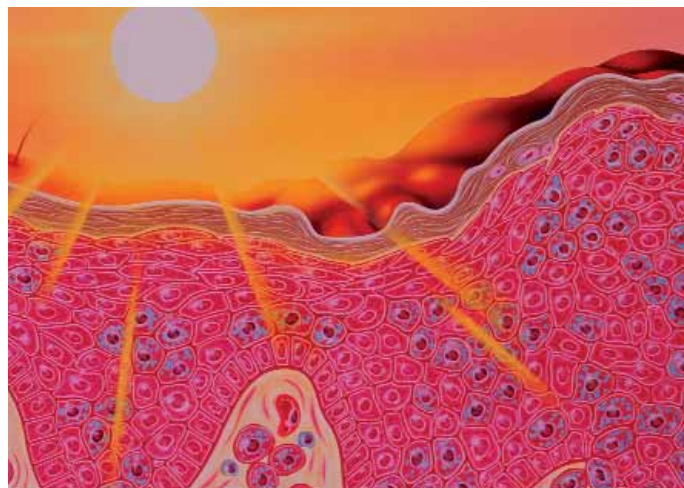


Skin cancer

— identification and primary prevention

By John Smithson, BPharm, MPS, and Ian Heslop, AACPA, MRPharmS

Skin cancer is the most common form of cancer in the UK. There are many types of skin cancer, all of which vary in their risk of metastasis and mortality. This article examines the most prevalent cancers and the strategies used to prevent them



An illustration of cancer cells (blue) spreading through the epidermis (pink)

Skin cancer is the most common form of cancer in the UK and the most costly to the NHS. Its prevalence in the UK continues to rise despite public health promotions that encourage people to be “sun smart”. However, it is also the most preventable type of cancer.

Skin cancer can be classified as non-malignant (eg, seborrhoeic keratoses, see Panel 1), pre-malignant and malignant. This article will focus on the three most common types of malignant skin cancer:

- Basal cell carcinoma (BCC)
- Squamous cell carcinoma (SCC)
- Melanoma

Malignant skin cancers can also be classed as melanoma and non-melanoma skin cancers (NMSC).

— Melanoma

A malignant melanoma is a life-threatening cancerous tumour that is derived from epidermal melanocytes (the main cell types in the epidermal layer of the skin are described in

Panel 2, p40). Although it represents only 4 per cent of all skin cancers, malignant melanoma is responsible for 80 per cent of all deaths attributed to skin cancer.¹

The age-standardised rate of malignant melanoma has been increasing steadily in England and Wales for the past 20 years.² Malignant melanoma represents around 10 per cent of skin cancers in England and Wales. There were approximately 7,800 new cases of malignant melanoma reported in 2004.

Although it is far less common than NMSC, its mortality rate is much higher. In England and Wales during 2005, there were 1,622 deaths attributed to melanoma compared with 453 for NMSC.³

Malignant melanoma has a slightly higher incidence rate in women (female-to-male ratio of 5:4), but becomes more prominent in men over the age of 60 years.

The importance of early diagnosis of malignant melanoma cannot be overemphasised. The treatment of thin, malignant melanomas provides an excellent prognosis.⁴

The four main types of malignant melanoma are:

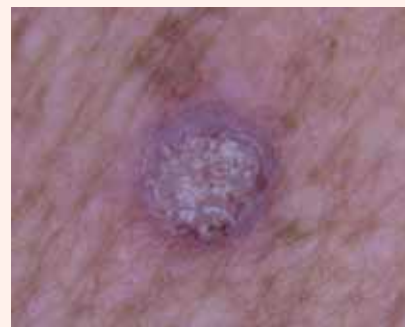
- Lentigo maligna
- Superficial spreading
- Nodular
- Acral lentiginous

Panel 1: Seborrhoeic keratoses

Seborrhoeic keratoses, also known as senile warts, are common, benign epidermal tumours that usually affect the face and trunk, particularly in the elderly. They are often pigmented and range in colour from a dirty yellow to black.

The tumour is often raised and either round or oval-shaped, with a “warty” appearance, a defined border and a “greasy” feel.

Small seborrhoeic keratosis can be removed using a curette, cryotherapy or diathermy if required (see p50).



A seborrhoeic keratosis

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Panel 2: The main cell types in the epidermis

The epidermis is comprised of four major cell types:

- Keratinocytes are the most common cells in the epidermis. They are rapidly dividing cells that develop over a period of weeks into keratin plates that are eventually shed from the outer layer of the skin.
- Melanocytes are large cells that are interspersed among the keratinocytes at a ratio of one melanocyte to every five to 10 keratinocytes. They produce melanin — a pigment that prevents DNA damage in the basal and spinous layers of the epidermis by absorbing ultraviolet radiation. The amount of melanin that these melanocytes produce can differ depending on genetics and the level of UV exposure.
- Langerhans cells are antigen-presenting cells that phagocytose foreign substances as part of the immune system.
- Merkel cells are present at the inner edge of the epidermis. Together with disc-like sensory nerve endings, they function as a sensory receptor for touch.

Although skin cancers can originate in deeper tissue or appendages within the skin, the most common types of skin cancers originate in the epidermis and the cells of the basement membrane.

Characteristics With the exception of nodular melanoma, all malignant melanomas share similar features and only differ slightly in presentation, location and aggression. They are usually asymmetrical with irregular margins and range in colour from tan-brown to black. Traditionally, they are described as having a diameter greater than 6mm, though early detection

may yield a malignant melanoma that has a diameter smaller than this.

Nodular melanoma usually presents with a regular border and uniform pigment, (usually red or pink) and is often elevated and firm. After several months, it often starts to ulcerate, crust and bleed.⁵

An example of a superficial, spreading malignant melanoma is shown in Figure 1.



Figure 1: A superficial, spreading malignant melanoma

Detection Self-examination and examination by a physician or other healthcare professional all offer opportunities to detect suspicious skin lesions.

Pharmacists and patients are not trained in detecting and diagnosing skin cancer, however there are several characteristics to look out for. These characteristics are listed in Panel 3 (p41).

Melanomas do not always present with all of the classic features. For example, a



Figure 2: A large number of atypical naevi on a man's back

nodular melanoma may not be black or brown, asymmetrical or have an irregular border. However, it will display some worrying characteristics (eg, it may be elevated, growing rapidly and starting to crust and bleed), therefore it is imperative to refer the patient to his or her GP if any of these characteristics is present.

Risk factors Some genetic or lifestyle factors can increase a patient's risk of developing a malignant melanoma.



Figure 3: An example of a squamous cell carcinoma

Ultraviolet radiation During adult life, recreational (intermittent) sun exposure of sufficient level to cause sunburn or blistering of the skin, appears to be the strongest determinant of melanoma risk, followed by a high total lifetime sun exposure and occupational ultraviolet radiation exposure.⁶

Atypical naevi Also known as dysplastic naevi, atypical naevi (moles) are acquired (ie, not present at birth), pigmented lesions

Panel 3: Characteristics of malignant melanoma

When a naevus (mole) develops into a malignant melanoma, it is likely to alter in appearance. The detection of these changes follows the ABCDEFG rule.

This rule suggests that if a naevus develops the following characteristics, it warrants referral to a skin cancer specialist:

- A Asymmetry
- B Border irregularity
- C Colour variation (especially any change in colour)
- D Diameter greater than 6mm (although a smaller size should not deter referral)
- E Elevated above the surface of the skin
- F Firm
- G Growing (report any naevus that changes in size or shape)

found predominantly on the trunk that are often larger than ordinary naevi (moles). They are elevated above the surrounding skin but may have ill-defined borders.

They tend to have a “pebbly” texture and range in colour from tan-brown to dark brown (and may contain some pink).

The presence of atypical naevi puts the patient at increased risk of developing a malignant melanoma, so suspicious naevi are often surgically removed.

However, surgery is not practical if multiple lesions are present, such as in patients that suffer from atypical naevi syndrome. These patients often have 80 or more of these naevi present on their skin. It is more cost-effective to manage these patient with baseline photography of the lesions and a once or twice yearly follow-up.

Atypical naevi on a man’s back is shown in Figure 2 (p41).

— Non-melanoma skin cancer

NMSCs encompasses a group of skin cancers that include BCC, SCC and a number of other less common malignancies, which are all derived from epidermal keratinocytes. They are the most common of human cancers. In 2004, there were over 59,000 cases reported in England alone.⁷ The reporting of NMSC is typically low, resulting in an underestimate of the true incidence of these lesions.

BCCs are slow-growing, invasive epithelial tumours arising from the basal layer of the epidermis. They are the most common malignancy among the caucasian population and their incidence is increasing by approximately 10 per cent every year.⁸

SCCs tend to occur in areas of the body that have been heavily exposed to sunlight. They are more likely than BCCs to metastasise with the greatest risk of metastatic spread being attributed to lesions on the ear, lower lip and scalp.⁹

However, in contrast to melanoma, NMSCs rarely metastasise, so have a low mortality rate, particularly in patients under 50 years of age.¹⁰ However, they can still cause significant morbidity.



Figure 4: A nodular basal cell carcinoma

Characteristics SCCs are characterised by tender, erythematous papules or nodules that may enlarge over weeks or months. They may also ulcerate or bleed. A well differentiated SCC is shown in Figure 3 (p41).

The three types of BCC are:

- Nodular (Figure 4)
- Superficial, multifocal (Figure 5)
- Morphoeic (Figure 6)

All three types may display ulceration, pigmentation or a pearly presentation. They are usually found on the trunk, limbs, head or neck.

Diagnosis NMSC may present with or without pigmentation, have clear borders and be of uniform colour. Although they are less likely to cause a fatality than malignant melanoma, they are also more difficult to identify.

Any lesion that shows signs of inflammation, bleeding or oozing should be referred to a skin specialist. In addition, any lesion that alters in sensation (eg, starts to itch), size or shape should be treated with suspicion. The presence of hair in the lesion is of little diagnostic value.

Risk factors Some patients are at increased risk of developing a NMSC. This can be due to an increased level of UV exposure or because they have developed pre-malignant lesions (eg, solar keratoses or Bowen disease) that are a precursor to a NMSC.

UV radiation Exposure to sunlight is a risk factor for both SCC and BCC.

The risk of developing SCC is associated with high accumulative exposure to sunlight, so it tends to be more common in older people. The risk of developing BCC is greatly increased by exposure to strong sunlight (ie, enough to cause sunburn), especially in childhood.



Figure 5: A superficial, multifocal basal cell carcinoma

Suggestions for future special features

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It should also be noted that high levels of sun exposure in childhood are associated with an increased risk of developing all types of NMSC.

Solar keratoses Also known as actinic keratoses, solar keratoses are common, pre-malignant lesions that are usually caused by the dysplasia (proliferation of cells of an abnormal type or the formation of abnormal tissue) of basal keratinocytes. They can potentially progress to invasive SCC, although this progression is rare.

They appear on parts of the body that are chronically exposed to solar radiation (eg, the back of the hands, forearms, face, bottom lip, neck and ears) and predominantly affect middle-aged or elderly people.

They usually appear as dry, scaly and rough lesions with sharp edges. The scales may be picked off, albeit with some difficulty, to reveal a hyperaemic base (“pinkish” than normal due to increased blood flow) with punctate (dotted) bleeding points.¹¹ Over time, the scale may become thick and horny.

Solar keratoses may disappear, either spontaneously or after a period of sun avoidance (eg, by using sunscreen). An example of solar keratoses is shown in Figure 7 (p44).



Figure 6: A morphoeic basal cell carcinoma



Figure 7: A keratotic horn arising from a dysplastic solar keratosis on a man's thigh

Bowen's disease Bowen's disease is a common, pre-malignant condition that is classified as an "intraepidermal SCC." It differs from SCC because it does not invade the basement membrane of the skin.

It is characterised by a flat, red plaque with white or yellow scale or crust. It usually develops on sun-exposed skin, particularly on the legs, but can present anywhere on the skin or any mucosal surface. The condition mostly presents in older women.

The lesion gradually enlarges in an irregular fashion while maintaining a well-defined border. Its progression to SCC may occur after many years, although the incidence of this is low. Ulceration of the lesion can be an indication that this progression has occurred. An example of Bowen's disease on the lower leg is shown in Figure 8.

Panel 4: Summary of risk factors for developing skin cancer

Patients who are at the greatest risk of developing skin cancer are those who have:

- An occupation that exposes them to high levels of natural or artificial ultraviolet radiation
- A history of blistering sunburns
- A large number of atypical naevi
- A personal or family history of malignant melanoma or NMSC
- A degree of immunosuppression
- Fair skin
- Blonde or red hair
- Blue eyes
- Difficulty tanning or a propensity to burn easily

— Ultraviolet radiation

UV radiation is a major causative factor in developing NMSC and malignant melanoma, although the amount of radiation that induces skin cancer is not known. Exposure to UV radiation that is sufficient to cause sunburn, and high accumulative exposure to any UV radiation during child and adult life, both contribute to the risk of developing skin cancer.

UV radiation can be subclassified as follows:

- UVA — wavelength: 320–400nm
- UVB — wavelength: 290–320nm
- UVC — wavelength: 200–290nm

UVA Most of the UV radiation that reaches the earth's surface is UVA. It is responsible for tanning the skin, but also photoageing and photosensitivity reactions. It penetrates deeper into the skin than UVB and UVC, and there is strong evidence to suggest that it damages DNA.

UVB The UV radiation most associated with the development of skin cancers is UVB.⁶ Most UVB is absorbed by the ozone layer, but sufficient still reaches the earth's surface to cause erythema and DNA damage. UVB is 1,000 times more likely to cause erythema and sunburn than UVA, and also contributes to photoageing.

UVC UVC radiation from the sun is almost completely absorbed by the ozone layer, so it has minimal risk of causing skin cancer. UVC radiation from artificial sources (eg, arc welders or bactericidal lamps) may increase the risk of skin cancer, although this is not proven. Individuals who are exposed to high levels of artificial UVC, such as welders, are encouraged to use a sunscreen that provides protection against all forms of UV radiation.

Sunbeds Sunbeds can emit UVA radiation that is 10–15 times stronger than that experienced from exposure to the midday sun. They also can emit a small proportion of UVB radiation.¹²

Their increased use, particularly by light-skinned individuals, is of major concern. Sunbed use appears to be associated with increased rates of melanoma and SCC, but not BCC.¹³

There is no evidence to suggest that using a sunbed protects the skin against damage from subsequent sun exposure. The use of these devices is discouraged, especially in young adults.

— Primary prevention

Over the past 30 years, public awareness campaigns have been shown to promote the primary prevention of skin cancers. For

Panel 5: The affect of increasing SPF on the amount of UVB block

SPF of sunscreen	Percentage of UVB blocked
15	93.3
30	96.7
50	98.0

(Adapted from Australian radiation protection and nuclear safety agency guidelines 2003)

example, these campaigns have focused on the early detection of skin cancer and the importance of reducing sunlight exposure.

These campaigns have altered the demographics of skin cancer and also the prevalence of the different types of skin cancers.

While the incidence of skin cancer continues to rise in Australia, the rate of BCC among young people has decreased. In addition, the ratio of BCC to SCC has changed from 4:1 in 1985 to 5:2 in 1995.¹⁴ This suggests that the campaigns have caused a reduction in the high-intensity UV exposure that is associated with holidaymakers. It may also reflect a greater public awareness of the damage that sun exposure can cause.

Children, teenagers and fair-skinned adults should be particularly aware of the dangers of excess sun exposure and sunburn.

The Australian campaigns have emphasised the following principles:

- Wearing sun-protective clothing
- Wearing a hat
- Seeking shade
- Wearing sunglasses
- Using sunscreens



Figure 8: An example of Bowen's disease on the shin of a female viewed using a dermatoscope

The major risk factors for developing skin cancer are listed in Panel 4 (p44).

Sun-protective clothing Wearing tightly woven, collared, long-sleeved shirts and long trousers is advised. Darker materials absorb more light and therefore provide more protection. It should be noted that many fabrics offer diminished protection when they are wet.

Hat Wearing a wide-brimmed hat is advised, to protect the head, neck, face and ears from excessive sun exposure.

Shade Direct exposure to the sun should be avoided between 10am and 3pm, so shade should be sought if outdoors. Also, reflected sunlight is responsible for up to half of the UV radiation that reaches the skin, therefore extra care should be taken when near reflective surfaces such as water, concrete, snow and white sand.

Sunglasses Individuals are advised to wear large, close-fitting sunglasses that wrap around the eye. Sunglasses should be assigned an eye protection factor (EPF) between one and 10, for which a higher rating indicates greater protection. Using a darker lens does not necessarily confer a greater protection.

Sunscreen Sunscreen should be applied 30 minutes before sun exposure. It should be reapplied every two to three hours, and also after sweating or swimming. The use of sunscreens in babies is considered safe for small areas of the skin (eg, hands and face), but primarily, exposure to the sun should be avoided.

— Choice of sunscreens

Sunscreens are designed to protect against sunburn, but there is debate about their role in preventing sun-related skin cancer. There is evidence to suggest that the use of sunscreen has reduced the incidence of SCC and solar keratosis.¹⁵

However, it has also been suggested that the use of sunscreens may encourage people to spend longer periods exposed to high levels of UV radiation — exposing them to a greater risk of BCC and malignant melanoma.

It is prudent to advise the public against relying solely on sunscreen for protection from UV radiation. It should be used as part of a complete sun-avoidance regimen.

SPF Sun protection factor (SPF) refers to the ratio of UV light needed to cause erythema on sunscreen-protected skin, compared with unprotected skin. The protection that a sunscreen affords will vary under different environmental conditions. It should not be assumed that if

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one individual uses a sunscreen that has an SPF that is twice as high as another, the individual can safely spend twice as much time exposed to UVB radiation.

Panel 5 (p44) outlines the percentage of UVB radiation that is blocked by sunscreens with different SPF values. The results demonstrate the relatively minor increase in physical UVB protection on increasing the SPF from 15 to 30, and from 30 to 50.

It should be noted that SPF is tested using an application of sunscreen that is up to four times thicker than a typical consumer application. Clearly, some people are not applying a thick enough application of sunscreen.

There is no universal system for classifying sunscreens according to the degree of UVA protection they afford. In general, the public should be advised to select a sunscreen that has an SPF rating above 30, offers broad spectrum cover (against UVA and UVB) and is water-resistant.

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