Review

# Sunlight (actinic) keratosis: an update

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## Introduction

There is considerable controversy regarding the nature of sunlight (solar/actinic) keratosis. One view is that sunlight keratosis is a premalignant condition [1-6]; another view is that *ab initio* it is a form of superficial squamous cell carcinoma (SCC) [7-9]. Sunlight keratosis results from abnormal proliferation of keratinocytes of sun-exposed skin. Common sites of occurrence are neck, hands, arms and head including the vermilion border of the lips, most frequently the lower lip [10, 11]. Sunlight keratotic lesions are dry, skin-coloured or brownish, rough macules or papules [1, 4]. The term sunlight keratosis refers only to the appearance of the lesion and to its aetiology, but not to its pathobiological behaviour or histopathological features.

If left untreated the risk of progression of sunlight keratosis to invasive SCC can be as high as 20% per year [4, 9]. Keratinocytes of sunlight keratosis that are destined to remain stable and those that are destined to progress to SCC are morphologically indistinguishable. They both arise from keratinocytes that have undergone initial sunlight-induced transformation [7, 8, 12]. Sunlight keratosis may represent the first change in the continuum of sunlight-induced carcinogenesis [13, 14] and the potential for progression to SCC can only be judged retrospectively on the basis of DNA molecular profile and their behaviour. Sunlight keratosis should be treated promptly as soon as it is diagnosed [9, 11].

The aetiology of sunlight keratosis is long-term cumulative exposure to the ultraviolet-B (UVB) component of sunlight. Those at risk of sunlight keratosis include people with fair complexions, those in outdoor occupations, those who are immunocompromized, and those with certain hereditary conditions, importantly oculocutaneous albinism and xeroderma pigmentosum [4, 11]. Protective measures against sunlight keratosis should be related to the aetiological and risk factor [15].

## Mechanisms of UVB-induced keratinocyte transformation and carcinogenesis

Ultraviolet radiation in the range of 290 to 320 nm (UVB) is strongly erythrogenic and melanogenic, and more than 90% of the energy of UVB to which anyone is exposed is absorbed by the epidermis in which it induces these changes. Depending on the intensity and the duration of the exposure to UVB, the keratinocytes may proliferate, and may also sustain DNA damage [16, 17].

In keratinocytes with UVB-induced DNA damage, the p53 tumour suppressor gene arrests the cell cycle allowing the repair of damaged DNA; or it promotes apoptosis of those keratinocytes with irreparable DNA. However the p53 gene itself may undergo UVB-induced mutation and the consequent dysregulation of its function will allow damaged DNA to propagate by cell division. This can promote the evolution of a clone or indeed a field of keratinocytes with UVB-induced DNA alterations [3, 9, 13, 17], which can then be referred to as a field of cancerization. The keratinocytes in such a field may constitute a monoclone of genetically transformed cells from which superficial or overt carcinoma may develop [18].

Once initiated, the sunlight-induced skin carcinogenesis is irreversible and predisposes the affected cells to chromosomal instability increasing the likelihood of time-related additional UVB-induced genetic alterations. The additional genetic alterations, referred to as carcinogenic promotion, culminates in the selective clonal expansion of the initially transformed cells [3, 13, 17, 19-21].

Although in most cases of sunlight-induced SCC the UVB acts as both initiator and promoter, it may well be that during organogenesis some keratinocytes undergo genetic or epigenetic changes and subsequently form a field of developmentally altered cells that are vulnerable to promotion of carcinogenesis by subsequent UVB-induced genetic lesions [18].

Squamous cell carcinoma confined to the epithelium (carcinoma in situ) arising from sunlight keratosis has similar UVB-induced genetic alterations to the lesion of origin and the fact that additional sunlight-induced genetic alterations can give rise to invasive SCC suggest that the sunlight keratosis itself should be regarded as superficial SCC [7, 8, 13, 17]. However, regardless of how persuasive the genetic and histological arguments in favour of this concept may be the ultimate verdict as to whether sunlight keratosis was in fact a superficial

SCC can only be made retrospectively by observing the clinical and biological behaviour.

## Epidemiology

Sunlight keratosis occurs as a result either of accumulative lifetime exposure or of shorter intense exposure to the UVB component of sunlight [2, 22]. It is difficult to establish the general rates of prevalence and incidence of sunlight keratosis worldwide because of differences in racial, geographic, climatic and educational factors in different parts of the world or even the same country [11, 16].

UVB radiation is absorbed by epidermal melanin which provides substantial protection to dark-skinned persons, whereas white skinned persons lack this protection [1]. Fair skinned persons tan poorly, burn readily, and are at high risk of sunlight keratosis and its sequelae [23]. Outdoor occupations or recreational pursuits, increase the risk of sunlight keratosis [3, 11]. Persons with oculocutaneous albinism and xeroderma pigmentosum are most at risk [1, 11].

About 90% of the spectrum of the electromagnetic radiation originating from the sun is blocked by the ozone layer, but as a result of the ongoing depletion of ozone, more of the sun's UVB radiation is reaching the earth with consequently increasing incidence of sunlight-induced cutaneous lesions [2, 3]. Characteristics of the geographic locality greatly influence the prevalence and incidence of sunlight keratosis in different parts of the world. The intensity of UVB radiation increases substantially with increasing altitude [23, 24], with decreasing latitude [3, 11, 23, 24], and with reflection from sand or snow [25]. Sunlight keratosis is more common in males than in females and its prevalence increases with age. The reported prevalence rates from different climatic regions are highly variable [1, 9, 11].

## Clinical features

Sunlight keratoses are irregular rough, scaly, hyperkeratotic papules or plaques ranging from skin-colour to reddish brown. They occur most frequently on sun exposed areas of the scalp, ears, face, lower lip, neck, arms, hands and legs. Sometimes, the lesions may be detected more readily by the feel of the rough, scaly, sandpaper-like surfaces than by their visual appearance [1, 9, 26]. The lesions may be single, multiple or may become confluent, ranging in size from 2mm to 6mm and rarely exceed 1cm (Fig. 1) [1, 7, 9, 26]. Usually the lesions are asymptomatic but uncommonly may be itchy or painful [1, 11].

Sunlight keratosis should be differentiated from other cutaneous conditions with similar clinical features such as discoid lupus erythematous, seborrhoeic keratosis, verruca vulgaris, lichenoid keratosis and incipient SCC [1, 11]. Sunlight keratosis of the lip (sunlight chei-

litis) most frequently affects the lower lip and appears as a diffuse, slightly scaly lesion that may involve the entire lip which loses its usual elasticity. In addition to the list of clinical differential diagnoses given for the skin, the clinical differential diagnosis of sunlight cheilitis includes leukoplakia, plasma cell cheilitis; allergic cheilitis and cheilitis granulomatosis [11].

Sunlight cheilitis is associated with greater risk of progression to invasive SCC than sunlight keratosis of cutaneous surfaces [8, 11]. About 20% of squamous cell carcinomata of the lower lip that originate as sunlight cheilitis will metastasize.[11] Since neither the outcome of sunlight cheilitis nor of sunlight keratosis can be predicted, they should be treated as soon as they are diagnosed to reduce the risk of morbidity and mortality [7, 8, 14].

## Histopathological features

Sunlight keratosis is characterized by a disturbed sequence of maturation, and by cellular atypia of keratinocytes [9, 11]. The epidermis is irregularly acanthotic and atrophic, surfaced by patches of orthokeratosis and parakeratosis [1]. Small buds of atypical keratinocytes protrude into the papillary dermis but the basement membrane remains intact. The dermis shows features of solar elastosis [7].

Most cases of sunlight-induced SCC appear to arise from sunlight keratosis and the epidermis adjacent to the SCC still seems to show microscopical features of sunlight keratosis [3, 7, 14, 23]. This frequently-occurring close contiguity of sunlight keratosis to SCC is strongly suggestive of the probability of the existence of a field of cancerization in UVB damaged skin [18]. It may even be that apparently normal epithelium sur-



**Fig. 1.** Solar keratosis of the medial surface of the lower lip in a 38-years old black female with mucocutaneous albinism. Note the brownish scales and superficial erosion on an erythematous base. (Image courtesy of Dr MH Motswaledi, Department of Dermatology, School of Medicine, University of Limpopo, Medunsa Campus).

rounding lesions of sunlight keratosis may already have undergone UVB-induced genetic alterations making them susceptible to transformation [9, 26]; or they may already represent a genetically altered pre-cancerous clone of cells [26].

It is possible that UVB-induced solar elastosis in the dermis may precede detectable changes in the epithelium, and the damaged dermis may dysregulate mediation pathways between the connective tissue to the overlying keratinocytes that contribute or act synergistically with the direct UVB effect on the epithelium in inducing the initial genetic alterations in the keratinocytes.

## Diagnosis

Diagnosis of sunlight keratosis is frequently based on the clinical appearance alone since biopsy of multiple affected sites is not feasible [26]. Therefore the clinical criteria of rapid growth, size, pruritis, bleeding, ulceration, erythema, or induration [1, 7] are used to decide which lesions should be biopsied [1, 2, 26].

Diagnosis of sunlight keratosis based on clinical grounds alone is not always reliable although between 74% and 94% of cases of sunlight keratosis can be correctly diagnosed clinically [26]. However, in this regard it is important to remember that on the basis of clinical examination alone it is impossible to determine where sunlight keratosis ends and where SCC begins [8]. Histopathological diagnosis remains the ultimate investigative procedure.

## The natural course of sunlight keratosis

Sunlight keratosis is a step in the continuum initiated by UVB-induced alterations to the genome of sun-exposed keratinocytes. The clone of altered keratinocytes may remain stable but further sun exposure can bring about transformation conferring a selective growth advantage upon the keratinocytes which then possesses the potential to become SCC [7]. In this continuum, from the outset, sunlight keratosis is already a clonal expansion of transformed keratinocytes [7, 8].

Although it would be clinically advantageous to be able to predict which specific sunlight keratotic lesion will progress to SCC, or when this will happen, there are several factors making it problematical. Firstly, the genetic transformational events and their sequences are not fully understood [27]. Secondly, dysplasia may remain stable indefinitely or may progress very rapidly to frank SCC [28]. Thirdly, even the keratinocytes of normal looking sunlight exposed epithelium without dysplasia may have undergone the initial genetic transformation of an extent that can result in accelerated progression to malignancy [18]; and lastly, the possibility of regression of dysplastic lesions has been documented [1, 2, 9, 11].

Notwithstanding the difficulties of predicting the 'which' and 'when' of malignant transformation of sunlight keratosis, there are certain factors including the skin type, the palpable thickness and depth of the lesion, the severity of dysplasia and the immune suppression of the host that must increase one's index of suspicion [11, 14].

## Prevention

Sunlight keratosis is caused by cumulative exposure to UVB radiation, therefore the risk of sunlight keratosis and consequent malignant transformation can be decreased by limiting outdoor activities at peak sunlight hours, sensible sun tanning, protective clothing and the use of effective sunscreen [4, 15]. The reduction of sunlight exposure should start in childhood and should be achieved by sun protection education programs incorporated into school health education systems [11].

## Treatment

As the chance of any particular sunlight keratotic lesion undergoing malignant transformation cannot be predicted they should all be properly treated despite the fact that most of them are innocuous [8]. Although clinicians will often treat sunlight keratosis based on their experience, ideally the treatment modality should be chosen according to the location, size and appearance of the lesion, age, medical status, personal preference, biopsy results and aesthetics [4, 8, 11].

Topical chemotherapy (5-flourouracil and imiquimod), physical methods (cryosurgery, laser therapy, electrodessication or photodynamic therapy) and surgical excision are modalities commonly used in the treatment of sunlight keratosis [1, 4, 11].

Without microscopic examination it is impossible to distinguish between simple sunlight keratosis, sunlight keratosis that has progressed to intraepithelial carcinoma or sunlight keratosis that has already become invasive [1, 2]. However, for practical reasons not all sunlight keratoses can be biopsied and clinical judgement must be used to decide which lesions are at risk of becoming invasive SCC and must be biopsied, and which can be treated on the basis of clinical judgement. Regular follow-up is mandatory [8].

## Conclusion

Sunlight keratosis is common in sunny climates. Diagnosis can be made on the basis of clinical experience supported by histopathology. Treatment of established lesions is by topical chemotherapy, physical methods, or by excision, followed by regular follow up.

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*Note on terminology*
In the medical/dental literature the terms solar (of or relating to the sun, with the implication of short-wave light of the sun), and actinic (relating to light of short wavelength) are used interchangeably as descriptors of lesions of the skin or lip caused by these agents.
The arbitrary use of the two terms, the one of Latin and the other of Greek origin, seems unjustified, or at least unnecessary.
We have chosen to use the simple English terms *sunlight* or *sunlight-induced*.