at age 70.
- Melanoma is uncommon among African Americans, but when it does occur, survival times tend to be shorter than when it occurs in whites. Some studies have found that melanoma tends to be more serious if it occurs on the sole of the foot or palm of the

hand, or if it is in a nail bed. (Cancers in these areas make up a larger portion of melanomas in African Americans than in whites.)

- People with melanoma who have weakened immune systems, such as people who have had organ transplants or who are infected with HIV, also are at greater risk of dying of their melanoma.

How is melanoma skin cancer treated?

General treatment information

Once melanoma has been diagnosed and staged, your cancer care team will discuss your treatment options with you. Depending on your situation, you may have different types of doctors on your treatment team. These doctors may include:

- A **dermatologist**: A doctor who treats diseases of the skin
- A **surgical oncologist** (or oncologic surgeon): A doctor who uses surgery to treat cancer
- A **medical oncologist**: A doctor who treats cancer with medicines such as chemotherapy, immunotherapy, or targeted therapy
- A **radiation oncologist**: A doctor who treats cancer with radiation therapy

Many other specialists might be part of your treatment team as well, including physician assistants (PAs), nurse practitioners (NPs), nurses, nutrition specialists, social workers, and other health professionals. To learn more about who may be on your cancer care team, see *Health Professionals Associated With Cancer Care*.

It's important to discuss all of your treatment options as well as their possible side effects with your treatment team to help make the decision that best fits your needs. If there is anything you do not understand, ask to have it explained. (See the section "What should you ask your doctor about melanoma skin cancer?" for some questions to ask.)

Based on the stage of the cancer and other factors, your treatment options might include:

- Surgery
- Immunotherapy
- Targeted therapy
- Chemotherapy
- Radiation therapy

Early-stage melanomas can often be treated effectively with surgery alone, but more advanced cancers often require other treatments. Sometimes more than one type of

treatment is used. Follow this link to learn more about the most common treatment options based on the stage of the melanoma.

When time permits, getting a second opinion is often a good idea. It can give you more information and help you feel good about the treatment plan that you choose.

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-of-the art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service at 1-800-303-5691 for a list of studies that meet your medical needs, or see *Clinical Trials* to learn more.

Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn't mentioned to treat your cancer or relieve symptoms. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods refer to treatments that are used along with your regular medical care. Alternative treatments are used instead of a doctor's medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be dangerous.

Be sure to talk to your cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision. See *Complementary and Alternative Medicine* to learn more.

Help getting through cancer treatment

Your cancer care team will be your first source of information and support, but there are other resources for help when you need it. Hospital- or clinic-based support services are an important part of your care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services – including rides to treatment, lodging, support groups, and more – to help you get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our trained specialists on call 24 hours a day, every day.

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

Surgery for melanoma skin cancer

Surgery is the main treatment option for most melanomas, and usually cures early stage melanomas.

Wide excision

When a diagnosis of melanoma is made by skin biopsy, the site will probably need to be excised again to help make sure the cancer has been removed completely. This fairly minor surgery will cure most thin melanomas.

Local anesthesia is injected into the area to numb it before the excision. The site of the tumor is then cut out, along with a small amount of normal non-cancerous skin at the edges. The normal, healthy skin around the edges of the cancer is referred to as the *margin*. The wound is carefully stitched back together afterward. This will leave a scar.

The removed sample is then viewed under a microscope to make sure that no cancer cells were left behind at the edges of the skin that was removed.

Wide excision differs from an excisional biopsy. The margins are wider because the diagnosis is already known. The recommended margins vary depending on the thickness of the tumor. Thicker tumors need larger margins (both at the edges and in the depth of the excision).

Tumor thickness	**Recommended margins**
In situ	0.5 cm
1 mm (about 1/25 of an inch) or less	1 cm
1 to 2 mm	1 to 2 cm
2 to 4 mm	2 cm
Over 4 mm	2 cm

These margins might need to be altered based on where the melanoma is on the body and other factors. For example, if the melanoma is on the face, the margins may be smaller to

avoid large scars or other problems. Smaller margins may increase the risk of the cancer coming back, so be sure to discuss the options with your doctor.

Mohs surgery: In some situations, the surgeon may use Mohs surgery. This type of surgery is used more often for some other types of skin cancer, but not all doctors agree on using it for melanoma. In this procedure, the skin (including the melanoma) is removed in very thin layers. Each layer is then viewed under a microscope for cancer cells. If cancer cells are seen, the surgeon removes another layer of skin. The operation continues until a layer shows no signs of cancer. In theory, this allows the surgeon to remove the cancer while saving as much of the surrounding normal skin as possible.

Amputation: If the melanoma is on a finger or toe and has grown deeply, part or all of that digit might need to be amputated.

Lymph node dissection

In this operation, the surgeon removes all of the lymph nodes in the region near the primary melanoma. For example, if the melanoma is on a leg, the surgeon would remove the nodes in the groin region on that side of the body, which is where melanoma cells would most likely travel to first.

Once the diagnosis of melanoma is made from the skin biopsy, the doctor will examine the lymph nodes near the melanoma. Depending on the thickness and location of the melanoma, this may be done by physical exam, or by imaging tests (such as CT or PET scans) to look at nodes that are not near the body surface.

If the nearby lymph nodes feel abnormally hard or large, and a fine needle aspiration (FNA) biopsy or excisional biopsy finds melanoma in a node or nodes, a lymph node dissection is usually done.

If the lymph nodes are not enlarged, a sentinel lymph node biopsy may be done, particularly if the melanoma is thicker than 1 mm. (See the section “How is melanoma of the skin diagnosed?” for a description of this procedure.) If the sentinel lymph node does not contain cancer, then there is no need for a lymph node dissection because it’s unlikely the melanoma has spread to the lymph nodes. If the sentinel lymph node contains cancer cells, removing the remaining lymph nodes in that area with a lymph node dissection is usually advised. This is called a *completion lymph node dissection*.

It’s not clear if a lymph node dissection can cure melanomas that have spread to the nodes. This is still being studied. Still, some doctors feel it might prolong a patient’s survival and at least avoid the pain that may be caused by cancer growing in these lymph nodes.

A full lymph node dissection can cause some long-term side effects. One of the most troublesome is called *lymphedema*. Lymph nodes in the groin or under the arm normally help drain fluid from the limbs. If they are removed, fluid may build up. This can cause limb swelling, which may or may not go away. If severe enough, it can cause skin problems and an increased risk of infections in the limb. Elastic stockings or compression

sleeves can help some people with this condition. For more information, see our document *Understanding Lymphedema (for Cancers Other Than Breast Cancer).*

Lymphedema, along with the pain from the surgery itself, is a main reason why lymph node dissection is not done unless it is necessary. Sentinel lymph node biopsy, however, is unlikely to have this effect. It is important to discuss the possible risks of side effects with your doctor before having either of these procedures done.

Surgery for metastatic melanoma

If melanoma has spread from the skin to distant organs such as the lungs or brain, the cancer is very unlikely to be curable by surgery. Even when only 1 or 2 metastases are found by imaging tests such as CT or MRI scans, there are likely to be other areas of metastasis that are too small to be found by these scans.

Surgery is sometimes done in these circumstances, but the goal is usually to try to control the cancer rather than to cure it. If 1 or even a few metastases are present and can be removed completely, this surgery may help some people live longer. Removing metastases in some places, such as the brain, might also relieve symptoms and help improve a person's quality of life.

If you have metastatic melanoma and surgery is offered as a treatment option, talk to your doctor and be sure you understand what the goal of the surgery would be, as well as its possible benefits and risks.

Immunotherapy for melanoma skin cancer

Immunotherapy is the use of medicines to stimulate a patient's own immune system to recognize and destroy cancer cells more effectively. Several types of immunotherapy can be used to treat patients with melanoma.

Immune checkpoint inhibitors for advanced melanoma

An important part of the immune system is its ability to keep itself from attacking normal cells in the body. To do this, it uses "checkpoints", which are molecules on immune cells that need to be turned on (or off) to start an immune response. Melanoma cells sometimes use these checkpoints to avoid being attacked by the immune system. But newer drugs that target these checkpoints hold a lot of promise as melanoma treatments.

PD-1 inhibitors

Pembrolizumab (Keytruda) and **nivolumab (Opdivo)** are drugs that target PD-1, a protein on immune system cells called *T cells* that normally help keep these cells from attacking other cells in the body. By blocking PD-1, these drugs boost the immune response against melanoma cells, which can often shrink tumors and help people live longer (although it's not yet clear if these drugs can cure melanoma).

These drugs are given as an intravenous (IV) infusion every 2 or 3 weeks.

Side effects of these drugs can include fatigue, cough, nausea, itching, skin rash, decreased appetite, constipation, joint pain, and diarrhea.

Other, more serious side effects occur less often. These drugs work by basically removing the brakes from the body's immune system. Sometimes the immune system starts attacking other parts of the body, which can cause serious or even life-threatening problems in the lungs, intestines, liver, hormone-making glands, kidneys, or other organs.

It's very important to report any new side effects to your health care team promptly. If serious side effects do occur, treatment may need to be stopped and you may get high doses of corticosteroids to suppress your immune system.

CTLA-4 inhibitor

Ipilimumab (Yervoy) is another drug that boosts the immune response, but it has a different target. It blocks CTLA-4, another protein on T cells that normally helps keep them in check.

This drug is given as an intravenous (IV) infusion, usually once every 3 weeks for 4 treatments. In patients with melanomas that can't be removed by surgery or that have spread to other parts of the body, this drug has been shown to help people live an average of several months longer, although it's not clear if it can cure the melanoma.

The most common side effects from this drug include fatigue, diarrhea, skin rash, and itching.

Serious side effects seem to happen more often with this drug than with the PD-1 inhibitors. Like the PD-1 inhibitors, this drug can cause the immune system to attack other parts of the body, which can lead to serious problems in the intestines, liver, hormone-making glands, nerves, skin, eyes, or other organs. In some people these side effects have been fatal.

It's very important to report any new side effects during or after treatment to your health care team promptly. If serious side effects do occur, you may need to stop treatment and take high doses of corticosteroids to suppress your immune system.

Cytokines for advanced melanoma

Cytokines are proteins in the body that boost the immune system in a general way. Man-made versions of cytokines, such as interferon-alfa and interleukin-2 (IL-2), are sometimes used in patients with melanoma. They are given as intravenous (IV) infusions, at least at first. Some patients or caregivers may be able to learn how to give injections under the skin at home. Both drugs can help shrink advanced (stage III and IV) melanomas in about 10% to 20% of patients when used alone. These drugs may also be given along with chemotherapy drugs (known as *biochemotherapy*) for stage IV melanoma.

Side effects of cytokine therapy can include flu-like symptoms such as fever, chills, aches, severe tiredness, drowsiness, and low blood cell counts. Interleukin-2, particularly in high doses, can cause fluid to build up in the body so that the person swells up and can

feel quite sick. Because of this and other possible serious side effects, high-dose IL-2 is given only in the hospital, in centers that have experience with this type of treatment.

Interferon-alfa as adjuvant therapy

Patients with thicker melanomas often have cancer cells that have spread to other parts of the body. Even if all of the cancer seems to have been removed by surgery, some of these cells may remain in the body. Interferon-alfa can be used as an added (adjuvant) therapy after surgery to try to prevent these cells from spreading and growing. This may delay the recurrence of melanoma, but it is not yet clear if it improves survival.

High doses must be used for the interferon to be effective, but many patients can't tolerate the side effects of high-dose therapy. These can include fever, chills, aches, depression, severe tiredness, and effects on the heart and liver. Patients getting this drug need to be closely watched by a doctor who is experienced with this treatment.

When deciding whether to use adjuvant interferon therapy, patients and their doctors should take into account the potential benefits and side effects of this treatment.

Oncolytic virus therapy

Viruses are a type of germ that can infect and kill cells. Some viruses can be altered in the lab so that they infect and kill mainly cancer cells. These are known as *oncolytic viruses*. Along with killing the cells directly, the viruses can also alert the immune system to attack the cancer cells.

Talimogene laherparepvec (Imlygic) is an oncolytic virus that can be used to treat melanomas in the skin or lymph nodes that can't be removed with surgery. The virus is injected directly into the tumors, typically every 2 weeks. This treatment can sometimes shrink these tumors, but it has not been shown to shrink tumors in other parts of the body. It's also not clear if this treatment can help people live longer. Side effects can include flu-like symptoms and pain at the injection site.

Bacille Calmette-Guerin (BCG) vaccine

BCG is a germ related to the one that causes tuberculosis. BCG does not cause serious disease in humans, but it does activate the immune system. The BCG vaccine works like a cytokine by enhancing the entire immune system. It is not directed specifically at melanoma cells. It is sometimes used to help treat stage III melanomas by injecting it directly into tumors.

Imiquimod cream

Imiquimod (Zyclara) is a drug that is applied as a cream. It stimulates a local immune response against skin cancer cells. For very early (stage 0) melanomas in sensitive areas on the face, some doctors may use imiquimod if surgery might be disfiguring. It can also

be used for some melanomas that have spread along the skin. Still, not all doctors agree it should be used for melanoma.

The cream is applied anywhere from once a day to 2 times a week for around 3 months. Some people have serious skin reactions to this drug. Imiquimod is not used for more advanced melanomas.

Newer treatments

Some other types of immunotherapy have shown promise in treating melanoma in early studies. At this time they are available only through clinical trials (see "What's new in research and treatment of melanoma skin cancer?").

To learn more about this type of treatment, see our document *Cancer Immunotherapy*.

Targeted therapy for melanoma skin cancer

As doctors have found some of the gene changes that make melanoma cells different from normal cells, they have begun to develop drugs that attack these changes. These targeted drugs work differently from standard chemotherapy drugs, which basically attack any quickly dividing cells. Sometimes, targeted drugs work when chemotherapy doesn't. They can also have less severe side effects. Doctors are still learning the best way to use these drugs to treat melanoma.

Drugs that target cells with *BRAF* gene changes

About half of all melanomas have changes (mutations) in the *BRAF* gene. These changes cause the gene to make an altered BRAF protein that signals the melanoma cells to grow and divide quickly. Some drugs target this and related proteins.

If you have advanced melanoma, a biopsy sample of it might be tested to see if the cells contain a *BRAF* mutation. Drugs that target the BRAF protein (or the MEK proteins) are not likely to work in patients whose melanomas have a normal *BRAF* gene.

BRAF inhibitors

Vemurafenib **(Zelboraf)** and dabrafenib **(Tafinlar)** are drugs attack the BRAF protein directly.

These drugs shrink tumors in about half of the people whose metastatic melanoma has a *BRAF* gene change. They can also prolong the time before the tumors start growing again and help some patients live longer, although the melanoma typically starts growing again eventually.

These drugs are taken as pills or capsules, twice a day. Common side effects can include skin thickening, headache, fever, joint pain, fatigue, hair loss, rash, itching, sensitivity to the sun, and nausea. Less common but serious side effects can include heart rhythm problems, liver problems, kidney failure, severe allergic reactions, severe skin or eye problems, and increased blood sugar levels.

Some people treated with these drugs develop new skin cancers called *squamous cell carcinomas*. These cancers are usually less serious than melanoma and can be treated by removing them. Still, your doctor will want to check your skin often during treatment and for several months afterward. You should also let your doctor know right away if you notice any new growths or abnormal areas on your skin.

MEK inhibitors

The *MEK* gene is in the same signaling pathway inside cells as the *BRAF* gene, so drugs that block MEK proteins can also help treat melanomas with *BRAF* gene changes.

The MEK inhibitors **t**rametinib **(Mekinist)** and **cobimetinib (Cotellic)** have been shown to shrink some melanomas with *BRAF* changes. They are pills taken once a day. Common side effects can include rash, nausea, diarrhea, swelling, and sensitivity to sunlight. Rare but serious side effects can include heart damage, excess bleeding, loss of vision, lung problems, and skin infections.

When used by themselves, these drugs don't seem to shrink as many melanomas as the BRAF inhibitors. A more common approach is to combine a MEK inhibitor with a BRAF inhibitor. This seems to shrink tumors for longer periods of time than using either type of drug alone. Some side effects (such as the development of other skin cancers) are actually *less* common with the combination.

Drugs that target cells with *C-KIT* gene changes

A small portion of melanomas have changes in a gene called *C-KIT* that help them grow. These gene changes are more common in melanomas that start in certain parts of the body:

- On the palms of the hands, soles of the feet, or under the nails (known as *acral melanomas*)
- Inside the mouth or other mucosal (wet) areas
- In areas that get chronic sun exposure

Some targeted drugs, such as imatinib (Gleevec) and nilotinib (Tasigna), can affect cells with changes in *C-KIT*. If you have a melanoma that started in one of these places, your doctor may test your melanoma cells for changes in the *C-KIT* gene, which might mean that one of these drugs could be helpful.

Drugs that target different gene changes are also being studied in clinical trials (see "What's new in research and treatment of melanoma of the skin?").

Chemotherapy for melanoma skin cancer

Chemotherapy (chemo) uses drugs that kill cancer cells. The drugs are usually injected into a vein or taken by mouth as a pill. They travel through the bloodstream to all parts of

the body and attack cancer cells that have already spread beyond the skin. Because the drugs reach all areas of the body, this is called a *systemic* therapy.

Chemo can be used to treat advanced melanoma, but it is not often used as the first treatment since newer forms of immunotherapy and targeted drugs have become available. Chemo is usually not as effective in melanoma as it is in some other types of cancer, but it may relieve symptoms or extend survival for some patients.

Doctors give chemo in cycles, with each period of treatment followed by a rest period to give the body time to recover. Each chemotherapy cycle typically lasts for a few weeks.

Several chemo drugs can be used to treat melanoma:

- Dacarbazine (also called DTIC)
- Temozolomide
- Nab-paclitaxel
- Paclitaxel
- Carmustine (also known as BCNU)
- Cisplatin
- Carboplatin
- Vinblastine

Some of these drugs are given alone, while others are often combined with other drugs. It's not clear if using combinations of drugs is more helpful than using a single drug, but it can add to the side effects.

Some studies suggest that combining chemo drugs with immunotherapy drugs such as interferon-alpha and/or interleukin-2 (see "Immunotherapy for melanoma skin cancer") may be more effective than a single chemo drug alone, although it's not clear if this helps people live longer. This type of treatment is also called *biochemotherapy* or *chemoimmunotherapy*.

Isolated limb perfusion: This is a type of chemotherapy sometimes used to treat advanced melanomas that are confined to an arm or leg. It is done during a surgical procedure. The blood flow of the arm or leg is separated from the rest of the body, and a high dose of chemotherapy is circulated through the limb for a short period of time. This lets doctors give high doses to the area of the tumor without exposing internal organs to these doses, which would otherwise cause severe side effects.

To do this, a tube is placed into the artery that feeds blood into the limb, and a second tube is placed into the vein that drains blood from it. The tubes are connected to a special machine in the operating room. A tourniquet is tied around the limb to make sure the chemotherapy doesn't enter the rest of the body. A high dose of chemotherapy (usually with a drug called melphalan) is then infused into the blood in the limb through the

artery. During the treatment session, the blood exits the limb through the tube in the vein, is heated by the machine (to help the chemo work better), and is then returned back to the limb through the tube in the artery. By the end of the treatment the drug is completely washed out of the limb, and the tubes are removed so that the circulation is returned to normal.

Possible side effects of chemotherapy

Chemo drugs attack cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow (where new blood cells are made), the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemotherapy, which can lead to side effects.

The side effects of chemo depend on the type and dose of drugs and the length of time they are given. These side effects may include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea or constipation
- Increased risk of infection (from having too few white blood cells)
- Easy bruising or bleeding (from having too few blood platelets)
- Fatigue (from having too few red blood cells)

These side effects usually go away once treatment is finished. There are often ways to lessen side effects. For example, you can be given drugs to help prevent or reduce nausea and vomiting. Be sure to ask your doctor or nurse about drugs to help reduce side effects.

Some chemo drugs can have other side effects. For example, some drugs can damage nerve endings (a condition called *neuropathy*). This can lead to symptoms (mainly in the hands and feet) such as pain, burning or tingling sensations, sensitivity to cold or heat, or weakness. This usually goes away once treatment is stopped, but for some people it can last a long time. For more information, see *Peripheral Neuropathy Caused by Chemotherapy*.

Be sure to talk with your cancer care team about what to expect in terms of side effects. While you are getting chemo, report any side effects to your medical team so that they can be treated promptly. In some cases, the doses of the chemo drugs may need to be reduced or treatment may need to be delayed or stopped to prevent side effects from getting worse.

To learn more, see the Chemotherapy section of our website.

Radiation therapy for melanoma skin cancer

Radiation therapy uses high-energy rays (such as x-rays) or particles to kill cancer cells. External beam radiation therapy focuses radiation from outside the body on the skin tumor. This type of radiation therapy is used to treat some patients with melanoma.

Before treatments start, the radiation team will take careful measurements to determine the correct angles for aiming the radiation beams and the proper dose of radiation. The treatment is much like getting an x-ray, but the radiation is stronger. The procedure itself is painless. Each treatment lasts only a few minutes, although the setup time – getting you into place for treatment – usually takes longer.

When might radiation therapy be used?

Radiation therapy is not often used to treat the original melanoma that started on the skin, although it is sometimes used after surgery for a type of melanoma known as *desmoplastic melanoma*.

Sometimes, radiation is given after surgery in the area where lymph nodes were removed, especially if many of the nodes contained cancer cells. This is to try to lower the chance that the cancer will come back.

Radiation therapy can also be used to treat melanoma that has come back (recurred) after surgery, either in the skin or lymph nodes, or to help treat distant spread of the disease.

Radiation therapy is often used to relieve symptoms caused by the spread of the melanoma, especially to the brain or bones. Treatment with the goal of relieving symptoms is called *palliative therapy*. Palliative radiation therapy is not expected to cure the cancer, but it might help shrink it or slow its growth for a time to help control some of the symptoms.

Stereotactic radiosurgery (SRS)

SRS is a type of radiation therapy that can sometimes be used for tumors that have spread to the brain. (Despite the name, there is no actual surgery involved.) In one version of this treatment, a machine called a Gamma Knife® focuses about 200 beams of radiation on the tumor from different angles over a few minutes to hours. The head is kept in the same position by placing it in a rigid frame. In another version, a linear accelerator (a machine that creates radiation) that is controlled by a computer moves around the head to deliver radiation to the tumor from many different angles. These treatments can be repeated if needed.

Possible side effects of radiation therapy

Common side effects depend on where the radiation is aimed and can include:

- Sunburn-like skin problems
- Hair loss where the radiation enters the body
- Fatigue
- Nausea
- Loss of appetite and weight loss

Often these go away after treatment. When radiation is given with chemotherapy, the side effects are often worse.

Radiation therapy to the brain can sometimes cause memory loss, headaches, trouble thinking, or reduced sexual desire. Usually these symptoms are minor compared with those caused by a tumor in the brain, but they can still affect your quality of life.

To learn more about radiation, see the Radiation Therapy section of our website.

Treatment of melanoma skin cancer, by stage

The type of treatment(s) your doctor recommends will depend on the stage and location of the melanoma and on your overall health. This section lists the options usually considered for each stage of melanoma.

Stage 0

Stage 0 melanomas have not grown deeper than the top layer of the skin (the epidermis). They are usually treated by surgery (wide excision) to remove the melanoma and a margin of about 1/2 cm (about 1/5 of an inch) of normal skin around it. If the edges of the removed sample are found to contain cancer cells, a repeat excision of the area may be done. Some doctors may consider the use of imiquimod cream (Zyclara) or radiation therapy, although not all doctors agree with this.

For melanomas in sensitive areas on the face, some doctors may use Mohs surgery or even imiquimod cream if surgery might be disfiguring, although not all doctors agree with these uses.

Stage I

Stage I melanoma is treated by wide excision (surgery to remove the melanoma as well as a margin of normal skin around it). The amount of normal skin removed depends on the thickness and location of the melanoma, but no more than 2 cm (4/5 inch) of normal skin needs to be removed from all sides of the melanoma. Wider margins make healing more difficult and have not been found to help people live longer.

Some doctors may recommend a sentinel lymph node biopsy, especially if the melanoma is stage IB or has other characteristics that make it more likely to have spread to the lymph nodes. This is an option that you and your doctor should discuss.

If cancer cells are found on the sentinel lymph node biopsy, a lymph node dissection (removal of all lymph nodes near the cancer) is often recommended, but it's not clear if it can improve survival. Some doctors may recommend adjuvant (additional) treatment with interferon after the lymph node surgery as well.

Stage II

Wide excision (surgery to remove the melanoma and a margin of normal skin around it) is the standard treatment for stage II melanoma. The amount of normal skin removed depends on the thickness and location of the melanoma, but it should be no more than 2 cm (4/5 inch) around all sides of the melanoma.

Because the melanoma may have spread to lymph nodes near the melanoma, many doctors recommend a sentinel lymph node biopsy as well. This is an option that you and your doctor should discuss. If it is done and the sentinel node contains cancer cells, then a lymph node dissection (where all the lymph nodes in that area are surgically removed) will probably be done at a later date.

For some patients (such as those with lymph nodes containing cancer), doctors may advise treatment with interferon after surgery (adjuvant therapy). Other drugs or perhaps vaccines may also be recommended as part of a clinical trial to try to reduce the chance the melanoma will come back.

Stage III

These cancers have already reached the lymph nodes when the melanoma is first diagnosed. Surgical treatment for stage III melanoma usually requires wide excision of the primary tumor as in earlier stages, along with lymph node dissection. Adjuvant therapy with interferon may help keep some melanomas from coming back longer. Other drugs or perhaps vaccines may also be recommended as part of a clinical trial to try to reduce the chance the melanoma will come back. Another option is to give radiation therapy to the areas where the lymph nodes were removed, especially if many of the nodes contain cancer.

If melanomas are found in nearby lymph vessels in or just under the skin (known as *in-transit tumors*), they should all be removed, if possible. Other options include injections of Bacille Calmette-Guerin (BCG) vaccine, interferon, or interleukin-2 (IL-2) directly into the melanoma; radiation therapy; or applying imiquimod cream. For melanomas on an arm or leg, another option might be isolated limb perfusion (infusing the limb with a heated solution of chemotherapy). Other possible treatments might include targeted therapy, immunotherapy, chemotherapy, or a combination of immunotherapy and chemotherapy (biochemotherapy).

Some patients might benefit from newer treatments being tested in clinical trials. Many patients with stage III melanoma might not be cured with current treatments, so they may want to think about taking part in a clinical trial.

Stage IV

Stage IV melanomas are very hard to cure, as they have already spread to distant lymph nodes or other areas of the body. Skin tumors or enlarged lymph nodes causing symptoms can often be removed by surgery or treated with radiation therapy. Metastases in internal organs are sometimes removed, depending on how many there are, where they are, and how likely they are to cause symptoms. Metastases that cause symptoms but cannot be removed may be treated with radiation, immunotherapy, targeted therapy, or chemotherapy.

The treatment of widespread melanomas has changed in recent years as newer forms of immunotherapy (known as *immune checkpoint inhibitors*) and targeted drugs have been shown to be more effective than chemotherapy.

Ipilimumab (Yervoy), a newer immunotherapy drug, has been shown to help some people with advanced melanoma live longer. It can sometimes have severe side effects, so patients who get it need to be watched closely. Other new immunotherapy drugs, including pembrolizumab (Keytruda) or nivolumab (Opdivo), might also be options. These drugs seem to be more likely to shrink tumors than ipilimumab and are less likely to cause severe side effects. Other types of immunotherapy might also help, but these are only available through clinical trials at this time.

In about half of all melanomas, the cancer cells have changes in the *BRAF* gene. If this gene change is found, treatment with newer targeted drugs such as vemurafenib (Zelboraf), dabrafenib (Tafinlar), trametinib (Mekinist), and cobimetinib (Cotellic) might be helpful. They might be tried before or after the newer immunotherapy drugs, but they are not used at the same time. Like ipilimumab, these drugs can help some people live longer, although they have not been shown to cure these melanomas.

A small portion of melanomas have changes in the *C-KIT* gene. These melanomas might be helped by targeted drugs such as imatinib (Gleevec) and nilotinib (Tasigna), although, again, these drugs are not known to cure these melanomas.

Immunotherapy using interferon or interleukin-2 can help a small number of people with stage IV melanoma live longer. Higher doses of these drugs seem to be more effective, but they can also have more severe side effects, so they might need to be given in the hospital.

Chemotherapy can help some people with stage IV melanoma, but other treatments are usually tried first. Dacarbazine (DTIC) and temozolomide (Temodar) are the chemo drugs used most often, either by themselves or combined with other drugs. Even when chemotherapy shrinks these cancers, the effect often lasts for an average of several months before the cancer starts growing again. In rare cases they work for longer periods of time.

Some doctors may recommend biochemotherapy: a combination of chemotherapy and either interleukin-2, interferon, or both. For example, some doctors use interferon with temozolomide. The 2 drugs combined cause more tumor shrinkage, which might make patients feel better, although the combination has not been shown to help patients live longer. Another drug combination uses low doses of interferon, interleukin-2, and temozolomide. Each seems to benefit some patients. It's important to carefully consider the possible benefits and side effects of any recommended treatment before starting it.

Because stage IV melanoma is hard to treat with current therapies, patients may want to think about taking part in a clinical trial. Many studies are now looking at new targeted drugs, immunotherapies, chemotherapy drugs, and combinations of different types of treatments.

Even though the outlook for people with stage IV melanoma tends to be poor overall, a small number of people respond very well to treatment and survive for many years after diagnosis.

Recurrent melanoma

Treatment of melanoma that comes back after initial treatment depends on the stage of the original melanoma, what treatments a person has already had, where the melanoma comes back, and other factors.

Melanoma might come back in the skin near the site of the original tumor, sometimes even in the scar from the surgery. In general, these local (skin) recurrences are treated with surgery similar to what would be recommended for a primary melanoma. This might include a sentinel lymph node biopsy. Depending on the thickness and location of the tumor, other treatments may be considered, such as isolated limb perfusion chemotherapy; radiation therapy; tumor injection with BCG vaccine, interferon, or interleukin-2; or even systemic treatments such as immunotherapy, targeted therapy, or chemotherapy.

If nearby lymph nodes weren't removed during the initial treatment, the melanoma might come back in these nearby lymph nodes. Lymph node recurrence is treated by lymph node dissection if it can be done, sometimes followed by treatments such as interferon or radiation therapy. If surgery is not an option, radiation therapy or systemic treatment (immunotherapy, targeted therapy, or chemo) can be used.

Melanoma can also come back in distant parts of the body. Almost any organ can be affected. Most often, the melanoma will come back in the lungs, bones, liver, or brain. Treatment for these recurrences is generally the same as for stage IV melanoma (see above). Melanomas that recur on an arm or leg may be treated with isolated limb perfusion chemotherapy.

Melanoma that comes back in the brain can be hard to treat. Single tumors can sometimes be removed by surgery. Radiation therapy to the brain (stereotactic radiosurgery or whole brain radiation therapy) may help as well. Systemic treatments (immunotherapy, targeted therapy, or chemo) might also be tried.

As with other stages of melanoma, people with recurrent melanoma may want to think about taking part in a clinical trial.

What should you ask your doctor about melanoma skin cancer?

It’s important to have honest, open discussions with your cancer care team. You should ask any question, no matter how small it might seem. Here are some questions you might want to ask:

- How far has my melanoma spread within or beneath the skin? How thick is my melanoma?
- Do I need any other tests before we can decide on treatment?
- Do I need to see any other types of doctors?
- How much experience do you have treating this type of cancer?
- What are my treatment options? What are the possible risks and benefits of each?
- Which treatment do you recommend? Why?
- What is the goal of the treatment?
- How quickly do we need to decide on treatment?
- What should I do to be ready for treatment?
- How long will treatment last? What will it be like? Where will it be done?
- How will treatment affect my daily activities?
- What type of side effects might I expect?
- Will I have a scar after treatment?
- What are the chances of my cancer growing or recurring (coming back) with the treatment options we have discussed? What would we do if this happens?
- Should I take special precautions to avoid sun exposure?
- What type of follow-up will I need after treatment?
- Are my family members at risk for skin cancer? What should I tell them to do?

Along with these sample questions, be sure to write down your own questions. For instance, you might want more information about recovery times so you can plan your

work or activity schedule. Or you might want to ask about getting a second opinion or about clinical trials for which you may qualify.

Keep in mind that doctors aren't the only ones who can give you information. Other health care professionals, such as nurses and social workers, may have the answers to some of your questions. You can find more information about speaking with your health care team in our document *Talking With Your Doctor*.

What happens after treatment for melanoma skin cancer?

For many people with melanoma, treatment can remove or destroy the cancer. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about cancer growing or coming back. (When cancer comes back after treatment, it is called *recurrent cancer* or a *recurrence*.) This is a very common concern in people who have had cancer.

It may take a while before your fears lessen. But it may help to know that many cancer survivors have learned to accept this uncertainty and are living full lives. Our document *Living With Uncertainty: The Fear of Cancer Recurrence* talks more about this.

For others, melanoma may never go away completely. These people may get regular treatment with immunotherapy, targeted therapy, chemotherapy, or other treatments to try to help keep the cancer in check. Learning to live with cancer that does not go away can be difficult and very stressful. It has its own type of uncertainty. Our document *When Cancer Doesn't Go Away* talks more about this.

Follow-up care

Even if you have completed treatment, your doctors will still want to watch you closely. It's very important to keep all follow-up appointments. Follow-up is needed to check for signs of the cancer coming back, as well as possible side effects of certain treatments. This is a good time for you to ask your health care team any questions you need answered and to discuss any concerns you have.

Your follow-up schedule should include regular skin and lymph node exams by yourself and by your doctor. How often you need follow-up doctor visits depends on the stage of your melanoma when you were diagnosed and other factors. In addition to the exams, imaging tests such as x-rays or CT scans may be recommended for some patients.

A typical follow-up schedule for people with early-stage melanomas that were removed completely generally calls for physical exams every 6 to 12 months for several years. If these exams are normal, your doctor visits may be stretched to as long as once a year. Your doctor may recommend more frequent exams if you have many moles or atypical moles.

For thicker melanomas or those that had spread beyond the skin, a typical schedule might include physical exams every 3 to 6 months for 2 years, then every 3 to 12 months for the next few years. After that, exams are done at least once a year. Some doctors also recommend imaging tests such as chest x-rays or CT scans every 3 to 12 months for the first several years, especially for people who had more advanced stage disease.

It is also important for melanoma survivors to do regular self-exams of their skin and lymph nodes. Most doctors recommend this at least monthly. You should see your doctor if you find any new lump or change in your skin. You should also report any new symptoms (for example, pain, cough, fatigue, loss of appetite) that do not go away. Melanoma can sometimes come back many years after it was first treated.

People with melanoma that does not go away completely with treatment will have a follow-up schedule that is based on their specific situation.

If melanoma does come back, treatment will depend on where the cancer is, what treatments you've had before, and your overall health. For more information on how recurrent cancer is treated, see the section "Treatment of melanoma skin cancer by stage." For more general information on dealing with a recurrence, you might also want to read *When Your Cancer Comes Back: Cancer Recurrence*.

A person who has had one melanoma is at higher risk for developing other melanomas or other skin cancers. It's important for people who have had melanoma to examine their skin every month for new skin cancers, and to avoid getting too much sun exposure.

Seeing a new doctor

At some point after your treatment, you may be seeing a new doctor who doesn't know about your medical history. It's important to be able to give your new doctor the details of your diagnosis and treatment. Gathering these details during and soon after treatment may be easier than trying to get them at some point in the future. Make sure you have this information handy (and always keep copies for yourself):

- A copy of your pathology report(s) from any biopsies or surgeries
- Copies of imaging tests (CT or MRI scans, etc.), which can usually be stored digitally on a DVD, etc.
- If you had surgery, a copy of your operative report(s)
- If you stayed in the hospital, a copy of the discharge summary that the doctor wrote when you were sent home
- If you had radiation therapy, a copy of your treatment summary
- If you had immunotherapy, targeted therapy, or chemotherapy, a list of your drugs, drug doses, and when you took them
- Contact information for doctors who have treated your cancer

It is also very important to keep health insurance. Tests and doctor visits cost a lot, and even though no one wants to think of their cancer coming back, this could happen.

Can I get another cancer after having melanoma of the skin?

Cancer survivors can worry about a number of things, but often their greatest concern is facing cancer again. If a cancer comes back after treatment it is called a *recurrence*. But some cancer survivors may develop a new, unrelated cancer later. This is called a *second cancer*. Unfortunately, being treated for one cancer doesn't mean you can't get another type of cancer. In fact, certain types of cancer and cancer treatments can be linked to a higher risk of certain second cancers.

Survivors of skin melanoma can get any type of second cancer, but they have an increased risk of:

- Another skin cancer, including melanoma (this is different from the first cancer coming back)
- Salivary gland cancer
- Small intestine cancer
- Breast cancer (in women)
- Prostate cancer
- Kidney cancer
- Thyroid cancer
- Soft tissue cancer
- Non-Hodgkin lymphoma (NHL)

The most common second cancer seen in survivors of skin melanoma is another skin cancer.

Follow-up after treatment

After completing treatment for melanoma, you should still see your doctor regularly and have regular skin exams to look for signs the cancer has come back or new skin cancers (see "What happens after treatment for melanoma skin cancer?"). Let your doctor know about any new symptoms or problems, because they could be caused by the cancer coming back or by a new disease or second cancer.

Survivors of skin melanoma should follow the American Cancer Society guidelines for the early detection of cancer and stay away from tobacco products. Smoking increases the risk of many cancers.

To help maintain good health, survivors should also:

- Get to and stay at a healthy weight
- Be physically active
- Eat a healthy diet, with an emphasis on plant foods
- Limit alcohol to no more than 1 drink per day for women or 2 per day for men

These steps may also lower the risk of some cancers.

See our document *Second Cancers in Adults* for more information about causes of second cancers.

Lifestyle changes after having melanoma skin cancer

You can't change the fact that you have had melanoma. What you can change is how you live the rest of your life, making choices to help you stay healthy and feel as well as you can. This can be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even start during cancer treatment.

Make healthier choices

For many people, a diagnosis of cancer helps them focus on their health in ways they may not have given much thought in the past. Are there things you could do that might make you healthier? Maybe you could try to eat better or get more exercise. Maybe you could cut down on alcohol, or give up tobacco. Even things like keeping your stress level under control might help. Now is a good time to think about making changes that can have positive effects for the rest of your life. You will feel better and you will also be healthier.

You can start by working on the things that worry you most. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society at 1-800-227-2345.

Eating better

Eating right can be hard for anyone, but it can get even tougher during and after some types of cancer treatment. Treatment may change your sense of taste. Nausea can be a problem. You may not feel like eating and lose weight when you don't want to. Or you might have gained weight that you can't seem to lose. All of these things can be very frustrating.

If treatment causes weight changes or eating or taste problems, do the best you can and keep in mind that these problems usually get better over time. You may find it helps to eat small meals every 2 to 3 hours until you feel better. You may also want to ask your cancer team about seeing a dietitian, an expert in nutrition who can give you ideas on how to deal with side effects of these treatments.

One of the best things you can do after cancer treatment is start healthy eating habits. You may be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Getting to and staying at a healthy weight, eating a healthy diet, and limiting your alcohol intake may lower your risk for a number of types of cancer, as well as having many other health benefits.

You can get more information in our document *Nutrition and Physical Activity During and After Cancer Treatment: Answers to Common Questions*.

Rest, fatigue, and exercise

Extreme tiredness, called *fatigue*, is very common in people treated for cancer. This is not a normal tiredness, but a bone-weary exhaustion that often doesn't get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them to be active and do other things they want to do. But exercise can help reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel better physically and emotionally and can cope better, too.

If you were sick and not very active during treatment, it's normal for your fitness, endurance, and muscle strength to decline. Any plan for physical activity should fit your own situation. If you haven't been active in a few years, you will have to start slowly – maybe just by taking short walks.

Talk with your health care team before starting anything. Get their opinion about your exercise plans. Then, think about finding an exercise buddy so you're not doing it alone. Involving family or friends when starting a new activity program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, you will need to learn to balance activity with rest. It's OK to rest when you need to. Sometimes it's really hard for people to allow themselves to rest when they are used to working all day or taking care of a household, but this is not the time to push yourself too hard. Listen to your body and rest when you need to. (For more on fatigue and other treatment side effects, see the Physical Side Effects section of our website.)

Keep in mind exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- Along with a good diet, it will help you get to and stay at a healthy weight.
- It makes your muscles stronger.
- It reduces fatigue and helps you have more energy.
- It can help lower anxiety and depression.
- It can make you feel happier.
- It helps you feel better about yourself.

Getting regular physical activity also plays a role in helping to lower the risk of some cancers, as well as having other health benefits.

Can I lower my risk of the melanoma progressing or coming back?

Most people want to know if there are specific lifestyle changes they can make to reduce their risk of cancer progressing or coming back. Unfortunately, for most cancers there isn't much solid evidence to guide people. This doesn't mean that nothing will help – it's just that for the most part this is an area that hasn't been well studied. Most studies have looked at lifestyle changes as ways of preventing cancer in the first place, not slowing it down or preventing it from coming back.

At this time, not enough is known about melanoma to say for sure if there are things you can do that will be helpful. We do know that people who have had melanoma are at higher risk for developing another melanoma or other type of skin cancer. Because of this, it's very important to limit your exposure to UV rays (from the sun or tanning beds) and to continue to examine your skin every month for signs of melanoma coming back or possible new skin cancers. Skin cancers that are found early are typically much easier to treat than those found at a later stage.

Adopting healthy behaviors such as not smoking, eating well, being active, and staying at a healthy weight may also help, but no one knows for sure. However, we do know that these types of changes can have positive effects on your health that can extend beyond your risk of melanoma or other cancers.

How might having melanoma skin cancer affect your emotional health?

During and after treatment, you may find yourself overcome with many different emotions. This happens to a lot of people.

You may find yourself thinking about death and dying. Or maybe you're more aware of the effect the cancer has on your family, friends, and career. You may take a new look at your relationships with those around you. Unexpected issues may also cause concern. For instance, you might be stressed by financial issues resulting from your treatment. You might also see your health care team less often after treatment and have more time on your hands. These changes can make some people anxious.

Almost everyone who is going through or has been through cancer can benefit from getting some type of support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, religious or spiritual groups, online support communities, or one-on-one counselors. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It's not necessary or good for you to try to deal with everything on your own. And your friends and family may feel shut out if you don't include them. Let them in, and let in anyone else you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-227-2345 and we can put you in touch with a group or resource that may work for you. You can also read our document *Distress in People With Cancer* or see the Emotional Side Effects section of our website for more information.

If treatment for melanoma skin cancer is no longer working

If a melanoma keeps growing or comes back after one kind of treatment, it may be possible to try another treatment plan that might still cure the cancer, or at least keep it under control enough to help you live longer and feel better. Clinical trials also might offer chances to try newer treatments that could be helpful. But when a person has tried many different treatments and the cancer is still growing, even newer treatments might no longer be effective. If this happens, it's important to weigh the possible limited benefits of trying a new treatment against the possible downsides, including treatment side effects. Everyone has their own way of looking at this.

This is likely to be the hardest part of your battle with cancer, when you have been through many treatments and nothing's working anymore. Your doctor might offer you new options, but at some point you might need to consider that treatment is not likely to improve your health or change your outcome or survival.

If you want to continue to get treatment for as long as you can, you need to think about the odds of treatment having any benefit and how this compares to the possible risks and side effects. Your doctor can estimate how likely it is the cancer will respond to treatment you are considering. For instance, the doctor might say that more treatment might have about a 1 in 100 chance of working. Some people will still be tempted to try this. But it is important to have realistic expectations if you do choose this plan.

Palliative care

No matter what you decide to do, it is important that you feel as good as you can. Make sure you are asking for and getting treatment for any symptoms you might have, such as nausea or pain. This type of treatment is called *palliative care*.

Palliative care helps relieve symptoms, but it is not expected to cure the disease. It can be given along with cancer treatment, or can even be cancer treatment. The difference is its purpose. The main goal of palliative care is to improve the quality of your life, or help you feel as good as you can for as long as you can. Sometimes this means using medicines to help with symptoms like pain or nausea. Sometimes, though, the treatments used to control your symptoms are the same as those used to treat cancer. For instance, radiation might be used to help relieve pain caused by cancer that has spread. But this is not the same as treatment to try to cure the cancer.

Hospice care

At some point, you may benefit from hospice care. This is special care that treats the person rather than the disease; it focuses on quality rather than length of life. Most of the time, it is given at home. Your cancer may be causing problems that need to be managed, and hospice focuses on your comfort. You should know that while getting hospice care often means the end of treatments such as chemo and radiation, it doesn't mean you can't have treatment for the problems caused by the cancer or other health conditions. In hospice, the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult time. You can learn more about hospice in our document *Hospice Care*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there's still hope for good times with family and friends—times that are filled with happiness and meaning. Pausing at this time in your cancer treatment gives you a chance to refocus on the most important things in your life. Now is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do. Though the cancer may be beyond your control, there are still choices you can make.

To learn more

You can learn more about the changes that occur when treatment stops working, and about planning ahead for yourself and your family, by reading *Advance Directives* and *Nearing the End of Life*.

What's new in research and treatment of melanoma skin cancer?

Research into the causes, prevention, and treatment of melanoma is being done in medical centers throughout the world.

Causes, prevention, and early detection

Sunlight and ultraviolet (UV) radiation

Recent studies suggest there may be 2 general ways that UV exposure is linked to melanoma, but there is likely some overlap.

The first link is to sun exposure as a child and teenager. People with melanoma often have an early history of sunburns or other intense sun exposures, although not everyone does. This early sun exposure may cause changes in the DNA of skin cells (melanocytes) that starts them on a path to becoming melanoma cells many years later. Some doctors think this might help explain why melanomas often occur on the legs and trunk, areas that generally aren't exposed to the sun as much in adulthood.

The second link is to melanomas that occur on the arms, neck, and face. These areas are chronically exposed to sun, particularly in men.

Tanning booths may encourage either kind of melanoma to develop.

Researchers are looking to see if melanomas that develop from these types of UV exposure have different gene changes that might require them to be treated differently.

Public education

Most skin cancers can be prevented. The best way to reduce the number of skin cancers and the pain and loss of life from this disease is to educate the public, especially parents, about skin cancer risk factors and warning signs. It's important for health care professionals and skin cancer survivors to remind everyone about the dangers of too much UV exposure (both from the sun and from man-made sources such as tanning beds) and about how easy it can be to protect your skin against too much UV radiation.

Melanoma can often be detected early, when it is most likely to be cured. Monthly skin self-exams and awareness of the warning signs of melanomas may be helpful in finding most melanomas when they are at an early, curable stage.

The American Academy of Dermatology (AAD) sponsors annual free skin cancer screenings throughout the country. Many local American Cancer Society offices work closely with the AAD to provide volunteers for registration, coordination, and education efforts related to these free screenings. Look for information in your area about these screenings or call the American Academy of Dermatology for more information. Their phone number and website are listed in the "Additional resources" section.

Along with recommending staying in the shade, the American Cancer Society uses a slogan popularized in Australia as part of its skin cancer prevention message in the United States. "Slip! Slop! Slap!®… and Wrap" is a catchy way to remember when going outdoors to slip on a shirt, slop on sunscreen, slap on a hat, and wrap on sunglasses to protect your eyes and the sensitive skin around them.

Melanoma genetic research

Scientists have made a great deal of progress during the past few years in understanding how UV light damages DNA inside skin cells and how these changes can cause normal skin cells to become cancerous.

Some people, though, inherit mutated (damaged) genes from their parents. For example, changes in the *CDKN2A* (*p16*) gene cause some melanomas to run in certain families. People who have a strong family history of melanoma should speak with a cancer genetic counselor or a doctor experienced in cancer genetics to discuss the possible benefits, limits, and downsides of testing for changes in this gene.

Lab tests to help determine prognosis

Most melanomas found at an early stage can be cured with surgery. But a small portion of these cancers eventually spread to other parts of the body, where they can be hard to treat.

Recent research has shown that certain gene expression patterns in melanoma cells can help show if stage I or II melanomas are likely to spread. A lab test based on this research, known as *DecisionDx-Melanoma*, is now available. The test divides melanomas into 2 groups based on their gene patterns:

- Class 1 tumors have a low risk of spreading.
- Class 2 tumors have a higher risk of spreading.

This test might help tell if someone with early stage melanoma should get additional treatment or if they need to be followed more closely after treatment to look for signs of recurrence.

Treatment

While early-stage melanomas can often be cured with surgery, more advanced melanomas can be much harder to treat. But in recent years, newer types of immunotherapy and targeted therapies have shown a great deal of promise and have changed the treatment of this disease.

Immunotherapy

This type of treatment helps the body's immune system attack melanoma cells more effectively. Some forms of immune therapy are already used to treat some melanomas (see "Immunotherapy for melanoma skin cancer").

Drugs that block CTLA-4: Ipilimumab targets CTLA-4, a protein that normally suppresses the T-cell immune response, which might help melanoma cells survive. Ipilimumab has been shown to help some people with advanced melanomas live longer, and is already being used to treat some people with advanced melanoma.

A recent early study found that combining ipilimumab with another immunotherapy drug known as GM-CSF helped patients with advanced melanoma live longer than those who got just ipilimumab alone. The people who got the combination also seemed to have fewer serious side effects. Further clinical trials are testing ipilimumab combined with this or other drugs.

Drugs that block PD-1 or PD-L1: Melanoma cells also use other natural pathways in the body to help avoid being detected and destroyed by the immune system. For example, they often have a protein called PD-L1 on their surface that helps them evade the immune system.

New drugs that block the PD-L1 protein, or the corresponding PD-1 protein on immune cells called *T cells*, can help the immune system recognize the melanoma cells and attack them. Two drugs that block PD-1, pembrolizumab (Keytruda) and nivolumab (Opdivo), are now approved to treat advanced melanoma. In early studies, these drugs have shrunk tumors in about one quarter to one-third of people with melanoma, which is better than most results seen with ipilimumab. These drugs appear to have fewer serious side effects as well, and many of the tumor responses have been long-lasting so far. Larger studies of these new drugs are now being done, including some that use one of these drugs with ipilimumab to see if the combination might work even better.

Melanoma vaccines: Vaccines directed at melanoma are being studied in clinical trials. These are experimental therapies that have not yet been proven to be helpful.

These vaccines are, in some ways, like the vaccines used to prevent diseases such as polio, measles, and mumps that are caused by viruses. Such vaccines usually contain weakened viruses or parts of a virus that cannot cause the disease. The vaccine stimulates the body's immune system to destroy the more harmful type of virus.

In the same way, killed melanoma cells or parts of cells (antigens) can be used as a vaccine to try to stimulate the body's immune system to destroy other melanoma cells in the body. Usually, the cells or antigens are mixed with other substances that help boost the body's immune system as a whole. But unlike vaccines that are meant to prevent infections, these vaccines are meant to treat an existing disease.

Making an effective vaccine against melanoma has proven to be harder than making a vaccine to fight a virus. The results of studies using vaccines to treat melanoma have been mixed so far, but many newer vaccines are now being studied and may hold more promise.

Other immunotherapies: Other forms of immunotherapy are also being studied. Some early studies have shown that treating patients with high doses of chemotherapy and radiation therapy and then giving them tumor-infiltrating lymphocytes (TILs), which are immune system cells found in tumors, can shrink melanoma tumors and possibly prolong life as well. Newer studies are looking at changing certain genes in the TILs before they are given to see if this can make them more effective at fighting the cancer. This approach has looked promising in early studies, but it is complex and is only being tested in a few centers.

Many studies are now looking to combine different types of immunotherapy, which may be more effective than any single treatment for advanced melanoma.

Targeted drugs

As doctors have discovered some of the gene changes in melanoma cells, they have developed drugs that attack these changes. These targeted drugs work differently from standard chemotherapy drugs. They may work in some cases when chemotherapy doesn't. They may also have less severe side effects.

Drugs that target cells with changes in the *BRAF* gene: As noted in the section "Targeted therapy for melanoma skin cancer," about half of all melanomas have changes in the *BRAF* gene, which helps the cells grow. Drugs that target the BRAF protein, such as vemurafenib (Zelboraf) and dabrafenib (Tafinlar), as well as drugs that target the related MEK proteins, such as trametinib (Mekinist) and cobimetinib (Cotellic), have been shown to shrink many of these tumors. These drugs are now often used in melanomas that test positive for the *BRAF* gene change. Other, similar drugs are now being studied as well.

One of the drawbacks of these drugs is that they seem to work for only a limited time before the cancer starts growing again. A new approach is to combine a BRAF inhibitor with a MEK inhibitor. Study results have been promising, showing that combining the drugs results in longer response times and that some side effects (such as the development of other skin cancers) might actually be *less* common with the combination.

Drugs that target cells with changes in the *C-KIT* gene: A small number of melanomas have changes in the *C-KIT* gene. This is more likely in melanomas that start on the palms of the hands, soles of the feet, under the nails, or in certain other places.

Clinical trials are now testing drugs such as imatinib (Gleevec) and nilotinib (Tasigna), which are known to target cells with changes in *C-KIT*.

Drugs that target other gene or protein changes: Several drugs that target other abnormal genes or proteins, such as sorafenib (Nexavar), bevacizumab (Avastin), pazopanib (Votrient), and everolimus (Afinitor), are now being studied in clinical trials as well.

Researchers are also looking at combining some of these targeted drugs with other types of treatments, such as chemotherapy or immunotherapy.

Additional resources for melanoma skin cancer

More information from your American Cancer Society

We have a lot more information that you might find helpful. Explore www.cancer.org or call our National Cancer Information Center toll-free number, 1-800-227-2345. We're here to help you any time, day or night.

National organizations and websites*

Along with the American Cancer Society, other sources of information and support include:

American Academy of Dermatology (AAD)
Toll-free number: 1-888-462-3376 (1-888-462-DERM)

Website: www.aad.org
Spot Skin Cancer website www.aad.org/spot-skin-cancer

For information on melanoma, a skin cancer risk assessment, a locator for free skin cancer screenings, and a dermatologist locator

Environmental Protection Agency (EPA)
Website: www.epa.gov/sunwise/

Has free sun safety information

Melanoma Research Foundation
Toll-free number: 1-877-673-6460
Website: www.melanoma.org

For more on melanoma and chat rooms, patient stories, and bulletin boards – all to support and educate anyone affected by melanoma

Skin Cancer Foundation
Toll-free number: 1-800-754-6490 (1-800-SKIN-490)
Website: www.skincancer.org

Has pictures and descriptions of skin cancers, information and educational materials, and newsletters

National Cancer Institute
Toll-free number: 1-800-422-6237 (1-800-4-CANCER)
TTY: 1-800-332-8615
Website: www.cancer.gov

Part of the US National Institutes of Health, the NCI offers accurate, up-to-date information about cancer to patients, their families, and the general public

National Comprehensive Cancer Network (NCCN)
Website: www.nccn.org

Made up of experts from many of the nation's leading cancer centers, the NCCN develops guidelines for doctors to use when treating patients. Some of these guidelines, including one on melanoma, are available in versions for patients as well.

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

References: Melanoma skin cancer detailed guide

American Academy of Pediatrics. Policy statement – Ultraviolet radiation: A hazard to children and adolescents. *Pediatrics*. 2011;127:588-597.

American Cancer Society. *Cancer Facts & Figures 2016*. Atlanta, Ga: American Cancer Society; 2016.

American Joint Committee on Cancer. Melanoma of the skin. In: *AJCC Cancer Staging Manual*. 7th ed. New York: Springer; 2010:325-344.

Berman B, Villa AM. Immune response modulators in the treatment of skin cancer. In: Rigel DS, Friedman RJ, Dzubow LM, Reintgen DS, Bystryn JC, Marks R, eds. *Cancer of the Skin*. Philadelphia, Pa: Elsevier Saunders; 2005:499-513.

Curtin JA, Fridlyand J, Kageshita T, et al. Distinct sets of genetic alterations in melanoma. *New Engl J Med*. 2005;353:2135-2147.

Dudley ME, Yang JC, Sherry R, et al. Adoptive cell therapy for patients with metastatic melanoma: Evaluation of intensive myeloablative chemoradiation preparative regimens. *J Clin Oncol*. 2008;26:5233-5239.

El Ghissassi, Baan R, Straif K, et al. A review of human carcinogens – part D: Radiation. *Lancet Oncol*. 2009;10:751-752.

Flaherty KT, Infante JR, Daud A, et al. Combined BRAF and MEK inhibition in melanoma with BRAF V600 mutations. *N Engl J Med*. 2012;367:1694-703.

Flaherty KT, Robert C, Hersey P, et al. Improved survival with MEK inhibition in BRAF-mutated melanoma. *N Engl J Med*. 2012;367:107-114.

Freedman DM, Miller BA, Tucker MA. New Malignancies Following Melanoma of the Skin, Eye Melanoma, and Non-melanoma Eye Cancer. In: Curtis RE, Freedman DM, Ron E, Ries LAG, Hacker DG, Edwards BK, Tucker MA, Fraumeni JF Jr. (eds). New Malignancies Among Cancer Survivors: SEER Cancer Registries, 1973-2000. National Cancer Institute. NIH Publ. No. 05-5302. Bethesda, MD, 2006. Accessed on 4/18/2014 at http://seer.cancer.gov/archive/publications/mpmono/MPMonograph_complete.pdf.

Gangadhar TC, Fecher LA, Miller CJ, et al. Chapter 69: Melanoma. In: Niederhuber JE, Armitage JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa. Elsevier: 2014.

Hamid O, Robert C, Daud A. Safety and tumor responses with lambrolizumab (anti-PD-1) in melanoma. *N Engl J Med*. 2013;369:134-144.

Hauschild A, Grob JJ, Demidov LV, et al. Dabrafenib in BRAF-mutated metastatic melanoma: A multicentre, open-label, phase 3 randomised controlled trial. *Lancet*. 2012;380:358-365.

Hodi FS, Lee S, McDermott DF, et al. Ipilimumab plus sargramostim vs ipilimumab alone for treatment of metastatic melanoma: A randomized clinical trial. *JAMA.* 2014;312:1744-1753.

Howlader N, Noone AM, Krapcho M, et al (eds). SEER Cancer Statistics Review, 1975-2011, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2011/, based on November 2013 SEER data submission, posted to the SEER website, April 2014.

Kubica AW, Brewer JD. Melanoma in immunosuppressed patients. *Mayo Clin Proc*. 2012;87:991-1003.

Kushi LH, Doyle C, McCullough M, et al. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: Reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin*. 2012;62:30-67.

Leachman SA, Lowstuter K, Wadge LM. Genetic testing for melanoma. In: Rigel DS, Friedman RJ, Dzubow LM, Reintgen DS, Bystryn JC, Marks R, eds. *Cancer of the Skin*. Philadelphia, Pa: Elsevier Saunders; 2005:281-290.

National Cancer Institute. Physician Data Query (PDQ). Melanoma Treatment. 2014. Accessed at www.cancer.gov/cancertopics/pdq/treatment/melanoma/HealthProfessional on December 30, 2014.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Melanoma. Version 1.2015. Accessed at www.nccn.org/professionals/physician_gls/PDF/melanoma.pdf on December 30, 2014.

Olsen CM, Carroll HJ, Whiteman DC. Estimating the attributable fraction for melanoma: A meta-analysis of pigmentary characteristics and freckling. *Int J Cancer*. 2010;127:2430-2445.

Robbins PF, Morgan RA, Feldman SA, et al. Tumor regression in patients with metastatic synovial cell sarcoma and melanoma using genetically engineered lymphocytes reactive with NY-ESO-1. *J Clin Oncol*. 2011;29:917-924.

Robert C, Long GV, Brady B, et al. Nivolumab in previously untreated melanoma without BRAF mutation. *N Engl J Med*. 2015;372:320-330.

Slingluff CL, Flaherty K, Rosenberg SA, Read PW. Cutaneous melanoma. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 9th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2011:1643-1691.

Topalian SL, Hodi FS, Brahmer JR, et al. Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. *N Engl J Med*. 2012;366:2443-2454.

Wolchok JD, Kluger H, Callahan MK, et al. Nivolumab plus ipilimumab in advanced melanoma. *N Engl J Med*. 2013;369:122-133.

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For additional assistance please contact your American Cancer Society
1-800-227-2345 or www.cancer.org