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Risk Factors: Close to Home

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Most people are aware excessive sun exposure puts you at risk for developing melanoma. But overall risk is a combination of nature and nurture, quality and quantity. Few formal studies have been done to determine which risk factors are most predictive of future development of melanoma. “I think most of us would agree that there is some component of sun exposure in the etiology of melanoma, plus your genetic heritage,” says Jeffrey Weber, MD, PhD, of the H. Lee Moffitt Cancer Center.

To date, the only concrete risk factor for melanoma is a rare mutation in a gene called p16 that causes patients to develop large numbers of unusual-looking moles—a genetic disease called familial atypical multiple mole melanoma syndrome. The mutation, which shuts off a protein that limits cell division, is found in only 10 to 40 percent of patients with a family history of melanoma.

Other genetic changes have been associated with melanoma, including a common mutation in a protein called BRAF. This mutation can also be found in benign moles, however, so exactly how it may contribute to disease is unclear.

Family heritage is also a factor because melanomas occur more frequently in people with fair skin who burn easily and are less common in darkskinned individuals and those who rarely sunburn. The risk increases further for people with a family history of melanoma (one or more first-degree relatives). Higher risk also comes with a large number of moles or a rare familial tendency for clusters of irregularly shaped moles called atypical nevus syndrome. Suspicious changes—irregular borders, multiple colors, or increased size—often indicate early melanoma.

The cumulative amount of time a person spends in the sun is a well-established risk factor for melanoma, but the timing of that exposure may also be important. Some studies suggest sun exposure as a child is more risky than exposure as an adult, although additional research has failed to back up this finding. The caveat of all these studies is the difficulty of accurately measuring sun exposure, which is typically assessed using patient surveys.

Large-scale genetic studies may soon clarify how these risk factors contribute to melanoma. Dr. Weber, for example, has launched a study in search of genetic signatures that may help predict who is most at risk for developing metastatic disease and who might respond best to a particular therapy. He’s now collecting more than 500 tumor and blood samples from patients at different stages of disease, which will be tested for various genetic changes.

As Dr. Weber puts it: “Understanding why 15 percent of the population responds

[to a therapy] and another 15 percent [don't progress], and figuring out how to filter out the 30 percent so you can treat the other 70 percent with something else would be invaluable."