Indoor Tanning: The Link To Melanoma Is No Longer Deniable

Elena B. Hawryluk, MD, PhD
Dermatology Program, Boston Children’s Hospital, Harvard Medical School
Department of Dermatology
Massachusetts General Hospital
Harvard Medical School, Boston, MA

Alan C. Geller
School of Public Health
Harvard Medical School, Boston, MA

David E. Fisher, MD, PhD
Department of Dermatology
Massachusetts General Hospital
Harvard Medical School, Boston, MA

Indoor tanning devices such as sun lamps, tanning beds, and tanning booths expose the skin to concentrated amounts of ultraviolet radiation (UVR), and a growing body of research now links this exposure more convincingly than ever to an increased risk of melanoma and other skin cancers. While some early studies pointing to the carcinogenic effects of indoor tanning started emerging as early as the 1990s, in the past few years, with advances in scientific scrutiny and the results of multiple investigations, the weight of evidence has become virtually irrefutable.

The Source of the Damage

We now know that tanning beds darken the skin through a process that requires UV-induced DNA damage; this damage activates transcription of cellular repair signals that ultimately increase skin pigmentation as a partial barrier against further damage. Unfortunately, some damage has already been done, and the repairs are probably never complete; the remaining damage is what produces genetic mutations that can lead to skin cancers.

As its name suggests, artificial tanning (tanning machines, not to be confused with sunless tanning) essentially mimics or reproduces natural UVR from the sun. Natural sunlight produces UVR of different wavelengths – UVA, UVB, and UVC – but UVC rays are largely filtered out by stratospheric ozone before reaching the earth. While older tanning lamps (before the late 1970s) also produced a broad spectrum of radiation including UVA, UVB, and UVC, more recent tanning lamps primarily emit UVA, the most effective wavelength for inducing a tan without incurring sunburn.
When tanning machines were altered in this way, it was widely believed that because UVB caused sunburn and UVA didn’t, UVB was far more dangerous. We now know differently. UVA has longer wavelengths than UVB (320-400 nm vs. 290-320 nm), penetrates the skin more deeply, and unlike UVB, which causes direct DNA damage and mutation, UVA inflicts DNA damage indirectly, by producing free radicals that cause oxidative damage and stress. In short, both UVA and UVB cause skin damage and skin cancer. [Figure 1.]

In 2009, the World Health Organization’s International Agency for Research on Cancer classified UV radiation, from both the sun and artificial UV tanning devices, as carcinogenic to humans.1 Both old and newer tanning lamps have been shown to increase risk of skin cancer,2,3 and a recent report linked indoor tanning to 170,000 nonmelanoma skin cancer cases per year in the US.4 The impact of indoor tanning on an individual’s total UV exposure can be substantial: in fact, the UV emission spectra of sunbeds exceed the UV index of the noontime summer sun at intermediate latitudes.5 While the sunbed emission spectra of UVB are similar to those of the sun, the UVA emission spectra of sunbeds are 10-15 times that of solar emission.5 Frequent tanners (with 100 or more sessions in their lifetime) who use modern high-pressure sunlamps may have up to 12 times the annual UV exposure of suntanners.6

The Problem is Widespread

The amount of damage caused by indoor tanning is especially alarming in light of its popularity. The U.S. Food and Drug Administration (FDA) estimates that more than 30 million Americans use tanning devices annually. These machines can be found not just at tanning salons, but increasingly at spas, health clubs, and hair salons as a service for patrons. A 2008 cross-sectional, interview-based survey of 29,394 individuals examined the prevalence of indoor tanning and found the rates highest among those who were young, white, and female.7 The highest prevalence (20.4 percent) was among individuals 18 to 29 years of age.7 More recently, according to the 2010 National Health Interview Survey, 32 percent of non-Hispanic white women aged 18-21 reported indoor tanning, with the tanners reporting an average of 28 sessions per year.8

The practice unfortunately is very common among adolescents as well: the 2011 national Youth Risk Behavior Surveillance System found that 13 percent of high school students engaged in indoor tanning, including 29 percent of white high school girls, and 32 percent of girls in the 12th grade.6 Guy and colleagues further noted that 16.7 percent of these girls had tanned during the preceding year.9 And including even younger teens, a 2011 cross-sectional interview-based study of 6,125 adolescents (ages 14-17) in the 100 most populated American cities found that over the preceding year, indoor tanning was utilized by 17.1 percent of girls and 3.2 percent of boys.9 Greater use of tanning beds is associated not just with being white and female, but also with having a parent who practices indoor tanning, having a greater allowance, and living within two miles of a tanning facility.

Figures

**Figure 1: Molecular Mechanism of Skin Pigmentation Induced by UV Radiation**

Ultraviolet light triggers DNA damage in the nucleus of keratinocytes, resulting in the activation of p53, which transcriptionally up-regulates the expression of the gene encoding proopiomelanocortin (POMC). POMC is post-translationally processed to produce melanocyte-stimulating hormone (MSH) and $\beta$-endorphin. After secretion, MSH acts on its receptor, the melanocortin 1 receptor, located on melanocytes at the basal layer of the epidermis, thereby inducing the production of pigment, which is subsequently transported out of melanocytes to overlying keratinocytes, where the pigment vesicles coalesce over the UV-exposed side of the nucleus, resulting in tanning.
use (independent of sun exposure) to an increased risk of the disease, especially among patients younger than 30 years of age. Among this population, for those with more than 10 sessions per year, only melanomas on the trunk were significantly associated with tanning. In 1998, however, Swerdlow and Weinstock came to the conclusion that while there were “several reasons for concern” that tanning beds cause melanoma, new meta-analyses and more precise data were required before arriving at that conclusion.

In 2002, Karagas and colleagues took a notable stride, publishing a well-respected study showing that tanning bed users were 2.5 times more likely to develop squamous cell carcinoma (SCC) and 1.5 times more likely to develop basal cell carcinoma (BCC), but the study looked only at these nonmelanoma skin cancers.

In the past few years, finally, the meta-analyses and more precise data Swerdlow and Weinstock were looking for have come to light, along with striking increases in melanoma incidence among young people that appear to parallel the increases in indoor tanning. In 2010, a US analysis by the Surveillance, Epidemiology, and End Results (SEER) Program showed that melanoma incidence has risen preferentially among young American women, prevalently on body sites naturally photoprotected by clothing, such as the trunk; as an aside, the researchers observed that this sizable melanoma increase in young women happened to coincide with the massive increase in indoor tanning in the US. SEER data was also analyzed by Purdue and colleagues, who similarly reported that the annual incidence of melanoma among young women increased from the 1990s onward, for thinner and thicker melanomas, regional and distant tumors alike. Again, these increases took place concurrently with the rise in young women’s tanning bed usage.

The Evidence Mounts

Other large, convincing studies have continued amassing the evidence, further explicating and quantifying the increase in risk of melanoma and other skin cancers due to tanning.

• In 2010, Lazovich and colleagues conducted a population-based case-control study comparing 1,167 cases of invasive cutaneous melanoma to age- and gender-matched controls in Minnesota, finding that 63 percent of the melanoma patients and 51 percent of the controls had indoor tanning exposure. The authors demonstrated that melanoma risk increased with indoor tanning years (P <0.006), hours (P<0.0001), and sessions (P=0.0002). These increased risks were found across device types and regardless of the age when tanning initiated.

• In 2011, a case-control-family study by Cust and colleagues examined 604 melanoma cases in Australia and determined that 76 percent of the melanomas were attributable to sunbed use. This risk was increased with earlier age at first exposure as well as increased frequency of use, and was associated with earlier onset melanoma. Similarly, a year later, Wehner et al. found that the risk of developing melanoma was especially increased for individuals who started indoor tanning before age 25.

• In 2012, Boniol and colleagues provided a systematic review and meta-analysis of 27 case-control, cohort, and cross-sectional studies that demonstrated an association between tanning bed use and melanoma risk among individuals who had ever used indoor tanning. As with Cust et al. and Wehner et al., this risk increased with both number of tanning sessions and initial usage at a young age (<35 years).

A 1.8 percent increase in melanoma risk occurred for each additional sunbed session per year, and the authors calculated an estimated 3,438 melanoma cases attributed annually to sunbed use in European countries.

• Also in 2012, Zhang and colleagues utilized a large, well-characterized cohort (73,494 female nurses from 1989-2009) to identify a dose-response relationship between the use of tanning beds and the risk of skin cancers, with 11 percent increased risk of melanoma among participants who used tanning beds four times per year, in addition to a 15 percent increased risk of both SCC and BCC. With SCC comprising over 20 percent of all skin cancer deaths and melanoma the vast majority of skin cancer deaths, the elevated risk of both cancers caused by indoor tanning is of major public health importance. Also of note were the researchers’ findings that the increased risk of skin cancer due to tanning bed use was similar among participants of different natural pigmentation (both fair skin and darker skin) — a clear indication that public health messages about the dangers of tanning need to be emphasized across all populations.

These and many other significant studies have appeared in just the past few years. With each new bit of research showing a dose-dependent relationship between tanning, melanoma, and other skin cancers, and special vulnerability in those who start young, the certainty of the link becomes more solidified, as well as the urgency for imparting this message to people everywhere as early in life as possible.

Regulation of Tanning

The increased appreciation of skin cancer risks associated with indoor tanning has brought increased restrictions to tanning access worldwide. In 2003, only France and Brazil had any nationwide tanning laws, but just nine years later, a 2012 review of international legislation found 11 countries with legislation that restricts indoor tanning for individuals under age 18.

In the US, the FDA device classification of tanning beds is Class I, indicating that they present minimal potential to cause harm (offering no more danger than a tongue depressor), and they are subject only to general controls to ensure safety and efficacy; however, given the mounting evidence, in 2010 the General and Plastic Surgery Devices Panel made the recommendation to change this classification. In May 2013, the FDA proposed raising the classification for tanning devices to a Class II level, which would require special controls including labeling requirements, performance standards, surveillance, patient registries, and guidance documents. A final rule on this proposed administrative order is pending.

In 2011, California became the first state to ban indoor tanning for anyone under age 18. Next came Vermont in 2012, followed closely by a succession of other states. In 2013 alone, Illinois, Nevada, Texas, and Oregon (where under-18s are prohibited unless they provide a prescription) have all banned
indoor tanning for people under age 18. Connecticut, New York, and New Jersey have bans for young people under age 17, and Wisconsin for those under age 16. Many other states have enacted bans for those under age 14, or require a prescription, parental accompaniment, and/or parental consent along with various age limitations. Currently at the state level, 35 states and the District of Columbia now have tanning restrictions in place for minors of varying ages, and an additional 11 states have introduced legislation.

The efficacy of these developments, however, was called into question by a 2011 study of adolescent tanning by Mayer and colleagues, who found that the practice is being strongly discouraged by most prominent health organizations, including the World Health Organization, the American Medical Association, the American Academy of Dermatology, and the American Academy of Pediatrics, as well as The Skin Cancer Foundation. All have issued strong statements about the dangers of tanning. It is time for the FDA to revisit the safety data, and to move forward with raising the classification of tanning devices to Class II, requiring increased regulation. It is time, in fact, to pass nationwide laws banning all minors under age 18 from indoor tanning.

The problem is, federal oversight of the tanning industry is lacking. While the FDA has provided recommended exposure limits, a 2003 community-based survey study in North Carolina showed that the FDA-recommended exposure limits for tanning were exceeded by 95 percent of users.

Now that the melanoma risk associated with indoor tanning is more firmly established than ever, the practice is being strongly discouraged by most prominent health organizations, including the World Health Organization, the American Medical Association, the American Academy of Dermatology, and the American Academy of Pediatrics, as well as The Skin Cancer Foundation. All have issued strong statements about the dangers of tanning. It is time for the FDA to revisit the safety data, and to move forward with raising the classification of tanning devices to Class II, requiring increased regulation. It is time, in fact, to pass nationwide laws banning all minors under age 18 from indoor tanning.

**References**

People who regularly tan are often more knowledgeable about the dangers of ultraviolet light exposure and the risk of skin cancer than are non-tanners. So why do they knowingly keep exposing themselves to a carcinogen? Social influences and so-called “appearance motivation” have been posited as possible reasons, but these are only part of the picture. It turns out that many physical addiction factors may be involved.

**To Tan or Not To Tan**

In a recent study, researchers investigating the behavioral models that predict sunbathing and indoor tanning sampled 589 college females to study the appearance factors related to tanning (sociocultural influences, appearance-related reasons to tan, and appearance-related reasons not to tan) and the perceived threat of skin cancer. In addition, both indoor tanning and sunbathing intentions and behaviors were collected over a six-month time frame. Among the study’s participants, both sociocultural influences (media, family, friends) and appearance-related reasons to tan outweighed the perceived threats of tanning and the appearance-related reasons not to tan.

**Biology of Tanning Addiction**

Once thought to be a purely behavioral characteristic, tanning may have biological effects that lead some patients to continue exposing themselves to ultraviolet light. In a seminal survey study by Warthan and colleagues, UV light (UVL) tanning was investigated as a type of substance-related disorder (SRD); 145 beachgoers in Galveston Island, Texas, were evaluated to assess their dependence on UVL tanning, based on two models used to identify SRDs. The researchers employed modified versions of both the standard CAGE questionnaire (normally used for alcoholism screening) and the American Psychiatric Association’s DSM-IV-TR, which includes seven criteria for diagnosing SRDs. Of the 145 participants, 26 percent met the modified CAGE criteria and 53 percent met the modified DSM-IV-TR criteria for a substance-related disorder (p=0.03).

A similar study conducted by Harrington, et al. also sought to determine the presence of addictive behaviors in participants who frequented indoor tanning salons. As in the Warthan study, the 100 participants completed both a modified CAGE questionnaire and a modified DSM-IV questionnaire. Forty-one percent of the subjects met the criteria for a “tanning addictive disorder.” These studies provided a new paradigm for understanding why people seek out exposure to UV light. The authors suggested that recognizing tanning as a potential SRD might alter future strategies to decrease or eliminate this addictive behavior.

**Natural Narcotic Effects**

In keeping with this survey research, in vitro and in vivo studies provided a biologic foundation for the addictive properties of tanning. Wintzen and colleagues, conducting in vitro studies designed to assess how UV light induces pigmentation, found that UV light exposure induces keratinocytes to synthesize alpha-melanocyte stimulating hormone (α-MSH), a polypeptide derived from the larger protein proopiomelanocortin (POMC). Yet another polypeptide hormone contained within POMC, β-endorphin, was released in addition to the α-MSH. β-endorphin, which binds to narcotic receptors, is the “feel-good” molecule in the body. The possibility that endorphin production underlies tanning behavior provided an exciting new basis for explaining why tanners frequently seek both outdoor and indoor tanning sites, despite knowing the harmful effects (Figure 1).

*The Center for Dermatology Research is supported by an unrestricted educational grant from Galderma Laboratories, L.P. Dr. Feldman is the founder and holds stock in Causa Research and www.DrScore.com. Jean-Phillip Okhovat has no conflicts to disclose.

Figure 1. Vicious Circle: the link between tanning and the sensation of a rewarding stimulus

UV exposure stimulates keratinocytes to release alpha-melanocyte stimulating hormone (α-MSH), a polypeptide derived from the larger protein proopiomelanocortin (POMC). β-endorphin, the body’s “feel good” molecule which binds to narcotic receptors, is also released and is potentially a mechanism that leads to habitual tanning behavior.

Continued on page 6
A 2004 in vivo study by Feldman et al. investigated whether UV exposure can have physiologically reinforcing effects separate from appearance motivation that may contribute to tanning behavior. The researchers enrolled frequent tanners, identified as those tanning three times a week or more. Subjects tanned in two tanning beds designed to appear the same, except that one emitted UV light and the other did not. Both tanning beds transmitted visible light and appeared identical; however, tanning beds include acrylic sheets that people lie on, and one of the tanning beds had acrylic filters that blocked UV, while the other had no such filters. This allowed for controlled, blinded UV administration. The tanners had sessions in both beds on Mondays and Wednesdays and were then allowed to choose one of the two beds on Fridays. The Monday, Wednesday, and Friday sessions were repeated for six weeks. There were 41 Friday “choice” sessions total, and in 39 of those sessions (95 percent), tanners chose the UV bed; only twice did anyone choose the non-UV bed. Study participants reported a more relaxed mood after UV exposure than after non-UV exposure. This study provided strong confirmation of a biologic mechanism that at least partly drives tanning behavior in frequent tanners. [Figure 2.]

To test whether endorphin production underlies this drive, expanding on an earlier preliminary study, Kaur et al. subsequently conducted a study to determine whether opioid antagonism would block the potential reinforcing effect of indoor tanning in eight frequent tanners and eight infrequent tanner control subjects. In the earlier study (2005), Kaur and colleagues had given three frequent tanners 50 mg of naltrexone, a narcotic antagonist that effectively blocks central and peripheral opioid receptors. Two of the subjects developed unexpected nausea, vomiting, and disorientation—symptoms similar to those seen in cases of opioid withdrawal.

In Kaur et al.’s larger study, done the next year, the eight frequent and eight infrequent tanners were given escalating doses of naltrexone. At each dose level, subjects were randomized to receive either naltrexone or placebo, then switched to the other at the next visit. Drug screening was done to assure that the subjects were not taking exogenous narcotics. All eight infrequent tanners completed the trial without adverse events (nausea and/or jitteriness). In contrast, two frequent tanners discontinued the study due to adverse events at a dose of 15 mg naltrexone, and two others also experienced adverse events at 15 mg naltrexone but remained in the study. In the placebo and 5 mg dose of naltrexone conditions, frequent tanners preferred the UV stimulus; but at naltrexone doses of 15 and 25 mg, frequent tanners showed a reduced preference for UV exposure.

Thus, the earlier in vitro studies and confirmatory in vivo human trials provided strong evidence to support the theory that the reinforcing effects of UV exposure may be at least partly mediated by opioids, such as β-endorphin. As opposed to the previous prevailing notion that frequent tanners tan purely for appearance-related motivations, frequent tanning behavior appears to have, at least in part, a physiologic basis. The Role of the Central Nervous System

Further advances in elucidating the addictive properties of tanning are coming from brain imaging studies designed to assess whether tanning has an effect on the central nervous system (CNS). The brain’s “reward pathway” contains three important structures: the ventral tegmental area (VTA), the nucleus accumbens, and the prefrontal cortex. The VTA is connected to both the nucleus accumbens and the prefrontal cortex via this pathway. [Figure 3.] When activated by a rewarding stimulus, the neurons of the VTA release dopamine into the nucleus accumbens and the prefrontal cortex.

Researchers have sought to investigate the effects of UV radiation (UVR) on the central nervous system by assessing the effects of commercially available tanning on regional cerebral blood flow (rCBF) — a measure of brain activity — using single-photon emission computed tomography (SPECT). In a study by Harrington et al., seven frequent tanners were placed under UVA/UVB tanning light during two sessions, one session involving UVR exposure and the other employing filtered UVR. During the unfiltered UVR sessions only, the participants showed a relative increase...
Conclusions

In the past several years, a wave of research has helped to delineate the complex internal and external (physiologic, psychological, and biochemical) reasons for tanning behavior and tanning addiction. As we improve our understanding of why people continue to engage in an activity that is potentially so harmful, this knowledge may allow investigators to develop better interventions to reduce or even eliminate habitual tanning.

References


From the Editors, from page 1

these actions could engrain in everyone's minds the dangers of artificial tanning the same way warning labels and banned sale to minors did when it came to smoking.

But changing hearts and minds will be complex. Just as lighting up was once the epitome of cool, a tan remains for many young people the symbol of health and beauty. Paradoxically, these young tanners are more knowledgeable than ever about the dangers, but often this does not change their behavior — the quest for cool, the desire to “belong,” and the need to be attractive hold sway. Hopefully, the preponderance of scientific proof, unflagging public education, and reduced access will have the same effect that the war on smoking did, making it marginal. Already, with numerous celebrities speaking out about the dangers (and especially the aging effects) of tanning, we can envision a time when attitudes shift towards making one's natural skin color the desired norm.

The last piece of the puzzle may prove the most difficult. Even if all of the above conspire to discourage tanning, once the habit starts, it is extremely hard to break. The reason may surprise some: like smoking, tanning is physically addictive. In our second story, Jean-Phillip Okhovat and Dr. Steven Feldman scrupulously trace the recent in vitro and in vivo research that has led scientists to this conclusion. This new knowledge could be the first step toward developing treatments — interventions to help people stop what we now know is an addictive behavior that could kill them before their time.

Allan C. Halpern, MD
Editor-in-Chief

Ashfaq A. Marghoob, MD
Associate Editor

Figure 3. The central nervous system “reward pathway”

The central nervous system reward pathway consists of the ventral tegmental area (VTA), the nucleus accumbens, and the prefrontal cortex. These areas become active when the skin is exposed to ultraviolet light.