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# Treatment Update Melanoma

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## Researchers are studying the causes of melanoma to find new ways to diagnose and treat it in earlier stages.

#### Each year, more than 68,000 Americans are

**diagnosed with melanoma.** Melanoma is the most serious type of skin cancer. It begins in cells called melanocytes that give the skin its pigment, or color. While most melanocytes are located in the skin, they can also be located in the eye and other organs. Melanocytes make the skin pigment, melanin. Normal skin cells grow and divide to form new skin cells, replacing old ones that wear off the skin's surface. Normal cells know when to stop growing and dividing once they have fully developed, but cancer cells continue to grow and divide, forming a tissue mass called a growth or tumor. In melanoma, melanocytes become cancerous (malignant) when they do not stop growing. Because they continue to grow, they can spread and damage other parts of the body.

Although it is a very serious cancer, melanoma is quite treatable in its early stages. Researchers are studying the causes of melanoma to find new ways to diagnose and treat it earlier. Knowing more about how melanoma starts and spreads has led to new ways of treating it.

## About Melanoma

Melanoma can appear on any skin surface and on parts of the body that never see the sun, such as inside the mouth. Even though it is more common in light-skinned people of European descent, melanoma occurs in men and women of all races and ages. In women, it usually develops on the lower legs, between the shoulders, or on the hips. In men, melanoma is seen mostly on the head, the neck, the back, between the shoulders, or on the hips.

#### **Types of Melanoma**

There are four main types of melanoma:

**Superficial spreading melanoma** is the most common type of melanoma. It looks like a brown-black stain that spreads and is at least one-quarter of an inch wide. This type usually starts from a growth that is not cancerous (mole). It is found most often on the legs or on the back.

**Nodular melanoma** starts as a mole and then becomes raised and dome-shaped. It is found on women's legs and on women's and men's backs. This is the most aggressive form of melanoma.

**Lentigo maligna melanoma** is less common and usually seen in older adults. This kind of melanoma most often appears on the face or other body parts exposed to the sun. It looks like a dark, odd-shaped stain. It is not associated with moles.

Acral lentiginous melanoma is usually found on the soles of the feet, palms of the hands, undersides of the fingers, fingernails, or toenails.

### Stages of Melanoma

Not everyone with melanoma will receive the same treatment. The right treatment depends on your individual situation. To plan the best treatment for you, your doctor needs to know the stage of your cancer—that is, whether and how much it has spread in your body. If your doctor thinks you might have melanoma, he or she will remove a skin sample of that area (skin biopsy). The lab will check the skin sample to see if cancer cells are present. Your doctor may also order other tests, such as blood tests, chest X-rays, CT scans, MRIs, and PET scans, to see whether cancer cells have spread in your body.

Based on the results of your skin biopsy and other tests, the melanoma is given a number from 0 to 4. This is known as the stage of the cancer.

Stage 0	The melanoma involves only the top layer of skin. This is also called melanoma in situ.
Stage 1	<ul> <li>1a The tumor is no more than 1 millimeter thick (about as wide as a pencil tip). The surface may look like it is worn out or broken down, or</li> <li>1b The tumor is between 1 and 2 millimeters thick, and the surface is not broken down.</li> </ul>
Stage 2	<ul> <li>2a The tumor is between 1 and 2 millimeters thick, and the surface appears broken down, or</li> <li>2b The thickness of the tumor is more than 2 millimeters thick, and the surface may appear broken down.</li> </ul>
Stage 3	The melanoma cells have spread to at least one nearby lymph node (lymph nodes are the small "filtering stations" that rid the body of waste and fluids and help fight infections), or The melanoma cells have spread from the original tumor to nearby tissues.
Stage 4	Cancer cells have spread to the lung or other organs, skin areas, or lymph nodes far away from the original growth. This is also called metastatic melanoma.

## **Treatment Options for Melanoma**

Treatment of melanoma depends on the type and stage of your cancer and the size and location of the tumor, as well as your overall health and medical history. Sometimes, all of the melanoma is removed during a biopsy and no more treatment is required. If more treatment is needed, treatment options may include surgery, radiation, chemotherapy, immunotherapy, targeted treatment, and clinical trials.

#### Surgery

Surgery is the main way to treat all stages of melanoma, and it is also used to treat melanoma that comes back after treatment (recurrent melanoma). There are a few different ways in which the surgeon can remove the tumor:

**Local excision** removes the melanoma and a small amount of normal tissue around it.



Wide local excision removes the melanoma and a larger amount of normal tissue around it. Nearby lymph nodes may also be removed. Lymph nodes, also called lymph glands, are small bean-shaped groups of immune system tissue. They remove cell waste, germs, and other harmful substances from the immune system.

If a large area of tissue is removed from the body, the surgeon may need to use skin from another part of your body to replace the missing skin (skin graft). If you have a skin graft, you may have to take special care of the area until it has healed.

In addition to removing the tumor, your doctor may also perform one of the following surgical procedures:

Sentinel lymph node biopsy removes the first lymph node that the cancer is likely to spread to from the tumor (sentinel lymph node). That lymph node is looked at under a microscope. If cancer cells are found, taking out more lymph nodes may be recommended.

**Lymphadenectomy** removes the lymph nodes and examines them to see if they have cancer cells.

### Radiation

Radiation therapy uses forms of energy—X-rays and gamma rays—to kill cancer cells. The two main types of radiation therapy are external radiation and internal radiation. External radiation uses a machine *outside* the body that transmits radiation to the cancer site. Internal radiation uses a radioactive substance that is placed *inside* the body. Microscopic spheres with a radioactive drug inside can be injected into or near the cancer site. The spheres deliver low-dose radiation treatment directly at the tumor site. Radiation therapy is sometimes used in stage-3 melanoma after surgery to keep it from coming back. It may also be used in stage-4 melanoma when surgery is not an option or may be hard to do. Radiation therapy cannot cure melanoma that has spread in the body, but it can shrink tumors that are painful. It is also used to relieve symptoms in cases where melanoma comes back after treatment.

### Chemotherapy

Chemotherapy is a cancer treatment that uses drugs to kill cancer cells or stop them from growing. It may be used to treat stage-3 melanoma that cannot be removed using surgery, and stage-4 melanoma, or if the melanoma comes back after treatment. Even if the surgeon removes the whole tumor in the surgery, you may be given chemotherapy to kill any cancer cells that may be left behind. Usually these drugs are given by an injection or are taken by mouth in a pill form.



Chemotherapy can be given daily or in 14-day, 21-day, or 28-day cycles followed by a time of rest. Some chemotherapy drugs used to treat melanoma include:

- Dacarbazine (DTIC-Dome)
- Temozolomide (Temodar)
- Dacarbazine or temozolomide combined with other chemotherapy drugs
- Paclitaxel (Taxol), alone or with cisplatin (Platinol) or carboplatin (Paraplatin)

These drugs may be used alone or given together. Chemotherapy is not the most effective treatment option for melanoma, but often it can lessen cancer symptoms and extend life.



### Immunotherapy

Immunotherapy is a treatment that helps boost the immune system's ability to find and destroy cancer cells. It may be used after surgery to reduce the chance of the cancer returning. Immunotherapy may also treat melanoma that comes back after treatment.

One immunotherapy is interferon alfa-2b (Intron A), which is a treatment approved by the Food and Drug Administration (FDA) for use after surgery to try to decrease the risk of melanoma returning. It is approved for patients with stage-2b and stage-3 melanoma. Another form of interferon, called peginterferon alfa-2b (Sylatron), was approved by the FDA in March 2011. Peginterferon alfa-2b can be used after the melanoma is completely removed by surgery even if it had spread to the lymph nodes.

Other immunotherapies approved for the treatment of stage-4 melanoma include interleukin-2 (Proleukin) and Ipilimumab (Yervoy). Ipilimumab was also approved by the FDA in March 2011. Interferon alfa-2b, interleukin-2, and ipilimumab are given by needle into a vein. Interferon alfa-2b can also be given by needle under the skin. Peginterferon alfa-2b should only be given by needle under the skin.

**Interferon alfa-2b and Peginterferon alfa-2b** act like proteins made by normal cells when the body is fighting an infection or disease. It slows down the growth of melanoma.

**Interleukin-2** is a protein made by blood cells in the body. It helps the body make more of the immune cells that can destroy melanoma tumors.

**Ipilimumab** (or "Ipi") is a newer treatment that acts by "taking the brakes off" of the immune system to help destroy melanoma.

### **Targeted Therapy**

Targeted therapy is a form of treatment in which drugs are developed to destroy cancer cells while leaving normal cells intact. These drugs find cancer cells based on special features of a tumor. Tumors have genetic mutations, and these mutations can cause certain proteins to become overactive. Targeted therapy blocks the function of these proteins, shutting down the ability of the cell to grow. Because they are "targeted" to the tumor, these therapies may be more effective and have less side effects compared to chemotherapy and radiation.

The FDA approved vemurafenib (Zelboraf), a targeted therapy, in August 2011. Vemurafenib can be used to treat patients who have melanoma that cannot be removed by surgery or has spread throughout the body. Vemurafenib works by blocking the activity of a mutated form of BRAF, a protein that is part of the mechanism cells use to grow. By blocking the activity of this protein, it can shut down the ability of the tumor cells to grow out of control. In clinical trials, vemurafenib has been shown to extend life in patients with metastatic melanoma.

### **Clinical Trials**

Melanoma researchers are conducting studies called clinical trials to find out whether promising new treatments are effective. Clinical trials can test for new uses of existing drugs, different ways to give treatment, and new ways to detect cancer.

Many researchers are studying vaccines that trigger the immune system to find and destroy cancer cells. Different types of antimelanoma vaccines are being tested in trials for patients with stage-3 or stage-4 melanoma. Ask your doctor about clinical trials and whether or not one may be right for you.

## **Managing Side Effects**

The different surgeries and drugs used to treat melanoma can cause many side effects. Many of these side effects are treatable and/or may stop when treatment is stopped. Be alert for *any* side effects and report them to your doctor. Here are different side effects related to some treatments.

#### Surgery

**Pain** Your doctor may give you a pain medicine or tell you other ways to relieve pain. Some strong pain relievers, such as *opioids*, can lessen very severe pain. Morphine is an example of an opioid. Other pain relievers, like acetaminophen (Tylenol), may be used along with opioids. Keeping a pain diary can help you track and describe your pain to your health care team.

**Bleeding** Your doctor or nurse may show you how to take special care of the wound left by the surgery.

**Scars** Your doctor can use creams, injectable medicines, and lasers to improve problem scars that cause pain, itching, discomfort, are large in size, or that may worry you.

Lymphedema This is a build-up of fluid, usually in an arm or a leg, that may occur when lymph nodes are removed. A physical therapist and/or special exercises can help improve your ability to move. To prevent infection you may also have special instructions to clean or protect the skin of the swollen area. To lessen swelling, compression stockings or machines may also be used.

#### Radiation

**Red, dry, tender, or itchy skin** Your doctor may recommend or prescribe creams or lotions containing topical corticosteroids or antibiotics, to help relieve the discomfort.

**Fatigue** Your doctor may recommend exercising, if possible, and other ways to stay active. Taking short naps (less than one hour at a time) during the day and getting a good night's rest can also help. Other options include changing your work schedule and saving your energy for the activities you find most important.

### Chemotherapy

**Infections, fevers, low immunity** Your treatment may affect your body's ability to fight off infection. Your doctor will run blood tests before treatment and either delay or reduce your dose depending on your tests. During treatment, tell your doctor if you have a fever higher than 101° F.

**Bleeding or bruising** Your doctor will check certain blood cells, called platelets. Treatment may be given if you have a low level of platelets.

**Nausea and vomiting** Your doctor can give you medicine to avoid or lessen nausea and vomiting. If your doctor tells you to take these drugs before coming for treatment, it is important that you do so. Avoiding nausea and vomiting is easier than stopping it after it starts.

**Other temporary side effects** Temporary side effects may include loss of appetite, fatigue, mouth sores, or hair loss.

#### Immunotherapy

**Nausea, vomiting, and other flu-like symptoms** Your doctor may give you medicines to lessen nausea and vomiting. Staying hydrated is very important if you have these symptoms.

**Fatigue** Your doctor may change your diet or have you drink more fluids. Alternating periods of activity and rest or increasing your physical activity may also be suggested.



Weight loss Your doctor may tell you to eat small, frequent meals, take vitamins, or drink high-protein shakes. A dietician can also give you helpful eating tips.

**Mood changes** Your doctor may give you medicines that help your mood or suggest other options, such as counseling and support groups.

**Damage to organs** Some side effects may be serious and cause damage to different parts of your body. Organ damage would show different signs or symptoms. For example, yellowing of the skin and darkened urine may be a sign of damage to your liver. Diarrhea or stomach pain could be caused by damage to your intestines. Ask your doctor about the signs of serious side effects before you start your treatment. These side effects may start during treatment but can also happen months later. If you see signs of a serious side effect, call your doctor right away.

**Skin problems** Rash, with or without itching, blisters, and sores in the mouth are examples of side effects of the skin. If these side effects occur or get worse, call your doctor for instructions.

## **Coping With Melanoma**

A diagnosis of melanoma can bring up many feelings and concerns. It is normal for you and your loved ones to need help coping with all of the life changes that result. Here are some ways to cope with a diagnosis of melanoma.

Talk with your health care team. People with cancer often feel more in control when they know as much as they can about their cancer and their treatment.

• Write down all of your questions and concerns. Share them with your health care team. Do not worry about asking too many questions. Tell your health care team when you do not understand their instructions or when you need more information.



- Take notes on the conversations you have with your health care team so you can review the information later.
- Enlist a supporter. Bring a friend or family member with you to your appointments to help you remember details, take notes, and serve as a second "set of ears."
- Ask your doctor to recommend books, articles, and websites about melanoma and its treatment.
- Get a second opinion. Doing this helps many patients feel more comfortable about their treatment decisions.

#### Stay as active as possible during and after treatment.

Staying active has health benefits. Ask your doctor about:

- The type of physical activities you can do, how long, and how many days a week.
- A healthy, tasty diet that you can easily follow.
- Whether you should adjust your daily routine, such as by taking time off from work.
- Stress-relieving activities such as meditation.
- Sources of support available to you and your loved ones.

For ways to learn about melanoma, find self-care tips, and connect with others for emotional support, see the "Resources" section on page 21 for more information.

Join a melanoma support group. People with cancer often find it easier to cope when they get help from others. Support groups allow you and your loved ones to talk with others who have similar concerns. You can talk about what it is like to cope with melanoma and be part of a larger community of support.

## After Treatment Ends: Following Up With Your Doctor

After treatment for melanoma, regular checkups are important. Your doctor will monitor your recovery and check for any new cancer. During a checkup, your doctor will ask you questions about your health and may do a physical exam, run blood tests, and take scans of your chest, liver, bones, and brain to check for whether or not the melanoma returned.

There is a greater chance of a new melanoma appearing in people who have been treated for melanoma in the past. To lessen the chance of this happening, follow up with your doctor regularly after your treatment ends. Practice sun safety by:

- Using sunscreen with a sun protection factor (SPF) of 30 or more.
- Wearing sun-protective clothing, sunglasses, and wide-brimmed hats to protect your skin.
- Avoiding sunlamps and tanning booths.

In addition, check your skin for:

- A new mole that looks different from your other moles.
- A new red- or darker-colored flaky patch that may be a little raised.
- A new flesh-colored, firm bump.
- A change in the size, shape, color, or feel of a mole.
- A sore that does not heal.

**Changes may not mean you have melanoma again.** Follow up regularly with your doctor and tell your doctor as soon as possible about any new skin changes.

To find melanoma support groups, ask your doctor, social worker, or other member of your health care team, or call your local hospital and ask about its cancer support programs. Cancer*Care* offers free face-to-face, telephone, and online support groups for people with cancer.

**Contact Cancer***Care.* Cancer*Care* is a national nonprofit organization that provides free, professional support services to anyone affected by cancer. We offer individual counseling, support groups, education, financial assistance, and practical help. All of our services are completely free of charge.

# To learn more about how we help, call 1-800-813-HOPE (4673) or visit www.cancercare.org.



## **MORE ABOUT MELANOMA** Frequently Asked Questions

#### Q. If my biopsy results are negative for cancer • cells after treatment, what are the chances that melanoma will come back?

After treatment, it's possible that the melanoma can recur at or near the site of the original tumor or in another part of the body. The likelihood that melanoma will return is broken up into three groups: low-risk (less than a 20% chance of returning), intermediate-risk (between a 20% and 50% chance of returning), or high-risk (more than a 50% chance of returning). You and your doctor should work together to craft a follow-up care plan based on your risk of recurrence.

Because people who have had melanoma are also at increased risk of developing a second, unrelated melanoma, your follow-



up plan should include regular skin check-ups by your doctor. You should also learn as much as you can about skin self-exams and how to practice sun safety (See the "After Treatment Ends: Following Up With Your Doctor" section on page 17).

# Q. How do I know if I am a good candidate to enroll in a clinical trial?

A. Each clinical trial has its own checklist for patient enrollment. For example, some trials may include only patients with a certain stage of melanoma or patients who have already received cancer treatment. Clinical trial researchers need patients to meet the trial's terms in order to be a part of it. If you have melanoma and are interested in being part of a clinical trial, talk to your doctor. He or she will be able to tell you if clinical trials are available for someone with your type and stage of cancer.

#### Q. I have been diagnosed with melanoma and have read that this increases my children's risk of developing this cancer. Is there anything we can do to reduce their chances of developing melanoma?

A. Family history is one risk factor for melanoma. Other risk factors include high sun exposure and having many or unusual moles. Because melanoma is most treatable when it is found early, people at increased risk for melanoma should check their skin from head to toe regularly and have a doctor check their skin. You can help your children reduce their risk for melanoma by teaching them about sun safety. This includes spending less time in the sun between 10:00 AM and 4:00 PM, when the sun's rays are strongest, wearing sun-protective clothing, regularly applying broad-spectrum sunscreen with an SPF 30 or higher, and avoiding sunlamps and tanning booths.

### Q I am taking interferon for my treatment of melanoma. What can I do to cope with its side effects?

A. Interferon can cause side effects such as flu-like symptoms, fatigue, weight loss, and changes in mood. These side effects are more common if you are getting a higher dose of the drug. Before making any changes to your treatment, diet, or daily routine to help manage your side effects, talk to your doctor. Depending on your history, the side effects that you are having, and results from other tests, your doctor may change how you are given interferon. He or she may also recommend over-the-counter medicines or tips to help you manage your side effects, or switch you to another treatment.

Taking over-the-counter medicines like acetaminophen (Tylenol), or drinking more fluids, may help to lessen flu-like symptoms.

### Resources

CancerCare 1-800-813-HOPE (4673) www.cancercare.org

American Cancer Society 1-800-227-2345 www.cancer.org

**Cancer.Net** Patient information from the American Society of Clinical Oncology www.cancer.net

Melanoma International Foundation 1-866-463-6663 www.melanomaintl.org

Melanoma Research Foundation 1-877-673-6460 www.melanoma.org

National Cancer Institute 1-800-422-6237

www.cancer.gov

The Skin Cancer Foundation 1-800-754-6490

www.skincancer.org

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for Help and Hope, visit or call:

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