



Melanoma Skin Cancer

What is cancer?

The body is made up of trillions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn't die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called *metastasis*. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

No matter where a cancer may spread, it is always named for the place where it started. For example, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Not all tumors are cancerous. Tumors that aren't cancer are called *benign*. Benign tumors can cause problems – they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening.

What is melanoma?

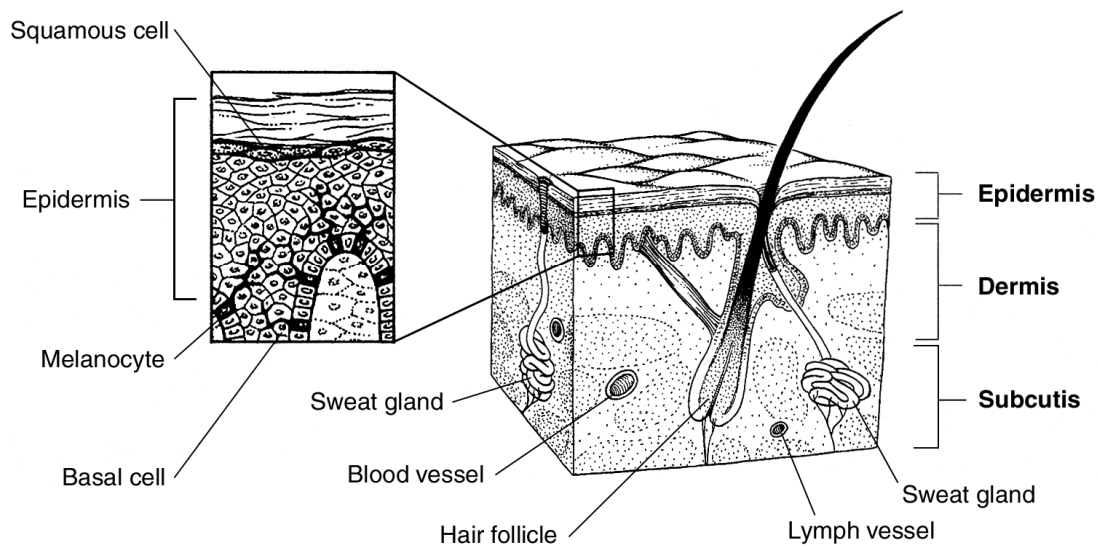
Melanoma is a cancer that starts in a certain type of skin cell. To understand melanoma, it helps to know about the normal structure and function of the skin.

Normal skin

The skin is the largest organ in your body. It does several different things:

- Covers the internal organs and protects them from injury
- Serves as a barrier to germs such as bacteria
- Prevents the loss of too much water and other fluids
- Helps control body temperature
- Protects the rest of the body from ultraviolet (UV) rays
- Helps the body make vitamin D

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



Epidermis

The top layer of skin is the epidermis. The epidermis is very thin, averaging only 0.2 millimeters thick (about 1/100 of an inch). It protects the deeper layers of skin and the organs of the body from the environment.

Keratinocytes are the main cell type of the epidermis. These cells make an important protein called keratin. Keratin helps the skin protect the rest of the body.

The outermost part of the epidermis is called the *stratum corneum*, or horny layer. It is composed of dead keratinocytes that are continually shed as new ones form. The cells in this layer are called *squamous cells* because of their flat shape.

Living squamous cells are found below the stratum corneum. These cells have moved here from the lowest part of the epidermis, the basal layer. The cells of the basal layer, called *basal cells*, continually divide to form new keratinocytes. These replace the older keratinocytes that wear off the skin's surface.

Melanocytes, the cells that can become melanoma, are also present in the epidermis. These skin cells make the 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.

The epidermis is separated from the deeper layers of skin by the basement membrane. The basement membrane is an important structure because when a skin cancer becomes more advanced, it generally grows through this barrier.

Dermis

The middle layer of the skin is called the *dermis*. The dermis 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. Collagen, made by cells called fibroblasts, gives the skin its resilience and strength.

Subcutis

The deepest layer of the skin is called the subcutis. 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.

Melanocytic tumors

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

A **Spitz nevus** is a kind of skin tumor that sometimes looks like melanoma. 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.

Other benign tumors

Benign tumors that develop from other types of skin cells include:

- Seborrheic keratoses: tan, brown, or black raised spots with a "waxy" texture or rough surface
- Hemangiomas: benign blood vessel growths often called cherry or strawberry spots, or port wine stains
- Lipomas: soft growths of benign fat cells
- Warts: rough-surfaced growths caused by a virus

Most of these tumors rarely, if ever, turn into cancers. There are a lot of 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*. Because most melanoma cells still produce melanin, melanoma tumors are usually brown or black. But this is not always true, as some melanomas can be non-pigmented and appear pink, tan, or even white.

Melanomas can occur anywhere on the skin, but are more likely to start in certain locations. The trunk (chest and back) is the most common site in men. The legs are the most commonly affected site 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 10% of melanomas in whites.

Melanomas can also form in other parts of your body such as the eyes, mouth, and vagina, but these are much less common than melanoma of the skin. Melanomas in these organs are discussed in our other documents.

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 melanoma are sometimes grouped together 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 in different ways.

Non-melanoma skin cancers include basal cell and squamous cell cancers (by far the most common skin cancers, and actually 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 less worrisome and are treated differently from melanoma. Merkel cell carcinoma is an uncommon type of skin cancer that is sometimes harder to treat. These cancers are discussed in our document called *Skin Cancer: Basal and Squamous Cell*.

Still other types of non-melanoma skin cancers are discussed in our documents called *Kaposi Sarcoma* and *Lymphoma of the Skin*.

What are the key statistics about melanoma?

Cancer of the skin is by far the most common of all cancers. Melanoma accounts for less than 5% of skin cancer cases but causes a large majority of skin cancer deaths.

The American Cancer Society's most recent estimates for melanoma in the United States are for 2012:

- About 76,250 new melanomas will be diagnosed (about 44,250 in men and 32,000 in women). Incidence rates for melanoma have been rising for at least 30 years.
- About 9,180 people are expected to die of melanoma (about 6,060 men and 3,120 women). From 2004 to 2008, the death rate in whites has been dropping in those younger than 50, but has been stable in women or rising in men older than 50.

Melanoma is more than 10 times more common in whites than in African Americans. Although before age 40, incidence rates are higher in women than in men, after 40, rates are almost twice as high in men as in women. Overall, the lifetime risk of getting melanoma is about 2% (1 in 50) 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 called "What are the risk factors for melanoma?"

Unlike many other common cancers, melanoma has a wide age distribution. It occurs in younger as well as older people. Rates continue to increase with age and are highest among those in their 80s, but melanoma is not uncommon even among those younger than 30. In fact, it is one of the more common cancers in young adults.

For information on survival rates for melanoma, see the section called "How is melanoma staged?"

What are the risk factors for melanoma?

A risk factor is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. For example, smoking is a risk factor for cancers of the lung, mouth, larynx (voice box), bladder, kidney, and several other organs.

But risk factors don't tell us everything. Having a risk factor, or even several risk factors, does not mean that you will get the disease. And many people who get the disease may not have any known risk factors. Even if a person with melanoma has a risk factor, it is often very hard to know how much that risk factor may have contributed to the cancer.

Scientists have found several risk factors that may make you more likely to develop melanoma.

Ultraviolet (UV) light exposure

Ultraviolet (UV) radiation is a major risk factor for most melanomas. Sunlight is the main source of UV radiation, which can damage the genes in your skin cells. Tanning lamps and beds are also sources of UV radiation. People with high levels of exposure to light from these sources are at greater risk for skin cancer, including melanoma.

Ultraviolet radiation is divided into 3 wavelength ranges:

- *UVA rays* cause cells to age and can cause some damage to cells' DNA. They are linked to long-term skin damage such as wrinkles, but are also thought to play a role in some skin cancers.
- *UVB rays* can cause direct damage to the DNA, and are the main rays that cause sunburns. They are also thought to cause most skin cancers.
- *UVC rays* don't get through our atmosphere and therefore are not present in sunlight. They are not normally a cause of skin cancer.

While UVA and UVB rays make up only a very small portion of the sun's wavelengths, they are the main cause of the damaging effects of the sun on the skin. UV radiation damages the DNA of skin cells. Skin cancers begin when this damage affects the DNA of genes that control skin cell growth. Both UVA and UVB rays damage skin and cause skin cancer. UVB rays are a more potent cause of at least some skin cancers, but based on what is known today, there are *no* safe UV rays.

The amount of UV exposure depends on the strength of the rays, the length of time the skin is exposed, and whether the skin is protected with clothing or sunscreen.

The nature of the UV exposure may play a role in melanoma development. Many studies have linked the development of melanoma on the trunk (chest and back) and legs to frequent sunburns (especially in childhood). The fact that these areas are not constantly exposed to UV light may also be important. Some experts think that melanomas in these areas are different from those on the face and neck, 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.

For information on how to protect yourself and your family from UV exposure, see the section called "Can melanoma be prevented?"

Moles

A *nevus* (the medical name for a mole) is a benign (non-cancerous) melanocytic tumor. Moles are not usually present at birth but 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.

Dysplastic nevi: Dysplastic nevi (nevi is the plural of nevus), also called atypical nevi, often look a little like normal moles but also look a little like melanoma. They are often larger than other moles and have an abnormal shape or color. (See the section called "Can melanoma be found early?" 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 and scalp.

A small number of dysplastic nevi may develop into melanomas. But most dysplastic nevi never become cancerous, and many melanomas seem to arise without a pre-existing dysplastic nevus.

Lifetime melanoma risk may be higher than 10% for those with many dysplastic nevi (sometimes referred to as *dysplastic nevus syndrome*). Dysplastic nevi often run in families. Someone with many dysplastic nevi and with several close relatives who have had melanoma has a 50% or greater lifetime risk of developing melanoma.

People with this condition should have very thorough, regular skin exams by a dermatologist (a doctor who specializes in skin problems). In some cases, full body photographs are taken to help the doctor recognize which moles are changing and growing. Many doctors recommend that patients be taught to do monthly skin self-exams and be counseled about sun protection.

Congenital melanocytic nevi: Moles present at birth are called congenital melanocytic nevi. The lifetime risk of getting melanoma for people with congenital melanocytic nevi has been 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 smaller for those with small nevi.

Congenital nevi are sometimes removed by surgery so that they do not have a chance to become cancerous. Whether or not 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 at regular intervals 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 more than 10 times 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 1 or more first-degree relatives (mother, father, brother, sister, child) has had melanoma. Around 10% of all people with melanoma have a family history of the disease.

The increased risk might be due to a shared family lifestyle of frequent sun exposure, a family tendency to have fair skin, or a combination of both factors. It may also be due to inherited gene changes (mutations) in a family. Gene mutations have been found in anywhere from about 10% to 40% of families with a high rate of melanoma. Most experts do not recommend genetic testing in these families at this time. Rather, they advise that people with a strong family history of melanoma do the following:

- Have regular skin exams by a dermatologist
- Thoroughly examine your skin once a month

- Be particularly careful about sun protection and avoid artificial UV rays (such as those from tanning booths)

Personal history of melanoma

A person who has already had melanoma has an increased risk of getting melanoma again. About 5% to 10% of people with melanoma will develop a second one at some point.

Immune suppression

People who have been treated with medicines that severely suppress the immune system, such as organ transplant patients, have an increased risk of melanoma.

Age

Although melanoma is more likely to occur in older people, this is a cancer that is also found in younger people. In fact, melanoma is one of the most common cancers in people younger than 30. Melanoma that runs in families may occur at a younger age.

Gender

In the United States, men have a higher rate of melanoma than women.

Xeroderma pigmentosum

Xeroderma pigmentosum (XP) is a rare, inherited condition resulting from a defect in an enzyme that normally repairs damage to DNA. People with XP have a high risk for developing melanoma and other skin cancers at a young age. Because people with XP are less able to repair DNA damage caused by sunlight, they can develop many cancers on sun-exposed areas of their skin.

Do we know what causes melanoma?

Researchers are beginning to understand 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 contain instructions for controlling when our cells grow, divide, and die. Genes that promote cell division are called *oncogenes*. Genes that slow down cell division 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) radiation can damage DNA. Sometimes this damage affects certain genes that control how and when cells grow and divide. If these genes do not function properly, the affected cells may form a cancer.

Most UV radiation comes from sunlight, but some may come from man-made sources such as tanning booths. 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 due to exposures that happened many years earlier. Children and young adults often get a lot of intense UV sun exposure that may not result in an actual cancer until many years or even decades later.

Scientists have found that the DNA of certain genes is often damaged in melanoma cells. Most of these DNA changes are not inherited. They are more likely the result of damage caused by sunlight. Some people's cells seem to repair their damaged DNA better than others. These people may be less likely to develop melanoma. In the future, better understanding of how these DNA changes lead to melanoma might be used to help treat or even prevent 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. Drugs that specifically target melanoma cells with this gene change are now being studied. Results from clinical trials of people with advanced melanomas have been promising (see the section called "What's new in melanoma research and treatment?").

In some families with inherited melanomas, gene mutations that greatly increase the risk of melanoma are 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 the growth of the cell. Scientists reason that this leads to overgrowth and eventually cancer.

Although most moles never turn into a melanoma, some do. Researchers have found some DNA changes that transform benign nevus (mole) cells into 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.

Can melanoma be prevented?

Not all melanomas can be prevented, but there are things you can do that may reduce your risk of getting melanoma.

Limiting ultraviolet (UV) exposure

The most important way to lower your risk of melanoma is to protect yourself from exposure to UV radiation. Practice sun safety when you are outdoors. "Slip! Slop! Slap!... and Wrap" is a catch phrase that can help you remember the 4 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.

Protect your skin with clothing

Clothes provide different levels of UV protection, depending on many factors. Long-sleeved shirts, long pants, or long skirts are the most protective. Dark colors generally provide more protection than light colors. A tightly woven fabric protects better than loosely woven clothing. Dry fabric is generally more protective than wet fabric.

Be aware that covering up doesn't block out all UV rays. If you can see light through a fabric, UV rays can get through too.

Some companies in the United States now make clothing that is lightweight, comfortable, and protects against UV exposure even when wet. These sun-protective clothes may have a label listing the ultraviolet protection factor (UPF) value – the level of protection the garment provides from the sun's UV rays (on a scale from 15 to 50+). The higher the UPF, the higher the protection from UV rays.

Newer products, which are used in the washing machine like laundry detergents, can increase the UPF value of clothes you already own. They add a layer of UV protection to your clothes without changing the color or texture.

Wear a hat

A hat with at least a 2- to 3-inch brim all around is ideal because it protects areas often exposed to intense sun, such as the ears, eyes, forehead, nose, and scalp. A shade cap (which looks like a baseball cap with about 7 inches of fabric draping down the sides and back) is also good, and will provide more protection for the neck. These are often sold in sports and outdoor supply stores.

A baseball cap can protect the front and top of the head but not the neck or the ears, where skin cancers commonly develop. Straw hats are not as protective as ones made of tightly woven fabric.

Use sunscreen

Use sunscreens and lip balms on areas of skin exposed to the sun, especially when the sunlight is strong (for example, between the hours of 10 am and 4 pm). Many groups, including the American Academy of Dermatology, recommend using products with a sun protection factor (SPF) of 30 or more. Use sunscreen even on hazy days or days with light or broken cloud cover because the UV light still comes through.

Always follow directions when applying sunscreen. Ideally, a 1-ounce application (about a palmful of sunscreen) is recommended to cover the arms, legs, neck and face of the average adult. Protection is greatest when sunscreen is used thickly on all sun-exposed skin. To ensure continued protection, sunscreens should be reapplied. It is often recommended to do so every 2 hours. Many sunscreens wash off when you sweat or swim and then wipe off with a towel, so they must be reapplied for maximum effectiveness. And don't forget your lips; lip balm with sunscreen is also available.

Some people use sunscreens in order to stay out in the sun for long periods of time without getting sunburned. Sunscreen should not be used to spend more time in the sun than you otherwise would, as you will still end up with damage to your skin.

Sunscreens may help reduce your exposure to UV light and reduce your risk of melanoma. But there is no guarantee, and if you stay in the sun a long time, you are at risk of developing skin cancer even if you have put on sunscreen.

If you want a tan, one option is using a "sunless" tanning lotion. These can provide the look, without the danger. Sunless tanning lotions contain a substance called *dihydroxyacetone* (DHA). DHA works by interacting with proteins on the surface of the skin to produce color. You do not have to go out in the sun for these to work. The color tends to wear off after a few days. Most sunless tanning lotions provide very little protection from UV rays, so if you use one, you should still use sunscreen and wear protective clothing when going outside.

Wear sunglasses

Wrap-around sunglasses with at least 99% UV absorption provide the best protection for the eyes and the skin area around the eyes. Look for sunglasses labeled as blocking UVA and UVB light. Labels that say "UV absorption up to 400 nm" or "Meets ANSI UV Requirements" mean the glasses block at least 99% of UV rays. If there is no label, don't assume the sunglasses will give any protection.

Seek shade

Another way to limit exposure to UV light is to avoid being outdoors in direct sunlight too long. This is particularly important in the middle of the day between the hours of 10 am and 4 pm, when UV light is strongest. If you are unsure about the sun's intensity, use the shadow test: if your shadow is shorter than you are, the sun's rays are the strongest, and it is important to protect yourself.

When you are outdoors, protect your skin. Keep in mind that sunlight (and UV rays) can come through light clouds, can reflect off water, sand, concrete, and snow, and can reach below the water's surface.

The UV Index: The amount of UV light reaching the ground in any given place depends on a number of factors, including the time of day, time of year, elevation, and cloud cover. To help people better understand the intensity of UV light in their area on a given day, the National Weather Service and the US Environmental Protection Agency have

developed the UV Index. It gives people an idea of how strong the UV light is in their area, on a scale from 1 to 11+. A higher number means a higher chance of sunburn, skin damage, and ultimately skin cancers of all kinds. Your local UV Index should be available daily in your local newspaper, on TV weather reports, and online (www.epa.gov/sunwise/uvindex.html).

Avoid tanning beds and sunlamps

Many people believe the UV rays of tanning beds are harmless. This is not true. Tanning lamps give out UVA and usually UVB rays as well, both of 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 the age of 30. Most 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. Older children need to be cautioned about sun exposure as they become more independent. It is important, particularly in parts of the world where it is sunnier, to cover your children as fully as is reasonable. You should develop the habit of using sunscreen on exposed skin for yourself and your children whenever you go outdoors and may be exposed to large amounts of sunlight.

Babies younger than 6 months should be kept out of direct sunlight and protected from the sun using hats and protective clothing. Sunscreen may be used on small areas of exposed skin only if adequate clothing and shade are not available.

A word about sun exposure and vitamin D

Doctors are learning that vitamin D has many health benefits. It may even help to lower the risk for some cancers. Vitamin D is made naturally by your skin when you are in the sun. How much vitamin D you make depends on many things, including how old you are, how dark your skin is, and how intensely the sun shines where you live.

At this time, doctors aren't sure what the optimal level of vitamin D is. A lot of research is being done in this area. Whenever possible, it is better to get vitamin D from your diet or vitamin supplements rather than from sun exposure, because dietary sources and vitamin supplements do not increase risk for skin cancer, and are typically more reliable ways to get the amount you need.

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

Watching for abnormal moles and having them removed

Certain types of moles have an increased risk of developing into a melanoma (see the section called "What are the risk factors for melanoma?"). 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 may be changing into a melanoma.

Routine removal of many moles is not generally 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 called "Can melanoma be found early?" for descriptions of what to look for.

Genetic counseling and testing

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

Genes such as CDKN2A (also known as p16) have been found to be mutated in some families with high rates of melanoma. 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.

Before getting any type of genetic testing, it's important to know ahead of time 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 be able to provide solid answers. This is why meeting with a genetic counselor before testing is crucial in deciding if testing should be done.

Because it's not clear how useful the test results might be, most melanoma experts do not recommend genetic testing for people with a personal or family history of melanoma at this time. 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.

Learning more about skin cancer prevention

Many organizations conduct skin cancer prevention activities in schools and recreational areas. Others develop brochures and public service announcements. For more information, see the section called "Additional resources."

Can melanoma 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 curable.

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. A hand-held mirror should be used to help look at areas that are hard to see, such as the backs of your thighs.

All areas should be examined, including your palms and soles, scalp, ears, nails, and your back. (For a more thorough description of a skin self-exam, see our documents called *Skin Cancer: Prevention and Early Detection* and *Why You Should Know About Melanoma*) Friends and family members can also help you with these exams, especially for those hard-to-see areas, such as your back. Be sure to show your doctor any area that concerns you and ask your doctor to look at areas that may be hard for you to see. In men, about 1 of every 3 melanomas occurs on the back.

Spots on the skin that are new or changing in size, shape, or color should be seen by a doctor promptly. Any unusual sore, lump, blemish, marking, or change in the way an area of the skin looks or feels may be a sign of skin cancer or a warning that it might occur. The skin might become scaly or crusty or begin oozing or bleeding. It may feel itchy, tender, or painful. Redness and swelling may develop. Spots on the skin that look different from the surrounding moles (the "ugly duckling sign") should be evaluated.

It is sometimes hard to tell the difference between melanoma and an ordinary mole, even for doctors, so it is important to show your doctor any mole that you are unsure of.

What to look for

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). A mole can be present at birth, or it can 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 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 **ABCD** 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 $\frac{1}{4}$ inch – the size of a pencil eraser), but melanomas can sometimes be smaller than this.

Some melanomas do not fit the rules described above, so it is important to tell your doctor about any changes in skin lesions, new skin lesions, 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 to surrounding skin
- Redness or a new swelling beyond the border
- Change in sensation – itchiness, tenderness, or pain
- Change in the surface of a mole – scaliness, oozing, bleeding, or the appearance of a bump or nodule

Exam by a health care professional

Part of a routine cancer-related checkup should include a skin exam by a health care professional qualified to diagnose skin cancer. Your doctor should be willing to discuss any concerns you might have about this exam.

Any suspicious lesions or unusual moles should be seen by your primary doctor or by a dermatologist, a doctor who specializes in skin problems. 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 called "How is melanoma diagnosed?" for more information.)

How is melanoma diagnosed?

If an abnormal area of skin raises the suspicion of skin cancer, certain medical exams and tests may be used 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 is for your doctor to take your medical history. The doctor probably will ask when the mark on the skin first appeared, if it has changed in size or appearance, and if it has caused any symptoms (pain, itching, bleeding, etc.). You may also be asked about exposures to known causes of skin cancer (including sunburns) and if 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 there is bleeding or scaling. The rest of your body will be checked for spots and moles that may be related to skin cancer.

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

If you are being seen by your primary doctor and melanoma is suspected, 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 oil is used with this instrument. A digital or photographic image of the spot may be taken.

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 lesion is likely benign (non-cancerous) without the need for a biopsy.

Skin biopsy

If the doctor thinks a spot may be a melanoma, he or she will take a sample of skin from the suspicious area to be looked at under a microscope. This is called a *skin biopsy*. Different methods can be used for a skin biopsy. The choice depends 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 may produce different types of scars, so ask your doctor about scarring before the biopsy is done.

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 biopsy

For this type of biopsy, the doctor first numbs the area with a local anesthetic. The doctor then shaves off the top layers of the skin (the epidermis and the outer part of the dermis) with a surgical blade.

A shave biopsy is useful in diagnosing many types of skin diseases and in sampling moles when the risk of melanoma is very low. But it is not generally recommended if a melanoma is suspected because a shave biopsy sample may not be thick enough to measure how deeply a melanoma has invaded the skin.

Punch biopsy

A punch biopsy removes a deeper sample of skin. The doctor uses a tool that looks like a tiny round cookie cutter. Once the skin is numbed with a local anesthetic, the doctor rotates the punch biopsy tool on the surface of the skin until it cuts through all the layers of the skin, including the dermis, epidermis, and the upper parts of the subcutis.

Incisional and excisional biopsies

To examine a tumor that may have grown into the deeper layers of the skin, the doctor may use an incisional or excisional biopsy technique. After numbing the area with a local anesthetic, 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 wound are 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.

Examining the biopsy samples

All skin biopsy samples are looked at under a microscope by a pathologist, a doctor trained in the examination and diagnosis of tissue samples. Often, the sample is sent to a dermatopathologist, a doctor who has special training in making diagnoses from skin samples.

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 in a skin lesion, biopsies of nearby lymph nodes may be done to see if the cancer has spread that far (or farther).

In rare cases, biopsies may be needed to figure out what type of cancer someone has. For example, some melanomas may spread so quickly that they reach the lymph nodes, lungs, brain, or other areas while the original skin melanoma is still small. Sometimes these tumors are found before the skin lesion is discovered. In other cases they may be found long after a skin melanoma has been removed, so it's not clear that it might be the same cancer.

In still other cases, metastatic melanoma may be found without ever finding a skin lesion. 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 quite rare, and if melanoma has spread widely throughout the body, it may not be possible to tell which tumor was the first one.

When such spread has occurred, the metastatic melanoma in certain organs might 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 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 typically given different treatments.

These types of biopsies may be 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 to biopsy large lymph nodes near a melanoma to find out if the melanoma has spread to them. This type of biopsy uses a syringe with a thin, hollow needle to remove very small tissue fragments from a 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 near the body surface, 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 internal organ such as the lung or liver, an ultrasound or computed tomography (CT) scan (a special type of x-ray; see below) is often used to guide the needle into place.

FNA biopsies are not as invasive as some other types of biopsies, but they may not always provide enough of a sample to tell if melanoma is present. 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 skin incision. Local anesthetic is generally used. This is often done if a lymph node's size suggests spread of melanoma 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 determine if it has spread to nearby lymph nodes. 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. That is why 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), the doctor injects a small amount of radioactive material (and sometimes a blue dye) into the area of the melanoma. After an hour or so, the doctor checks various lymph node areas with a radioactivity detector (which works like a Geiger counter). The surgeon makes a small incision in the identified lymph node area. The lymph nodes are then checked to find which one(s) turned blue or became radioactive. These nodes are then removed and looked at under a microscope.

If the sentinel node does not contain melanoma cells, 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*.

If a lymph node near a melanoma is abnormally large, the sentinel node procedure may not be needed. The enlarged node is simply biopsied.

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 in people with very early-stage melanoma, which is very unlikely to have spread. Imaging tests may also be done to help determine how well treatment is working or to look for possible signs of cancer recurrence after treatment.

Chest x-ray

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

Computed tomography (CT)

The CT scan is a type of x-ray test that produces 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 or organs such as the liver are enlarged, which might be due to the spread of melanoma. It can also identify 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. 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 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 or have ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays. You need to lie still on a table while they are being done. During the test, the table slides in and out of the scanner, a ring-shaped machine that completely surrounds the table. You might feel a bit confined by the ring you have to lie in when the pictures are being taken.

Spiral CT (also known as helical CT) is now used in many medical centers. This type of CT scan uses a faster machine that reduces the dose of radiation and yields more detailed pictures.

CT-guided needle biopsy: CT scans can also be used to guide a biopsy needle precisely into a suspected metastasis. For this procedure, you remain on the CT scanning table while a radiologist moves a biopsy needle through the skin and toward the location of the mass. CT scans are repeated until the needle is within the mass. A fine needle biopsy sample (tiny fragment of tissue) or a larger core needle biopsy sample (a thin cylinder of tissue) is then removed to be looked at under a microscope.

Magnetic resonance imaging (MRI)

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. The energy from the radio waves is absorbed by the body and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a very detailed image of parts of the body. 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. 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. The MRI machine also makes loud buzzing noises that you may find disturbing. Some places provide earplugs to help block this noise out.

Positron emission tomography (PET)

For a PET scan, you receive an injection of a radioactive substance (usually a type of sugar related to glucose, known as FDG). The amount of radioactivity used is very low. Because cancer cells in the body are growing rapidly, they absorb large amounts of the radioactive sugar. A special camera can then create a picture of areas of radioactivity in the body. The picture is not finely detailed like a CT or MRI scan, but it can provide helpful information about your whole body.

This test can be useful to see if the cancer has spread to lymph nodes. PET scans are also useful when your doctor thinks the cancer has spread but doesn't know where. Doctors find it most useful in people with advanced stages of melanoma. It is not very helpful in people with early stage melanoma.

Some newer machines are able to perform 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 with the more detailed appearance of that area on the CT.

Bone scan

A bone scan is used to look for cancer that has spread to the bones, but it is rarely used in melanoma. It is only done when other test results or symptoms suggest that the cancer may have spread to the bones.

For this test, a slightly radioactive chemical is injected into the bloodstream. It collects in the bones at cancer sites or other areas where there is metabolic activity. You then lie on a table for about 30 minutes while a special camera detects the radioactivity and creates a picture of your skeleton. The images from these scans are seen as "hot spots" in the body, but they don't provide much detail. If an area lights up on the scan, x-rays of the affected area can be done to get a more detailed look. If melanoma is a possibility, a biopsy of the area may be needed to confirm this.

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

Lab tests

Tests of biopsy samples

Samples from any biopsies you have will be sent to a lab, where a pathologist (a doctor who is specially trained to diagnose disease) will look at them under a microscope for melanoma cells. 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 cancer (see the section called "How is melanoma staged?"), which in turn affects treatment options and prognosis (outlook).

In the near future, doctors may also test biopsy samples for specific gene changes in the melanoma cells. Some newer drugs now being studied for advanced melanomas are only likely to work if the cells have certain gene changes, so these tests may become important in determining treatment options.

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 for blood levels of a substance called lactate dehydrogenase (LDH) before treatment. If the melanoma has spread to distant parts of the body, a higher than normal level of LDH is a sign that the cancer may be harder to treat.

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

How is melanoma staged?

Staging is a process of finding out how widespread a cancer is. This includes describing its size, whether it has spread to the lymph nodes or any other organs, and certain other factors. The stage is based on the results of the physical exam, imaging tests (CT or MRI scan, etc.), biopsies, and other tests, which are described in the section called "How is melanoma diagnosed?"

The American Joint Committee on Cancer (AJCC) TNM system

A staging system is a standard way of summarizing how far a cancer has spread. This helps members of the cancer care team determine a patient's prognosis (outlook) as well as the best treatment options.

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 contains 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** (small bean-shaped 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 actually 2 types of staging for melanoma:

- *Clinical staging* is based on what is found on physical exam, 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 node biopsy) may actually be higher than the clinical stage (determined before the node biopsy) if the biopsy finds cancer in new areas. Doctors use the pathologic stage once it is available, as it provides a more accurate picture of the extent of the cancer.

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*. The thinner the melanoma, the better the prognosis. In general, melanomas less than 1 millimeter (mm) in depth (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: Another important aspect for tumors is the mitotic rate. To measure this, the pathologist counts the number of cells that are in the process of dividing (mitosis) in a specified 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: The melanoma tends to have a worse prognosis if the pathologist says it is *ulcerated* (the outermost layer of skin is absent).

The possible values for T are:

TX: Primary tumor cannot be assessed.

T0: No evidence of primary tumor.

Tis: Melanoma in situ (The tumor remains in the epidermis).

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/mm².

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/mm².

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 or toward a nearby lymph node area (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 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 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 $1/\text{mm}^2$. 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 $1/\text{mm}^2$, 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 of 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 of 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 of 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 of any thickness, but it is not ulcerated. It has spread to small areas of nearby skin or lymphatic channels 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 of 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 of any thickness and is ulcerated. It has spread to small areas of nearby skin or lymphatic channels around the original tumor, but the nodes do not contain melanoma. There is no distant spread.

Any T, N3, M0: The melanoma can be of 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 or lymphatic channels 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 by stage?

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some patients 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. Whether or not you want to read about the survival statistics below for melanoma is up to you.

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).

In order 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 more favorable outlook for people now being diagnosed with melanoma.

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they cannot predict what will happen in any particular person's case. Knowing the type and the stage of a person's cancer is important in estimating their outlook. But many other factors may 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 if the numbers below may apply, as he or she is familiar with the aspects of your particular situation.

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 III C: The 5-year survival rate is around 40%. The 10-year survival is around 24%.

Stage IV: The 5-year survival rate for stage IV melanoma 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, or if the blood level of lactate dehydrogenase (LDH) is normal.

Other factors affecting survival

Other factors aside from stage may also affect survival. For example, stage for stage, older people generally have shorter survival times. The biggest drop 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 shown that melanoma is more serious if it occurs on a foot, palm, or nail bed. People with HIV infection and melanoma also are at greater risk of dying of their melanoma.

How is melanoma treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the 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.

General treatment information

Once melanoma has been diagnosed and staged, your cancer care team will discuss your treatment options with you. Based on the stage of the cancer and other factors, treatment options may include:

- Surgery
- Chemotherapy
- Immunotherapy
- Radiation therapy

Early stage cancers 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.

It is important to consider your options carefully. If there is anything you do not understand, ask to have it explained.

The next few sections describe the various types of treatments used for melanoma of the skin. This is followed by a description of the most common treatment options based on the stage of the melanoma.

Surgery for melanoma

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

Simple excision

Thin melanomas can usually be completely cured by a fairly minor surgery called simple excision. The tumor is 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*.

Simple 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 call for larger margins.

Tumor thickness	Recommended margins
In situ	0.5 cm
Less than 1 mm	1 cm
1 to 2 mm	1 to 2 cm
2 to 4 mm	2 cm
Over 4 mm	At least 2 cm

Local anesthesia is injected into the area to numb it before the excision. The wound is carefully stitched back together afterwards. This will leave a scar.

Re-excision (wide excision)

When a diagnosis of melanoma is made by biopsy, the site will probably need to be excised again. More skin will be cut away from the melanoma site, and the sample will be viewed under a microscope to make sure that no cancer cells remain in the skin. The size of the margin depends on the thickness of the tumor (see the table above).

If the melanoma is on the face, the margins may be smaller to avoid disfigurement. In some cases, the surgeon may use Mohs surgery (but doctors disagree on its use for melanoma). In this procedure, the skin (including the melanoma) is removed in very thin layers. Each layer is viewed under a microscope for signs of cancer. 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 skin tissue as possible.

Amputation

If the melanoma is on a finger or toe, the treatment may require amputation of all or part of that digit. At one time, some melanomas of the arms and legs were also treated by amputation, but this is no longer done.

Lymph node dissection

In this operation, the surgeon removes all of the lymph nodes in the region near the primary melanoma. (For example, if a skin melanoma is found 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 nearest the melanoma. Depending on the thickness and location of the melanoma, this may be done by physical exam, or by imaging tests for nodes that are not near the surface.

If the nearby lymph nodes feel abnormally hard or large, and a fine needle aspiration 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 called "How is melanoma diagnosed?" for a description of this procedure.) If the sentinel lymph node does not show cancer, then it is unlikely the melanoma has spread to the lymph nodes and there is no need for a lymph node dissection. 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*.

In the past, a lymph node dissection was sometimes done to see if the melanoma had spread to the nodes. Today, a sentinel lymph node biopsy is done first because it is a less invasive surgery that is less likely to cause side effects such as lymphedema (see below). A lymph node dissection may then be done afterward if needed.

It is 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 over time. 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. Sometimes special devices that squeeze the limbs are used and may be helpful. For more information, see

our document called *Understanding Lymphedema (for Cancers Other Than Breast Cancer)*.

Lymphedema, along with the pain from the surgery itself, is why lymph node dissection is not done unless the doctor thinks 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 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 completely removed, this surgery may help some patients live longer. Removing metastases in some places, such as the brain, might also relieve symptoms and help improve the patient's quality of life.

If you have metastatic melanoma and surgery is recommended 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.

Chemotherapy for melanoma

Chemotherapy (“chemo”) uses drugs that kill cancer cells. The drugs are usually injected into a vein or given by mouth. They travel through the bloodstream to all parts of the body and attack cancer cells that have already spread beyond the skin to lymph nodes and other organs. Because the drug reaches all areas of the body, it is called a *systemic* therapy.

Chemo is often used to treat advanced melanoma. Although it is usually not as effective in melanoma as it is in some other types of cancer, chemo may relieve symptoms or extend survival for some patients.

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

Several chemotherapy drugs may be used to treat melanoma:

- Dacarbazine (also called DTIC)
- Temozolomide
- Paclitaxel
- Carmustine (also known as BCNU)

- Cisplatin
- Carboplatin
- Vinblastine

Dacarbazine, temozolomide, and paclitaxel may be given either alone or along with some of the other drugs on the list. It is 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 chemotherapy drugs with 1 or more immunotherapy drugs, such as interferon-alpha and/or interleukin-2 (see the document called "Immunotherapy"), may be more effective than a single chemotherapy 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 injected into the limb for a short period of time.

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. A tourniquet is tied around the limb to make sure the chemotherapy does not enter the rest of the body. A high dose of chemotherapy (usually with a drug called melphalan) is then injected into the limb. During the session, the blood exits the limb through the tube in the vein, is heated by a machine in the operating room, and is then recirculated back into 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.

Isolated limb perfusion 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.

Possible side effects of chemotherapy

Chemotherapy 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, 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 chemotherapy depend on the type and dose of drugs given and the length of time they are taken. These side effects may include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting

- Diarrhea
- Increased risk of infection (from low white blood cell counts)
- Easy bruising or bleeding (from low blood platelets)
- Fatigue (from low red blood cells)

These side effects are usually short-term and go away once treatment is finished. Some drugs may have specific effects that are not listed above, so be sure to talk with your cancer care team about what you might expect in terms of side effects.

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.

You should report any side effects you notice while getting chemotherapy to your medical team so that they can be treated promptly. In some cases, the doses of the chemotherapy drugs may need to be reduced or treatment may need to be delayed or stopped to prevent side effects from getting worse.

Immunotherapy for melanoma

Immunotherapy stimulates a patient's own immune system to recognize and destroy cancer cells more effectively. Several types of immunotherapy can be used in treating patients with advanced melanoma.

Ipilimumab for advanced melanoma

Ipilimumab (Yervoy) is a monoclonal antibody, a man-made version of an immune system protein. It targets CTLA-4, a protein that normally helps keep immune system cells called T cells in check. By blocking the action of CTLA-4, ipilimumab is thought to boost the immune response against melanoma cells in the body.

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, it has been shown to help people live an average of several months longer. Doctors are now studying its use for earlier stage melanomas as well.

This drug works by basically removing the brakes off the body's immune system. This can be helpful against cancer cells, but it can also lead to serious side effects. In some cases the immune system starts to attack other parts of the body, which can cause serious problems in the intestines, liver, hormone-making glands, nerves, skin, eyes, or other organs. In some people these side effects have been fatal.

These immune-related side effects most often occur during treatment, but some have been reported up to a few months after treatment has finished. It is 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.

Cytokines for advanced melanoma

Cytokines are proteins that boost the immune system in a general way. Two man-made versions of natural cytokines, interferon-alpha 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 may 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 centers that have experience with this type of treatment.

Interferon-alpha as adjuvant therapy

Patients with thicker melanomas often have cancer cells that have spread to other parts of the body. Even after all apparent cancer has been removed by surgery, some of these cells may remain. Interferon-alpha 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 cannot 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 therapy, patients and their doctors should take into account the potential benefits and side effects of this treatment.

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 kind of like a cytokine, 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 (Aldara) is a drug that, when applied as a cream, 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 may also be used for some melanomas that have spread along the skin. Still, not all doctors agree on whether 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 may have serious skin reactions to this drug. Imiquimod is not used for more advanced melanomas.

Radiation therapy for melanoma

Radiation therapy uses high-energy 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 for treating some patients with melanoma. The treatment is much like getting an x-ray, but the radiation is more intense. 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.

Radiation therapy is not often used to treat the original melanoma that started on the skin. In some cases, it may be given as an adjuvant to surgery in the area where lymph nodes were removed, especially if many of the nodes contained cancer cells. This is to try to reduce the chance that the cancer will come back.

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

Radiation therapy is often used to relieve symptoms caused by metastases to the brain or bone. Treatment with the goal of relieving symptoms is called palliative therapy. Palliative radiation therapy is not expected to cure the cancer, but it may help shrink it for a time to control some of the symptoms.

Side effects of external radiation therapy depend on where it is aimed. They might include sunburn-like skin problems and hair loss where the radiation enters the body, fatigue, nausea, and vomiting. Often these go away after treatment.

Clinical trials for melanoma

You may have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is choosing which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. They are done to get a closer look at promising new treatments or procedures.

If you would like to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our Web site at www.cancer.org/clinicaltrials. You

can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinicaltrials

There are requirements you must meet to take part in any clinical trial. If you do qualify for a clinical trial, it is up to you whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the art cancer treatment. They are the only way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

You can get a lot more information on clinical trials in our document called *Clinical Trials: What You Need to Know*. You can read it on our Web site or call our toll-free number (1-800-227-2345) and have it sent to you.

Complementary and alternative therapies for melanoma

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and Web sites may offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help you feel better. Some methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not to be helpful, and a few have even been found harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delays or interruptions in your medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It is easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with few or no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or

they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating cancer.

As you consider your options, here are 3 important steps you can take:

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking about using.
- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods in general and to find out about the specific methods you are looking at.

The choice is yours

Decisions about how to treat or manage your cancer are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

Treatment of melanoma 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 epidermis. They are usually treated by surgery to remove the melanoma and a margin of about 1/2 cm (about 1/5 inch) of normal skin. For melanomas in sensitive areas on the face, some doctors may use a cream containing the drug imiquimod (Aldara) if surgery might be disfiguring, although not all doctors agree with this use.

Stage I

Stage I melanoma is treated by surgery to remove the melanoma as well as a margin of normal skin. The amount of normal skin removed depends on the thickness of the melanoma. When the thickness is less than 1 mm, wide excision with 1 cm (2/5 inch) margins is recommended. For stage I melanomas between 1 mm and 2 mm thick, the tumor and 1 cm to 2 cm (4/5 inch) of surrounding skin are removed. No more than 2 cm of normal skin needs to be removed from all sides of the melanoma in stage I. 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 the sentinel lymph node biopsy is positive, 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.

Stage II

Wide excision is the standard treatment for stage II melanoma. If the melanoma is between 1 mm and 2 mm thick, a margin of 1 to 2 cm of normal skin will be removed as well. If the melanoma is thicker than 2 mm, about 2 cm of normal skin will be removed from around the tumor site.

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, then a lymph node dissection (where all the lymph nodes in that area are surgically removed) will be done at a later date.

In certain cases (such as if the tumor is found to be more than 4 mm thick or if lymph nodes contain cancer), some doctors may advise adjuvant therapy (additional treatment) with interferon after surgery. 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 reached the lymph nodes at the time of diagnosis. Surgical treatment for stage III melanoma usually requires lymph node dissection, along with wide excision of the primary tumor as in stage II. Adjuvant therapy with interferon may help some patients with stage III melanomas fight off recurrence longer.

If several melanomas are present, they should all be removed. If this is not possible, injections of bacille Calmette-Guerin (BCG) vaccine or interleukin-2 directly into the melanoma or applying the topical immunotherapy imiquimod are treatment options. For melanomas on an arm or leg, another possible option is to isolated limb perfusion (infusing the limb with a heated solution of chemotherapy). In some cases, radiation therapy may be given as an adjuvant to surgery in the area where lymph nodes were removed, especially if many of the nodes were found to contain cancer. Other possible treatments include chemotherapy, immunotherapy with cytokines, or both combined (biochemotherapy).

Newer treatments being tested in clinical trials may benefit some patients. Many patients with stage III melanoma may 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 lymph node metastases causing symptoms can often be removed by surgery. Metastases in internal organs are sometimes removed, depending on how many are present, where they are located, and how likely they are to cause symptoms. Metastases that cause symptoms but cannot be removed surgically may be treated with radiation, immunotherapy, or chemotherapy.

Ipilimumab (Yervoy), a newer immunotherapy drug, has been shown to help some people with advanced melanoma live longer. It is just now coming into use, but some doctors may prefer it over other treatment options, such as chemotherapy or other types of immunotherapy.

The chemotherapy drugs in use at this time are of limited value in most people with stage IV melanoma. Dacarbazine (DTIC) and temozolomide (Temodar) are the ones most often used, either by themselves or combined with other drugs. Even when chemotherapy can shrink these cancers, the effect is often only temporary, with an average time of about 3 to 6 months before the cancer starts growing again. In rare cases they are effective for longer periods of time, however.

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

Some doctors 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 may 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. Patients should carefully consider the possible benefits and side effects of any recommended treatment before starting.

Because stage IV melanoma is very hard to treat with current therapies, patients may want to think about taking part in a clinical trial. Clinical trials of new chemotherapy drugs, targeted drugs, new methods of immunotherapy such as vaccines, and combinations of different types of treatments may benefit some patients.

Even though the outlook for patients with stage IV melanoma tends to be poor overall, a small number of patients have responded very well to treatment or have survived for many years after diagnosis.

Recurrent melanoma

Treatment of melanoma that comes back after initial treatment depends on the stage of the original melanoma, the prior treatment, and the site of recurrence.

Melanoma may come back in the skin near the site of the original tumor. In general, these local (skin) recurrences are treated with surgery similar to that recommended for a

primary melanoma. This may 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, systemic chemotherapy, immunotherapy, radiation therapy, or tumor injection with BCG vaccine or interferon.

If nearby lymph nodes weren't removed during the initial treatment, the melanoma may come back in these nearby lymph nodes. This may appear as a swelling or tumor mass. Lymph node recurrence is treated by lymph node dissection, and may include adjuvant therapy such as interferon or radiation therapy.

The cancer can also come back in distant sites. Almost any organ can be affected. Most often, the melanoma will come back in the lung, bone, 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 sites of recurrence can sometimes be removed by surgery. Most chemotherapy drugs aren't able to reach the brain, although temozolomide may be useful. Radiation therapy to the brain may help as well.

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

More melanoma treatment information

For more details on treatment options – including some that may not be addressed in this document – the National Comprehensive Cancer Network (NCCN) and the National Cancer Institute (NCI) are good sources of information.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. These are available on the NCCN Web site (www.nccn.org). The NCCN also has a patient version of treatment guidelines for melanoma, which can be found at www.nccn.com.

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its Web site (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov.

What should you ask your doctor about melanoma?

It is important to have honest, open discussions with your cancer care team. They want to answer all of your questions, no matter how minor you might think they are. Some questions to consider:

- What type of skin cancer do I have?

- How far has my melanoma spread within or beneath the skin? How thick is my melanoma?
- Are there other tests that need to be done before we can decide on treatment?
- Are there other doctors I need to see?
- 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 long will treatment last? What will it involve? Where will it be done?
- What is my expected prognosis (outlook), based on my cancer as you view it?
- Will I have a scar after treatment? What other side effects might I have?
- What should I do to be ready for 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?
- Do I need follow-up appointments to check for recurrence or formation of a new cancer?
- Are my family members at risk for skin cancer? Should I arrange to have my family members screened?

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.

What happens after treatment for melanoma?

For some people with melanoma, treatment may 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 live with this uncertainty and are leading full lives. Our document called *Living With Uncertainty: The Fear of Cancer Recurrence*, gives more detailed information on this.

For others, the melanoma may never go away completely. These people may get regular treatment with immunotherapy, 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.

Follow-up care

If you have completed treatment, your doctors will still want to watch you closely. It is very important to keep all follow-up appointments. Follow-up is needed to check for cancer recurrence or spread, as well as possible side effects of certain treatments. This is the time for you to ask your health care team any questions you need answered and to discuss any concerns you might have.

Your follow-up 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. In addition to the exams, imaging tests may be recommended for some patients.

A typical follow-up schedule for melanomas thinner than 1 mm generally calls for physical exams every 3 to 12 months for several years. If these exams are normal, you can return for a checkup once a year. Your doctor may recommend more frequent exams if you have many moles or atypical moles.

For thicker melanomas, 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 6 to 12 months for the first several years, especially for people who had more advanced stage disease.

It is also important for melanoma skin cancer survivors to do regular self-exams of the skin and lymph nodes (most doctors recommend 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 come back as many as 10 or (rarely) more years after it was first treated.

Patients with stage IV melanoma whose cancer has been completely removed or disappeared after treatment usually have the same follow-up schedule as for those with thicker melanomas (see above). Patients with stage IV melanoma that does not go away completely have a follow-up schedule that is based on their specific situation.

If melanoma does recur, treatment will depend on the location of the cancer, what treatments you've had before, and your overall health. For more information on how recurrent cancer is treated, see the section called "Treatment of melanoma by stage." For more general information on dealing with a recurrence, you may also want to see our document called *When Your Cancer Comes Back: Cancer Recurrence*. You can get this document by calling 1-800-227-2345.

A person who has had one melanoma may still be at risk for developing another melanoma or a non-melanoma type of skin cancer. People cured of one melanoma should

continue to examine their skin every month for new skin cancers, and should avoid too much sun exposure.

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself seeing a new doctor who does not know about your medical history. It is important that you be able to give your new doctor the details of your diagnosis and treatment. Make sure you have this information handy:

- 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 on a CD, 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 doctors prepare when patients are sent home
- If you had radiation therapy, a summary of the type and dose of radiation and when and where it was given
- If you had chemotherapy or immunotherapy, a list of your drugs, drug doses, and when you took them

It is also 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.

Lifestyle changes after having melanoma

You can't change the fact that you have had cancer. 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 thought much about 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 the 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 those 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 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 may have gained weight that you can't seem to lose. All of these things can be very frustrating.

If treatment caused 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 portions 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 these treatment side effects.

One of the best things you can do after cancer treatment is put healthy eating habits into place. 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.

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 doesn't get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them to exercise 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 is normal for your fitness, endurance, and muscle strength to decline. Any plan for physical activity should fit your own situation. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis twice a week. If you haven't exercised 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, try to find an exercise buddy so you're not doing it alone. Having family or friends involved when starting a new exercise 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 balance activity with rest. It is 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 information on dealing with fatigue, please see *Fatigue in People With Cancer* and *Anemia in People With Cancer*.)

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.

And long term, we know that getting regular physical activity 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 cancer 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 is little 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. People who have had melanoma are at higher risk for developing another melanoma or other type of skin cancer. Because of this, it is important to avoid too much sun exposure and to continue to examine your skin every month for signs of possible new skin cancers. Skin cancers that are found early are typically much easier to treat than those discovered at a later stage.

Adopting healthy behaviors such as not smoking, eating well, and maintaining 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 cancer.

How does having melanoma 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 may 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, church 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 is 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 do not include them. Let them in, and let in anyone else who 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.

What happens if melanoma treatment is no longer working?

If cancer 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 shrink the tumors enough to help you live longer and feel better. But when a person has tried many different treatments and the cancer has not gotten any better, the cancer tends to become resistant to all treatment. If this happens, it's important to weigh the possible limited benefits of 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 medical treatments and nothing's working anymore. Your doctor may offer you new options, but at some point you may 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. In many cases, your doctor can estimate how likely it is the cancer will respond to treatment you are considering. For instance, the doctor may say that more treatment might have about a 1 in 100 chance of working. Some people are still tempted to try this. But it is important to think about and understand your reasons for choosing this plan.

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 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 purpose 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 drugs 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 bone pain caused by cancer that has spread to the

bones. Or chemo might be used to help shrink a tumor and keep it from blocking the bowels. But this is not the same as treatment to try to cure the cancer.

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 your 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 called *Hospice Care*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there is 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.

What's new in research and treatment of melanoma?

Research into the causes, prevention, and treatment of melanoma is under way in many 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 to 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 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.

Public education

Most skin cancer can be prevented. The best way to reduce the number of skin cancer cases 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 is important for health care professionals and skin cancer survivors to remind everyone about the dangers of excess UV exposure (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 should be detected early, when it is most likely to be completely 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. The American Cancer Society works 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 telephone number and Web site are listed in the "Additional resources" section.

The American Cancer Society uses a slogan popularized in Australia as 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 DNA research

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

On the other hand, some people may 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, limitations, and downsides of testing for changes in this gene.

Molecular staging

Advances in melanoma DNA research are also being applied to molecular staging. In ordinary staging, a lymph node removed from a patient is looked at under a microscope to see if melanoma cells have spread to the lymph node.

In molecular staging, RNA (a chemical related to DNA), is extracted from cells in the lymph node. Certain types of RNA are made by melanoma cells but not by normal lymph node cells. A sophisticated test called reverse transcription polymerase chain reaction (RT-PCR) is used to detect these types of RNA.

Early studies have found that RT-PCR is better than routine microscopic testing at detecting the spread of melanoma to lymph nodes. This test may eventually help identify some patients who might benefit from additional treatment such as immunotherapy after surgery. However, some doctors are concerned that this test may lead to unnecessary treatment for some patients, which is why this test is not currently recommended. Studies are now in progress to learn more about how results should influence choice of treatment.

Treatment

Immunotherapy

This type of melanoma treatment includes several approaches for helping the body's immune system attack melanoma cells more effectively. Some forms of immune therapy, such as ipilimumab (Yervoy), cytokines (interferon-alpha and interleukin-2), and the BCG vaccine are already used to treat some melanomas. They work by boosting the immune system in a general way.

Ipilimumab targets CTLA-4, a protein that normally suppresses the T-cell immune response, which might help melanoma cells to survive. This drug has been shown to help some people with advanced melanomas live longer. Researchers are now trying to determine if it might be useful earlier in the course of the disease. Other drugs that counteract CTLA-4 are now being studied as well.

Melanoma vaccines

Vaccines directed at melanoma are being studied in clinical trials. They are experimental therapies that do not yet have proven benefit.

These vaccines are, in some ways, similar to 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 injected into a patient as a vaccine in an attempt 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. Clinical trials are testing the value of treating advanced melanoma patients with vaccines, sometimes combined with cytokine therapy as well. The results of these studies have been mixed so far, but newer vaccines may hold more promise.

In a recent clinical trial of patients with advanced melanoma, adding a vaccine to high-dose interleukin-2 (IL-2) increased the portion of tumors that shrank and the length of

time before they started growing again better than just giving IL-2 alone. But it's not yet clear if this vaccine can help people live longer.

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), 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. Further studies of these new treatments are now under way.

Targeted drugs

As doctors have discovered some of the gene changes in melanoma cells, they have begun to develop 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 changes in the BRAF gene

About half of all melanomas have changes in a gene called BRAF. These changes cause the gene to make an altered BRAF protein that signals the melanoma cells to grow and divide. A drug called vemurafenib (PLX4032 or Zelboraf™) acts against the altered BRAF protein. In studies of people whose metastatic melanoma has a certain BRAF gene change (mutation), it caused tumors to shrink in about half of the patients treated. It also seemed to prolong the time before the tumors started growing again and helped patients live longer. In August 2011, vemurafenib was approved by the FDA to treat advanced melanomas that contain the BRAF mutation. This drug is not likely to work in patients whose melanomas have a normal BRAF gene, so a sample of your melanoma must be tested to see if it contains the BRAF mutation before the drug can be used. This drug is given as a pill, taken twice a day. The most common side effects seen in the studies were joint pains, fatigue, hair loss, rash, itching, sensitivity to the sun, and nausea. Serious side effects can occur, such as heart rhythm problems, liver problems, severe allergic reactions, severe skin problems, and severe eye problems. Also, some of the patients treated with vemurafenib in the studies developed new skin cancers, including some melanomas.

Other drugs that target BRAF gene changes are now being developed and studied as well.

Drugs that target changes in the c-kit gene

Certain types of melanomas often have unusual gene changes. This often includes melanomas that start in certain areas:

- On the palms of the hands, soles of the feet, or under fingernails
- Inside the mouth or in other mucosal areas

- In areas that get chronic sun exposure

About one third of these uncommon melanomas have changes in a gene called c-kit. Some drugs that are already used to treat other cancers, such as imatinib (Gleevec) and nilotinib (Tasigna), are known to target cells with changes in c-kit. Clinical trials are now under way to see if these and other drugs might help people with these types of melanoma.

Drugs that target other gene or protein changes

Several drugs that target other abnormal genes or proteins, such as sorafenib (Nexavar), bevacizumab (Avastin), temsirolimus (Torisel), 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

More information from your American Cancer Society

The following related information may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-227-2345.

A Parent's Guide to Skin Protection (also available in Spanish)

After Diagnosis: A Guide for Patients and Families (also available in Spanish)

Clinical Trials: What You Need to Know

Immunotherapy

Living With Uncertainty: The Fear of Cancer Recurrence

Pain Control: A Guide for Those With Cancer and Their Loved Ones (also available in Spanish)

Skin Cancer: Prevention and Early Detection

Sun Basics: Skin Protection Made Simple (information for children aged 8 to 14)

Surgery (also available in Spanish)

Understanding Chemotherapy: A Guide for Patients and Families (also available in Spanish)

Understanding Lymphedema (for Cancers Other Than Breast Cancer)

Understanding Radiation Therapy: A Guide for Patients and Families (also available in Spanish)

When Your Cancer Comes Back: Cancer Recurrence

Why You Should Know About Melanoma (also available in Spanish)

National organizations and Web sites*

In addition to the American Cancer Society, other sources of patient information and support include:

American Academy of Dermatology

Toll free number: 1-888-462-3376 (1-888-462-DERM)

Web site: www.aad.org

Environmental Protection Agency

Web site: www.epa.gov/ebtpages/humasunprotection.html

Melanoma Research Foundation

Toll free number: 1-800-673-1290

Web site: www.melanoma.org

Melanoma Patients Information Page: www.melanoma.org/community/mpip-melanoma-patients-information-page

National Cancer Institute

Toll-free number: 1-800-422-6237 (1-800-4-CANCER)

Web site: www.cancer.gov

Skin Cancer Foundation

Toll-free number: 1-800-754-6490 (1-800-SKIN-490)

Web site: www.skincancer.org

**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 detailed guide

Altekruse SF, Kosary CL, Krapcho M, Neyman N, Aminou R, Waldron W, Ruhl J, Howlander N, Tatalovich Z, Cho H, Mariotto A, Eisner MP, Lewis DR, Cronin K, Chen HS, Feuer EJ, Stinchcomb DG, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2007, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2007/, based on November 2009 SEER data submission, posted to the SEER web site, 2010.

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 2012*. Atlanta, Ga: American Cancer Society; 2012.

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.

Chapman PB, Hauschild A, Robert C, et al. Improved survival with vemurafenib in melanoma with BRAF V600E mutation. *N Engl J Med*. 2011 Jun 30;364(26):2507-16.
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, Puzanov I, Kim KB, et al. Inhibition of mutated, activated BRAF in metastatic melanoma. *N Engl J Med*. 2010;363:809-819.

Huang CL, Halpern AC. Management of the patient with melanoma. In: Rigel DS, Friedman RJ, Dzubow LM, Reintgen DS, Bystryn JC, Marks R, eds. *Cancer of the Skin*. Philadelphia, Pa: Elsevier Saunders; 2005:265–273.

Lange JR, Fecher LA, Sharfman WH, et al. Melanoma. In: Abeloff MD, Armitage JO, Niederhuber JE, Kastan MB, McKenna WG, eds. *Abeloff's Clinical Oncology*. 4th ed. Philadelphia, Pa: Elsevier; 2008:1229–1252.

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. 2011. Accessed at www.cancer.gov/cancertopics/pdq/treatment/melanoma/HealthProfessional on April 8, 2011.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Melanoma. Version 2.2011. Accessed at www.nccn.org/professionals/physician_gls/PDF/melanoma.pdf on April 8, 2011.

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.

Schwartzentruber DJ, Lawson D, Richards J, et al. A phase III multi-institutional randomized study of immunization with the gp100:209-217(210M) peptide followed by high-dose IL-2 compared with high-dose IL-2 alone in patients with metastatic melanoma. *J Clin Oncol*. 2009;27:18s (suppl; abstr CRA9011).

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*. 8th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2008:1897–1951.

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