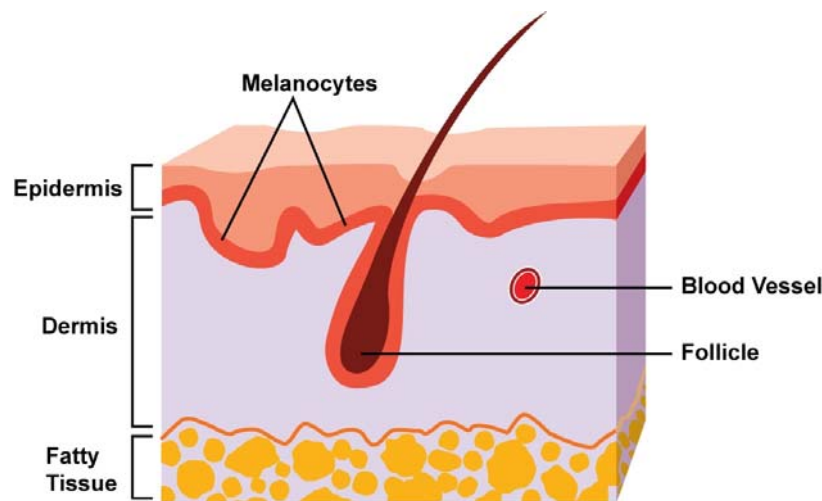


BACKGROUNDER: Melanoma

Disease Overview

Melanoma is a type of cancer that begins in skin cells called melanocytes. Melanocytes produce melanin, the pigment that gives skin its natural color and causes it to tan or darken. Clusters of melanocytes and surrounding tissue sometimes form benign (non-cancerous) moles. These cells can mutate (change) and begin to grow and divide faster than normal cells. Melanoma occurs when the melanocytes become malignant (cancerous). Melanoma can metastasize (spread) from skin cells to healthy tissues, including the lymph nodes or other organs.¹



Risk Factors for Melanoma

The exact cause of melanoma is unknown, but there are a number of factors that can increase a person's risk. These include the number of moles on the skin; previous or family history of melanoma; a weakened immune system; having at least one severe, blistering sunburn as a child or teenager; and cumulative exposure to UV radiation. Melanoma is more common in people with fair skin that burns or freckles easily; however, anyone can get it.²

The best ways to prevent melanoma are to avoid sun exposure between the hours of 10 a.m. and 4 p.m.; to use a "broad spectrum" sunscreen with a sun protection factor (SPF) of at least 15 that blocks both UVA and UVB rays; and to wear protective clothing, a hat and sunglasses when outside during peak sun hours.³

Quick Facts on Melanoma

Skin cancer is very common, accounting for more than 50% of all cancers. Although melanoma is rare (3% of skin cancer cases), it causes a majority of skin cancer deaths—approximately 80%.^{4,5} It is predicted that more than 64,500 cases of melanoma will be diagnosed in the United States and Canada in 2007, and that more than 9,000 people will die from the disease.^{6,7}

Melanoma tends to occur at a younger age than do most cancers, with half of all cases found in people under age 57.⁸ The incidence and mortality rates have risen significantly over the past several decades. Melanoma is one of the fastest growing forms of cancer. By the year 2010, it is estimated that one in 50 people will have been diagnosed with melanoma.⁹

Melanomas are frequently characterized as “local” vs. “distant,” where “local” means there is no spread, and “distant” means that the tumor has metastasized. If melanoma is detected early and hasn’t gone beyond the skin, it can be easily treated with surgery. For localized melanoma, the 5-year survival rate is 98%. The majority (83%) of melanomas are diagnosed at this stage. If the cancerous cells have spread and reached the lymph nodes or other parts of the body, the 5-year survival rate drops dramatically: 64% for regional stage disease and just 16% for distant stage disease.¹⁰

Signs and Symptoms

The most frequent signs of melanoma are changes in the size, shape, color, or feel of an existing mole. Most melanomas have a black or blue-black area.¹¹ Dermatology and oncology groups suggest evaluating moles and skin changes for signs of melanoma using the “ABCDE” approach:^{12,13}

- **A**symmetry – the shape of one half doesn’t match the other
- **B**order – edges are ragged, notched, blurred or irregular in outline
- **C**olor – uneven skin tone, with shades of black, brown, tan or areas of white, grey, red, pink or blue
- **D**iameter – increase in size, usually larger than a pencil eraser or 1/4 inch (6 mm)¹⁴
- **E**levation – a mole is raised above the skin and has a rough surface

Melanomas can occur anywhere on the skin, but are more likely to develop in certain locations. In men, they are most often found on the torso; in women, on the lower legs. Melanomas can also appear on the palms of the hands, soles of the feet, buttocks, back, scalp, and under the nails.

Diagnosis and Staging

Melanoma is usually first suspected during a physical examination, at which time the doctor will assess the patient’s medical history: when the skin lesion first appeared, whether it has changed in size or appearance, past exposures to UV radiation, and family history of the disease.¹⁵ If a spot on the skin is suspected to be melanoma, a biopsy often is suggested.¹⁶ This is a procedure where a small sample of tissue is removed. The tissue is examined under a microscope by a pathologist to check for cancer cells.¹⁷

In order to detect whether the cancer cells have metastasized, additional procedures may be performed, such as removal of the lymph nodes closest to the area where the melanoma developed, removal of lymph node cells, or removal of abnormally large lymph nodes suspected to have melanoma cells.¹⁸

If melanoma has been diagnosed, other tests will be conducted to see if the cancer has spread. These typically include chest x-rays or blood tests to assess liver function and other factors

(sometimes called biomarkers) to help determine specific sites where the cancer may have spread. Advanced imaging techniques may also be used to look for cancer cells in the liver, bones and brain.

Melanoma is classified by several stages according to tumor thickness, involvement of the lymph nodes, the presence of distant metastases, or the presence of ulceration. While melanomas are usually about the size of a pencil eraser when diagnosed, they can be smaller.

- **Stage 0**—melanoma cells are found in the outer layer of skin cells and have not invaded deeper tissues
- **Stage I**—the tumor is no more than 1 mm thick (about the width of a comma) with some ulceration, or between 1 and 2 mm thick with no ulceration; there is no spread to nearby lymph nodes
- **Stage II**—the tumor is at least 1 mm thick, or between 1 and 2 mm thick with ulceration, or more than 2 mm thick with possible ulceration; there is no spread to nearby lymph nodes
- **Stage III**—the melanoma cells have spread to regional lymph nodes
- **Stage IV**—cancer cells have spread to other organs, lymph nodes or skin areas far from the original tumor¹⁹

Treatment Options and Prognosis

Surgery is the standard treatment for melanoma in all stages. In most cases, the tumor and some of the surrounding normal tissue are removed; lymph nodes near the tumor may also be removed.

Advanced melanoma (Stage IV) may require further treatment, including chemotherapy—taken orally or via injection, biological therapy (immunotherapy), or radiation therapy. For patients with metastatic melanoma or a high risk of recurrence, there are few effective treatment options available. Standard biologic treatments such as interferon alpha and high-dose interleukin-2 may be recommended.²⁰

Leading melanoma experts have voiced the urgent need for innovative approaches to treat metastatic melanoma given that standard treatments, like interferon alpha, have shown minimal effect on survival and sometimes cause significant toxicity.^{21,22} One example currently under investigation is a therapeutic cancer vaccine designed to stimulate the body's own defenses—the immune system—to find and fight cancer cells. There are now several clinical trials investigating the use of therapeutic cancer vaccines in combination with standard treatment regimens in melanoma patients.^{23,24} The safety and efficacy of therapeutic cancer vaccines are still under investigation and market authorization has not yet been obtained. For more information on therapeutic cancer vaccines, including one trial currently enrolling patients, **call 1-800-xxx-xxxx** or visit www.cancervaccines.com.

Patients with all stages of melanoma should consider enrollment in clinical trials, which evaluate new, potentially more effective therapies. Despite the fact that these research studies are often the key to finding new treatment options for metastatic melanoma, only three to five % of adult cancer patients enroll in clinical trials. For information on clinical trials, visit www.clinicaltrials.gov.

¹ National Cancer Institute: “What You Need to Know About Melanoma”

² Ibid

³ Ibid

⁴ American Cancer Society: “How Many People Get Melanoma Skin Cancer”

⁵ Miller, AJ and MC Mihm, Jr (2006). Mechanisms of Disease: Melanoma. *New England Journal of Medicine*. 355; 1:51-65.

⁶ American Cancer Society: “How Many People Get Melanoma Skin Cancer”

⁷ Canadian Cancer Society: “Melanoma Statistics”; accessed from www.cancer.ca

⁸ American Cancer Society: “What are the Key Statistics About Melanoma?”

⁹ Melanoma Research Foundation: “Facts About Melanoma”

¹⁰ American Cancer Society: “Cancer Facts & Figures 2007”

¹¹ National Cancer Institute: “What You Need to Know About Melanoma”

¹² Atkins, MB, Elder, DE, Essner, R, et al (2006): “Innovations and Challenges in Melanoma: Summary Statement from the First Cambridge Conference”, *Clinical Cancer Research*, 12 (7 Suppl), 2291-2296.

¹³ American Academy of Family Physicians, Melanoma: A Kind of Skin Cancer, <http://familydoctor.org/online/famdocen/home/common/cancer/types/666.html>

¹⁴ National Cancer Institute: “What You Need to Know About Melanoma”

¹⁵ American Cancer Society/National Comprehensive Cancer Network: “Melanoma: Treatment Guidelines for Patients”, 2005

¹⁶ National Cancer Institute: “What You Need to Know About Melanoma”

¹⁷ American Cancer Society Glossary: accessed from www.cancer.org

¹⁸ American Cancer Society/National Comprehensive Cancer Network: “Melanoma: Treatment Guidelines for Patients”, 2005

¹⁹ National Cancer Institute: “What You Need to Know About Melanoma”

²⁰ Ibid.

²¹ Kirkwood, JM, Moschos, S and W Wang (2006): “Strategies for the Development of More Effective Adjuvant Therapy of Melanoma: Current and Future Explorations of Antibodies, Cytokines, Vaccines and Combinations”, *Clinical Cancer Research*, 12 (7 Suppl), 2231-2236.

²² Ibid.

²³ National Cancer Institute “Cancer Vaccines Fact Sheet”

²⁴ Kirkwood, JM, Moschos, S and W Wang (2006): “Strategies for the Development of More Effective Adjuvant Therapy of Melanoma: Current and Future Explorations of Antibodies, Cytokines, Vaccines and Combinations”, *Clinical Cancer Research*, 12 (7 Suppl), 2231-2236.