

Too much sun comes back to haunt the elderly

by Professor Gregory Peterson

Mrs B is a 60-year-old lady, who has presented to the pharmacy seeking advice on products to get rid of her facial 'sun spots', as she is worried that they could turn cancerous. She is very active, swimming and playing tennis at least twice-weekly. She and her retired husband usually spend 6 months of each year at their unit in Port Douglas.

'It's a good thing that beauty is only skin deep, or I'd be rotten to the core.'

Phyllis Diller

As people age, their chances of developing skin-related disorders increase. Skin, which constitutes about one-sixth of the total body weight, forms the most visible indicator of age.¹ Although skin is incredibly durable, it is affected, like other organ systems, by ageing.^{2,3} Skin ageing can be separated into two components.²⁻⁷ The first component, intrinsic ageing, occurs as a consequence of chronological ageing in all individuals. Changes over time occur at variable yet unalterable genetically determined rates and are influenced by gender, race and skin colour. The inevitable facial fine lines and wrinkles that accompany ageing occur because the skin atrophies and loses its elasticity, allowing the skin to sag.

It is, however, estimated that 90% of what is perceived as skin ageing is not due to intrinsic ageing, but due to extrinsic ageing – produced by factors that are, to varying degrees, controllable and include ultraviolet (UV) light exposure ('photo-ageing'), cigarette smoking, alcohol abuse, poor nutrition, environmental pollutants, and repetitive muscle movements like squinting or frowning.^{4,8} The extrinsic ageing of the skin is the focus of this article.

Australia has the highest skin cancer rate in the world. Solar keratoses are discovered in up to 40–50% of the Australian population older than 40 years.⁹

Solar (or actinic) keratoses, also known as sun spots, are scaly lesions, generally occurring on the sun-exposed skin of the face, hands, forearms, neck and, in balding men, the scalp (Figure 1). They particularly occur among older fair-skinned individuals.^{8,10} The lesions are scaly

sandpaper-like patches, varying in colour from skin-coloured to reddish-brown or yellowish-black.¹¹ They are usually painless but may be slightly tender.^{8,12} Lesions may be single or multiple. Individuals with solar keratoses have on average 6–8 lesions.

The aetiology of solar keratoses involves an interaction between constitutional factors such as skin colour, advancing age, sex, place of birth, sun exposure, latitude and ozone integrity. Cumulative sun exposure is the single most important cause of solar keratoses.¹³ Fair-skinned, blue-eyed people living in sunny climates are most likely to develop solar keratoses.¹² Individuals with many years of extensive sun exposure are at the greatest risk. Other risk factors include immunosuppression from organ transplantation, immunosuppressive therapy, or exhibition of genetic diseases of skin hypopigmentation, such as xeroderma pigmentosum or albinism.¹⁰

Solar keratoses are the most common type of premalignant skin lesion. In Australia, where the prevalence of solar keratoses is the highest in the world, up to 40% of caucasian adults may have solar keratoses. The lesions take years to develop and so the prevalence of solar keratoses increases with age, with a range in caucasian Queenslanders reported at below 10% in those aged 20 to 29 years and approximately 80% in 60 to 69-year-olds.^{12,14} They are more common in men than in women.

Figure 1. Solar keratoses



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A major concern with solar keratoses is the possibility of developing skin cancer. Reassuringly, most solar keratoses do not progress to cancer, and as many as 26% regress spontaneously.^{10,12} However, conversely, up to 60% of cutaneous squamous cell carcinomas do arise from solar keratoses.¹² Practically, patients should realise that there is a low rate of transformation of solar keratoses to squamous cell carcinoma. Despite this, the presence of solar keratoses indicates that they have a higher risk for skin cancers compared to the general population, and should therefore take preventive measures and be screened and checked regularly.^{11,13} Estimates of the precise risk of solar keratoses progressing to squamous cell carcinomas vary widely; published likelihoods of a lesion undergoing malignant transformation to a squamous cell carcinoma range from 0.025 to 20% per lesion per year.^{12,13} The relative risk for squamous cell carcinoma increases for people with more than five solar keratoses.¹³

Prevention is the most important treatment modality for solar keratoses. Avoidance of sun and artificial sources of ultraviolet light, wearing of appropriate outdoor clothing, applying sunscreen and self-examination are among the most effective preventive measures.^{9,11} It has been shown that regular use of sunscreen with a sun protection factor (SPF) exceeding 15 not only prevents the development of solar keratoses, but also hastens the remission of existing solar keratoses.^{10,13}

Ultimately, most patients want their solar keratoses treated, either because of their malignant potential, for cosmetic reasons or symptomatic relief.¹³ Owing to difficulties in predicting which solar keratosis will progress to cancer, the general rule is to treat all solar keratoses.⁹

'Cryotherapy using liquid nitrogen is most commonly used to treat solar keratoses. This method destroys the keratinocytes through freezing, while mostly preserving important dermal structures such as blood vessels, nerves and collagen due to their higher resistance to cold. This ranges from the 83% reported for freezing times longer than 20 seconds, to 39% for 5 seconds or less of freezing. Hypopigmentation is a recognised

*sequelae with cryotherapy because the melanocytes in the epidermis are also susceptible to freezing injury.'*¹³

Excision is another lesion-specific technique for solar keratoses that is quick and convenient to perform but requires local anaesthesia. An advantage of excision over cryotherapy is the availability of tissue for histological examination, particularly when cancer is suspected. However, scarring occurs more commonly than with cryotherapy.¹³

Topical therapies will be necessary in patients with multiple facial lesions.^{10,11} Salicylic acid (2% to 5% in either aqueous cream or an ointment base, applied once or twice daily) may be used for early lesions.^{8,10} More potent topical options are:⁸

- diclofenac 3% gel (*Solaraze*), twice daily for 12 weeks;
- fluorouracil 5% cream (*Efudix*), once or twice daily for two to four weeks on the face or three to six weeks on arms and legs; or
- imiquimod 5% cream (*Aldara*), once daily three times a week for three to four weeks (for 1 to 3 cycles with a 4-week treatment-free period between cycles).

*There are too few controlled trials comparing treatment modalities for physicians to make sound, evidence-based treatment decisions.*¹²

Each of these topical treatments can cause severe inflammation (typically, fluorouracil 5% cream does so most potently), so counselling and close supervision is required. Diclofenac 3% gel is the least potent agent and generally requires a longer course than the other therapies. Imiquimod 5% cream may have a rejuvenating effect on solar-damaged skin as an additional cosmetic advantage.⁸

Treatment with fluorouracil produces progressive erythema and burning and, after two to four weeks, ulceration followed by reepithelialisation over another two weeks. Treatment should be discontinued once ulceration occurs.¹¹ As noted in the product's Consumer Medicine Information (CMI), 'when *Efudix* is applied to the skin, the following usually happens: a redness of the affected area (generally within 3 to 5 days) followed by blistering, peeling, and cracking (within 11 to 14 days) with occasional open sores and some discomfort.

Although the skin seems to be worse, it is a sign that the medication is working. The treated skin will flake away. Some redness of the skin will continue for some time after the drug is stopped. Scarring would not be expected'.

Noncompliance can be an issue with this treatment because of the significant side effects such as erythema, itching, burning and crusting, which are inherently linked to the action of the drug.¹³ Although temporary, the side effects can be unpleasant and may cause discomfort and short term disfigurement. Complete healing usually occurs within two months.¹¹ Pharmacists can help promote compliance and lessen adverse effects by thoroughly counselling patients using topical fluorouracil e.g. patients must be told to avoid the eyes and mucous membranes when applying the cream, use a non-metal applicator or a rubber glove to apply the cream, follow the directions in the package circular and CMI exactly, and to never leave the medication on longer than directed.¹¹

The exact mechanism of topical diclofenac in treating solar keratoses is not established. The relatively long treatment duration (three months) is a disadvantage and reduces compliance, but a shorter treatment period is reported to have lower efficacy, probably due to the delayed onset of action.¹³ The advantage of diclofenac treatment is its higher tolerability due to limited local inflammation and irritation. Side effects and local reactions may include contact dermatitis, dry skin, pruritus and rash.¹³ Systemic absorption produces plasma levels of diclofenac that are much lower than with oral administration of the drug, but the product still has the typical precautions and contraindications associated with the nonsteroidal anti-inflammatory drugs.

Imiquimod cream is normally applied in a cyclic regimen for solar keratoses, with the intention of decreasing local skin reactions. The usual dosage is once a day, at bedtime, three times a week, continued for four weeks, followed by a period of four weeks without any treatment. The rest period also allows the doctor to assess the need for another 'cycle' of

treatment as the therapeutic effect continues while the inflammation subsides.¹¹ If any solar keratoses remain, the treatment should be repeated for another four weeks.

A newer treatment option is photodynamic therapy, which involves the application of a pre-photosensitiser (methyl aminolevulinate *Metvix*) to the area of the skin being treated. An incubation period with an occlusive dressing (1–3 hours) is necessary for it to preferentially accumulate in dysplastic and malignant cells. The area is then exposed to a red light source, leading to preferential tumour cell death. This is due to the generation of reactive oxygen species resulting in oxidative cell damage. The phototoxic reactions also cause adverse events such as erythema, stinging, itching, oedema and exudation. The pain associated with such reactions may be severe enough to require local anaesthesia, especially during the illumination process, or pre-treatment with an oral analgesic. Healing time is often less than 10 days, which

can result in high levels of patient satisfaction.¹¹

Interestingly, several trials have established the efficacy and safety of topical colchicine, usually as a 0.5 or 1% gel, for solar keratoses.^{15,16}

To return to our case, the avoidance of sun exposure through physical means and using a broad-spectrum sunscreen should be emphasised to Mrs EJ. She should be advised to have her sun spots examined and that there are several topical products available on prescription that can remove sun spots, although they can cause significant irritation.

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