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The Epidemiology, Prevention, and Detection of Melanoma

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ABSTRACT

We are seeing a record number of newly diagnosed skin cancers worldwide, with the incidence of melanoma increasing at a faster rate than almost all other cancers. As clinicians, we will have, by far, the greatest impact on reducing this incidence through better methods of early detection of melanoma and proven prevention methods and techniques. The medical community must enhance its efforts to increase its training of new health care personnel who are capable of diagnosing and treating this record number of patients with skin cancer. We must also try to increase the access to our limited number of dermatologists and provide novel ways of patient education such as through skin self-examinations, total body photography, and improved education for our children. By providing easier access to skin examinations, we will increase our chances of detecting melanoma in its earliest and most curable form. The dangers of indoor tanning beds and salons must be transparent to those that use them, focusing on expanding the oversight of such facilities by our local and federal governmental agencies while establishing legislation in several states to further limit their use to our youth, who are especially at high risk for developing melanoma in the future. This review will focus on the epidemiology, prevention, and detection of melanoma.

EPIDEMIOLOGY OF MELANOMA

According to the Surveillance Epidemiology and End Results data, melanoma is the sixth most common fatal malignancy in the United States, responsible for 4% of all cancer deaths and 6 of every 7 skin cancer-related deaths.[1] A thorough understanding about incidence trends, mortality rates, risk factors, and genetics of this deadly cancer is of critical importance in order to create a national and even worldwide social awareness of the relationship between overexposure to ultraviolet radiation (UVR) in all of its forms and cutaneous melanoma. It is predicted that 1 in 5 Americans will develop skin cancer in his/her lifetime, resulting in 1 million new cases per year.[2] It should be noted that although melanoma represents the most lethal form of cancer, basal cell and squamous cell carcinoma are ~100 times more common than melanoma, and only squamous cell carcinoma is rarely associated with resulting metastasis and death.

Notably, the American Academy of Dermatology (AAD) reports that melanoma is the second most common cancer in women 20 to 29 year old, with 68,000 newly diagnosed cases in the United States in 2010.[3,4] The annual direct cost of treating nonmelanoma skin cancer in the United States in 2007 was estimated to total $650 million, and when melanoma is included, this number increased to a staggering $2.9 billion.[5] According to a recent publication of the International Agency for Research on Cancer (IARC), Queensland, Australia, had the highest incidence of invasive cutaneous melanoma worldwide during the period from 1998 to 2002.[4,6] Additionally, the IARC placed North America as fourth in melanoma incidence worldwide, with 19.4 per 100,000 males and 14.4 per 100,000 females. However, the most recent data from Surveillance Epidemiology and End Results, encompassing the years of 2002 to 2006, shows a marked increase in incidence in non-Hispanic whites of 28.9 per 100,000 in males and 18.7 per 100,000 in females.[7] In 2010, current estimates indicate that 1 of every 39 people in the United States will be diagnosed with melanoma during his/her lifetime.[8] This risk is substantially greater than noted in 1985 and 1965, when the lifetime risks were estimated to be 1 in 150 and 1 in 600, respectively.[9,10]

Incidence rates vary throughout Europe as well, with the highest rates seen in Switzerland, Norway, Sweden, and Denmark compared with those countries in southern Europe.[7,11] MacKie et al[11] hypothesize that this latitudinal gradient may be related to sun-exposure behaviors, and in particular to the tendency for Northern Europeans to vacation in sunny climates, resulting in intense, intermittent sun exposure. A Swedish study reported 46,337 melanomas diagnosed during the period of 1960 through 2004,

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clearly revealing an increase in the incidence of melanomas of the trunk and lower limb.[12] The number of head and neck melanomas has also increased, but less rapidly than other locations, most commonly associated with older individuals, >70 years old. Primary melanomas of the trunk and lower limb have been associated with intermittent, high-intensity sun exposure, as opposed to head and neck melanomas, which appear to be associated more with chronic, long-term sun exposure.

Ultraviolet Radiation and the Development of Melanoma

It is now widely accepted that the major environmental risk factor for the development of primary cutaneous melanoma is UVR, which can be subdivided into ultraviolet A (UVA), ultraviolet B (UVB), and ultraviolet C (UVC). Immediate tanning is caused by UVA and fades within hours or days. Delayed tanning occurs 2 to 3 days after initial exposure to UVA or UVB and lasts several weeks to months.[13] Tanning after exposure to UVR depends on the skin type and the UV Index. UV Index as calculated by the US National Weather Service is reported as a scale from 0 to 11 and takes into account the wavelengths of UVB (290-320 nm), UVA (320-400 nm), strength of UVR relative to ground level, adjusted skin sensitivity to UVR, ozone concentration, and cloud amounts.[14] Burn frequency after exposure to UVR as related to UV index differs among the various skin types.[13.15] The contribution of UVC in the development of skin cancer is considered negligible as most is prevented from reaching the surface of the earth by the atmospheric ozone layer.[16]

Elmwood and Gallagher[17] identified that short, intermittent burning episodes of sun exposure is a major risk factor for the future development of melanoma, resulting in a higher incidence in those individuals with pale, nonacclimated white skin. The specific wavelengths that are known to cause squamous cell cancer in albino hairless mice are bimodal in nature (peaked at 293 and 354 nm), with the development of cutaneous melanoma seen after exposure to wavelengths of 290 to 320 nm, or the wavelength of UVB.[18]

A direct relationship between UVB and melanoma has been demonstrated, with a 10% increase in average annual UVB irradiation correlating with a 19% increased risk of melanoma.[19] The DNA mutations identified after UVB exposure can lead to the generation of pyrimidine dimers that cause cytosine to thymine and dimerization with associated DNA mutations.[20] Recent evidence also shows UVA causing similar DNA changes.[21] The tumor suppressor gene *p53*, which has the capacity to repair DNA damage via inducing apoptosis, is itself subjected in the skin to dipyrimidine mutagenesis. Thus, the carcinogenic effects of UVR to DNA are twofold in that it induces genomic mutations and impairs the normal function of *p53*.[22,23]

Melanoma is mostly seen in the non-Hispanic white population, making the phenotypes of pale white, red-haired, or blond-haired as established risk factors for developing cutaneous melanoma. The unique distinction between such phenotypes and the dark-skinned population is partly because of the type of melanin produced, which is greatly influenced by the gene, *MC1R*. Eumelanin is responsible for the dark pigmentation, while phaeomelanin is responsible for red hair and freckles. Loss of function of the wild-type *MC1R* gene with associated gene mutations and chromosomal arm variability prevent eumelanin production and are associated with most of the red-haired phenotypes observed in the human population.[16]

Invasive cutaneous melanoma in one or more first-degree relatives is an additional risk factor for melanoma. As stated by MacKie et al,[11] the work of 2 international melanoma genetics collaborative groups, Genomel and Gem, has shown that approximately one third of patients in melanoma families worldwide have an identifiable germline mutation in *CDKN2A*, a gene important in controlling entry into the cell cycle. *CDKN2A* codes for 2 different proteins, p16 and p14ARF. Tucker[24] identified *CDK4*, a second melanoma susceptibility gene found in 5 families to date worldwide. In addition, within melanoma-prone families, *MC1R* variation increases the risk of melanoma in families without *CDKN2A* and modifies the risk of melanoma associated with *CDKN2A* mutations[24-26] by conferring a sevenfold increase in the risk of developing melanoma.

Some familial cases of melanoma are also associated with the familial atypical multiple mole and melanoma syndrome. This syndrome was originally described in families showing concordance for melanoma and a cutaneous phenotype characterized by the multiple large moles of variable size and color with pigmentary leakage.[20] As stated by Tsao et al,[27] a family history of cutaneous melanoma in at least 2 first-degree relatives and younger age at diagnosis are important components of this syndrome. This is partly because of the increased rate of p16 mutations (protein encoded by CDKN2A) associated with this syndrome.[28] Thus, the identification of populations at high risk, such as those with a potential familial predisposition or gene mutation, is important in our efforts to identify high-risk groups that may benefit from intense surveillance and skin cancer screening efforts.

EARLY PREVENTION OF MELANOMA

Education of Our Youth

The most modifiable risk factor for skin cancer is UVR exposure. We must educate others as to the importance of using sunscreens, in combination with attempting to increase the number of people who use safe sun practices, such as avoiding the sun during peak hours, using protective clothing and head gear, and avoiding the use artificial sources of UV light.[29] There is great concern in regard to the total amount of sun exposure during early childhood, resulting in the implementation of several prevention programs worldwide to reduce the amount of sun exposure during these critical years. The Committee on Environmental Health of the American Academy of Pediatrics published its recommendations in 1999, urging pediatricians to promote the reduction of sun exposure in children by encouraging the use of sunscreen during outdoor activities, utilization of protective clothing, wide-brimmed hats, use of shaded areas, and being mindful of the daily UV index.[30]

Several recently established programs have resulted in an overall improvement in children's sun protection. Aulbert et al[31] established a feasible certification program for sun protection in a German child daycare center, with the goal to establish better policies for childhood sun protection and a long-term goal of decreasing the incidence of skin cancer. Several noted successes of this intervention included a significant gain in knowledge of staff members, an increased use of children wearing a hat from 13% to 72%, increased use of the reapplication of sunscreen, and an increased use of shaded areas on the playground. However, it did not succeed in keeping the children inside during the most intense UVR exposure or in educating the staff members to become a convincing example of sun protection by wearing protective clothing.

In the United States, Buller et al[32] randomly selected 1,000 public elementary schools within 27 metropolitan areas from 58 US cities in 1998 to assess current sun protection policies and the receptiveness to new policies. They found that only 3.4% of schools had an official sun protection policy, with the most common reason being the principal's lack of awareness and organizational barriers in place, such as lack of surplus funding to instill such changes in sun protection. In a separate study of secondary schools, Buller et al[33] performed a telephone survey of 484 secondary schools in 27 cities, addressing whether current Centers for Disease Control and Prevention-issued recommendations for school programs to reduce skin cancer were being implemented, in use, or followed.

Although a similarly low 10% of the schools reported having a sun protection policy, nearly all (96%) reported sun protection education occurring regularly, with limited and infrequent use of written educational materials on sun protection. Such public education efforts are questions as to their ultimate effectiveness in terms of the goal being to reduce the number of cases of melanoma in the future and possibly detecting melanoma at an earlier stage. Brackeen et al[34] examined the cause of the increased incidence of melanoma in Central Texas, suggesting that the increase in incidence is not the result of increased detection, rather it is a failure of the current public education efforts for sun protection.

Chemoprevention of Photocarcinogenesis

It is well-established that UVR exposure in humans results in tumor initiation and promotion, proceeding to complete transformation and carcinogenesis with excessive exposure.[35] Although considered an essential aspect of UVR protection, standard formulations of sunscreens have been shown to have limited or inadequate protection against reducing skin cancer.[35] Thus, considerable interest has developed in examining the potential use of naturally occurring botanicals for the prevention of UVR-induced photodamage and skin cancer. Several such naturally occurring compounds have been identified such as apigenin, a flavenoid found in herbs, fruits, vegetables, tea, and wine, that has been shown to prevent UV-induced tumorigenesis in mice.[36] Other compounds shown to have substantial photoprotective effects include curcumin, proanthocyanidins (grape seeds), resveratrol (grape skins, peanuts, red wine, mulberries), silymarin (milk thistle), and green tea.[35] In particular, the photoprotective effects of green tea polyphenols are well documented in the literature, protecting against UV-induced immunosuppression, premature aging, sunburn response, and carcinogenic activity.[37]

Indoor Tanning Salon as an Industry

It is imperative that public awareness increases as to the real dangers of UVR in all of its forms. This is especially true for the abuse of indoor tanning beds with its known association with the development of all forms of skin cancer, especially melanoma. The laws governing UVR exposure related to the use of indoor tanning beds or sunlamps are woefully inadequate. Given the rise in youth patronage of indoor tanning salons, we cannot ignore the potential immediate and long-term health risks to these young adults, especially when considering the formidable costs associated with the treatment of both melanoma and nonmelanoma skin cancers. Most compelling is the

recent classification by the World Health Organization (WHO) clarifying that all forms of UVR (UV A, B, C), broad-spectrum UVR, solar radiation, and exposure to sunlamps or tanning beds are designated as class 1 carcinogens, defined as known to cause cancer in humans. It is listed alongside cigarettes, asbestos, mustard gas, and plutonium-239 (in atomic bombs) as leading cancer-causing agents.

Despite such warnings, the indoor tanning salon industry is big business worldwide, with estimated annual revenue in 1992 of $1 billion, which grew to more than $5.5 billion in 2009 in the United States.[38,39] Although the absolute number of skin cancers related to tanning bed use is not known, a recent study strongly shows that exposure to tanning beds increases the risk for developing melanoma, especially in women aged 45 years or younger.[40] Of the 1 million Americans who use tanning salons regularly, 70% are females in the age range of 16 to 49 years old.[41,42] The groups of individuals that are at most danger are teenage girls and younger women who regularly use tanning salons, with a very high incidence found in women between the ages of 20 and 35. Among the US consumer base are 2.3 million teenagers, with the overall tanning trends increasing from 1% of American adults using tanning beds in 1988 to 27% in 2007.[38,43] At the same time, a decreased awareness as to the dangers of tanning has resulted in an increased risk in the developing of melanoma from 1994 through 2007.[44]

The number and density of indoor tanning facilities per 100,000 people in the 116 most populous cities in the United States have far exceeded other companies, such as the interval growth of Starbucks and McDonalds. In March 2006, the number and density of indoor tanning salons were 41.8 (SD 30.8) and 11.8 (SD 6), respectively. The mean numbers of indoor tanning salons exceeded Starbucks and McDonalds in the same cities, 29.6 (SD 22.5) and 19 (SD 25.2), respectively. Cities with higher percentages of whites and lower UV index scores had significantly higher facility densities than those with lower percentages of whites and higher UV index scores.[45]

The increasing trend of indoor tanning is encouraged by the indoor tanning industry as seen in a full-page advertisement in *The New York Times* on March 26, 2008: ''no compelling scientific evidence that tanning causes melanoma''…adding, ''UV light—both indoors and out—stimulates the natural production of vitamin D…vitamin D protects against heart disease and many types of cancer…It's time to rethink sun bathing.''[46] This type of unsubstantiated advertising is seen throughout the United States, with groups such as the Smart Tan Network, a lobbying group for the tanning industry, falsely implying that sunscreen is not needed every day and that it may completely block the body's ability to produce vitamin D.[47]

The UV Foundation, a division of the Indoor Tanning Salon, has falsely concluded that regular use of tanning bed leads to higher vitamin D serum concentrations, despite several groups disputing such unfounded conclusions.[48] Studies have shown that exposure through indoor tanning beds far exceeds the dosage required for vitamin D synthesis. The recommended UVB exposure dose is 25% of 1 minimal erythema dose, or 1 MED. The MED for type 2 skin is 12.6 minutes (ie, 25% of 1 MED requires 3 minutes) and for type 3 skin is 17.7 minutes (25% MED requires 4.5 minutes) using a standard tanning bed. A normal tanning session consists of 20 minutes of UVB exposure, or an extra 4.5 to 7 times the amount of UVB required for the production of vitamin D.[49]

A recent study shows that 0.5 to 2 hours per week of hands and face exposure was adequate for vitamin D biosynthesis.[50] A randomized double-blind controlled trial in Australia that compared a group wearing SPF 17 versus a placebo group showed that either group did not develop any deficiencies in the levels of vitamin D.[51] The recommendations of using a tanning bed as a means to induce vitamin D production was specifically advocated by Holick,[52] solely for those individuals with intestinal malabsorption via exposing hands, face, arms, and legs to an amount of time to reach 25% of what would develop a mild sunburn, that is, 1 MED for 2 to 3 times per week appears to be more than adequate.

The increase in indoor tanning is alarming when viewed relative to strong evidence that links indoor UV radiation exposure via tanning bed usage to skin cancer. A recent study analyzing patients diagnosed with basal cell carcinoma, squamous cell carcinoma, and 540 controls showed that those who have used a tanning device previously were at a 50% higher risk for developing basal cell carcinoma (odds ratio [OR] 1.5; 95% confidence interval [CI]: 1.1-2.1) and more than double the risk for squamous cell carcinoma (OR, 2.5; 95% CI: 1.7-3.8).[53] Ting et al[40] found that use of a tanning bed by 1,518 dermatologic patients showed a 64% increase in the risk of developing melanoma (OR, 1.64; 95% CI: 1.01-2.67), with a stronger risk in women <39 years old (OR, 3.22; 95% CI: 1.01-11.46).

A 2007 study by the IARC revealed that the first exposure to indoor tanning prior to the age of 35 was associated with a 75% increased risk of developing melanoma (RR, 1.75; 95% CI: 1.35-2.26).[54] A Swedish study showed that people who regularly use tanning beds have a relative risk for developing melanoma of 1.8, with a much higher risk for those <36 years old of 8.1, adjusting for hair color, raised nevi, skin type, and number of sunburns.[55] A Norwegian and Swedish

study of 106,379 women demonstrated that regular (at least once per month) solarium use at any age had a 55% increased risk of developing melanoma, with the greatest association in the 20- to 29-year-old age group.[56]

Youth Access to Tanning Salons

A telephone survey has previously shown that 10% of youth age 11 to 18 and 8% of their primary caregivers used tanning sunlamps in 1997, and 30% of youths whose caregivers used tanning beds also used them.[57] A cross-sectional study from 50 states included 10,079 boys and girls age 12 to 18 and showed only a basic understanding of UVR overexposure, the proper use of sunscreen, high rates of sunburning, and tanning bed use. Notably, girls were likely more than boys to report using tanning beds, with girls age 15 to 18 more so than girls age 12 to 14. The increase in tanning bed usage increased with age: 7% of girls 14 years old increased to 16% by age 15 and 35% by age 17.[58] Independent predictors associated with indoor tanning sunlamp use include age 17 to 18, female, parents who use sunlamps in the previous year, nonusers of sunscreening products at the beach, and pool and low sun sensitivity.[57]

Current Laws Governing the Indoor Tanning Salon Industry

In 1986, the Food and Drug Administration (FDA) recommended a schedule for tanning sessions, stating a maximum 0.75 MED $\times$ 3 in the first week, increased gradually to a total maintenance of 4 MED weekly or biweekly. The manufacturers were asked to formulate their own schedules based on these overriding recommendations.[59] Additionally, the FDA limited the amount of exposure to UVC, not the ratio of UVA to UVB. Moreover, compliance to the limits of dosage of UVR by tanning salons is not reviewed at the federal or state level. Not surprisingly, a survey in North Carolina showed that 95% of clients exceed the recommended daily dose.[60] Few inquiries have been made into the enforcement practices of indoor tanning salons. A recent review shows 28 states have some form of law in place as of 2006, with licensure required in 22 of 28 cities, less than half gave citations to facilities that violated the state laws as written, with 32% of the city officials not inspecting these facilities, and another 32% inspected them less regularly than annually.[61]

Pertaining to youth access, an analysis of 3,647 indoor tanning facilities demonstrated that states with youth access laws are more likely than states without to require parental consent, with parents required to be present during tanning sessions.[62] Infractions to the recommendations by the FDA are not isolated to the United States, with 83% of tanning salons in England exceeding the European standards for UVB radiation levels.[63] Similar increased UV intensity was found in Norway.[64] In the December 2008 Report to Congress, the FDA noted that UV exposures found in sunlamp products are excessive and that comparable cosmetic results can be obtained with exposures that are one-fourth to one-third current levels used.[3]

The state of North Carolina has taken the lead in attempting to restrict the use of tanning bed usage to adults only. They have passed legislation that includes an active inspection program of tanning salons to ensure that tanning beds are up to standards and enforcement of rules against minors from tanning. In 2004, North Carolina banned the use of indoor tanning salons/beds of adolescents under the age of 13. Other states have followed, such as Michigan; in December 2008, the Michigan legislature took an important step to help combat the rise in skin cancer rates by passing House Bill 4146, which regulates tanning salons by specifically requiring onsite parental consent for anyone under 18 years old. They additionally required larger warning signs in tanning salons, listing the potential health care consequences of tanning bed usage and also required a signed consent form for all customers.

Approximately 25 other states have some form of restricted access for minors who want to use tanning salons. The banning of tanning in minors is currently recommended by the WHO and the AAD. It should not go unsaid that physicians of all types should not be afraid to enter the political ring in order to bring about changes in the current laissez-faire attitude toward the tanning salon industry. Many physicians have done so; however, until an organized effort emerges in an attempt to bring about legislation that would outlaw the use of tanning beds, we must continue to educate our patients and the population of the substantial dangers of tanning beds.

EARLY DETECTION OF MELANOMA

Skin Cancer Screening

In February 2009, the US Preventive Services Task Force published an update stating that there is insufficient evidence available to recommend for or against skin cancer screening.[65] Furthermore, there has never been a randomized, controlled trial examining the efficacy of skin cancer screening. Thus, no data exist to demonstrate the effectiveness of early detection of skin cancer or the benefits on morbidity and mortality, including a reasonable calculation of the benefits of screening in the general population. However, many clinicians rightfully point out that the bar is held too high for such a screening test because this is one of the few cancers that merely requires a

visual examination to make the diagnosis, with no risk to the actual screening process itself. The minimal risks associated with a biopsy also are small compared with other screening tests, such as colonoscopy or mammography. Despite these strongly held perceptions, the US Preventive Services Task Force found no new evidence that proves that whole-body skin examinations, whether by the physician or self-examination by the patient, reduce morbidity and mortality from skin cancer.

Dermatologists in particular are quick to point out that it appears almost intuitive to think that screening for melanoma can be both effective and beneficial in their practices, citing a wealth of data in support of early detection of melanoma. Berwick[66] examined whether skin self-examination (SSE) was associated with a decrease in lethal melanomas by interviewing 650 people with newly diagnosed melanoma and 549 without disease on whether they had previously performed SSE. She found that the 15% who reported practicing SSE had a reduced risk for melanoma incidence (OR, 0.66; 95% CI: 0.44-0.99). Additionally, SSE was reported to reduce the risk for advanced disease among patients with melanoma (OR, 0.58; 95% CI: 0.31-1.11).

A recent US survey shows that only 22% of the adult population has ever had a full head-to-toe skin examination.[67] Young adults are especially lacking in basic knowledge of skin cancer awareness. Arnold and DeJong[68] sampled Boston-area young adults and found that more than half did not know what to look for on their skin or ever thought about performing an SSE. The National Skin Cancer Screening Programs of the AAD (1986-2001) showed that 80% of American adults did not have a regular dermatologist, 78% had never had a previous AAD skin cancer screening examination, and 60% had never had their skin checked by any doctor, with 51% not even willing to see a doctor unless the screening was offered at no charge.[67]

Thus, it will ultimately rely on the persons' ability to perform a sufficient SSE at home, in the hope that if they do find a suspicious skin lesion, that they will then be seen by their local dermatologist. Muhn et al[69] artificially enlarged skin spots by 2 mm and 4 mm and found that the sensitivity for self-detecting was 58% and 75%, respectively, with an overall specificity of 62%. Epstein et al[70] demonstrated that earlier and thinner melanomas were detected by physicians, nearly 0.7 mm difference in thickness, when compared with those detected by patients, spouses, or family friends. Schwartz et al[71] found similar results, with physician-detected melanoma (0.40 mm) showing the thinnest lesions compared with either patient-detected (1.17 mm) or spouse-detected (1.00 mm) lesions. A recent study from 2005 to 2008 showed 56.3% of melanomas and 60% of melanoma in situ were initially detected by dermatologists and were not part of the presenting complaint.[72]

Interestingly, Losina et al[1] found that one-time melanoma screenings of the general population were shown to be cost effective when compared with other cancer screening programs in the United States, with one-time, once every 2 years, and annual skin cancer screenings saving 2.5, 8.8, and 10.2 quality-adjusted life years, respectively, per 1,000 people screened. Despite current recommendations, many dermatologists continue to perform full-body skin cancer screening on their patients, acknowledging that it is a relatively no-risk, simple, cost-effective, and practical method for the early detection of nonmelanoma and melanoma skin cancers.

Role of Total Body Photography and Dermoscopy

Total body photography (TBP) is used to sequentially document the stability of skin lesions, detect subtle changes in existing lesions, and to recognize new lesions.[73] Additionally, TBP was shown to help identify melanoma in its earlier stages and promote continued surveillance of skin lesions via the patient performing SSE. It is still utilized in many practices today, and the most common reasons for its use are for those patients with multiple (>5) atypical nevi, reducing patient anxiety, and earlier detection of melanomas, and that it leads to fewer biopsies. Feit et al[74] reported on patients who were undergoing TBP as part of their regular follow-up skin examinations, showing that 74% of the melanomas detected were a direct result of a noted subtle change on serial TBP. Others have shown its role in increasing the rates and compliance of SSE when the patients are actually given the photographs to take home with them as part of the SSE.[75-78]

Dermoscopy is a simple and inexpensive technique that permits the visualization of morphologic characteristics that are not readily detectable with the naked eye. It is a real-time, in vivo method for the early detection of melanoma and other pigmented skin lesions. It has been shown to improve diagnostic sensitivity for melanoma by 10% to 27%.[79] Such improvements in diagnosis are the result of incorporating the use of various scoring algorithms, based on pattern analysis and pigmentary differences among others. For example, the Board of the Consensus Netmeeting on Dermoscopy in 2003 developed a 2-step process for the classification of melanocytic from nonmelanocytic skin lesions as well as a series of algorithms to differentiate between benign, suspicious, or malignant skin lesions.[80] These include

pattern analysis, ABCD rules of dermoscopy, Menzies scoring method, and the 7-point checklist.

The 7-point checklist includes 3 major criteria (atypical pigment network, blue-white veil, and atypical vascular pattern) and 4 minor criteria (irregular streaks, irregular pigmentation, irregular dots and globules, and regression structures). Blum et al[81] developed a simplified and highly accurate dermoscopic point list for cutaneous melanocytic lesions to diagnose a consecutive series of 269 melanocytic lesions. Using their modified ABC-point list, which was derived from the ABCD rule of Stolz, Menzies score, and the modified ABCD rule of Kittler, they achieved an overall sensitivity of 90.5%, specificity of 87%, and a diagnostic accuracy of 88.1% for the diagnosis of melanoma. Overall, dermoscopy has developed as a very useful tool for dermatologists as a method of increasing the diagnostic accuracy of up to 30% over clinical visual inspection.

Clinical Significance of Dysplastic Nevi

BK moles, Clark's nevi, and atypical nevi are terms that refer to lesions with specific clinical and pathologic characteristics associated with an increased risk for the development of melanoma. These typically become clinically apparent at puberty or adolescence and continue to appear throughout life. Some clinicians have described patients having many nevi as having ''dysplastic nevus syndrome,'' although the classic definition refers to a patient with a triad of >100 nevi, at least 1 nevi that is ≥8 mm in diameter, and at least 1 nevus with clinically atypical features. The clinical significance of dysplastic nevi is in their association with the development of melanoma, with an age-adjusted incidence of melanoma ~15 times higher in those patients with dysplastic nevi versus the general population (154 vs 10 per 100,000 person-years).[82] This risk also increases as the total number of dysplastic nevi increases and in the presence of a personal or family history of melanoma. For instance, there is a 100-fold increase in the incidence of melanoma in patients who previously were diagnosed with melanoma, a 200-fold increase in those with at least 2 family members with melanoma, and a >1,200-fold increase in those with both a personal history and a family history of melanoma.[82]

There is continued controversy as to the appropriate clinical management of dysplastic nevi. According to the available evidence, it is not necessary to confirm the diagnosis histologically.[82,83] Additionally, despite the recognized association between dysplastic nevi and the risk for developing melanoma, the majority of dysplastic nevi will never progress to melanoma.[84] For example, based on the assumption that in a population of 10 million people, up to 20% of all melanomas develop in contiguity with a dysplastic nevus, it is estimated that only 1 in 10,000 dysplastic nevi per year will progress to melanoma.[85] These estimates underscore the argument against prophylactic excision of dysplastic nevi as it is not cost effective and can provide the patient with a false sense of security, because an increased risk of developing melanoma remains the same after these nevi have been removed. In regard to the surveillance and overall management of dysplastic nevi, there are 2 published sets of guidelines, one from the US National Institutes of Health and the second from the Melanoma Working Group in the Netherlands.

CONCLUSION

In conclusion, it is clear that UVR is the primary culprit for the development of melanoma. The WHO has again highlighted this important information for the general public, thoroughly showing that UVR is now considered a class I carcinogen, known to cause cancer in humans. We must continue our educational efforts to make the public aware of these dangers. The early prevention of melanoma through education of our youth will be essential if we are to have an impact on lowering the incidence rates for melanoma. Along these lines, parents must take personal responsibility and oversight in order to prevent their teenagers from using indoor tanning salons. As physicians and health care providers, we must actively become involved in the political process to bring about change in current practices related to indoor tanning. The early detection of melanoma must continue with full-body skin examinations by dermatologists who can use other tools to enhance early detection, such as full-body photography and dermoscopy. Lastly, it is imperative that we continue the community outreach efforts to increase the public's understanding of the eminent dangers of UVR overexposure.

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