

DRUG INFORMATION CENTER

PHARMA INFO-LINE

Ozone depletion, Ultraviolet radiation and Melanoma; the vicious triangle

The incidence of melanoma (one type of skin cancer) is rising dramatically in the last few decades, despite the efforts that governments are doing. Worldwide, the incidence of melanoma is increasing 3-7 % per year in people of European descent[1]. In Australia and New Zealand, where melanoma incidence rates are the highest in the world, it has nearly doubled every 10 years[2] and the US is ranked fourth worldwide in the incidence of invasive melanoma among men in year 2000[3].

Two-third of melanoma may be attributed to excessive sunlight exposure, therefore reducing sun exposure could theoretically reduce the incidence of this malignancy[4, 5].

For the last 3 decades there has been concern that ozone depletion will lead to increase of solar ultraviolet radiation and consequently increase the risk of adverse impact on human health in general and on the skin in particular[6]. Ultraviolet radiation (UV) that comes from the sun has a spectrum that ranges from 200-400 nm and can be categorized into 3 bands[7];

UVC band	200-280 nm
UVB band	280-315 nm
UVA band	315-400 nm

While UVB radiation causes the majority of DNA damage and appears to be more closely associated with the

development of melanoma, 10-100 times more UVA radiation reaches the earth surface, and may also be important in the pathogenesis of melanoma[8].

The exact pathways by which sunlight can cause melanoma are incompletely understood.

In an epidemiologic population – based data[9], two different pathogenic pathways may explain how UV can result in cutaneous melanoma, the authors of this study have suggested a "divergent pathway" model for the development of cutaneous melanoma, under this model;

× People with an inherently low propensity for melanocyte proliferation require chronic sun exposure to drive clonal expansion of transformed epidermal melanocytes, assuming that the hypothesis is correct; then melanomas arising in this group of people should occur on habitually sun-exposed body sites such as the face.

× In contrast, among people with an inherently high propensity for melanocyte proliferation, the authors predicted that exposure to sunlight is required early in the process of carcinogenesis, after which host factors drive melanoma development. This group of patients would be expected to have less solar damage than the former group of melanoma patients and would be expected to develop their tumors on body sites with unstable melanocyte populations such as the trunk[9].

Who is at high risk?

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Article summary

- 2/3 melanoma may be attributed to excessive sunlight exposure.
- Incidence of melanoma in Egyptian population is low despite of increased sun exposure.
- Generous application of sunscreen and avoidance of direct sun exposure between 10 AM— 4 PM are important measures in order to prevent melanoma.

Risk factors for melanoma can be classified into environmental and genetic, this may in part explained why the incidence varies from one place and ethnic group to another.

People at high risk can be summarized in the following points;

Those with fair skin (white) are at higher risk than black, in an analysis from the Surveillance, Epidemiology and End Results (SEER) database from 1992 to 2002, the incidence rates in whites, Hispanics, Asians/Pacific islanders, blacks, and Native Americans were 18.4, 2.3, 0.8, 1.6, and 1.0 per 100,000 individuals, respectively[10].

Males are at higher risk to develop melanoma than females[11, 12].

Those who have repeated intense exposure to sunlight, and repeated sunburn in childhood and adolescence. While occupational exposure does not confer increased risk[13].

Who live in equatorial areas or near the equator, however this should be adjusted for skin type (white people who live in these areas)[14].

Protection measures:

Before we discuss the protection measures let us first go through some characteristics and definitions of sun-block, sunscreen, and sun protection factor (SPF).

Sun-block (physical sunscreen) are opaque formulations which absorb, reflect and scatter up to 99% of both UV and visible light. Because they are messy and may stain clothing, sun-block is often used on such sun-sensitive areas as the nose, lips, ears and shoulders. Examples of ingredients in sun-block are zinc oxide and titanium dioxide[15, 16].

Sunscreen (chemical sunscreen) absorbs specific wavelengths (range of 200-400 nm i.e. protect against both UVA and UVB) and is classified as drug by the FDA because it is "...intended to protect the structure and function of the human integument against actinic damage." Sunscreen formulations are considered more cosmetically refined due to their pleasing consistency and are, therefore, typically used over a prolonged time for effective protection[15].

Since sunscreens can now either chemically absorb UV rays, or deflect them, the term sunblock is no longer used[17].

Sun protection factor (SPF) is a measure of the ability of an intervention (typically clothing or sunscreen) to prevent erythema in response to sun exposure.

The SPF can be multiplied by the time of exposure necessary to produce minimal erythema in an unprotected individual to get the expected time until minimal erythema using that protection. This can be numerically explained as follows;

If unprotected person develops minimal erythema after 20 minutes of sun exposure, then after using a sunscreen with SPF-15, minimal erythema would be expected to occur after $20 \times 15 = 300$ minutes (5 hours) of exposure.

The protective measures that were endorsed initially by The National Council on Skin Cancer Prevention (in the US) have been adapted in many other countries and can be summarized in the following points[18]:

1. Do not burn; avoid sun tanning and tanning beds. Ultraviolet light from the sun and tanning beds causes skin cancer and wrinkling. Consider using a sunless self-tanning product to simulate the appearance of having been in the sun, but continue to use sunscreen.
2. Generously apply sunscreen to all exposed skin using a Sun Protection Factor (SPF) of at least 15 which provides broad-spectrum protection from both ultraviolet A (UVA) and ultraviolet B (UVB) radiation. Re-apply every two hours, even on cloudy days, and after swimming or sweating.
3. Wear protective clothing such as a long-sleeved shirt, pant, a wide-brimmed hat and sunglasses, where possible.
4. Seek shade when appropriate, remembering that the sun's rays are the strongest between 10 AM and 4 PM.
5. Use extra caution near water, snow and sand as they reflect the damaging rays of the sun which can increase the chance of sunburn.

The incidence rate of melanoma in Egypt is not known. However, Hussein et al 2006[19] in studying the clinicopathological features of melanocytic skin lesions have noticed that fortunately the incidence of melanoma seems to be rare in Egypt; this was based on the fact that among 41400 pathology accessions that were reviewed only 43 cutaneous melanocytic lesions were included in their study, of which; only 21 were cutaneous malignant melanomas (CMM). The authors concluded that ;the fact that Egypt has a hot, sunny climate and therefore people wear less clothing which together with frequency of melanoma on sun-exposed areas of the body suggest UV as a possible contributor to melanomagenesis. Nevertheless, compared with Western societies, the authors suggested that CMM is rare in Egypt probably due to lack of genetic predisposition among Egyptians (i.e. melanoma in Egypt is sporadic rather than familial in nature).

The authors also postulated that it is still possible that rarity of melanoma in Egypt is due to the amelioration of the effects of sun exposure by the relative impenetrability of the wheatish (color of the wheat) to black skin of the Egyptians to UV.

In support of this theory it has been found that split preparations of the stratum corneum and epidermis from fair and black skin (relatively impenetrable) can transmit 29 and 7% of UVB, respectively [19].

Conclusion:

Ozone layer depletion in addition to the concerns of global warming effect has also risen up the concern of excessive penetrated UV radiation to the earth with consequent increased risk of melanoma. It was only recently that protective measures have been circulating in the Egyptian media and they are more or less the same measures that have been previously adopted by the National Council on Skin Cancer Prevention (in the US). Fortunately Egyptians due to their skin type seem to be naturally protected against melanoma. However for people at increased risk; those of fair skin, and children and adolescents who are frequently get sunburn during summer vacation, protection measures are highly recommended.

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Patient Education Corner

What Should mom Know about her Child's oral medicine?

Whenever a mother who has a sick child comes to your clinic or pharmacy to seek for your help, make sure to follow the instructions that are listed below;



1. Determine the appropriate medicine and dosage for the child's age and weight.
2. Tell the mother the reason for using this specific medicine.
3. Demonstrate to the mother how to measure a dose.
4. Watch the mother practice measuring a dose by herself.
5. Ask the mother to give the first dose to her child.
6. Explain both verbally and by writing the instructions on the medicine package.
7. In case of antimicrobial agents explain that the course should be completed even if the child is completely cured.
8. Check the mother's understanding before she leaves the clinic or the pharmacy.

Milk thistle potential benefit in oncology

Silybum marianum (milk thistle) is a herb that is originally found in the Mediterranean region. The used part is the seed, which contains silymarin (4-6%). Silymarin is flavonolignan complex that is responsible for the herb's pharmacological benefits, which are supportive and protective effects in liver diseases[1].

Historically, it has been used for gastrointestinal and liver diseases since the Greco-Roman era, and today it remains in folk use as a digestive aid, aperients, anti-inflammatory, antineoplastic, hypotensive and general tonifier[2]. The German Commission E currently recommends its use for toxin-induced liver damage, hepatic cirrhosis and as supportive therapy for chronic inflammatory liver conditions[3]

In Chinese and Ayurvedic medicine, the herb represents major component in detoxification protocols, which aims to reduce the negative effects of excess weight, a history of heavy alcohol use, exposure to steroids, exogenous hormones, chemicals, heavy metals and drugs; including chemotherapy[4]

Silymarin is available in the Egyptian market alone as Legalon® tablets and in combination with other antioxidants as Silymarin plus®, and it is indicated for both acute and chronic hepatitis, active liver cirrhosis, and during administration of drugs that are hazardous to the liver.

This background in addition to silymarin safety profile make its use to prevent hepatotoxicity during chemotherapy very tempting. Many chemotherapeutic agents are metabolized by the liver and can cause hepatotoxicity, in addition silymarin is well tolerated, hence human studies have only shown minimal adverse effects with its use, such as rare reports of mild laxative effect, and mild allergic reactions that have been seen only with large doses (1500mg/day).

In a randomized double-blind study that was conducted by Ladas et al 2006 [5], whereas fifty (50) children with acute lymphoblastic leukemia and grade 2 or higher hepatic toxicity were randomized to receive milk thistle supplement in a dose of 5.1mg/kg/d or placebo for 28 days, the authors reported significant reductions in mean aspartate aminotransferase (AST) and a trend toward a significant reduction in alanine aminotransferase (ALT). More children in the milk thistle group developed a greater than 50% reduction in total bilirubin, which was significant at day 28 compared with placebo[5].

The NCI Children Oncology Group is currently following these encouraging findings in another Phase II Randomized Pilot Study.

For details you can follow this link;

http://www.cancer.gov/clinicaltrials/CPMC-IRB-14117#StudyIdInfo_CDR0000270914

In conclusion, milk thistle is a herb that is generally safe and has been used since a long time for liver protection. Research in applications in oncological setting is still going on, although initial reports are promising in preventing liver damage by chemotherapy; its use for this indication still needs more evidence.

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