Carcinogenic to Humans: Why the International Agency for Research on Cancer Added Indoor Ultraviolet (UV) Tanning to Group I

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In 2009, a working group of 20 scientists from around the world, brought together by the International Agency for Research on Cancer (IARC), added ultraviolet radiation (UVR) from tanning machines to the IARC’s Group I list of the most carcinogenic forms of radiation. Citing evidence from years of international research on the relationship between indoor tanning and skin cancer, the IARC, affiliated with the World Health Organization, placed this type of UVR in its most dangerous cancer category for humans, alongside offenders such as radon, asbestos, cigarettes, plutonium, and solar UVR.

UVB and Skin Cancer
An estimated 90 percent of all skin cancers are associated with exposure to UV radiation, above all from the sun, reaching the earth as shortwave, ultra-

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From the Editors

In this issue of The Melanoma Letter, we address the developments underlying a recent flurry of media attention and public policy action related to artificial ultraviolet (UV) tanning devices. A major impetus for all this attention was the extensive, authoritative report on the subject prepared by the International Agency for Research on Cancer (IARC), a working group affiliated with the World Health Organization (WHO). We are very grateful to Dr. Philippe Autier, who headed up the Unit of Prevention Evaluation that issued the report, for providing an outstanding synopsis of the science covered in the 64-page document, which concluded that artificial tanning devices are carcinogenic in humans.

In a companion piece, we share some of the exciting tanning bed policy changes occurring internationally in response to the WHO’s addition of these devices to Group 1, its most dangerous cancer category. The data affirming the risks of tanning beds have continued to mount since the IARC review. The recently published results from an extended follow-up of a cohort study of more than 100,000 women from Sweden and Norway reveal that the increased melanoma risk associated with tanning bed use in young people continues to increase with use of the devices in adulthood. Furthermore, a new large case-control study from Minnesota has found that both UVB-enhanced and primarily UVA-emitting devices are strongly associated with increased melanoma risk. This rapidly growing evidence supports the blanket recommendation of a recently released FDA educational video: “Avoid using device-generated UV sources such as tanning beds entirely.”

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violet B (UVB) and long-wave, ultraviolet A rays (280 to 315 nm and 315 to 400 nm, respectively). UVB composes about 5 to 10 percent and UVA 90 to 95 percent of the UVR to which we are exposed. By the end of the 1980s, after decades of study, scientists had well documented the carcinogenic properties of UVB. They knew that in the lab, it caused DNA mutations in skin cells that led to the development of cancer; triggered the growth of squamous cell carcinomas in rodents; and was more responsible than UVA for inducing sunburn. At the same time, studies provided increasing evidence that sunlight was the main environmental cause of skin cancer, which at that time was strongly associated with a history of sunburn. Thus, UVB was believed to be the major cause of skin cancer. Far less information was available on the role of UVA in skin cancer, but scientists considered it of the utmost importance to learn more, believing that research could prompt innovations in sun protection, such as improved, broader spectrum sunscreen formulations.

After thorough review of all available data from laboratory, animal, and human studies, in 1992 a Working Group convened by the IARC determined that sufficient evidence existed to place solar radiation, and more specifically solar UVR, in the IARC’s Group I – the most dangerous carcinogenic agents for humans.2 (For details on the criteria for Group I, see www.iarc.fr, monograph program.) However, there wasn’t yet sufficient evidence to assign specific wavelength ranges, like UVB, to Group I – evidence suggested but was not yet conclusive that UVB was a human carcinogen, and UVA was suspected to be a carcinogen – so both were classified as “probably carcinogenic to humans,” placing them in the IARC’s group IIa.

Uncertainties primarily stemmed from the many unanswered questions about the environmental causes of melanoma. In animal studies, UVB was found to induce squamous cell carcinoma (SCC), but had not yet been found to cause tumors akin to human melanomas; nor had DNA mutations specific to UVB exposure been found in melanoma. Epidemiologic studies suggested that melanoma was primarily caused by intermittent, intense sun exposure, acquired mainly during tanning, leisure, or sports activities. This would explain why melanoma was frequently found on areas normally sun-protected in everyday life, such as the trunk and thighs. In contrast, SCC occurred most frequently on chronically sun-exposed areas (e.g., the head and neck) of elderly subjects, and was considered to be mainly due to cumulative sun exposure. At that point, the involvement of sun exposure, and of UVB in particular, in the development of melanoma simply was not as clear as it was in SCC. With even less known about UVA, it was deemed premature to make a clear-cut distinction between UVB’s and UVA’s roles in skin cancer.

The Role of UVA

The marketing of modern UV tanning devices started at the end of the 1980s, with the advent of fluorescent lamps mainly emitting UVA rays. (Some UVB — less than five percent of the lamps’ UV output — was also emitted, since this wavelength is better at inducing a deep, long-lasting tan; UVA induces tanning quickly, while a UVB tan may take some days to develop, but stays dark longer.) With no convincing proof yet of UVA’s link to skin cancer and only a low amount of UVB included, tanning vendors could argue that acquiring a tan was safe (or safer) when obtained at a salon.

During the 1990s and into the 2000s, indoor tanning became very popular among light-skinned populations, and is now suspected to be one cause of the rise in melanoma incidence; nearly 30 million people tan indoors every year in the US alone,3 about 2.3 million of them teens,4 and melanoma is now the most common form of cancer for young adults 25–29 years old and the second most common for adolescents and young adults 15–29 years old.5 Powerful UV tanning units may be 10 to 15 times stronger than the midday sunlight on the Mediterranean Sea, subjecting indoor tanners to UVA doses well above those experienced during daily life or even when sunbathing outdoors. The fact is, repeated exposure to large, concentrated amounts of UVA constitutes a new experience for human beings.

Studies have gradually strengthened the evidence for a causal relationship between high doses of UVA exposure, indoor tanning, and skin cancer, especially melanomas of the skin and...
eyes. These data were systematically reviewed in an IARC monograph in June 2009,\textsuperscript{9} and the main results can be summarized as follows:

1. Extensive laboratory data and animal experiments (on DNA mutations and repair, immune function, cell integrity, cell cycle regulation, and other critical biological functions) document a role for UVA in skin carcinogenesis.\textsuperscript{6,7} The studies show that the carcinogenic mechanisms of UVB differ but sometimes overlap with those of UVA. Exposure to the sun causes a specific mutation pattern – cytosine to thymidine transition — due to cyclobutane pyrimidine dimers in DNA, and UVB was long assumed to be the culprit. But the same transition pattern has now been found in the skin of UVA-exposed mice, the Tp53 gene of UVA- or UVB-induced skin tumors in hairless mice, and the Tp53 gene in human actinic keratosis and malignant skin tumors.\textsuperscript{1,6} UVA actually penetrates the skin more deeply than UVB and can damage DNA in the skin cells. In either case, the mutations can lead to cancer. Recent evidence also shows that the body’s repair and removal of damaged DNA is less effective when the damage is caused by UVA.\textsuperscript{8}

2. Experiments in human volunteers show that tanning lamps produce the types of skin DNA damage associated with photocarcinogenesis.\textsuperscript{3}

3. Experiments in human volunteers also show that UVA and UVB can weaken the immune system through interacting and overlapping mechanisms, increasing vulnerability to cancer as well as other diseases.\textsuperscript{9}

4. Systematic reviews of epidemiological studies provide strong evidence that intermittent, intense sun exposure – the type of exposure often sustained on weekends or sunny vacations, leading to sunburn – is the main environmental risk factor for melanoma;\textsuperscript{10} this pattern can be simulated by indoor UV tanning, and has a greater potential to cause melanomas at younger ages than chronic sun exposure.\textsuperscript{11}

5. While epidemiological studies have not consistently shown that indoor UV tanning is a risk factor for cutaneous melanoma, in a 2006 IARC meta-analysis, all seven studies examined (six case-control and one cohort) found a significant increase in melanoma risk (ranging from a 40 to a 228 percent increase) when indoor UV tanning started during adolescence or young adulthood.\textsuperscript{5,12} The meta-analysis found an overall 75 percent increase in melanoma risk when indoor UV tanning began before age 35 [Figure 1]. In another meta-analysis, the Working Group found some evidence that UV tanning increased the risk of squamous cell carcinoma, especially when tanning bed use started before age 20. These results were highly consistent with the considerable data pointing to childhood and adolescence as the key periods for initiation and development of melanoma in adulthood.\textsuperscript{13}

6. Four case-control studies have reported consistently increased risk for ocular melanoma among UV-tanning device users,\textsuperscript{14} with a clear dose-response relationship – increased risk with increased indoor tanning. Again, the risk of this rare but dangerous cancer was greater for subjects who started indoor tanning before age 20.

Further review of the studies by the IARC found no indication that the findings were due to biased or otherwise problematic study design. No evidence supported a protective effect from sun bed use against future sun damage,\textsuperscript{9,12} and all the research substantiated a role for both UVA and UVB in human carcinogenesis. Thus, the entire UV spectrum and UV-emitting tanning devices were classified as carcinogenic to humans.\textsuperscript{1}

UV tanning’s role in the rise in melanoma incidence has been corroborated by a number of recent epidemiological observations. A few years ago, we predicted that we would begin seeing an increase in melanomas associated with tanning bed use on the trunk, especially in women.\textsuperscript{15} In areas where indoor UV tanning is popular, especially among teenagers and young adults, such as

![Figure 2: Melanoma in Sweden, 1960-2004](http://www.SkinCancer.org)
Nations Unite Against Tanning: The Impact of the IARC Report

When the International Agency for Research on Cancer (IARC), an affiliate of the World Health Organization, added UV radiation from tanning machines to Group I, its list of the most dangerous carcinogens for humans, it set off a chain of events worldwide that even its authors could scarcely have predicted. It was as if everyone had been primed and waiting for a signature event to launch all-out war on indoor tanning; the event turned out to be the IARC’s “Special Report” published in August, 2009 in The Lancet, announcing its latest review of human carcinogens and prominently featuring its addition of “UV-emitting tanning devices” to Group I.1 The new arrival joined a list of about 120 substances and compounds which already included solar radiation, as well as infamous agents from tobacco and radon to plutonium.2

Spurred by key findings in the IARC’s report – such as an increase in basal cell carcinomas, squamous cell carcinomas, and ocular melanomas among tanning bed users and a 75 percent increase in cutaneous melanoma risk among those who started tanning before age 301 – nations across Northern Europe, Australia, New Zealand, North America, and even South America sought legislation to restrict tanning bed use, especially among young people.

United by Tanning Legislation

France, Belgium, Germany, Scotland, Spain, Portugal, and the province of New Brunswick in Canada all now limit sunbed use for people under age 18. In France, all UVR-emitting devices must be declared to the national Health Authority; trained personnel must supervise all commercial establishments, and any claim that they provide health benefits is forbidden. Along with banning under-18s from using sunbeds, Scotland has mandated that all sunbed salons be supervised, with proper information provided to customers.3-6

Probably the greatest impact has been made in Brazil and Australia. For Brazil, the IARC’s report was the last straw, and on November 9, 2009, after extensive review and discussion between health authorities and a government working group, the Brazilian National Health Surveillance Agency (ANVISA) banned UV cosmetic tanning altogether nationwide – the only country to have taken such a sweeping step to date.7

Australia, already a worldwide leader in sun safety education, had been driven to action against tanning salons even before the IARC report. Clare Oliver, a budding 26-year-old Aussie journalist, had developed and died from melanoma just a few years after several visits to a tanning parlor, and her very public death (she wrote a newspaper story and gave broadcasts from her hospice bed calling for a ban on tanning beds) stirred public outrage that drove legislators to institute far greater controls over the tanning industry. The IARC report has only strengthened the country’s resolve. Today, all five major states in Australia have banned access to tanning beds for everyone under age 18. Most states also ban access to fair-skinned people (skin type I), and operators must display health warnings or risk up to million-dollar fines. All this legislation has driven scores of tanning parlors out of business, leaving the industry hanging by a thread. After more than a 300 percent increase in tanning parlors between 1996 and 2006, the number dropped by 32 percent in the past three years, and sometime this year, the number is expected to have dropped by up to 60 percent.8,10

The Battle Stateside

In the US, the attack on sunbed tanning has been waged from several directions. California, Texas, and at least 29 other states have passed their own legislation restricting use of tanning facilities by minors,11 and now, in the wake of the IARC report, there is a chance that the FDA will strengthen its regulations nationally.

After the IARC report appeared late last year, The Skin Cancer Foundation commissioned a white paper to the FDA urging greater regulation of tanning salons, and began lobbying legislators. This helped lead the FDA to hold a meeting on March 25 of this year to discuss upgrading tanning machines from a Class I medical device, the lowest regulatory category (the same class as tongue depressors) to Class II or III, thereby allowing the FDA to increase safety regulations and oversight. Leading up to the meeting, the Foundation launched a citizen’s petition in favor of reclassification, garnering nearly 300 signatures, and encouraged members and friends to submit testimony in favor of reclassification to the FDA via the Foundation’s website, www.SkinCancer.org. When the meeting took place, physician members of the Foundation presented key testimony about the dangers of tanning and tanning salons.12

After four hours of testimony, the FDA’s Medical Devices Advisory Committee unanimously recommended that the FDA upgrade its classification of tanning devices. The Panel concluded that Class I was inappropriate, incorrectly including tanning machines among “devices that present minimal potential for harm to the user.” The majority of the panel also favored an age restriction to limit minors’ access; approved of more disclosure to users about tanning’s dangers, and recommended better placement of labels warning users about these risks. The FDA is now weighing the panel’s recommendations. [Keep posted on the latest news on reclassification at www.SkinCancer.org]12

Even as the FDA deliberates its next move, other government bodies have been inspired by the IARC report to take action. A new 10 percent tax on indoor tanning — included in the

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in Sweden, Iceland, and Northern Ireland, sharp increases in the incidence of melanoma on the trunk have indeed been described.16,17,18 [See Figure 2].

In view of all the amassed knowledge on the detrimental effects of indoor UV tanning, public health officials need to increase control over indoor tanning, starting by preventing exposure to UV lamps by teenagers and young adults.

References

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health reform bill signed in recent months by President Obama — may especially make some cash-strapped young people think twice about tanning. The tax, scheduled to take effect July 1, is expected to raise $2.7 billion over 10 years.13

The Federal Trade Commission also has been cracking down on the marketing of indoor tanning, and in late May, the agency made its final settlement on a suit brought against the Indoor Tanning Association (ITA) in January for making false or unsubstantiated health and safety claims in a 2008 advertising campaign. The ITA has had to pull the disputed ads, and in addition to a ban on misleading claims, any ITA ads suggesting that tanning is safe or healthy must henceforth prominently display this disclosure: “NOTICE: Exposure to ultraviolet radiation may increase the likelihood of developing skin cancer and can cause serious eye injury.”14

The bottom line is that the IARC report has had a massive impact, providing impetus for multiple actions worldwide to reduce the dangers of indoor tanning.

Mark Teich, Executive Editor

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