

## New Evidence Provides Insight Regarding Rates of NMSC in Men

Research in mice suggests that males respond to UVB irradiation differently than women do, suggesting a possible basis of higher cancer rates

American Cancer Society estimates for last year suggested that more than one million individuals would be diagnosed with nonmelanoma skin cancer (NMSC), and 2,740 individuals would die from NMSC. Overall, men are more likely than women to develop both non-melanoma and melanoma skin cancers, although researchers failed to demonstrate a higher incidence of SCC in men younger than 40 compared to age-matched women.<sup>1</sup>

Taking account of all age groups, men are three times more likely than women to develop SCC, the American Cancer Society says.<sup>2</sup> There has been little scientific investigation of this difference. Increased risk in men has been attributed to lifestyle or habit differences between men and women, such as the assumption that men are less likely than women to use sunscreen on a consistent basis, there has been little scientific investigation of this difference.

It has been documented that men and women historically have had differing rates of skin cancer development at different anatomic sites. For example, men have traditionally had higher rates of melanoma of the back, chest, and abdomen, likely due to occupational exposure. Women traditionally have had higher rates of melanoma of the upper and lower extremities.

Interestingly, changing occupational and recreational trends in recent years coupled with changes in fashion may all have contributed to recent findings showing that these historical anatomic distributions are changing. (For more

on this, see the August 2007 issue, available online at [practicaldermatology.com](http://practicaldermatology.com)).

Research in mouse models now suggests males and females may respond differently to UVB exposure, prompting new understanding of sex-based differences in NMSC incidence.<sup>2</sup>

### The Male Response

Researchers<sup>2</sup> showed that after chronic exposure to equal doses of UVB, male Skh-1 mice developed tumors more quickly than did female mice, and males developed more total tumors. Histologic assessment showed that

tumors of male mice were more advanced than those of females.

In efforts to understand these differences in tumor development, researchers exposed additional male and female Skh-1 mice to a single UVB dose of 2,240J/m<sup>2</sup> and examined the skin 48 hours after exposure. Among measures assessed were skin fold thickness and myeloperoxidase activity—a marker of inflammation, as well as oxidative DNA damage, and antioxidant levels. Male mice demonstrated lower rates of inflammatory response compared to females, but they had

## NEW In Your Practice

**Gone in a Puff of Smoke.** While Asian men generally have less trouble than Caucasians with hereditary male baldness, new evidence suggests that smoking cigarettes may erase that line. According to data published in the *Archives of Dermatology* (November), smoking may destroy hair follicles, interfere with the way blood and hormones are circulated in the scalp, or increase production of estrogen. An examination of 740 men in Taiwan with an average age of 65 found cigarette use played a strong role in the development of moderate or severe hair loss. Researchers recommend that men showing early signs of hair loss be advised about the potential role of smoking in hair loss.

**Melanoma Vaccine?** Results from a recent trial indicate that Uvidem (IDD-3) showed clinical activity and induction of immune response and was well-tolerated in patients with advanced melanoma. Out of 33 patients treated, nine showed evidence of clinical benefit, two exhibited partial response, and six achieved stable disease with duration of response ranging from 7.2-29.7 months. To date, none of the patients who had an objective response has relapsed. Moreover, 18 of 29 patients showed a significant increase in TAA-specific cytokine-producing cells.

**Wash Those Hands.** Wearing masks, gloves, and gowns, along with regular hand-washing may be more effective than drugs for preventing the spread of respiratory viruses such as influenza and SARS, a study published in the *British Medical Journal* finds. The study examines data from various studies, where researchers found that simple, low-cost physical measures should be given higher priority in national pandemic contingency plans.

lower antioxidant levels and higher rates of oxidative damage.

The findings seem to suggest that increased and accelerated rates of tumor development in male mice may be attributed to a gender-mediated response to UVB exposure. Although inflammation is generally thought to be a prominent component of the etiology of various cancer types, these findings suggest that in the case of SCC formation, inflammatory response is less important than is UVB-induced oxidative damage.

### A Guy Thing?

Future research will hopefully uncover why male mice respond differently to UVB irradiation than females do. And, of course, studies in humans will have to confirm that men and women demonstrate the differing responses that were seen in mice in this study.

Based on current knowledge and previous research, it is reasonable to believe that hormonal expression could play a role; hormones have been shown to mediate tumor development and progression as well as immune response. Studies have implicated female sex hormones in the pathogenesis of various tumor types,<sup>3</sup> specifically in skin cancer formation.<sup>4,5</sup> Estrogens previously have been linked to inflammatory response following UVB exposure.<sup>6</sup> A recent study in the zebra finch showed that higher levels of testosterone were associated with increased susceptibility to oxidative stress, prompting development of “the oxidation handicap hypothesis.”<sup>7</sup> Androgens are also known to mediate immune response.<sup>8</sup>

Recognizing historical differences in anatomical distribution of skin cancer between men and women, we acknowledge that differences in UV exposure influence the development of skin cancer. It will be interesting to learn whether inflammatory or oxidative response to UV exposure varies based on body site of exposure as well as sex.

## Sunscreen Labeling Update

There have been some recent developments regarding sun protection, with the American Academy of Dermatology Association on behalf of its membership providing feedback to the FDA about proposed sunscreen labeling changes. The AADA's primary concern is with UVA testing methods. The letter to the FDA states in part:

We are of the opinion that the modified Boots method will give preferential merit to the significance of UVA I wavelengths and not the entire UVA spectrum, and that it will still be possible to generate a disproportionately high final UVA rating using a ratio method for products with low UVB and UVAII absorbances. This modified Boots method also lacks the supporting evidence base and the FDA does not provide the rationale for elimination of other accepted methodologies. Lastly, based on currently available UV filters in the US, the ratio needed to attain the “highest” rankings will be impossible for many sunscreens, hence diminishing the significance of the PPD test. The Academy favors the use of the Critical Wavelength (CW) as the in vitro test for UVA coverage for the following reasons:

- Contrary to the FDA statements, CW is a measure of the breadth of a sunscreen's potential, as CW is based on the inherent shape of a sunscreen's absorbance curve across the totality of the UVB/UVA spectrum.
- CW is highly corroborated by basic research and industry and has a significant evidence base for its validity in distinguishing low vs. high broad-spectrum products.
- CW is the in vitro method of choice that has been endorsed by the European Commission as one part of a dual methodology for assessment of UVA (broad-spectrum) protection.
- When evaluated within the context of comparable SPF sunscreens, an increase in CW can only be accomplished with an increase in UVA protection, and allows CW to differentiate products based on long-wave efficacy in a non-redundant manner with SPF.
- CW has been shown to be a sensitive indicator of photostability if sunscreens are pre-irradiated prior to the test procedure.
- Opponents of CW have based their claims on comparisons to in vivo testing methods or the inability of CW to differentiate products based on a biological endpoint. This point becomes irrelevant in the context of a dual methodology system.

**We await a response and further FDA action. The comment period, originally slated to close November 26, only recently closed (December 26).**

Until we know why and how men develop NMSC—and melanoma—and higher rates than women, our best prevention strategy remains sun avoidance and protection strategies. There has been interest in the role of topically applied and/or orally-administered antioxidants in the prevention of skin and other neoplasms. Although there is promising data that antioxidant supplementation can provide preventive health benefits to humans, no standard, agreed-upon prevention protocol has yet been identified, and potential problems with available products (insufficient active ingredient, unstable formulations, etc.) persist. ■

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