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ASK THE DOCTOR

Protecting Yourself Against the Deadliest Skin Cancer: Melanoma

By Joel Wiszniak, md

Q: My sister lives in Arizona and loves to spend time outdoors in the sun. I have told her to be careful about melanoma. What can she do to protect herself, and what are the warning signs of melanoma?

A: You are wise to advise your sister to take steps to protect against melanoma, since early diagnosis and treatment can stop this deadly cancer in its tracks. She can help prevent melanoma by limiting her sun exposure, using sunscreen, optimizing her nutritional intake, examining her skin regularly for unusual lesions, and regularly seeing a dermatologist for a head-to-toe skin check-up. Any skin lesion or mole that is asymmetric, does not have a well-demarcated border, has an uneven color, is greater than 6 mm in diameter, or that has changed in appearance should be examined by a professional for possible biopsy and removal.



MELANOMA BASICS

Of the three main skin cancer types—melanoma, basal cell carcinoma, and squamous cell carcinoma—melanoma is by far the most dangerous. The good news is that melanoma is the least frequently occurring type of skin cancer, but the bad news is that it can affect people of all ages. The American Cancer Society estimates that more than 62,000 new melanomas will be diagnosed in the United States in 2008, during which time more than 8,000 people nationwide are expected to die from melanoma.¹

Fortunately, most cases of melanoma are detected early and are classified as thin melanomas—less than or equal to 1 mm in thickness—that usually have a good prognosis.² Early diagnosis of melanoma is absolutely crucial as it makes treatment relatively easy. The superficial lesion is cut out with a clear margin and the patient is cured most of the time. But lesions thicker than 1 mm and especially more than 2 mm are associated with a poor prognosis. Deeper melanomas tend to metastasize (spread to other locations), with potentially dire consequences.

WHAT CAUSES MELANOMA?

Before I discuss how melanoma is diagnosed, let me explain how it occurs. Melanoma arises from cells called melanocytes, which are normal pigment-producing cells in the skin. The melanocytes make a pigment called melanin, which gives skin its color and also acts as a sunscreen to protect against ultraviolet radiation. Light-skinned people have less melanin and are thus at more risk for damage from sun exposure than darker-skinned people, who have more melanin. In fact, the risk of developing melanoma is 10 times higher in the white population versus the non-white population.³

The most common cause of melanoma is exposure to ultraviolet radiation from the sun, which can damage the DNA of melanocytes. If melanocytes sustain genetic damage, the cells may not grow and divide properly. The cells can become “immortal”—that is, they won’t die, but keep growing and spreading, possibly becoming cancerous. This is when melanoma arises.

In nearly one-third of melanomas, melanoma cells produce a protein called beta-catenin, which silences the expression of a gene that normally suppresses cancer, triggering the cells’ passage into immortality and malignancy.⁴

Another factor in the development of melanoma is genetic history. Some genetic characteristics make people more susceptible to developing melanomas, such as a high prevalence of abnormal moles (dysplastic nevi) and a family history of melanoma. Furthermore, genetic mutations that increase the risk of developing melanomas can be passed from one generation to the next.⁵



IDENTIFYING MELANOMA

As I explained, the earlier melanoma is diagnosed, the better the outcome. While physicians diagnose melanoma, patients also play an important role in early detection. Everyone should get into the habit of self-examination to detect changes in the appearance of moles, blemishes, freckles, and other marks on the skin. Examine your entire body in a well-lit room and using a full-length mirror. Use a hand-held mirror to see areas such as your back and the back of your thighs.

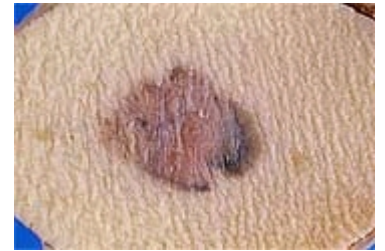
What should arouse suspicion is any type of change in skin moles or lesions. Use the A-B-C-D rule—looking for asymmetry, border irregularity, color variegation (different colors), and diameters greater than 6 mm wide.

- A. Asymmetry: one half of the mole/lesion doesn't match the other half.
- B. Border: edges of the mole/lesion are ragged, blotched, or blurred.
- C. Color: the color of the mole/lesion is not uniform.
- D. Diameter: the mole/lesion is greater than 6 mm wide.

For instance, imagine if you have had a mole on your arm all your life and you are very familiar with its color, size, and shape. During an examination, you suddenly notice that instead of its typical uniform oval shape, the mole now has a slightly irregular shape. Perhaps the color is darker on one side than on the other, or it is even a different color altogether. All of these are warning signs and you should be examined by a dermatologist as soon as possible.

While the A-B-C-D rule is a good one, bear in mind that all melanomas may not manifest with these signs. Furthermore, many benign (non-cancerous) lesions and moles can be A-B-C positive, such as the scenario I just described. Often, signs such as these are perfectly harmless, and thus the A-B-C-D rule is not absolute. But it is far better to be safe than sorry, and self-examination by the A-B-C-D rule is still the best way for the general public to be vigilant.

In the past 10 years, dermatologists have considered adding the letter “E” to the rule to signify an “evolving lesion.” Many consider this to be the most important criterion for evaluating a skin lesion. Basically, any mole or lesion that has evolved, or changed, is cause to see a dermatologist.



Skin cancer. Specimen of a malignant melanoma (dark area), a type of skin cancer. This cancer arises from the skin's melanocytes, the cells that produce the pigment (melanin) that gives skin its color.

SKIN BIOPSY AND DERMOSCOPY

A skin biopsy will likely be performed on any mole or lesion that the dermatologist believes is suspicious. This can be done in several ways, depending on its size and location. An incisional biopsy removes a portion of a mole or lesion that has grown into the deeper layers of the skin. An excisional biopsy removes the entire lesion. Both are performed under local anesthetic and using a surgical knife. A punch biopsy is used to obtain deeper samples of skin using an instrument that looks like a cookie cutter. After numbing the skin, the tool is used to punch through several layers to obtain a sample. These are the most common biopsy methods used when melanoma is suspected.⁶ A pathologist examines the tissue samples to determine if cancer may be present.

Another technique that I perform, which is widely used in Europe, is called epiluminescence microscopy (ELM), or dermoscopy.⁷ This provides a microscopic view of the lesion using a dermatoscope, which magnifies the lesion between 10 and 50 times. Thanks to a double-polarized light, the dermatologist can see two or three microns below the skin level and has a more specific way to tell if the lesion is benign, suspicious, or malignant. Dermoscopy allows for much earlier detection of smaller lesions and helps reduce the need for potentially unnecessary biopsies. If the dermatoscope is connected to a computer, digital photographs of the mole or lesion can be taken, which allows the dermatologist to monitor it over time.

Dermoscopy is thus a powerful tool to help ensure early diagnosis. Anyone who has a lot of moles should have a dermoscopic exam. However, a biopsy is still the most precise method of diagnosing skin cancer. If there is any doubt about the cancerous potential of a pigmented lesion, a biopsy will still be performed.



TREATMENT

If melanoma is diagnosed, it must then be typed and staged, like any cancer, in order to guide treatment options. The primary treatment for thin melanomas is excision. If there is a concern that the cancer has spread, the lymph nodes nearest the

melanoma must be examined. A melanoma that is 1 mm or more in depth is already in the danger zone.

The standard approach is to perform a sentinel lymph node (SLN) biopsy. As the sentinel node is the first lymph node that drains cancerous fluid, this procedure can detect early-stage melanoma in the lymph nodes and determine whether the cancer has spread. The sentinel lymph node is removed and examined for the presence of cancer cells. A negative SLN biopsy means the cancer has likely not spread to the node, which is good for the prognosis. A positive result indicates that cancer is present in the node and may also be present in other nodes nearby, in which case it is usually advised to remove the remaining lymph nodes in the area.⁸

In general, I prefer to have a more accurate diagnosis of a patient's condition as with the SLN biopsy, although some surgeons believe it has no effect on patient survival and requires the patient to undergo an extra procedure that may have adverse effects, such as lymphedema (swelling in the limbs). However, a recent study showed that individuals who underwent SLN biopsy had a significantly higher rate of 5-year disease-free survival (78%) compared with patients who had wide-excision surgery, in which the cancer is cut away together with a margin of tissue around it (73%). Although there was no difference in overall survival between the two groups, the strongest predictor of outcome in these patients was tumor status of the sentinel node.⁹

In the case of thick melanomas, patients are referred to an oncologist. There are many protocols for treatment, including chemotherapy, radiation, and immunotherapy using agents such as interferon-alpha or interleukin-2. Vaccine therapy is undergoing intensive study and shows great promise in the treatment of melanoma. Studies are also ongoing to find ways to inhibit beta-catenin, the cancer-causing protein found in melanocytes, as a treatment for melanoma.

PREVENTION

Prevention is, of course, the most important aspect of this discussion. And fortunately, the number one risk factor—sun exposure—is the one that is most easily controlled. Interestingly, some studies suggest that the intermittent sun exposure one receives on vacation or at leisure is a greater risk factor than chronic sun exposure. There are two possible explanations for this. One is that chronic exposure darkens the skin, which may provide more protection. Another possible explanation is that chronic sun exposure increases the level of vitamin D, which has been shown to offer protection against many types of cancer.¹⁰

Sun avoidance can be accomplished by simply staying out of the sun, by using sunscreens with a sun protection factor (SPF) of 15 or more,¹¹ and by wearing sun-protective clothing with a special weave that helps block ultraviolet radiation. Avoiding sunburn is crucial in reducing the risk of melanoma.¹²

Nutritional supplements may also protect against melanoma. Some studies suggest that higher levels of vitamin D confer greater protection against cancer in general, and possibly melanoma.^{10,13} The catch here is that staying out of the sun can decrease vitamin D levels, so it may be necessary to consume vitamin D supplements to maintain healthy levels. Certain foods are rich in vitamin D as well, such as salmon and cod liver oil. Cancer-fighting nutritional strategies include curcumin, which has been shown to inhibit melanoma cells, as well as other phytonutrients such as apigenin, grape seed proanthocyanidins, resveratrol, and milk thistle-derived silymarin.^{14,15}

CONCLUSION

Sun avoidance, self-examination, regular visits to the dermatologist, and nutritional strategies form a comprehensive melanoma prevention program. When identified and diagnosed early, the outcome of melanoma can be excellent.

If you have any questions on the scientific content of this article, please call a Life Extension Health Advisor at 1-800-226-2370.

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NOVEL CLINICAL STUDY SEEKS ADVANCED MELANOMA PATIENTS

Scientists are now recruiting patients for a clinical trial to investigate a promising new treatment for advanced melanoma. A novel method called in situ photo-immunotherapy (ISPI) has produced impressive results in all patients in whom it has so far been tested.

Immunotherapy—stimulating the body's own immune system to recognize and destroy cancerous cells—is considered one of the most promising ways to treat advanced forms of the disease. ISPI may improve on this approach, as it enlists patients' specialized defensive cells and sensitizes them to the patient's specific tumor characteristics. ISPI makes use of an immune-stimulating, topically applied skin cream used in conjunction with infrared lasers. The topical cream, imiquimod (Aldara®), binds with receptors on tumor cells and stimulates them to activate proteins that "broadcast" the presence of the tumor cells to the immune system. In essence, the patient's own tumor cells become a unique anti-tumor vaccine.

A preliminary case report examined the use of ISPI in two patients with late-stage melanoma. Following a six-week treatment cycle, both patients are still alive—more than 46 months later in one case, and 38 months later in the second case. The median life expectancy for stage IV melanoma cases is typically six to eight months. In addition, researchers observed shrinkage of untreated systemic metastases following therapy in at least one subject. These preliminary findings indicate that ISPI therapy may be a useful and relatively non-toxic way to treat patients with advanced melanoma.

Based on these findings, ISPI has received investigational new drug status from the FDA. Researchers at the University of Oklahoma are recruiting patients with stage III or IV melanoma for a clinical trial assessing ISPI's effectiveness in treating advanced-stage melanoma. All stage III and stage IV melanoma patients who enroll will receive the treatment. Prospective subjects must have at least one qualifying melanoma lesion (an unresected cutaneous metastasis), be willing to travel to Tulsa for the treatment cycle (five visits over a two-month period), and have a life expectancy of at least four months, even without therapy.

Patients accepted for the clinical trial will apply imiquimod cream twice a day to a specified area of the skin, for a total of six weeks. At weeks two and four, investigators will expose the area to an infrared laser, which is expected to enhance the effectiveness of the topical cream.

"The goal of the treatment is to stimulate significant anti-tumor host immune responses to palliate metastatic disease and potentially prolong life," notes co-principal investigator Dr. Mark Naylor. Dr. Naylor hopes to enroll at least 20 stage IV and 50 stage III melanoma patients for the trial. To inquire about participating in this study, contact:

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References

1. Available at: http://www.cancer.org/docroot/cric/content/cric_2_4_1x_what_are_the_key_statistics_for_melanoma_50.asp. Accessed March 11, 2008.
2. Available at: http://www.cancer.org/docroot/CRI/content/CRI_2_4_3X_How_is_melanoma_staged_50.asp?rnav=cric. Accessed March 18, 2008.
3. Available at: http://www.cancer.org/docroot/CRI/content/CRI_2_4_2X_What_are_the_risk_factors_for_melanoma_50.asp?rnav=cric. Accessed March 18, 2008.
4. Delmas V, Beermann F, Martinozzi S, et al. Beta-catenin induces immortalization of melanocytes by suppressing p16INK4a expression and cooperates with N-Ras in melanoma development. *Genes Dev.* 2007 Nov 15;21(22):2923-35.
5. Available at: http://www.cancer.org/docroot/CRI/content/CRI_2_4_2X_Do_we_know_what_causes_melanoma_50.asp?rnav=cric. Accessed March 11, 2008.
6. Available at: http://www.cancer.org/docroot/cric/content/cric_2_4_3x_how_is_melanoma_diagnosed_50.asp. Accessed March 11, 2008.
7. Available at: <http://www.emedicine.com/derm/topic557.htm>. Accessed March 18, 2008.
8. Available at: http://www.cancer.org/docroot/CRI/content/CRI_2_4_4X_Types_of_Surgery_for_Melanoma_Skin_Cancer_50.asp?rnav=cric. Accessed March 11, 2008.
9. Atkins MB, Elder DE, Essner R, et al. Innovations and challenges in melanoma: summary statement from the first Cambridge conference. *Clin Cancer Res.* 2006 Apr 1;12(7 Pt 2):2291s-2296s.
10. Grant WB, Holick MF. Benefits and requirements of vitamin D for optimal health: a review. *Altern Med Rev.* 2005 Jun; 10(2):94-111.
11. Available at: http://www.cancer.org/docroot/CRI/content/CRI_2_4_2x_Can_Melanoma_Be_Prevented_50.asp?rnav=cric.

12. Lew RA, Sober AJ, Cook N, Marvell R, Fitzpatrick TB. Sun exposure habits in patients with cutaneous melanoma: a case control study. *J Dermatol Surg Oncol.* 1983 Dec;9(12):981-6.
13. Schwartz GG, Skinner HG. Vitamin D status and cancer: new insights. *Curr Opin Clin Nutr Metab Care.* 2007 Jan;10(1):6-11.
14. Bush JA, Cheung KJ Jr, Li G. Curcumin induces apoptosis in human melanoma cells through a Fas receptor/caspase-8 pathway independent of p53. *Exp Cell Res.* 2001 Dec 10;271(2):305-14.
15. Baliga MS, Katiyar SK. Chemoprevention of photocarcinogenesis by selected dietary botanicals. *Photochem Photobiol Sci.* 2006 Feb;5(2):243-53.

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