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About Melanoma Skin Cancer

Overview

If you have been diagnosed with melanoma skin cancer or are worried about it, you likely have a lot of questions. Learning some basics is a good place to start.

What Is Melanoma Skin Cancer?

Research and Statistics

See the latest estimates for new cases of melanoma skin cancers in the US and what research is currently being done.

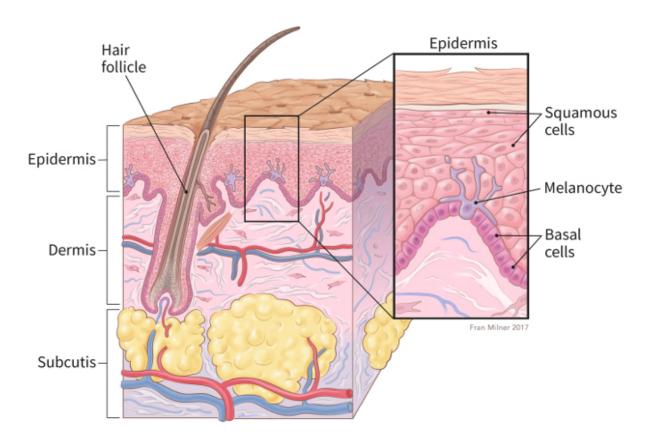
- Key Statistics for Melanoma Skin Cancer
- What's New in Melanoma Skin Cancer Research?

What Is Melanoma Skin Cancer?

Melanoma is a type of skin cancer that develops when melanocytes (the cells that give the skin its tan or brown color) start to grow out of control.

Cancer starts when cells in the body begin to grow out of control. Cells in nearly any part of the body can become cancer, and can then spread to other areas of the body. To learn more about cancer and how it starts and spreads, see What Is Cancer?¹

Melanoma is much less common than some other types of skin cancers. But melanoma is more dangerous because it's much more likely to spread to other parts of the body if not caught and treated early.



Where do skin cancers start?

Most skin cancers start in the top layer of skin, called the *epidermis*. There are 3 main types of cells in this layer:

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

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

Melanoma skin cancers

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

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

Having darkly pigmented skin lowers your risk of melanoma at these more common sites, but anyone can get melanoma on the palms of the hands, soles of the feet, or under the nails. Melanomas in these areas make up a much larger portion of melanomas in African Americans than in whites.

Melanomas can also form in other parts of your body, such as the <u>eyes</u>², mouth, genitals, and anal area, but these are much less common than melanoma of the skin.

Melanoma is much less common than some other types of skin cancer. But melanoma is more dangerous because it's much more likely to spread to other parts of the body if not caught and treated early.

Other types of skin cancer

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

Basal cell and squamous cell skin cancers

Basal cell and squamous cell cancers are by far the most common skin cancers, and actually are more common than any other form of cancer. Because they rarely spread (metastasize) to other parts of the body, basal cell and squamous cell skin cancers are

usually less concerning and are treated differently from melanoma. These cancers are discussed in <u>Basal and Squamous Cell Skin Cancer</u>.³

Less common skin cancers

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

- Merkel cell carcinoma⁴
- Kaposi sarcoma⁵
- Cutaneous (skin) lymphoma⁶
- Skin adnexal tumors (tumors that start in hair follicles or skin glands)
- Various types of sarcomas⁷

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

Benign skin tumors

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

Benign tumors that start in melanocytes

A **mole** (nevus) is a benign skin tumor that develops from melanocytes. Almost everyone has some moles. Nearly all moles (nevi) are harmless, but having some types can raise your risk of melanoma. See <u>Risk Factors for Melanoma Skin Cancer</u>⁸ for more information about moles.

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

Benign tumors that develop from other types of skin cells

- Seborrheic keratoses: tan, brown, or black raised spots with a "waxy" texture
- Hemangiomas: benign blood vessel growths, often called strawberry spots
- Lipomas: soft growths made up of fat cells

 Warts: rough-surfaced growths caused by some types of human papilloma virus (HPV)

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

Hyperlinks

- 1. www.cancer.org/treatment/understanding-your-diagnosis/what-is-cancer.html
- 2. www.cancer.org/cancer/eye-cancer.html
- 3. www.cancer.org/cancer/basal-and-squamous-cell-skin-cancer.html
- 4. www.cancer.org/cancer/merkel-cell-skin-cancer.html
- 5. www.cancer.org/cancer/kaposi-sarcoma.html
- 6. www.cancer.org/cancer/skin-lymphoma.html
- 7. www.cancer.org/cancer/soft-tissue-sarcoma.html
- 8. <u>www.cancer.org/cancer/melanoma-skin-cancer/causes-risks-prevention/risk-factors.html</u>

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Key Statistics for Melanoma Skin Cancer

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

How common is melanoma?

The American Cancer Society's estimates for melanoma in the United States for 2022 are:

- About 99,780 new melanomas will be diagnosed (about 57,180 in men and 42,600 in women).
- About 7,650 people are expected to die of melanoma (about 5,080 men and 2,570 women).

The rates of melanoma have been rising rapidly over the past few decades, but this has varied by age.

Risk of getting melanoma

Melanoma is more than 20 times more common in whites than in African Americans. Overall, the lifetime risk of getting melanoma is about 2.6% (1 in 38) for whites, 0.1% (1 in 1,000) for Blacks, and 0.6% (1 in 167) for Hispanics. The risk for each person can be affected by a number of different factors, which are described in Risk Factors for Melanoma Skin Cancer¹.

Melanoma is more common in men overall, but before age 50 the rates are higher in women than in men.

The risk of melanoma increases as people age. The average age of people when it is diagnosed is 65. But melanoma is not uncommon even among those younger than 30. In fact, it's one of the most common cancers in young adults² (especially young women).

For survival statistics, see Survival Rates for Melanoma Skin Cancer by Stage³.

Visit the American Cancer Society's Cancer Statistics Center⁴ for more key statistics.

Hyperlinks

1. www.cancer.org/cancer/melanoma-skin-cancer/causes-risks-prevention/risk-

factors.html

- 2. www.cancer.org/cancer/cancer-in-young-adults.html
- 3. <u>www.cancer.org/cancer/melanoma-skin-cancer/detection-diagnosis-staging/survival-rates-for-melanoma-skin-cancer-by-stage.html</u>
- 4. cancerstatisticscenter.cancer.org/

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What's New in Melanoma Skin Cancer Research?

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

Causes, prevention, and early detection

Sunlight and ultraviolet (UV) radiation

Recent research suggests there may be 2 main ways that exposure to UV rays1 is

linked to melanoma, but there is likely some overlap.

The first link is to **sun exposure as a child and teenager.** People with melanoma often have an early history of sunburns or other intense sun exposures, although not everyone does. This early sun exposure may damage the DNA (genes) in skin cells called melanocytes, which 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 thighs (in women) and trunk (in men), areas that generally aren't exposed to the sun as much in adulthood.

The second link is to **chronic sun exposure.** This type of exposure may be the cause of many melanomas that occur on the arms, neck, and face. These areas are chronically exposed to sun, particularly in men.

Tanning booths might help either kind of melanoma to develop.

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

Public education

Most melanomas (and other skin cancers) can be prevented². The best way to lower the number of skin cancers and the pain and loss of life from this disease is to educate people, especially parents, about <u>risk factors</u>³ and <u>warning signs and symptoms</u>⁴. It's important for health care professionals and skin cancer survivors to remind everyone about the dangers of too much UV exposure (both from the sun and from man-made sources such as tanning beds) and about how easy it can be to <u>protect your skin from UV rays</u>⁵.

Melanoma can often be found early⁶, when it is most likely to be cured. Monthly skin self-exams and awareness of the warning signs of melanomas may be helpful in finding most melanomas when they are at an early, curable stage.

The <u>American Academy of Dermatology (AAD)</u>⁷ sponsors annual free skin cancer screenings throughout the country. Many local American Cancer Society offices work closely with the AAD to provide volunteers for registration, coordination, and education efforts related to these free screenings. Look for information in your area about these screenings or contact the American Academy of Dermatology for more information.

Along with recommending staying in the shade, the American Cancer Society uses a slogan popularized in Australia as part of its skin cancer prevention message in the United States. "Slip! Slop! Slap!®... and Wrap" is a catchy way to remember when going

outdoors to slip on a shirt, slop on sunscreen, slap on a hat, and wrap on sunglasses to protect your eyes and the sensitive skin around them.

Melanoma genetic research

Scientists have made a great deal of progress in understanding how some of the DNA (gene) changes inside normal skin cells can lead them to become melanoma cells. In some cases, these gene changes can now be <u>targeted with newer treatments</u>⁸ for melanoma..

Some people <u>inherit mutated</u> (<u>damaged</u>) <u>genes</u>⁹ from their parents that raise their risk of melanoma. For example, changes in the *CDKN2A* (*p16*) gene cause some melanomas that run in certain families. People who have a strong family history of melanoma might want to speak with a cancer genetic counselor or a doctor experienced in cancer genetics to discuss the possible benefits, limits, and downsides of <u>testing for changes in this gene</u>¹⁰.

Diagnosis

Some newer approaches to diagnosing skin cancer don't require the removal of a skin sample.

One type of "optical biopsy" is **reflectance confocal microscopy (RCM)**. This technique allows the doctor to look at an abnormal area of skin to a certain depth without cutting into the skin.

RCM is used widely in Europe, and it's now available in some centers in the US. It may be especially useful for people with many unusual moles, as it can cut down on the number of skin biopsies these people need. RCM might also be helpful in determining the edges of a melanoma, which could help during surgery. This technique will likely become more widely available in the coming years.

Another technique now being studied is **adhesive patch testing**. Instead of cutting into the skin to get a biopsy sample, a sticky patch is placed over the suspicious area. When it's removed it takes some of the top layers of skin with it, which can then be tested for certain gene changes that are often linked with melanoma. If one of these gene changes is found, a standard biopsy of the area can then be done. If no gene changes are found, a biopsy isn't needed, and the area can be watched instead.

Lab tests to help determine prognosis (outlook)

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

Recent research has shown that certain gene expression patterns in melanoma cells can help show if <u>stage I or II melanomas</u>¹¹ are likely to spread. A lab test based on this research, known as *DecisionDx-Melanoma*, is now available. The test divides melanomas into 2 main groups, based on their gene patterns:

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

This test might help tell if someone with early-stage melanoma should get a sentinel lymph node biopsy (SLNB) or additional treatment, or if they need to be followed more closely after treatment to look for signs of recurrence. Doctors are still studying the best of use of this test.

Tests of other genes and gene patterns are now being studied as well.

Treatment

While early-stage melanomas can often be cured with <u>surgery</u>¹², more advanced melanomas can be much harder to treat. But in recent years, newer types of immunotherapy and targeted therapies have shown a great deal of promise and have changed the treatment of this disease.

Immunotherapy

This type of treatment helps the body's immune system attack melanoma cells more effectively. Some forms of immune therapy are now used to treat some melanomas (see Immunotherapy for Melanoma Skin Cancer).

Immune checkpoint inhibitors: Newer drugs such as pembrolizumab (Keytruda), nivolumab (Opdivo), and ipilimumab (Yervoy) block proteins that normally suppress the T-cell immune response against melanoma cells. These drugs are now one of the mainstays of treatment for advanced melanomas. Researchers are now looking for ways to make these drugs work even better. One way to do this might be by combining them with other treatments, such as other types of immunotherapy or targeted drugs.

Researchers are also studying if these drugs can be helpful for earlier stage

melanomas, as an adjuvant (additional) treatment after surgery. Some have already been shown to be useful after surgery for melanomas that have reached the lymph nodes, where they can help lower the chance that the cancer will come back. Researchers are now studying if these drugs might be helpful for even earlier stage melanomas, or if they might be helpful if used before surgery (called neoadjuvant treatment) for some people.

Newer immune checkpoint inhibitors with slightly different targets are now being studied as well.

Melanoma vaccines: Vaccines to treat melanoma are being studied in <u>clinical trials</u>¹⁴.

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

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

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

Adoptive cell therapy with tumor-infiltrating lymphocytes (TILs): Some studies have shown that treating patients with tumor-infiltrating lymphocytes (TILs) can shrink melanoma tumors and possibly prolong life as well. TILs are immune system cells inside a tumor. Once a tumor is removed with surgery, the TILs can be separated out and then multiplied in the lab, after which they can be given back to the patient as an IV infusion. In studies done so far, patients are usually given chemotherapy before this treatment to help the body accept the TILs. After getting the TILs, patients might also be given an immunotherapy such as interleukin-2 (IL-2)¹⁵, which might help these immune cells better attack the cancer.

Newer studies are looking at changing certain genes in the TILs before they are given to see if this can make them more effective at fighting the cancer. This approach has looked promising in early studies, but it's complex and is only being tested in a few centers.

Other immunotherapies: Other new forms of immunotherapy are also being studied. In addition, many studies are now looking at combining different types of immunotherapy, which may be more effective than any single treatment for advanced melanoma.

Targeted drugs

<u>Targeted therapy</u>¹⁶ drugs target parts of melanoma cells that make them different from normal cells. These drugs work differently from standard chemotherapy drugs. They work in some cases when chemotherapy doesn't. They can also have different (and sometimes less severe) side effects.

Drugs that target cells with *BRAF* **gene changes:** About half of all melanomas have changes in the *BRAF* gene, which helps the cells grow. Drugs that target the BRAF protein or the related MEK proteins have been shown to shrink many of these tumors, especially when BRAF and MEK inhibitors are combined. These drugs are now often used to treat advanced melanomas that test positive for the *BRAF* gene change. Researchers are now looking at whether these drugs might be helpful before or after surgery for some earlier stage melanomas.

Other, similar drugs are now being studied as well.

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

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

Drugs that target other gene or protein changes: Several drugs that target other abnormal genes or proteins are now being studied in clinical trials as well. Some examples include axitinib (Inlyta), pazopanib (Votrient), and everolimus (Afinitor).

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

Skin Cancer ACS Research Highlights¹⁷

See latest examples of how the Society conducts & funds research to help prevent, find, diagnose, treat, and live with skin cancers.

Hyperlinks

- 1. www.cancer.org/healthy/cancer-causes/radiation-exposure/uv-radiation.html
- 2. <u>www.cancer.org/cancer/melanoma-skin-cancer/causes-risks-prevention/prevention.html</u>
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