

Photodermatology: New concepts and recent controversies

Photodermatology is the study of how ultraviolet and visible light interact with the skin. These interactions may trigger carcinogenesis, photoageing, photodermatoses or exacerbate underlying photosensitive conditions such as SLE. Specific wavelengths have therapeutic uses including narrowband UVB phototherapy for psoriasis and red light photodynamic therapy (PDT) for actinic keratosis (AK). This brief update will summarize some of the recent developments in a rapidly expanding field.

Visible light

The effects of ultraviolet and infrared light on skin have been well-described. Visible light comprises 50% of the solar radiation reaching the earth's surface and can be subdivided by colour. Non-visual opsins have been demonstrated in skin and their role as cutaneous photoreceptors has been the subject of recent debate.

Darkly-pigmented skin undergoes greater hyperpigmentation compared to lightly-pigmented skin following visible light exposure.¹ It has been proposed that blue light increases tyrosinase activity in melanocytes through opsin 3 (OPN3) signalling in darkly-pigmented skin.² Conflicting evidence suggests that OPN3 functions independent of light.^{3,4} Further research is required to define the precise role of opsins in skin. Given the clinical evidence, ultraviolet and visible light photoprotection is recommended for conditions such as melasma in darker skin types.^{5,6} Broad spectrum sunscreens protect against UVB and UVA. The only available photoprotection against visible light is tinted sunscreen, which reduces transmission from 93 to 98%.⁷

Photodynamic therapy

PDT involves the use of a topical prodrug, such as aminolaevulinic acid (ALA), that is metabolized intracellularly to a photosensitizer, protoporphyrin IX. Red light illumination precipitates a phototoxic reaction. PDT is often used in the treatment of AK, superficial basal cell carcinoma (sBCC) and squamous cell carcinoma in-situ (SCCis). Pain is the main limiting factor. The use of daylight PDT for the treatment of AK is a painless alternative, however is weather-dependent.

Daylight PDT is ineffective for sBCC and SCCis. Efforts have been made to develop artificial white light sources that may provide year round treatment in a controlled environment.

Recently, artificial white LED light PDT has been investigated for the treatment of AK and sBCC using a theatre light.^{8,9} White light PDT was equivalent to daylight PDT for AK in a split-scalp randomized controlled trial.⁸ A cohort study demonstrated 100% clearance of sBCC at 28 days.¹⁰ One third of lesions recurred at one year, however the majority of these recurrences were peripheral and amenable to cryotherapy. Pain was negligible in both studies.^{8,9} Dedicated artificial white light sources have since been developed which may provide more uniform exposure and more durable clearance.^{11,12}

Mild-to-moderate acne is typically treated with topical retinoids and antibiotics. Concerns regarding antibiotic resistance and poor adherence to topicals have led to renewed interest in PDT. Two treatments of PDT demonstrated superiority to doxycycline and adapalene at 6 and 12 weeks, however pain scores up to 7/10 were reported.¹³ Three treatments of red-light PDT or four daylight exposures using low dose ALA (5%) have shown significant improvements in acne with minimal discomfort.^{14,15}

Vitamin D

UVB is essential for vitamin D synthesis. There is evidence that 1,25-dehydroxycholecalciferol plays a role in regulating the innate and adaptive immune systems.¹⁶ Meta-analyses have demonstrated that vitamin D supplementation can reduce the incidence of acute respiratory infections.¹⁷ The effect of vitamin D supplementation on reducing incidence and severity of SARS-CoV-2 infection remains unknown. Despite the absence of definitive evidence, normalising vitamin D levels through supplementation is a low risk intervention with clear musculoskeletal benefits.¹⁸

The effect of sunscreen on vitamin D production has been debated. Two recent reviews concluded that recreational sun protection does not compromise vitamin D synthesis.^{19,20} Many studies are limited to sunny climates or conducted during summer

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months and there is limited data on the effect of daily high factor sunscreen year round in temperate climates.²¹ Regardless, the daily ultraviolet dose requirement for vitamin D synthesis in lightly-pigmented skin is very low. Individuals with darker skin types have a greater risk of deficiency at shorter latitudes, especially during winter.^{22,23} When counselling patients, a balanced discussion of sun protection, dietary advice, vitamin D supplementation and skin cancer risk is required.

Sunscreen

An association between frontal fibrosing alopecia (FAA) and sunscreen use was found through survey data.²⁴⁻²⁸ Titanium dioxide (TiO₂) has been demonstrated in the follicular infundibulum of the hair follicle and postulated as a potential cause of FAA.²⁶ However, sunscreen use is widespread, yet the overall incidence of FAA remains low.²⁴ At present, there is insufficient evidence to suggest a causal relationship between sunscreen use and FAA.

An estimated 14,000 tonnes of sunscreen enter the sea annually.^{29,30} There is in vitro evidence that organic filters in sunscreen cause coral bleaching and death, although comparable concentrations have not been demonstrated in seawater.³¹ It is well-established that oceanic warming is the main cause of coral bleaching. Bioaccumulation in fish allows UV filters to enter the food chain and the effects of this are unknown.^{32,33} The UV

filters oxybenzone and octinoxate are now banned in Hawaii and Palau. General advice stands that photoprotection should focus on sun avoidance, seeking shade, wearing protective clothing and applying sunscreens with inorganic filters such as TiO₂ on exposed areas.³⁴

In the US, Valisure analysed 294 sunscreens and after-sun products and found that 78 contained benzene, a known carcinogen, up to a concentration of 6.77 ppm.³⁵ Benzene levels varied between batches and over half of affected sunscreens were sprays. The route of contamination is unclear, although may be through manufacturing processes. European sunscreens have more varied ingredients with superior UVA protection, are regulated as cosmetics and are subject to good manufacturing practice.^{36,37} At present, Valisure's findings appear to be relevant to upcoming FDA regulatory changes and those who have purchased affected batches in the US.

These widely publicised issues may negate public health messaging on sun-safe behaviours. In the context of rising skin cancer rates and reduced access to healthcare during the Covid-19 pandemic, it remains essential to counsel patients on how best to mitigate the risks of sun exposure through sun avoidance and photoprotection.

References available on request