

MELANOMA AND OTHER SKIN CANCERS: A guide for medical practitioners



Australia has one of the highest rates of skin cancer in the world. About 2 in 3 people in Australia will develop some form of skin cancer before the age of 70 years.

Skin cancer is divided into two main types:

Melanoma

Melanoma develops in the melanocytic (pigment-producing) cells located in the epidermis. Untreated, melanoma has a high risk for metastasis. The most common clinical subtype is superficial spreading melanoma (SSM) and is most commonly found on the trunk in males and lower limbs in females. Melanomas can develop on any part of the body, including parts not heavily exposed to ultraviolet (UV) radiation.

In Victoria:

- Melanoma is the fourth most common cancer diagnosed.
- Every year, more than 2000 new cases are diagnosed and there are almost 300 deaths from the disease.
- The risk of developing melanoma increases with age. However, melanoma is the second most common cancer in males and females aged 25–59 and the third most common cancer in females aged 15–24 years.
- In Australia, the lifetime risk of developing melanoma by age 75 years is about 1 in 23 for males and 1 in 33 for females.

Non-melanocytic skin cancer (NMSC)

- **Squamous cell carcinoma (SCC)** develops from the keratinocytes in the epidermis and is associated with risk of metastasis. SCC is most commonly found on the face, particularly the lip region, ears, nose, cheek and eyelid, and then on the neck, dorsa of hands and forearms in both sexes. In males, SCC is commonly found on the head and neck, and in females, it is commonly found on the upper limbs, followed by the head and neck. It is believed that many SCCs arise from premalignant actinic keratoses.
- **Basal cell carcinoma (BCC)** also develops from keratinocytes in the epidermis and is the most frequently diagnosed cancer in Australians. BCC is most commonly found on the face: the eyelid, lip and nasolabial fold, followed by ears, nose and cheek in both sexes. In males, BCC is common on the neck, back and shoulders, and in females, on the neck, shoulders and outer arms.

Causes of melanoma and other skin cancers

- Unprotected exposure to UV radiation remains the single most important lifestyle risk factor for melanoma and other skin cancers.
- UVA and UVB radiation contribute to skin damage, premature ageing of the skin and skin cancer.
- Melanoma and BCC are associated with both amount and pattern of sun exposure, with an intermittent pattern carrying the highest risk.
- Premalignant actinic keratosis and SCC are associated with the total amount of sun exposure accumulated over a lifetime.
- Other risk factors for NMSC can include exposure to some chemicals (e.g. arsenic), radiation therapy, UVA and psoralen (PUVA) treatment for psoriasis, immunosuppressive therapy and some rare genetic conditions predisposing to skin cancer.

Risk factors for melanoma

- Personal history of melanoma
- Multiple dysplastic naevi (>5)
- Multiple naevi (>100 or >11 on arm)
- Family history of melanoma/Personal history of NMSC
- Having fair or red hair and blue or green eyes
- Fair skin that burns easily, freckles and does not tan
- High levels of intermittent sun exposure (e.g. during outdoor recreation or sunny holidays)
- Immune suppression and/or transplant recipients
- Increasing age

Gender

In Victoria, males are 1.3 times more likely to be diagnosed with melanoma and almost 2.5 times more likely to die from it than females (after allowing for differences in age).



Mortality from melanoma rises steeply for males from 60 years and increases with age.

Melanoma in non-Caucasians

The incidence of melanoma in non-Caucasians is low. However, non-Caucasians are more likely to experience delayed diagnosis and have poorer clinical prognosis compared to Caucasians.

Prevention

Cancer Council Victoria recommends five steps to protect against sun damage during daily sun protection times:

-  **Slip** on sun-protective clothing – that covers as much skin as possible.
-  **Slop** on SPF30 (or higher) sunscreen – make sure it is broad-spectrum and water-resistant.
-  **Slap** on a hat – that protects the face, head, neck and ears.
-  **Seek** shade.
-  **Slide** on sunglasses – that meet Australian Standards.

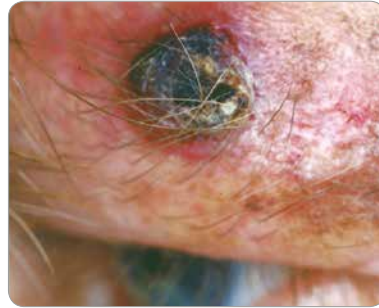
Check the daily sun protection times on the free SunSmart app.

Melanoma diagnosis

Superficial spreading melanoma (SSM)

Melanoma can develop in pre-existing moles in the skin, or more commonly in the melanocytes found in the epidermis (i.e. de novo).

- SSM is the most common form of melanoma.
- SSM can appear as a new spot, or an existing spot, freckle or mole that changes size, colour or shape.
- A patient diagnosed with melanoma is at increased risk of new primary melanomas (relative risks ranging above 10).



Nodular melanoma (NM)

This is an aggressive form of melanoma that grows quickly. NM differs from SSM in appearance and is easily misdiagnosed. NM has little radial growth within the epidermis but penetrates vertically into the dermis early. It is more likely to be symmetrical and uniform in colour (red, pink, brown or black), is more frequently less pigmented than SSM, and feels firm to touch. Over time, it may develop a crusty surface that bleeds easily.

- NM can become life threatening in 6–8 weeks.
- Approximately 15% of total melanomas diagnosed are NM.
- NM does not necessarily arise from a pre-existing mole and is commonly found on the head and neck.
- NM develops most commonly in older people, particularly men.



The ABCDE acronym can help distinguish a superficial spreading melanoma from a normal mole:

- A Asymmetry:** the lesion is irregular in shape or pattern.
- B Border:** the border or outline of a melanoma is usually irregular.
- C Colour:** there is variation in colour within the lesion.
- D Diameter:** the lesion is usually greater than 6 mm across. However, suspect lesions of smaller diameter should also be investigated.
- E Evolving:** the lesion changes over time (size, shape, surface, colour, symptoms e.g. itch).

The ABCDE acronym cannot be used to aid diagnosis of nodular melanoma; however, the following features can be of help:

- E Elevated:** the lesion can appear as a small, round and raised lump on the skin. Colour may be uniform throughout the lesion and may be black, brown, pink or red.
- F Firm:** the lesion feels firm to touch.
- G Growing:** a nodule that has been growing progressively for more than a month should be assessed as a matter of urgency.

If nodular melanoma is suspected, diagnosis should not be delayed, and urgent referral to a dermatologist or immediate excision is recommended.

Biopsy and excision for melanoma or suspicious naevi

- Complete excision biopsy with a 2 mm margin is recommended.
- Partial biopsies (e.g. punch biopsies and shave excisions) can be less accurate than excisional biopsy and should be performed by trained practitioners.
- If a thick melanoma is suspected, refer patient to a dermatologist or a surgeon with an interest in melanoma as a matter of urgency.

Treatment for melanoma

Selecting appropriate primary treatment will depend on the Breslow thickness (vertical depth) of the tumour. Breslow thickness is measured using the following system:

- (pTis) Melanoma *in situ*. The abnormal cells are found only in the non-vascular epidermis and have not penetrated into deeper tissue that contains blood vessels.
- (pT1) Melanoma cells reach the upper part of the dermis. The melanoma is less than 1 mm thick.
- (pT2) Melanoma cells reach the upper part of the dermis. The melanoma is between 1 mm and 2 mm thick.
- (pT3) Melanoma cells reach deeper into the dermis. The melanoma is between 2 mm and 4 mm thick.
- (pT4) Melanoma is more than 4 mm thick or it has invaded through the dermis and into the underlying fat.

Treatment is based on the T1–T4 classification. The surgical removal of the tumour with recommended margins of excision for each of the T-classification groups are:

- (pTis) Melanoma *in situ*: 5–10 mm clearance
- (pT1) Melanoma <1.0 mm: 1 cm clearance
- (pT2) Melanoma 1.0–2.0 mm: 1–2 cm clearance
- (pT3) Melanoma 2.0–4.0 mm: 1–2 cm clearance
- (pT4) Melanoma >4.0 mm: 2 cm clearance.

Note: evidence for optimal excision clearance for melanoma 2–4 mm thick is unclear. The *Clinical Practice Guidelines* recommend it may be desirable to take a wider margin (2 cm) for these tumours, depending on tumour site and surgeon/patient preference.

Other treatment options

Surgery

Sentinel lymph node biopsy (SLNB) should be discussed with patients with pT2 and thicker lesions, and performed by trained practitioners. Surgical resection of isolated metastases can be performed in both definitive and palliative treatment settings.

Immunotherapy

- For unresectable stage III or stage IV metastatic melanoma
- PD-1 inhibitors (Nivolumab, Pembrolizumab): given as IV infusion every 3 weeks
- CTLA-4 inhibitor (Ipilimumab): given as IV infusion every 3 weeks for 4 doses

Targeted therapy

- BRAF inhibitors (Dabrafenib and Vemurafenib): for treatment of BRAF V600 +ve unresectable stage III or stage IV metastatic melanoma, oral tablets
- ~50% of all melanomas have mutation in BRAF gene
- Used in combination with MEK inhibitor (Trametinib)

Chemotherapy

- May be offered for treatment of metastatic disease.
- Interferon may be offered following surgical removal of melanoma that has not progressed past lymph nodes.

Vaccines remain experimental, but may be offered within the context of clinical trials.

Radiation

Radiation treatment can be used to treat lentigo maligna when surgical approaches are considered less suitable. Post-operative radiotherapy can be performed for melanomas likely to recur locally or regionally. Radiotherapy can be used for palliative management of cerebral and bone metastases, and for other metastases where temporary local control is needed.

Follow-up for melanoma

Due to the risk of tumour recurrence and new primary melanomas, all patients require routine follow-up, the frequency of which will depend on the risk of both metastatic recurrence and further new melanomas.

Follow-up for metastatic disease is done more frequently in the early part of follow-up

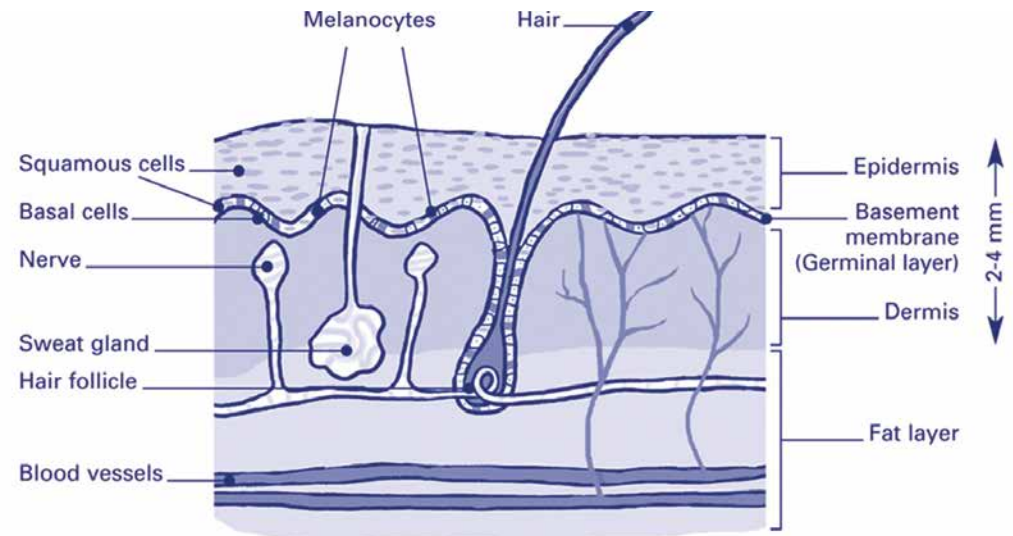
and not continued indefinitely because risk of recurrence diminishes with time. Follow-up for future primary melanomas is done at 6 to 12 month intervals and should be continued long term.

In Australia, up to 75% of patients detect their own recurring melanomas. Patients should be educated on recognising changes in their skin, have a professional full skin examination as deemed appropriate, and have further testing as required.

Survival

In Australia, for the period 2006–2010, the 5 year survival for melanoma was 94% for females compared with 89% for males.*

Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand. www.nhmrc.gov.au



Non-melanoma skin cancer (NMSC)

Diagnosis

Squamous cell carcinoma (SCC)

- SCC can spread to other parts of the body if not treated. Lesions on the ears and lips have a higher risk of metastasis.
- It appears as a thickened, red, scaly nodule that may bleed and ulcerate over time.
- It grows over a period of some months. Rapid growth is associated with increased risk of mortality.

Basal cell carcinoma (BCC)

- BCC is the most common and least dangerous form of skin cancer.
- It appears as a well-defined lump or scaly area that is red or pearly in colour.
- It may bleed or become ulcerated early on, then heal and break down again.
- It usually grows relatively slowly.



Victorian Melanoma Units

Melanoma Units provide specialised diagnostic services and treatment services. Melanoma management and treatment is guided by a multidisciplinary panel including pathology services, medical specialists, treatment options and clinical trials. Patients may be referred to these units by their GP or specialist.

Victorian Melanoma Service	Alfred Hospital, Commercial Road, Melbourne VIC 3004	Ph: 9076 0365 Fax: 9076 5799
Melanoma and Skin Service	Peter MacCallum Cancer Centre, 305 Grattan Street, Melbourne VIC 3000	Ph: 8559 5000
Royal Melbourne Hospital Melanoma Service	300 Grattan Street, Parkville VIC 3052	Ph: 9342 8187
Austin Hospital Melanoma Clinic	Medical Oncology Unit Level 6, Harold Stokes Building 145-163 Studley Road, Heidelberg VIC 3084	Ph: 9496 5763 Fax: 9457 6698
St Vincent's Dermatology Clinic	41 Victoria Parade, Fitzroy VIC 3065	Ph: 9231 2898 Fax: 9231 3489
Skin and Cancer Foundation	Level 1, 80 Drummond Street, Carlton VIC 3053	Ph: 9623 9400

Treatment

Treatment options for non-melanoma skin cancer include:

- Surgical excision of the tumour and surrounding tissue
- Curettage and cautery
- Application of topical agents (imiquimod cream, fluorouracil cream, photodynamic therapy)
- Cryotherapy
- Radiotherapy

The choice of treatment will depend on:

- Histological features
- Tumour size
- Thickness and grade
- Anatomical site
- Patient factors

Follow-up

Frequency of follow-up of patients treated for NMSC for evidence of recurrence, metastasis and/or any new primary skin cancers will depend on histological clearance and risk level of tumour. Patients should be educated on recognising changes in their skin (including examination of draining lymph nodes for patients with SCC), have a professional full skin examination as deemed appropriate, and have further testing as required.

Clinical Practice Guide: Basal cell carcinoma, squamous cell carcinoma (and related lesions) – a guide to clinical management in Australia.
www.cancer.org.au

Screening for melanoma and NMSC

There is no evidence demonstrating that population-based screening for melanoma and NMSC is effective in reducing morbidity or mortality, and it is not recommended.

Skin surveillance is recommended for patients identified to be at high risk of melanoma and NMSC, including patients with a previous diagnosis of melanoma.

Skin self-examination

Approximately 50% of melanomas are detected by the patient. There is no specific technique or recommended frequency of self-examination that has shown to reduce morbidity; however, regular skin examination may increase the probability of detecting skin cancer at an early and treatable stage.

Patients at high risk for melanoma should:

- Be taught to self-screen (including examination of draining lymph nodes) and recognise suspicious lesions
- Have a full body examination with a clinician every 6 to 12 months.

Patients treated for NMSC should:

- Be taught to self-screen and recognise changes to their skin
- Have a full body examination with a clinician every 12 months.

For the general population, the Australasian College of Dermatologists recommends that people examine their skin 4 times a year or as often as recommended by their medical practitioner.