Skin cancer types, diagnosis and prevention

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Skin cancer is one of the most common cancers that affects the UK population. There are two main types of skin cancer: melanoma and non-melanoma skin cancers — which consist of squamous cell carcinoma (SCC), basal cell carcinoma (BCC) and some of the rarer skin cancers.

The skin

The skin is the largest organ of the human body and has multiple physiological functions. It acts as a barrier to prevent infection, regulates temperature, controls fluid loss and is involved in the excretion of some waste products.

Skin comprises two main layers: the epidermis and the dermis. There are three types of cell that make up the epidermis. They are:

- Squamous cells — most of the epidermis consists of these
- Basal cells — round cells at the base of the squamous cells
- Melanocytes — situated between the basal cells and other cells, these cells produce the pigment melanin

The outermost layers of the epidermis are made of dead cells containing keratin — a substance that toughens the skin.

The dermis contains skin vasculature, nerves and sebaceous and sweat glands. Sebum produced by the sebaceous glands keeps the skin moist and waterproof. The dermis also contains collagen and elastin to provide the skin with strength and elasticity.

The thickness of the epidermis and the dermis varies in different parts of the body, from about 2–4mm. For example, skin on the back is quite thick, with an epidermis and dermis of around 4mm, whereas the skin on the face is much thinner.

Melanoma

Although other organs can be affected (eg, the eyes), melanoma usually starts in the skin — in a mole or on an area of skin that looks atypical. Melanomas develop from the uncontrolled cell division of melanocytes, which spread into surrounding surface layers of the skin. Because melanocytes have a dark coloration, melanomas usually look like a dark spot or mole on the skin (see Figure 1, p258). Women most commonly develop melanomas on the leg, whereas men develop them more often on the trunk.

Exposure to ultraviolet radiation is the leading cause of skin cancers such as melanoma. Early identification and prompt diagnosis are key to preventing metastases in other parts of the body.

SUMMARY

Some 11,000 people in the UK are diagnosed with melanoma, a type of skin cancer, each year and prevalence is higher in younger age groups. Other types of skin cancer include non-malignant melanomas, such as squamous cell carcinoma and basal cell carcinoma.

Exposure to ultraviolet radiation is the leading cause of skin cancer; other risk factors include genetics, skin type and reduced immunity. Early identification and treatment is vital to prevent advancement of the disease. People should be encouraged to be vigilant at checking their skin and existing moles for signs of skin cancer. Pharmacists can help promote awareness of skin cancer and educate their patients about protecting their skin from the sun.
Around 11,000 people are diagnosed with melanoma each year in the UK, where it is the most common cancer in people aged between 15 and 34 years and the fifth most common cancer overall. Melanoma is more common in women, particularly young women.

**Types of melanoma**

There are four types of skin melanoma. In order of prevalence they are:

- Superficial spreading melanoma — typically a slow growing melanoma
- Nodular melanoma — fast growing melanoma
- Lentigo maligna melanoma — usually affects older people on areas of their skin that have been extensively exposed to the sun for many years (lentigo maligna melanoma has a precursor condition called lentigo laigna, or Hutchinson’s freckle, which looks like a stain on the skin)²
- Acral melanomas — usually found on the soles of the feet or palms of the hands. More common in people of Afro-Caribbean origin³

**Risk factors for melanoma**

**Ultraviolet radiation** The leading risk factor for developing melanoma is exposure to ultraviolet (UV) radiation, either from natural sunlight or from sunbeds or sunlamps. UV radiation is highly mutagenic.⁴ DNA can be damaged by UV radiation by direct oxidative stress caused by reactive oxygen species or through indirect interference with DNA repair mechanisms.⁵

In the UK, incidence of melanoma is rising.¹ This is believed to be because more people are having holidays in the sun and exposing their skin to UV radiation. Being burnt by the sun, especially if the skin blisters, increases the risk of developing melanoma. An increase in the number of people using sunbeds and sunlamps in the past two decades has also added to the rising number of melanomas being diagnosed. People who use sunbeds frequently and those who start using them earlier in life are more at risk.¹

The Sunbeds (Regulation) Act 2010 prohibits the use of sunbeds by people aged under 18 years.

**Skin type** Different skin types react differently to sun exposure; having fair skin, red or fair hair, blue eyes and freckles makes skin more sensitive to the sun. People with these features are more likely to burn and have a higher risk of melanoma. Having numerous or atypical (large or irregular shape or colour) moles also increases an individual’s risk of developing melanoma.

**Genetics** Mutations in the BRAF gene are present in more than 50% of melanomas.⁷ BRAF kinase plays a role in regulating the mitogen-activated protein kinase/extracellular signal-regulated kinase (MAP/ERK) signalling pathway, which affects cell division and differentiation.

BRAF mutations allow for uncontrolled cell division of melanocytes — leading to cancer. The discovery of BRAF has led to the development of new therapies to treat melanomas.⁷

In melanomas that have a familial association, mutations most commonly occur in the TP53 gene, which codes for protein 53 (p53). When this protein is in its normal state it functions as a tumour suppressor, allowing damaged cells time to repair without progressing to cancer. However, mutations in TP53 make the protein unable to perform this function.⁶

Other gene mutations have also been associated with familial melanoma, notably the cyclin-dependent kinase inhibitor 2A gene.

In future, family members of people with melanoma may be able to be screened for defective genes. This will, hopefully, influence those affected to become more vigilant in monitoring their moles and have regular total-body skin examinations — allowing for early detection of a melanoma for which the chances of a cure are greater.

The faulty genes that can cause melanomas have also been linked to pancreatic cancers. This explains why some families have increased risk of melanoma and pancreatic cancers.⁹

**Reduced immunity** People with a lowered immune system have an increased risk of melanoma, including those with HIV and those taking immunosuppressants.
Signs and symptoms of melanoma

Half of all melanomas begin with a change in previously normal looking skin. This usually appears as a dark area or abnormal new mole. Other melanomas develop from an existing mole or freckle. It is important to refer patients to their GP if they complain of any of the following signs and symptoms:

- Any of the ABCDE signs (see Box 1)
- Unusual skin marks that last longer than a few weeks
- Moles that itch or tingle
- Moles that bleed or crust over
- Dark discoloration under a nail

Staging melanoma

For many patients, curative surgery is possible; therefore, early diagnosis and investigation of melanoma is important. The American Joint Committee on Cancer has produced a validated staging system — the tumour, nodes, metastasis (TNM) system — that describes a person’s cancer and is based on tumour depth, the presence of ulceration, lymph node involvement and the identification of metastases. The stages of melanoma according to the TNM system are described in Box 2.

Tumours are assessed according to certain features, such as the depth of the melanoma (Breslow thickness). This measurement is the distance from the surface of the skin to the deepest melanoma cells and is the most significant measurement for predicting prognosis of melanoma. It identifies the risk of a metastatic deposit in a sentinel lymph node.10 The deeper the melanoma, the higher the likelihood of sentinel node involvement. For example, a Breslow depth of less than 0.75mm is associated with a 1% risk of metastatic deposit in a sentinel node, whereas a Breslow depth of 4mm or more carries a 36% risk. The Clark scale, which relates to the depth of skin layer penetration, can also be used to stage melanoma. Whether the melanoma is ulcerated or not (a melanoma is ulcerated if the layer of skin covering it is missing) and mitotic rate (the number of cells undergoing mitosis in a certain area of melanoma tissue) are also taken into account; the presence of ulceration and a high mitotic rate are associated with a poorer prognosis. Metastases in the lymph nodes and other parts of the body are also considered when staging melanomas.

Non-melanoma skin cancer

Basal cell carcinoma

BCC is a cancer of the basal cells of the epidermis. It is common in the UK and accounts for 75% of all non-melanoma skin cancers.1 Fortunately, BCCs are slow growing and almost never metastasise (less than 0.1% do). BCCs occur more commonly on sun-exposed areas of the skin, but also on areas of chronic scars and certain anatomical sites, such as the lips. BCCs start as small red papules that bleed occasionally. The layer of skin covering a BCC can remain intact for months but will eventually develop into an ulcer that does not heal. For patients who detect BCCs early, the prognosis is good with 90% of cases being curable.10 However, some BCCs are aggressive and if left untreated can spread to deeper layers of tissue, such as the bone, making treatment difficult. A small number of BCCs may also return in the same area of skin post-treatment; this is known as local recurrence.

Squamous cell carcinoma

SCC is a cancer of the keratinocytes of the epidermis and makes up 20% of non-melanoma skin cancers.1 Like BCCs, SCCs appear on sun-exposed areas of the skin, but also on areas of chronic inflammation. SCC presents as a red papule or non-healing lesion, and ulceration and bleeding can occur (see Figure 3, p258). They are generally slow growing and prognosis is good with treatment. However, 5–10% will metastasise at an early stage, affecting the lymph nodes first.10 Risk factors for metastasis include: recurrent disease; large size; deep invasion; and disease associated with chronic scars and certain anatomical sites, such as the lips. Locally advanced metastatic disease is associated with a five-year survival rate of over 65%.10 Disseminated disease has a considerably poorer prognosis.

Box 1: The ABCDE signs of melanoma

The mnemonic ABCDE is a useful way to monitor the appearance of moles and detect the early signs of melanoma. The letters stand for:

- Asymmetry — the mole has an irregular shape
- Border — the border of the mole is irregular or has jagged edges
- Colour — there is a mix of colours in the mole
- Diameter — the diameter of the mole is greater than 7mm
- Evolution — the mole has changed size, shape or colour

Box 2: Stages of melanoma

A staging system is used to describe the characteristics of melanoma. It is used to guide treatment decisions and predict a likely prognosis.

Stage 0

Melanoma is present on the top surface of the skin and has not spread into deeper layers

Stage 1 (no metastases)

Stage 1a — melanoma is less than 1mm thick, not ulcerated and has a mitotic rate of less than 1/mm²
Stage 1b — melanoma is less than 1mm thick and ulcerated, or is 1.01–2mm thick, not ulcerated and has a mitotic rate of at least 1/mm²

Stage 2 (no metastases)

Stage 2a — melanoma is 1.01–2mm thick and ulcerated, or 2.01–4mm thick and not ulcerated
Stage 2b — melanoma is 2.01–4mm thick and ulcerated, or thicker than 4mm and not ulcerated
Stage 2c — melanoma is thicker than 4mm and ulcerated

Stage 3

Stage 3 melanomas have spread to lymph nodes or lymphatic vessels closest to the melanoma but not to other body parts. The depth of the melanoma in stage 3 is not relevant because staging is more dependent on the number of lymph nodes involved, the size of the melanoma cells and the infiltration of melanoma cells into lymphatic vessels

Stage 4

Stage 4 melanomas have metastasised to distant parts of the skin, distant lymph nodes or other organs, commonly the lung, liver or brain. This is termed advanced or metastatic melanoma
Associated with SCCs is Bowen’s disease, a pre-cancerous skin condition caused by abnormal cells growing in the epidermis. These cells are non-invasive and non-malignant, but if left untreated can develop into SCC.

Risk factors Sun exposure and lowered immunity are the main risk factors for BCC and SCC. Other risk factors include previous skin cancers, previous radiotherapy (particularly for BCC), exposure to chemicals (coal, soot, asphalt, paraffin and petroleum derivatives) and certain rare hereditary conditions, such as Gorlin syndrome or xeroderma pigmentosum.

Rarer types of non-melanoma skin cancer are described in Box 3.

Prevention of skin cancer
Exposure to UV radiation is a major modifiable risk factor for the prevention of all types of skin cancer. Pharmacists can educate the public about the risks of sun exposure. The main counselling points are:

- Seek shade when the UV rays from the sun are strongest. During the UK summer this is usually between 11am and 3pm, however, times may vary in other countries
- Cover up when there is no shade available. Wear loose clothing, a hat and good quality sun glasses to protect your skin from the sun
- Always wear sunscreen; sun protection factor (SPF) rating refers to the amount of UBV the sunscreen can filter, whereas the star rating refers to the extent to which UVA is filtered. Cancer Research UK recommends that a sunscreen with an SPF of at least 15 that also has UVA protection is used — the more stars the better. No sunscreen can provide 100% protection from UV radiation and will only provide protection if it is applied properly.
- Avoid sunbeds or sunlamps; sunbeds are estimated to be responsible for around 100 deaths from melanoma each year in the UK. Cancer Research UK recommends that anyone with fair skin, many moles or a family history of skin cancer should avoid using sunbeds. It is illegal for anyone under the age of 18 years to use sunbeds or sunlamps, except for specific medical reasons
- Protect children; young skin is particularly at risk from sun damage. Extra precautions are needed to ensure children are protected from the sun
- Watch out for fake tan. Although fake tan is a safer tanning alternative to sun exposure, most fake tan products do not protect the skin from UV radiation
- Avoid tanning supplements. Melanotan is a synthetic hormone that increases levels of melanin in the skin. There has been no research into the safety of this unlicensed product and it is illegal to sell it in the UK

Box 3: Rarer non-melanoma skin cancers
Rarer types of non-melanoma skin cancer include Merkel cell carcinoma, Kaposi’s sarcoma, cutaneous T-Cell lymphoma and sarcomas.

Merkel cell carcinoma Merkel cell carcinomas usually affect the head, neck or limbs and appear as red or purple nodules with a shiny surface. Merkel cell carcinomas have the propensity for local recurrence and regional or distant metastasis. Merkel cells are found in the top layer of skin and close to nerve endings.

Kaposi’s sarcoma Kaposi’s sarcoma is a systemic disease that presents with skin lesions. Four subtypes have been identified. They are: classic Kaposi’s sarcoma; African endemic Kaposi’s sarcoma; Kaposi’s sarcoma in the iatrogenic immunosuppressed; and AIDS-related Kaposi’s sarcoma (Kaposi’s sarcoma in HIV patients is an AIDS-defining illness).

Cutaneous T-cell lymphoma Cutaneous T-cell lymphoma is a class of non-Hodgkin’s lymphoma. Unlike most non-Hodgkin’s lymphomas — which are B-cell related — cutaneous T-cell lymphoma is associated with mutations of T lymphocytes (T-cells). Malignant T-cells migrate to the skin and form lesions, which change shape as disease progresses.

Sarcomas Sarcomas originate from mesenchymal cells such as bone and soft tissue (including the skin). Dermatofibrosarcoma is a sarcoma that specifically affects the skin.

References