

**FAST FACTS**



*All You Need to  
Keep up to  
Speed*

# Skin Cancer

by Karen L Agnew, Barbara A Gilchrest  
and Christopher B Bunker

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## Skin Cancer



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### Declaration of Independence

This book is as balanced and as practical as we can make it. Ideas for improvement are always welcome: [feedback@fastfacts.com](mailto:feedback@fastfacts.com)

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## Glossary

**Actinic keratosis (solar keratosis):** a sun-induced, precancerous, cutaneous lesion, presenting as a scaly patch or plaque, comprising atypical keratinocytes microscopically

**5-ALA:** 5-aminolevulinic acid – a naturally occurring substance in the human body that is converted to protoporphyrin IX, a photosensitizer, especially in actively growing cells; often present in precancers or cancers

**Basal cell carcinoma (BCC):** a low-grade skin cancer; the most common human malignancy, composed microscopically of basaloid cells, which are locally invasive and rarely metastasize

**Bowen's disease:** a scaly, erythematous plaque that is a type of in-situ squamous cell carcinoma

**Breslow thickness:** cutaneous melanoma thickness, measured histologically from the top of the viable epidermis (granular layer) to the deepest tumor cell in the skin; an important prognostic indicator

**Broders' histological grade:** classification system for squamous cell carcinoma in which grades 1, 2 and 3 denote ratios of differentiated to undifferentiated cells of 3:1, 1:1 and 1:3, respectively; grade 4 denotes tumor cells with no tendency towards differentiation

**Chondrodermatitis nodularis heliis:** a small, benign but painful papule on the helix of the ear caused by inflammation of the ear cartilage

**Clark's level of invasion:** a grading system for the level of invasion of primary cutaneous melanoma in which level I is confined to the epidermis, level II extends to the papillary dermis past the basement membrane, level III fills the papillary dermis and compresses the reticular dermis, level IV invades the reticular dermis and level V involves subcutaneous tissue. Like Breslow thickness, it correlates with risk of metastasis, with a worse prognosis for the higher levels

**Cryosurgery:** a dermatologic treatment in which a very cold substance or cryogen (usually liquid nitrogen) is applied to the skin to freeze cutaneous lesions and cause controlled necrosis

**Dermatoscope:** a handheld magnifying instrument that assists with the examination of cutaneous lesions

**Epidermolysis bullosa dystrophica:** an inherited blistering disease, characterized by atrophy of blistered areas, severe scarring and nail changes that occur after separation of the epidermis

**Erythema ab igne:** a red-brown hyperpigmentation of the skin caused by chronic local exposure to heat

**Erythroplasia of Queyrat:** squamous cell carcinoma in situ of the glans penis

**Gorlin's syndrome:** an inherited disease in which a mutated gene (*PTCH*) predisposes to development of tens to hundreds of BCC and to certain other developmental anomalies

**Hedgehog signaling pathway:** a cascade of signaling molecules that influence embryologic development and later cell division, in which mutations can lead to BCC and other malignancies

**HPV:** human papillomavirus, responsible for warts; only certain subtypes are related to the development of cancer

**Hyperkeratosis:** thickening of the outer layer of skin

**In situ:** in place – a cancer that has not spread to invade neighboring tissues

**Keratinocyte:** a cell of the epidermis characterized by keratin production

**Keratoacanthoma:** a rapidly growing epidermal tumor comprising well-differentiated atypical keratinocytes; the tumor usually regresses spontaneously; more aggressive forms are often difficult to differentiate from squamous cell carcinoma

**Lentigo (plural: lentiginos):** a dark spot with more pigment cells than normal skin; a sign of sun damage but lacking malignant potential

**Lentigo maligna (Hutchinson's melanotic freckle):** an irregularly pigmented macule most commonly found on the face and/or neck of older people representing in-situ melanoma with the potential to progress into invasive malignant melanoma (lentigo maligna melanoma)

**MAL:** methyl aminolevulinate – used as a photosensitizer in photodynamic therapy

**Mammillated:** having nipple-like projections

**Melanocyte:** a melanin-producing cell situated in the basal layer of the epidermis; the normal counterpart of a melanoma cell

**Melanoma:** a cutaneous tumor with strong metastatic potential, comprising malignant melanocytes

**Mohs' micrographic surgery:** a procedure in which a cutaneous neoplasm is excised and the margins frozen-sectioned and assessed histologically in stages as the tumor is removed; the wound is only repaired when there is histological confirmation of complete excision

**Nevomelanocyte:** precursor of a melanocytic nevus cell derived from either epidermal melanoblasts or dermal Schwann cells

**Nevus:** developmental abnormality. A melanocytic nevus (commonly a mole); a cluster of benign pigment cells that usually appear in the first decades of life ('bathing trunk' nevi are congenital lesions that cover a large area of the body)

**Parakeratosis:** retention of nuclei in the upper layers of the epidermis

**Photodynamic therapy (PDT):** a treatment in which a photosensitizer such as 5-ALA or MAL is applied to the tissue and then activated by a source of visible light, resulting in cell destruction

**Punch biopsy:** a small skin specimen for histological assessment obtained by using a circular blade attached to a handle

**PUVA:** administration of psoralen (a phototoxic drug), which acts as a skin sensitizer, followed by exposure to ultraviolet A (UVA) light; used to treat psoriasis, vitiligo and other skin diseases

**Seborrheic keratosis:** a benign, pigmented, often papillomatous cutaneous lesion generally seen in older individuals; also called stucco keratosis

**Squamous cell carcinoma (SCC):** a malignant cutaneous neoplasm, derived from keratinocytes, that usually presents as an enlarging nodule on sun-exposed sites; these tumors have metastatic potential

**Sunburn cells:** keratinocytes undergoing apoptosis as a result of ultraviolet irradiation

**Sun protection factor (SPF):** a number that quantifies the degree of protection given by a sunscreen from the erythemogenic wavelengths (primarily UVB). The SPF value is obtained by dividing the exposure time required to develop barely detectable erythema (sunburn) for sunscreen-protected skin by that for unprotected skin

**UV:** ultraviolet; the portion of sunlight energy responsible for sunburn, tanning and cancer

**Xeroderma pigmentosum:** a rare autosomal-recessive disorder of defective DNA repair characterized by more than a thousandfold risk of UV-induced skin cancer

## Introduction

Skin cancer is important to doctors, both generalists and specialists, and to the public because it is common (and becoming more so), preventable and treatable.

There are three main types: malignant melanoma and the two non-melanoma skin cancers, basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). Well over a million people in the USA and about 100 000 in the UK develop a skin cancer each year. Most of these cancers are BCC, and many of the affected people will have, or have had, at least one other skin cancer.

Twenty years ago, melanoma was the 27th most common cancer in the USA, but it is now the seventh, and it has become the most common solid tumor in adults. Melanoma, particularly, and SCC can kill – there are about 7500 deaths from melanoma in the USA each year and about 1800 in the UK, more than double the figures of 20 years ago.

In part, our current problems with skin cancer are the result of mass emigration from northern Europe over the last two centuries, with fair-skinned people settling in sunnier climes such as North America, Australia, New Zealand and South Africa. Climate change, longevity, recreation and hedonism are important additional factors.

Skin cancer is caused by damage to DNA from ultraviolet (UV) light combined with failure to repair that damage effectively and/or failure to eliminate or repair precancerous skin lesions.

Theoretically, skin cancer can be prevented by educating people about, for example, recreation, clothing, sunscreens and sunbeds (primary prevention), but this approach could take a generation or more before it has a sizeable effect. Serious morbidity and mortality can be prevented or reduced (secondary prevention) by educating patients and physicians alike, so that at-risk individuals and early lesions are identified with accuracy. In Australia, the 5-year survival of patients with melanoma increased to 85% by the year 2000, from around 50% in 1980.

Surgery is usually the treatment of choice, although there are other options, mainly for precancerous situations such as actinic (solar) keratoses. The increasing volume of skin-cancer work has implications for the planning of medical staffing levels and healthcare delivery systems. Although relatively simple surgery suffices for most cancers in most patients, some require multidisciplinary input (dermatologist, plastic surgeon, radiotherapist and oncologist).

National and international consensus guidelines have evolved, and these assist practice (especially by non-experts), education, training, audit and research. Mohs' micrographic surgery has resulted in significantly improved cure rates for selected skin cancers, particularly BCC. Unfortunately, effective treatment of disseminated disease, which has a high mortality, remains difficult. The management of advanced melanoma, for example, consumes a very high proportion of the overall budget for the disease.

Although the incidence of skin cancer is growing rapidly worldwide, most malignancies are treatable if they are diagnosed early enough. With this in mind, we aim to present the basic facts about the epidemiology, causation, presentation and management of skin cancer in an easily accessible way, and we hope that *Fast Facts – Skin Cancer* will be of interest and value to a wide readership. We have included key references throughout the book to support the principal points and to facilitate further inquiry.

### Basal cell carcinoma

Basal cell carcinoma (BCC) is the most common malignant neoplasm in white populations. Its incidence has increased in recent decades: the highest rates are in Australia, where it affects over 2% of men. The tumor most commonly arises on the head and neck (Figure 1.1) and, overall, the incidence is higher in men than in women.

**Risk factors.** The risk of BCC is increased in those who:

- have a history of severe childhood sunburn(s)
- have red hair
- tan poorly.

The association with sunlight is not well understood. Cumulative ultraviolet (UV) exposure was conventionally thought to be the most important risk factor. However, exposure to the sun during childhood and adolescence and, particularly, intense intermittent exposure may be of greater importance than previously thought in the development of BCC.



**Figure 1.1** BCC most commonly arises on the head and neck.

Other risk factors for BCC include:

- North European ancestry
- a positive family history
- immunosuppression
- exposure to arsenic
- previous radiotherapy.

BCC can develop in a sebaceous nevus (Figure 1.2). It is also associated with a number of conditions, including albinism, xeroderma pigmentosum (a rare autosomal-recessive disorder that affects DNA repair), nevoid BCC syndrome (Gorlin's syndrome) and human immunodeficiency virus (HIV) infection.

Table 1.1 summarizes the risk factors for BCC compared with squamous cell carcinoma and melanoma.

### **Squamous cell carcinoma**

Cutaneous squamous cell carcinoma (SCC) is the second most common skin cancer in white populations; SCC represents roughly 20% of all non-melanoma skin carcinomas. The incidence of non-melanoma skin cancer (BCC and SCC together) is approximately 18–20-fold greater than that of melanoma.

SCC is most commonly seen in the elderly and is three times more common in men than women. The incidence is rising, being



**Figure 1.2** Sebaceous nevus on scalp – BCC and SCC can develop from this type of birthmark.



**Figure 3.51** Pyogenic granuloma.

**Figure 3.52** Cutaneous metastases arising from an internal malignancy.



**Diagnosis.** Early diagnosis of melanoma is essential, as the survival rate decreases with increasing tumor thickness. Clinical diagnosis of malignant melanoma can be difficult, as the differential diagnosis is wide, and includes nevi, seborrheic keratosis, dermatofibroma, pyogenic granuloma (Figure 3.51), vascular lesions and cutaneous metastases (Figure 3.52). The ABCDEF rule (Table 3.1) is a simple guide that can assist with identifying early melanomas. However, the rule is only a guide, and it should not be applied

TABLE 3.1

**Clinical features of melanoma – the ABCDEF rule**

A	Lesion asymmetry
B	Irregular border
C	Multiple colors
D	Diameter > 7 mm
E	Evolution/elevation
F	'Funny' mole

TABLE 3.2

**Seven-point checklist for melanoma. Melanoma should be suspected if there is any one major feature or any combination of three minor features**

**Major features**

Change in size

Irregular shape

Irregular color

**Minor features**Diameter  $\geq$  7 mm

Inflammation

Oozing

Change in sensation

strictly – for example, early melanoma may be smaller than 7 mm and there may be no pigment in an amelanotic melanoma.

The UK guidelines for managing cutaneous melanoma promote the use of the seven-point checklist to assist with clinical diagnosis (Table 3.2). This system emphasizes the importance of irregular color or shape and change in size in the identification of suspect lesions.

**Dermoscopy.** The dermatoscope can assist with the clinical diagnosis of melanoma, enabling examination of the anatomic structures of the epidermis, dermoepidermal junction and superficial papillary dermis. Several pigment patterns that can be seen with this instrument are suggestive of melanoma. The usual approach is to put the dermoscopic findings into an algorithm to calculate the likelihood of a malignant melanoma. The most commonly used algorithms are the ABCD rule of dermoscopy, the seven-point checklist and Menzies' scoring method (Table 3.3). These have been developed from the initial technique of pattern analysis, and all are recognized as valid methods for evaluating pigmented lesions with dermoscopy. A meta-analysis of the usefulness of dermoscopy for the diagnosis of melanoma concluded that, for formally trained, experienced operators, dermoscopy gave a more accurate diagnosis than clinical examination alone. Although dermoscopy may improve diagnostic accuracy, it has not yet been shown to alter the physician's practice or increase the sensitivity of excision biopsy in malignant melanoma.