

# Melanoma Skin Cancer Causes, Risk Factors, and Prevention

Learn about the risk factors for melanoma skin cancer and what you might be able to do to help lower your risk of getting melanoma.

#### **Risk Factors**

A risk factor is anything that raises your chances of getting a disease such as cancer. Learn more about the risk factors for melanoma skin cancer.

Risk Factors for Melanoma Skin Cancer

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you can do to lower your risk of getting it. If you are at higher risk because of certain factors, there are also things you can do that might help find it early<sup>1</sup>, when it's likely to be easier to treat.

- What is a risk factor?
- Ultraviolet (UV) light exposure
- Moles
- · Lighter skin, hair, and eye color
- Family history of melanoma
- Personal history of melanoma or other skin cancers
- Having a weakened immune system
- Being older
- Being male
- Xeroderma pigmentosum

#### What is a risk factor?

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

Having a risk factor, or even many risk factors, does not mean that you will get melanoma. Many people with risk factors never get melanoma. And some people who get it may have few or no known risk factors.

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

### Ultraviolet (UV) light exposure

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

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

The pattern and timing of the UV exposure may play a role in melanoma development. For example, melanoma on the trunk (chest and back) and legs has been linked to frequent sunburns (especially in childhood). This might also have something to do with the fact that these areas aren't constantly exposed to UV light. Some research suggests that melanomas that start in these areas are different from those that start on the face, neck, and arms, where the sun exposure is more constant.

And different from either of these are melanomas on the palms of the hands, soles of the feet, or under the nails (known as **acral lentiginous melanomas**), or on internal surfaces such as the mouth and vagina (**mucosal melanomas**), where there has been little or no sun exposure.

To learn more about the effects of UV rays on the skin and what you can do to protect yourself and your loved ones, see <u>Ultraviolet (UV) Radiation</u><sup>2</sup> and <u>How Do I Protect</u> <u>Myself from Ultraviolet (UV) Rays</u><sup>3</sup>

#### Moles

A mole (also known as a *nevus*) is a benign (non-cancerous) pigmented tumor. Babies are not usually born with moles; they often begin to appear in children and young adults.

**Having many moles:** Most moles will never cause any problems, but someone who has many moles is more likely to develop melanoma.

**Atypical moles (dysplastic nevi):** These moles look a little like normal moles but have some features of melanoma. They are often larger than other moles and have an abnormal shape or color. (See <u>Signs and Symptoms of Melanoma Skin Cancer</u><sup>4</sup> for descriptions of how moles and melanomas look.) They can appear on skin that is exposed to the sun, as well as skin that is usually covered, such as on the buttocks or scalp.

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

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

People with this condition have a very high lifetime risk of melanoma, so they need to have very thorough, regular skin exams by a dermatologist (a doctor who specializes in skin problems). Sometimes full-body photos are taken to help the doctor recognize if

moles are changing and growing. Many doctors recommend that these patients be taught to do monthly <u>skin self-exams</u><sup>5</sup> as well.

**Congenital melanocytic nevi:** Moles present at birth are called *congenital melanocytic nevi*. The lifetime risk of melanoma developing in congenital melanocytic nevi is estimated to be between 0 and 5%, depending on the size of the nevus. People with very large congenital nevi have a higher risk, while the risk is lower for those with small nevi. For example, the risk for melanoma is very low in congenital nevi that are smaller than the palm of the hand, while those that cover large portions of the back and buttocks (*bathing trunk nevi*) have significantly higher risks.

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

### Lighter skin, hair, and eye color

The risk of melanoma is much higher for people with lighter skin color than for people with darker skin.

Among people with lighter skin, those with red or blond hair, blue or green eyes, or skin that freckles or burns easily are at increased risk.

### Family history of melanoma

Your risk of melanoma is higher if one or more of your first-degree relatives (parents, brothers, sisters, or children) has had melanoma. Around 1 in 10 people with melanoma have a family history of the disease.

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

For some people with a strong family history of melanoma, doctors might advise genetic counseling and testing to see if they have gene mutations that increase their risk.

#### Personal history of melanoma or other skin cancers

A person who has already had melanoma has a higher risk of getting melanoma again. In people who've had several melanomas or who've had melanoma at an early age, doctors might advise genetic counseling and testing to see if they have gene mutations that increase their risk.

People who have had basal or squamous cell skin cancers are also at increased risk of getting melanoma.

#### Having a weakened immune system

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

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

People infected with <u>HIV</u><sup>6</sup>, the virus that causes AIDS, often have weakened immune systems and are also at increased risk for melanoma.

### **Being older**

The risk of melanoma increases as people age, but melanoma can also develop in younger people. In fact, melanoma is one of the most common cancers in people younger than 30 (especially younger women).

Melanoma that runs in families may occur at a younger age.

### **Being male**

In the United States, men are more likely than women to get melanoma, although this varies by age. Before age 50, the risk is higher for women; after age 50, the risk is higher in men.

### Xeroderma pigmentosum

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

Tsao H, McCormick SR. Inherited susceptibility to melanoma. UpToDate. 2023. Accessed at https://www.uptodate.com/contents/inherited-susceptibility-to-melanoma on September 15, 2023.

## What Causes Melanoma Skin Cancer?

genes can result in cells growing out of control.

 Some genes normally help repair mistakes in a cell's DNA. Changes that turn off these DNA repair genes can result in the buildup of DNA changes within a cell, which might lead to them growing out of control.

Mutations or other changes in any of these types of genes might lead to cells growing out of control. Changes in several different genes are usually needed for a cell to become a cancer cell. To learn more, see <u>Oncogenes, Tumor Suppressor Genes, and DNA Repair Genes</u><sup>1</sup>.

### Acquired gene mutations

Most often, gene changes related to melanoma are acquired during a person's lifetime and are not passed on to a person's children (inherited). Sometimes these **acquired mutations** seem to happen randomly within a cell, without having a clear cause. At other times, they likely happen as the result of exposure to an outside cause.

For example, <u>ultraviolet (UV) rays</u><sup>2</sup> are a major cause of melanoma. Most UV rays come from sunlight, but some can come from man-made sources such as tanning beds. UV rays can damage the DNA in skin cells. Sometimes this affects certain genes that control how the cells grow and divide. If these genes no longer work properly, the affected cells may become cancer cells.

In many cases a melanoma might not appear until many years after the DNA damage from UV rays has been done. Children and young adults often get a lot of intense sun exposure that might not result in cancer until many years or even decades later.

The most common change in melanoma cells is a mutation in the *BRAF* oncogene, which is found in about half of all melanomas. Other genes that can be affected in melanoma include *NRAS*, *CDKN2A*, and

Less often, people inherit gene changes from a parent that clearly raise their risk of melanoma.

Familial (inherited) melanomas most often have changes in tumor suppressor genes, such as *CDKN2A* (also known as *p16*), *CDK4*, or *BAP1*,

#### Seek shade

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

## Slip! Slop! Slap!<sup>®</sup> and Wrap!

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

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

#### Avoid using tanning beds and sunlamps

Many people believe the UV rays of tanning beds are harmless. This is not true. Tanning lamps give off UV rays, which can cause long-term skin damage and can cancer.

Certain types of moles are more likely to develop into melanoma (see Melanoma Skin Cancer Risk Factors). 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 features that suggest they might change into a melanoma.

Routine removal of many moles is not usually recommended as a way to prevent melanoma. Some melanomas develop from moles, but most do not. If you have many moles, getting careful, routine exams by a dermatologist, along with doing monthly <u>skin self-exams</u><sup>3</sup>, 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 <u>Signs and Symptoms of Melanoma Skin</u> <u>Cancer</u><sup>4</sup> for descriptions of what to look for.

### Avoid weakening your immune system (when possible)

Having a weakened immune system increases your risk of getting melanoma and other types of skin cancer.

Infection with HIV, the virus that causes AIDS, can weaken the immune system. Avoiding known risk factors for HIV infection, such as intravenous (IV) drug use and having unprotected sex with many partners, might lower your risk of skin cancer, as well as many other types of cancer. (For more information, see <u>HIV Infection, AIDS, and</u> <u>Cancer<sup>5</sup></u>.)

Some people need to take medicines to suppress their immune system. This includes people who have had organ transplants and some people with autoimmune diseases. People with cancer also sometimes need to take medicines such as chemotherapy, which can lower their immune function. For these people, the benefit from taking these medicines will likely far outweigh the small increased risk of getting skin cancer.

## Hyperlinks

- 1. <u>www.cancer.org/cancer/risk-prevention/sun-and-uv/uv-radiation.html</u>
- 2. www.cancer.org/cancer/risk-prevention/sun-and-uv/uv-protection.html
- 3. <u>www.cancer.org/cancer/risk-prevention/sun-and-uv/skin-exams.html</u>

- 4. <u>www.cancer.org/cancer/types/melanoma-skin-cancer/detection-diagnosis-</u> staging/signs-and-symptoms.html
- 5. www.cancer.org/cancer/risk-prevention/infections/hiv-infection-aids.html

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# Genetic Counseling and Testing for People at High Risk of Melanoma

Gene mutations (changes) that increase melanoma risk can be passed down through families (inherited), but these account for only a small portion of melanomas.

You might have inherited a gene mutation that increases your risk of melanoma if:

• Several (typically at least 3) members on one side of your family have had melanoma

- You have had 3 or more melanomas
- You have had melanoma at an early age (typically before age 45)
- You or other family members have also had other cancers that might be from an inherited genetic syndrome (such as pancreatic cancer, breast cancer, or brain tumors)

The most common gene changes in families with high rates of melanoma are mutations in the *CDKN2A* gene (also known as *p16*). Genetic tests for changes in this gene have been available for several years, although it hasn't always been clear how useful they are. In part, this is because people with any of the factors above are already known to have a higher risk of melanoma whether they carry a mutated *CDKN2A* gene or not, so it's not always clear how genetic testing results would change what a person does (or what a doctor would recommend).

In recent years, researchers have found inherited changes in other genes that are linked with an increased risk of melanoma. While changes in some of these genes seem to be linked mainly with melanoma, changes in other genes result in inherited syndromes that increase the risk of other cancers, as well as melanoma. For example:

- Changes in the *BRCA2* gene are most often linked with increased risks of breast and ovarian cancers, but they're also linked with some other cancers, including melanoma.
- Changes in the *PTEN* gene are linked with breast, uterine, and thyroid cancer, as well as melanoma.
- Changes in the *TP53* gene can result in Li-Fraumeni syndrome, which is linked with increased risks of breast cancer, sarcoma, and brain tumors, as well as melanoma.
- Changes in the *BAP1* and *MITF* genes have also been linked with other cancers in addition to melanoma.

With advances in technology in recent years, the costs of genetic testing have come down, and testing can now be done to look for changes in several different genes at the same time. Still, most melanoma experts don't recommend genetic testing for all people with a personal or family history of melanoma. Testing is more likely to be helpful if you have any of the factors in the list above, or if your family history includes some of the cancer types listed above.

Whether or not your doctor recommends genetic testing – and which gene changes would be tested for – will depend on how likely it is that you might have an inherited gene change.

If you're considering genetic testing, it's very important to meet first with a genetic counselor or other health professional with knowledge of genetic testing. They can describe the tests to you and explain what the results may or may not tell you about your risk. Genetic testing is not perfect, and sometimes the tests might not provide clear answers. To learn more about genetic testing, see <u>Genetic Testing for Cancer Risk</u><sup>1</sup>

Written by