Between the diagnosis of melanoma and changes that take place in normal sun-exposed skin is a large gray area filled with uncertainty. New research from the Mayo Clinic, reported in the July issue of the *Archives of Dermatology*, has defined the "upper level of normal" in the changes that take place and should help in diagnosing true melanoma.

"The data from our study should help physicians to discern increased melanocyte density in sun-damaged skin from that in early melanoma," lead researcher Ali Hendi, MD, assistant professor of dermatology at the Mayo Clinic in Jacksonville, Florida, told Medscape. At present, there is a tendency to err on the side of caution and overdiagnose melanoma in sun-damaged skin to avoid the obvious medical and legal consequences of missing true melanoma. But this can result in unnecessary surgery to remove those areas of skin and lead to unnecessary morbidity and deformity, he pointed out.

New Research Differentiates Melanoma From Sun-Exposed Skin

The study was conducted in skin samples taken from 132 patients with nonmelanoma skin cancers (mostly basal cell carcinomas) on the head or neck. The patients underwent Mohs surgery to remove the affected skin, and the researchers cut samples from the edges of the excised tissue. Hence, the samples consisted of normal noncancerous skin that, because of its location, had been exposed to the sun. All the patients were white, with a mean age of 70 years, and most of them lived in western Pennsylvania. Only 11 of the patients reported recent intense sun exposure, defined as outdoor exposure in a sunny climate (such as that of Florida) within 2 weeks of surgery.

The researchers found that normal long-standing sun-exposed skin has an average of 15 to 20 melanocytes per high-power field (in 0.5 mm of skin). This contrasts with normal skin without sun damage, which has an average of 5 to 7 melanocytes per 0.5 mm of skin. The finding adds to the evidence that disproves the long-held belief that skin has a static number of melanocytes. It has now been established that sun exposure increases the number of melanocytes and that melanocyte density is proportional to cumulative sun exposure, the researchers comment.

In addition, the sun-exposed skin had a confluence of up to 9 adjacent melanocytes as well as melanocytes extending along hair follicles, the researchers report. Both of these features have previously been used by...
pathologists as indicators of early melanoma, but now Dr. Hendi and coauthors John Zitelli, MD, and David Brodland, MD, both from the University of Pittsburgh Medical Center, Pennsylvania, report finding them in normal sun-exposed skin.

However, there was no nesting or pagetoid spread of melanocytes, the team reports, and there was no "vertical stacking" of melanocytes in the epidermis, which is a common finding in melanomas. "We didn't see any of these features in the samples that we looked at," Dr. Hendi said.

"In melanoma, the pigment-producing melanocyte cells proliferate and run out of control, but it's not just that the melanocytes increase in number," Dr. Hendi commented in an interview. "The increase in number also happens in normal skin exposed to the sun, and this is where the gray zone starts — at what point does it stop being normal and become melanoma? What we have established is the range of normal melanocyte density in sun-exposed skin using the immunostain [melanoma antigen recognized by T cells] MART-1."

Increased melanocyte density and mild to moderate confluence on their own do not substantiate the diagnosis of melanoma, the researchers conclude. There should also be nesting, vertical stacking, or pagetoid spread. "If these features are not present, then it's unlikely to be melanoma, and the skin can be left in place," Dr. Hendi said.

"To be able to look in the microscope and have a measurement by which to determine successful removal of melanoma in situ is something we've hoped for for quite a while," Dr. Hendi says in a press release issued by Mayo Clinic. "In many cases, surgeons can stop removing tissue much sooner, which will result in less trauma to the skin."