Melanoma
clinical features and early diagnostic techniques

GPs are at the front line in the diagnosis of melanoma and are often required to assess pigmented lesions to determine if further investigation is warranted. Here is a review of the clinical features of melanoma and new techniques that have been developed to aid diagnosis.

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Australia has the highest incidence of melanoma in the world, and this continues to rise. The incidence rates in Australia are up to four times higher than those found in Canada, the USA and the UK.[1] In 2001, the estimated risk of developing an invasive melanoma before the age of 75 years was one in 25 for Australian men and one in 34 for Australian women. In the past 10 years the annual incidence has increased, on average, 2.1% per year for males and 1.2% for females.[1] When compared with other cancers, melanoma is the third most common cancer in women and the fourth most common cancer in men; however, in people aged between 15 and 44 years, melanoma is the most common cancer.[1]

Despite the increasing incidence of melanoma, the overall five-year survival rate has steadily improved, and is now greater than 85%.[2] However, early diagnosis is essential as the five-year survival rate of greater than 95% seen with patients with lesions thinner than 1 mm falls to less than 50% in those with lesions exceeding 4 mm in thickness.

Risk factors

Identification of high risk patients is an important aspect in the early detection of melanoma; Table 1 lists the main risk factors for the development of melanoma.[3]

Epidemiological studies have revealed that intermittent exposure to intense ultraviolet (UV) light, best characterised by sunburns, particularly those occurring during childhood and adolescence, is associated with an increased risk of melanoma.[4]

IN SUMMARY

- **Australia has the highest incidence of melanoma in the world, and GPs represent the front line of melanoma diagnosis.**
- **Assessment of melanoma risk factors enables GPs to identify high risk individuals and implement appropriate melanoma prevention and surveillance strategies.**
- **Dermoscopy and whole body photography add significant clinical information that may be used to identify new lesions or prevent unnecessary biopsy.**
- **Excisional biopsy with 2 mm margins is the preferred method for further investigation of suspicious pigmented lesions.**
- **Referral of patients to a multidisciplinary melanoma unit should be considered in complicated cases requiring specialist management.**
- **Computer assisted diagnosis is a new frontier in melanoma diagnosis. At present, this technology should be viewed with caution as it cannot reliably diagnose up to 20% of melanomas.**

Table 1. Clinical risk factors for melanoma

Stronger risk factors

Multiple dysplastic naevi
Multiple typical naevi (more than 200)
Previous melanoma
Strong family history (more than three first degree family members)

Weaker risk factors

Weak family history
History of blistering sunburn
Previous nonmelanoma skin cancer
Type I skin
Freckling
Blue eyes
Red hair
Transplant recipients/immunosuppression

Table 2. Clinical criteria for dysplastic naevi

A dysplastic naevus has three or more of the following:

- Ill-defined border
- Irregularly distributed pigmentation
- Background erythema
- Diameter greater than 5 mm
- Irregular border

There is also increasing evidence that regular use of tanning beds may increase melanoma risk, and their use, particularly by adolescents, should be discouraged.[5,6]

Numerous studies have examined the significance of total naevus counts in the development of melanoma, and it is clear that individuals with increased naevus numbers have an increased risk of melanoma. It should be noted, however, that more than half of melanomas arise *de novo* (on normal skin) and not from melanocytic naevi. For a 20-year-old individual, the estimated lifetime risk of any one naevus transforming into a melanoma by the age of 80 years is one in 3165 for men and one in 10,800 for women.[7] Thus, prophylactic removal of melanocytic naevi is not recommended.

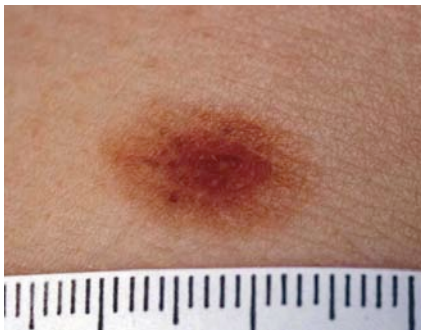


Figure 1. A dysplastic naevus.

Dysplastic naevi (atypical naevi, Clark's naevi) are a subset of melanocytic naevi with specific clinical features (Figure 1, Table 2).[8] It is estimated that 7 to 18% of the population have one or more dysplastic naevi. The risk of any one dysplastic naevus undergoing malignant transformation is low; however, individuals with multiple dysplastic naevi have a three- to 20-fold increased risk of developing melanoma, with the risk increasing the greater the total number of dysplastic naevi. For this reason, dysplastic naevi should be viewed primarily as a risk factor for melanoma and, therefore, prophylactic excision is not recommended.

Management of patients identified as high risk

It is generally recommended that those people identified as being at high risk for developing melanoma engage in programs of prevention and increased surveillance. An annual medical examination is recommended for high risk individuals; this should be carried out by a GP or dermatologist, depending on the individual's level of risk and access to specialist care. Baseline skin images should be taken for individuals with large numbers of naevi, and regular self-examination should also be encouraged.

Exposure to UV radiation is the only known preventable risk factor for melanoma and has been the major focus of public education campaigns. All patients, particularly those at high risk, should be encouraged to adopt sun protection strategies. Although sunscreens with a high sun protection factor (SPF) can be effective in protecting against UV radiation, physical protection through natural shade and clothing is preferable when possible.

Clinical assessment

Clinical assessment of patients for melanoma includes taking a thorough history and performing a complete skin examination under good lighting. Important aspects of the history include:

- history of any new or changing lesions
- past history of skin cancer (melanoma and nonmelanocytic skin cancers)
- family history of skin cancer
- history of severe, blistering sunburn, particularly in childhood
- history of immunosuppression (e.g. HIV infection, medications).

Important aspects on physical examination include:

- examination of any suspicious lesion (historically or visually)
- estimation of total naevus count
- presence and number of dysplastic naevi
- assessment of skin phototype (Table 3).

No area should be neglected during physical examination, including the scalp, breasts, buttocks, soles of the feet and between the toes. However, involvement of the genitalia is uncommon, and this area need not be examined unless there are specific concerns.

In 1985 the ABCD criteria for the early clinical detection of melanoma was adopted by the American Cancer Society.[9] This acronym describes the clinical features of melanoma that may be evident at any one point of time, including:

- Asymmetry
- Border irregularity
- Colour variegation
- Diameter greater than 6 mm.

The ABCD criteria have recently been revised to ABCDE (E for Evolution) to address the importance of change in malignant lesions.[10] A lesion with one or more ABCDE criteria should be considered suspicious.

Some limitations have been identified in the ABCDE system. Early melanoma may have a diameter of less than 6 mm, and some melanoma subtypes, including nodular melanoma and amelanotic melanoma, often do not fulfil the A, B and C criteria. There are also many benign lesions, including seborrhoeic keratoses and dysplastic naevi, that may satisfy all of the ABCDE criteria. Many experienced clinicians rely instead on overall pattern recognition or the 'ugly duckling' sign to differentiate between benign and malignant lesions.[11]

Characteristics of the common melanoma subtypes

Superficial spreading melanoma

Superficial spreading melanomas (SSM; Figure 2a) are the most common subtype of melanoma and account for about 70% of melanoma cases. Although they may be found anywhere on the body, SSM are most often found on the trunk in men and legs in women. Classically they present as an enlarging (over months), asymmetrical pigmented lesion with variegated pigmentation and irregular borders.

Nodular melanoma

Nodular melanomas (Figure 2b) comprise 15% of melanomas. They may occur anywhere but have a predilection for the head and neck. They may present as a rapidly enlarging, discrete nodule, often with evidence of ulceration. Nodular melanomas differ from superficial spreading melanomas because they lack a radial growth phase. About 50% of nodular melanomas lack pigment (amelanotic) and appear pink or red. The lack of pigment, regular borders and symmetrical appearance mean nodular melanomas often do not fulfil the ABCD criteria and instead a history of change or evolution (E) is relied upon for diagnosis. Thus, nodular melanomas represent a major challenge to early diagnosis because of their unusual clinical appearance and rapid growth.

Acral lentiginous melanoma

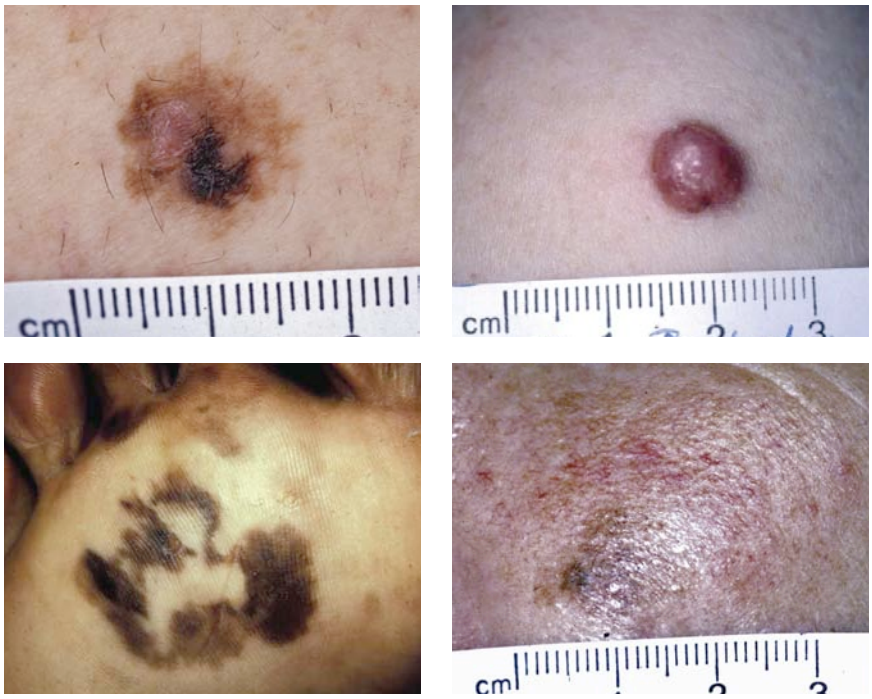
Acral lentiginous melanomas (ALM; Figure 2c) are a subtype of melanoma arising on the sole, palm, fingernail or toenail and account for 5% of melanoma cases. Subungual (nail bed) involvement may present with a longitudinal pigmented band in the nail or pigmentation of the nail fold surrounding the nail (Hutchinson's sign).

Lentigo maligna melanoma

Lentigo maligna melanomas (LMM; Figure 2d) arise from lentigo maligna, the *in situ* phase of LMM (previously often referred to as Hutchinson's melanotic freckle). LMM account for about 10% of melanoma cases. They are located in areas of frequent sun exposure (head and neck), usually in fair skinned older individuals. Clinically they present as a progressively enlarging pigmented macule with colour variation and other ABCDE features.

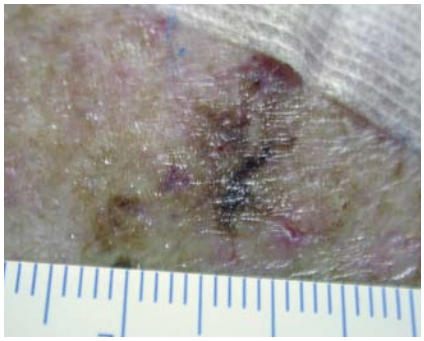
Table 3. Definition of skin phototype (Fitzpatrick)

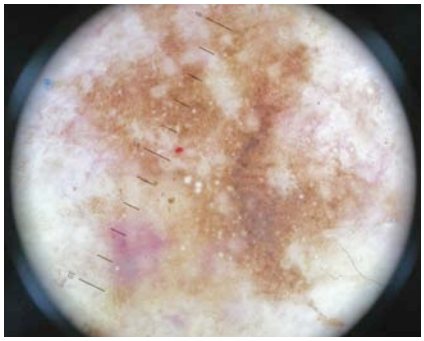
Skin phototype	Characteristics
Type I	Burns easily without tanning
Type II	Burns easily with slight tanning
Type III	Burns moderately and tans moderately
Type IV	Burns minimally and tans well
Type V	Rarely burns and tans deeply
Type VI	Never burns and deeply tans



Figures 2a to d. a (top left). Superficial spreading melanoma. b (top right). Nodular melanoma. c (above left). Acral lentiginous melanoma. d (above right). Lentigo maligna melanoma.

Figure 3. A dermoscope with digital dermoscope attachment.





Figures 4a and b. a (left). An area of pigmentation adjacent to a recently excised melanoma, which clinically is very suspicious for melanoma. b (right). Dermoscopy reveals the characteristic features of a benign seborrhoeic keratosis.

Baseline clinical photography

In the general practice setting, digital cameras can be extremely useful in the surveillance of individual skin lesions. If a lesion is thought clinically to be benign but melanoma is difficult to exclude, a short period of observation (two to three months) aided by a baseline photograph may prevent unnecessary biopsy.

Table 4. Dermoscopic features suggestive of melanoma

Blue-white veil
Multiple brown dots
Pseudopods
Radial streaming
Peripheral black dots and/or globules
Multiple (five or six) colours

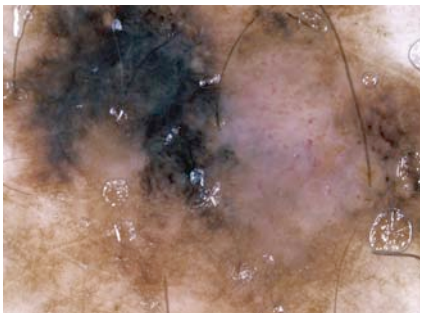


Figure 5. Dermoscopy of the lesion seen in Figure 2a showing many characteristic features of melanoma.

Total body surface imaging has proven useful in the surveillance of high risk patients with high mole counts or multiple dysplastic naevi in whom the detection of new or subtly changing lesions is difficult. These images are used for direct visual comparison of each body area and are an efficient and cost effective aid to skin surveillance. They are of much better quality when taken by a trained clinical photographer. If significant skin changes occur, these images may need to be updated (usually after five to 10 years).

Dermoscopy

Dermoscopy (epiluminescence microscopy, dermatoscopy) is an evolving field in dermatology that has been shown to improve the accuracy of diagnosing cutaneous lesion (Figure 3). Oil immersion, optical magnification and an oil–glass interface are used to make the epidermis more translucent, allowing for the noninvasive visualisation of subsurface structures. Dermoscopy has been shown to increase the accuracy of melanoma diagnosis by 5 to 30%, depending on the type of lesion and the experience of the clinician.[12] In experienced hands, dermoscopy can add vital clinical clues and prevent unnecessary biopsy (Figures 4a and b).

A short period of training can enable the confident diagnosis of benign lesions such as seborrhoeic keratoses, angiomas and junctional naevi, as these lesions often have characteristic dermoscopic appearances. The accurate diagnosis of atypical melanocytic naevi of various kinds and early melanoma requires considerably more experience.

Pigmented melanomas almost universally display evidence of asymmetry of pigment pattern and multiple colours on dermoscopy. Table 4 lists the more specific features of melanoma that should raise significant clinical suspicion if they are seen in any pigmented lesion on dermoscopy (Figure 5).

Differential diagnosis

Table 5 lists the common differential diagnoses to consider when assessing pigmented lesions, and Figures 6 to 10 illustrate these. Often these lesions have clinical or dermoscopic features that differentiate them from malignant or premalignant lesions. However, any lesion deemed suspicious through history or clinical examination should be investigated further. In this situation, management options for patients may include a short period of observation, possibly aided by imaging, excisional biopsy or referral to an appropriate specialist.

Biopsy

An excisional biopsy with 2 mm margins is the preferred method for obtaining tissue for diagnostic purposes. A partial biopsy may lead to misdiagnosis due to

sampling error or an insufficient specimen. Complete excision allows histological examination of lesion architecture and cellular detail, and the accurate assessment of tumour depth for malignant lesions.

An excisional biopsy may not be appropriate in some situations – for example, for large lesions requiring substantial excision or pigmented lesions of the nail apparatus. In these situations, a tissue diagnosis may be obtained through shave or incisional biopsy. Partial biopsies do not adversely affect survival or induce local recurrence or metastasis.[13] A shave biopsy is often used in the diagnosis of the atypical facial pigmented macule, to look for possible early lentigo maligna before definitive excision. Partial biopsies are best undertaken by those with expertise and training in the clinical diagnosis of melanocytic lesions.

Complicated skin closure with tissue flaps should be avoided for excisional biopsies, as flap closure distorts skin architecture and makes the planning for re-excision of malignant lesions more complicated. The use of skin flaps may also interfere with lymphatic drainage and decrease the accuracy of sentinel lymph node biopsy. Wide excision (margins greater than 5 mm) is not recommended for the initial biopsy.

Role of the multidisciplinary treatment centre

Several cities in Australia have multidisciplinary melanoma units for the management of patients with biopsy-proven melanoma or metastatic disease. These units offer comprehensive assessment and advice on all aspects of management including:

- pathology review by an expert dermatopathologist
- dermatological assessment with dermoscopy for the presence of further primary melanomas
- melanoma risk assessment and advice regarding future surveillance including body map imaging
- re-excision, particularly if a complicated closure is required
- advice regarding the role of sentinel lymph node biopsy and staging investigations
- surgery for metastatic disease, including regional lymph node dissections for patients with nodal melanoma
- medical oncology assessment for patients with metastatic disease
- radiation oncology assessment for palliation of metastatic disease and the treatment of certain primary lesions (lentigo maligna and desmoplastic melanoma)
- psychology support and counselling
- recommendations regarding future follow up and management
- advice regarding the most appropriate local resources for optimal local treatment and follow up for those aspects of care that can be undertaken outside a major centre
- support for referring doctors in the ongoing care of their patients.

Referral to such a centre should be considered for patients with with high-risk primary melanomas or metastatic melanoma as well as those melanomas in unusual sites or of unusual type. Anxious patients also often benefit from the opportunity to discuss their concerns in an expert setting and to receive ongoing psychological support if this is indicated.

New techniques and the future of melanoma diagnosis

Computer assisted diagnosis

Various new instruments have recently been developed to assist in the early diagnosis of melanoma. These machines digitally archive clinical and dermoscopic images for future follow up and often provide computerised image analysis as a diagnostic aid. At present they are not a sufficient substitute for clinical judgement and dermoscopic examination. More than 20% of melanomas are nodular or amelanotic, and these instruments are not designed to address such clinically difficult lesions. In addition, they do not take into consideration clinical history and patient risk factors, essential components in establishing thresholds for biopsy of pigmented lesions.

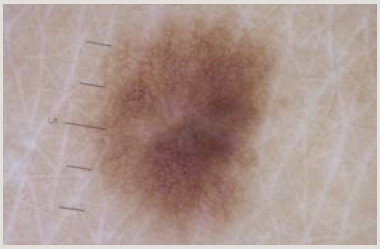
Digital dermoscopy

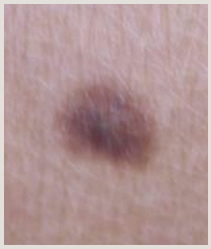
The digital storage of dermoscopic images for the follow up of lesions of concern is an exciting new frontier in dermoscopy. For lesions with an increased but still small potential to

Table 5. Differential diagnoses of pigmented lesions

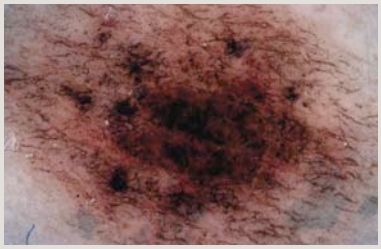
Pigmented lesion	Dermosopic features
Melanocytic naevus (Figure 6)	Symmetrical with regular pigment network and symmetrical structures
Dysplastic and/or atypical naevus (Figure 7)	Atypical pigment net
Seborrhoeic keratosis (Figure 8)	Horn cysts with or without crypts and fissures
Dermatofibroma (Figure 9)	Central hypopigmentation surrounded by delicate pigment network
Haemangioma (Figure 10)	Venous lakes and lacunes

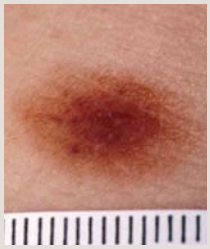
Characteristic dermoscopic appearances of common pigmented lesions



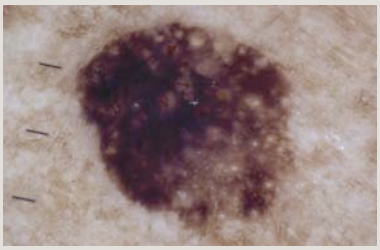


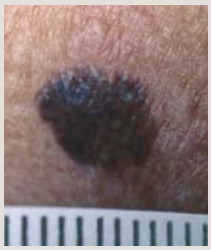
Figures 6a and b. Melanocytic naevus. a (above left). Dermoscopy reveals a regular pigment network. b (above right). Macroscopic image of same lesion.





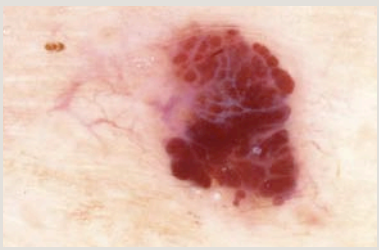
Figures 7a and b. Dysplastic naevus. a (above left). Dermoscopy reveals an atypical pigment net. b (above right). Macroscopic image of same lesion.

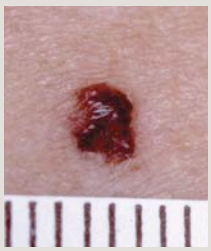




Figures 8a and b. Seborrhoeic keratosis. a (above left). Horn cysts and pseudofollicular openings are seen on dermoscopy. b (above right). Macroscopic image of same lesion.

Figures 9a and b. Dermatofibroma. a (above left). Dermoscopy shows a central scar-like patch and delicate pigment network. b (above right). Macroscopic image of same lesion.





Figures 10a and b. Haemangioma. a (far left). Venous lakes shown on dermoscopy. b (left). Macroscopic image of same lesion.

Scales shown are marked in millimetres.

undergo malignant transformation, such as dysplastic naevi, this technique provides the opportunity to follow lesions, looking for the dermoscopic changes indicating possible evolution into a melanoma before any grossly visible change is evident. In lesions where there is a low level of suspicion for the presence of early melanoma, short term monitoring over a three- to six-month period provides an excellent way to assess lesion stability and minimise rates of unnecessary excision of benign lesions.

Teledermoscopy

Teledermoscopy is a new diagnostic system currently being developed for geographic areas where dermatologists are not available. Advances in internet technology and digital compression software have allowed the transmission of dermoscopic images from remote areas. The feasibility of teledermoscopy has been established in numerous studies, with a similar sensitivity and specificity to that of face-to-face diagnosis.[14] There is also the potential for short or long term digital dermoscopic follow up of single or multiple lesions using teledermoscopy.

Benign to malignant ratio for biopsy

The benign to malignant ratio for biopsy is our best measure of the efficiency of physicians and the abovementioned techniques in the diagnosis of melanoma. In Australia, published ratios vary widely from 30:1 for GPs and skin cancer clinics to 3:1 for expert dermatologists using body map images and dermoscopy. Thus,

large savings to the health system are to be made from the use of these techniques, as well as gains in morbidity and mortality from more effective early melanoma diagnosis.

Conclusion

Melanoma is one of the most common cancers in Australia, and the probability of a GP seeing a patient with melanoma is high. The prognosis of patients with melanoma is directly related to tumour thickness, and so early diagnosis is essential. Although the early detection of melanoma may be challenging, thorough clinical examination can detect most cases. New technologies are being developed to assist in the early diagnosis of melanoma; however, at present they are no substitute for good clinical assessment. MT

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Further reading

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