

The prevention, diagnosis, referral and management of melanoma of the skin: concise guidelines

Julia Newton Bishop, Veronique Bataille, Alice Gavin, Marko Lens, Jerry Marsden, Tania Mathews and Catherine Wheelhouse*

ABSTRACT – Melanoma of the skin is an increasingly common tumour, which often has a slow early growth rate during which curable lesions may be detected and removed. Physicians therefore have the potential to reduce mortality and this guideline is intended to promote early diagnosis of melanoma. The majority of melanomas occur in white-skinned people. The most common risk factors are pale sun-sensitive skin and the presence of increased numbers of melanocytic naevi (moles). Melanoma is more common in women than men; the mean age of onset is 50 years; and a fifth of cases occur in young adults. In the UK population the most common sites are on the lower leg in women, and on the back in men. The predictors of melanoma are progressive change in the shape, size and colour of moles. This guideline provides a series of photographs of moles, melanomas and other skin lesions, which may resemble melanomas.

KEY WORDS: atypical naevi, early diagnosis, superficial spreading melanoma

What is melanoma and what is its epidemiology?

Melanoma of the skin is a malignant tumour, which arises from cutaneous melanocytes. Current UK lifetime risk is about 1:150 for men and 1:120 for women. It is therefore an uncommon cancer in the UK, so most physicians have a limited experience of it and the majority have not had the opportunity to develop diagnostic skills. The incidence of melanoma continues to increase: we have calculated that by 2007 the lifetime risk in men will be 1:120 and in women will be 1:95.

Melanoma is a tumour predominantly of white-skinned people¹ and the incidence correlates with latitude of residence,¹ providing strong evidence that sun exposure is causal. Although it is uncertain what decrement in UV dose reduction might produce a

decrement in melanoma risk, conventional advice to white-skinned populations at risk is to minimise sun exposure. The recent interest in vitamin D as a putative protective agent for other forms of cancer² makes it important that the advice to avoid sun exposure should be targeted at those most at risk [IIB]. It may also be sensible to advise those who avoid the sun to reduce their risk of skin cancer that they should ensure compensatory dietary intake of vitamin D.

Types of melanoma

Table 1 lists characteristics of the four clinical subtypes of melanoma. Figs 1–13 at the end of the article illustrate each type.

Who is at risk of melanoma?

The most important phenotypic markers are an above-average mole count and sun-sensitive skin (Table 2). Individuals with either are at increased risk. The phenotypic markers of sun sensitivity are hair colour (red or blonde hair), blue eyes and particularly freckles [IIA].³

The mean age of diagnosis in the UK is around 50 years, but the age distribution curve is relatively flat

*The Guideline Development Group was convened by the British Association of Dermatologists in conjunction with the Royal College of Physicians.

Concise Guidance to Good Practice Series Editor: **Lynne Turner-Stokes** FRCP

Clin Med 2007;7:283–290

Box 1. Levels of evidence.

Level	Type of evidence	Grade of recommendation
IA	Meta-analysis of randomised clinical trials (RCT) or inception cohort studies	A
IB	At least 1 RCT or well-designed cohort studies with good follow-up	A
IIA	At least 1 well-designed controlled study without randomisation or a meta-analysis of case control studies	B
IIB	At least one study with quasi-experimental design or case-control study	B
III	At least 1 non-experimental study (such as descriptive study)	C
IV	Expert committee reports or reports by recognised authorities	C

*For membership of the Guideline Development Group, see end of paper.

Table 1. Types of melanoma (see Figs 1–13).

Type	Description
Superficial spreading melanomas (Figs 5 and 6)	Slow growing initially: develop horizontally at first for months before they acquire the capacity for invasion. The physician therefore has the potential to diagnose at a curable phase. Commonest type of melanoma.
Nodular melanomas (Fig 10)	Grow more rapidly – vertical growth phase (having acquired the capacity for invasion) from the beginning. More common in older individuals.
Lentigo maligna melanomas (Fig 11)	Slow-growing at first then rapid when become invasive. Develop in a slow-growing precursor pigmented macule called a lentigo maligna or Hutchinson's freckle, which may remain in situ and incapable of metastasis for very many years. However, once a melanoma develops these variants are as aggressive as others of similar thickness. Much more common in people over 60 years old.
Acral lentiginous melanomas (Fig 12)	Rarest type. Found on the soles or palms or under the nail (subungual). Occur in all ethnic groups. Thought to be unrelated to sun exposure aetiologically.

and 20% of cases occur in young adults aged 15 to 39 years old.⁷ Although melanoma remains one of the less common forms of cancer, its occurrence in young people means that it has a large impact in terms of years of life lost.

Where do they occur on the body?

Melanomas may occur anywhere on the skin but they occur particularly as described below.

- Women most commonly develop melanomas on the lower limb (50% of women, 18% of men).⁷
- Men who develop superficial spreading or nodular melanomas most commonly develop them on the trunk (35% of men, 14% of women), especially the back.
- Patients with chronic sun exposure through life commonly develop their melanomas on the head and neck.

What is the relationship between moles and melanoma?

Moles are both markers of risk of melanoma⁴ and precursors. A long-standing mole which starts to change therefore justifies referral. Atypical moles are somewhere on the proliferative continuum from a common mole to a melanoma (Figs 1 to 3) but they rarely progress to melanoma. Like other moles the majority disappear in time but some may progress. An atypical mole which is changing in size, shape or colour should be reviewed by a specialist (see Fig 3).

Table 2. Risk factors for melanoma.

Risk factor	Relative risk (95% confidence interval)	Approximate prevalence in the population
High density freckles (compared with low density)	2.10 (1.24–3.29) ³	17% where a score of 50 or above using Gallagher's freckle score is used*
Red hair (compared with dark hair)	3.64 (2.56–5.37) ³	8%*
101–120 normal moles	6.89 (4.63–10.25) ⁴	6%
5 atypical moles	6.36 (3.80–10.33)	1% with 4 or more in the UK

*The prevalence of these risk factors varies considerably between populations and data within the UK are sparse. The figures given are from studies performed in the UK.^{5,6}

The progression in Diagram 1 is important to recognise, although it must be emphasised that the majority of such moles never progress and indeed disappear as the patient ages. Thus, atypical moles are those that must be monitored but the absolute risk of melanoma is so low that prophylactic excision is not justified.⁸ The indication for removal is to exclude melanoma [IIB].

Patients with many moles, especially clinically atypical moles, are at sufficiently increased risk of melanoma (relative risk

Diagram 1. The progressive development of an atypical mole, into a superficial spreading melanoma over time.

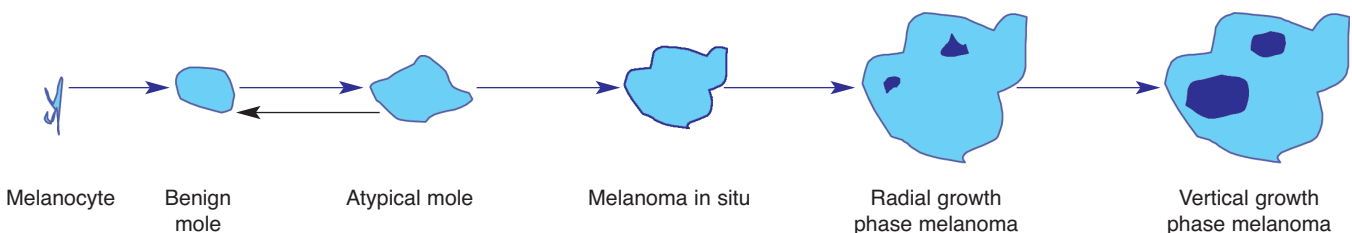


Table 3. Who and when to refer.

Signs and symptoms	How quickly to refer to the dermatologist	Purpose
Moley patient	Within 13 weeks	Risk estimation and education
A new mole which is growing quickly in an adult	Within 2 weeks	Assessment
A long standing mole which is changing in shape and colour	Within 2 weeks	Assessment and treatment
A mole which has: <ul style="list-style-type: none"> • 3 or more colours • lost its symmetry 	Within 2 weeks	Assessment
Any new nodule which is growing, and is pigmented or vascular in appearance	Within 2 weeks	Assessment and biopsy
New pigmented line in a nail	Within 2 weeks	Assessment and probably monitoring or biopsy of the nail bed
Something growing under a nail especially if there is vascular tissue or pigment	Within 2 weeks	Assessment and biopsy

around 10-fold compared with those with few moles, lifetime risk in the order of 1 in 15) to merit referral for assessment. Patients with two or more atypical moles should be referred to a dermatologist for risk assessment and education about self-monitoring, based on the risk of melanoma reviewed in a recent meta-analysis [IIA].⁴ In the UK around 2% of the population have this phenotype [IIB].⁶

What are the symptoms and signs of a melanoma?

Most melanomas are asymptomatic, although some patients report that their melanoma itches or tingles. Vertical growth phase melanomas may also bleed if ulcerated. However, normal moles may itch, particularly if they are inflamed, and they may bleed if caught. Both these symptoms are therefore poor discriminators and are unlikely to be of note unless the mole has changed in appearance over time or has the clinical features of irregularity of shape and colour. Only about 50% of melanomas develop in pre-existing moles – a large proportion appear de novo.

A patient who reports a history of progressive change in the shape, size or colour of a mole should be referred to a dermatologist promptly even if the lesion looks relatively banal. It is very important to realise that melanoma may look unremarkable early in its evolution – simply an asymmetrical and bigger version of the benign mole from which it may have grown. The clue to the diagnosis may lie only in the history.

What are the diagnostic signs of a melanoma?

Superficial spreading melanomas (Figs 5 and 6) are usually:

- larger in surface area than normal moles and increase in size progressively over time. Most (but not all) are therefore 7 mm or greater in diameter when diagnosed

- irregular in colour: commonly three or more different colours (browns, reds, blacks or blue-blacks)
- irregular in shape: lacking in symmetry, with geographical borders.

Nodular melanomas often also have irregular colour (Fig 10) but may be more uniform in colour than superficial spreading melanomas. Such tumours are usually black or red and may be ulcerated.

Lentigo maligna melanomas (Fig 11) may have the appearance of a superficial spreading or nodular melanoma but they arise in a longstanding flat pigmented precursor lesion known as a lentigo maligna. This precursor lesion has the appearance of a freckle but one which is larger, more sharply defined and darker than a normal freckle.

Acral lentiginous melanomas (Fig 12) appear on the palm and sole initially as flat pigmented lesions resembling moles, which start to increase in size and which ultimately develop irregular areas of pigmentation and which sometimes ulcerate. Such melanomas often present late partly because the patient may be unaware of the appearance of the sole of the foot and partly because they may be misdiagnosed as an ulcer, particularly in a diabetic. They may also be hidden by a layer of reactive keratin, appearing as a callus (corn). The diagnostic clue here may be bleeding.

Melanomas which grow under the nail (subungual) (Fig 13) are most common under the thumb nail or the nail of the great toe. They appear always to arise from the nail matrix and therefore first appear at the proximal nail fold. The classical subungual melanoma arises as a narrow pigmented band in the nail, which slowly widens and ultimately produces a subungual mass (often amelanotic and friable) and which lifts up the nail plate and tends to bleed. This form of melanoma is very easy to misdiagnose, commonly as a fungal infection or a pyogenic granuloma.

Table 4. Who not to refer.

Lesions which should not be referred	Suggested management
A typical seborrhoeic wart (basal cell papilloma) (Fig 9)	None needed unless inflamed when referral would be appropriate or curettage with histology
A maturing mole (Fig 2) which is slowly becoming dome shaped and losing its colour	Reassurance provided information is given (ideally written) to seek advice if significant change subsequently occurs

Management

Accurate diagnosis is most likely to result from an accurate history recording and lesion examination, comparison with a previous photograph, and prompt complete excision of suspicious lesions. This clinico-pathological correlation is important because melanoma may clinically and histologically mimic benign lesions and vice versa. It is strongly recommended that incisional or incomplete excisions be avoided, particularly because sampling error may result in inaccurate diagnoses. The British Association of Dermatologists and the Melanoma Study Group guidelines describe the management of melanoma.⁹

Recommendations on referral

Tables 3 and 4 provide details on referral and management for different types of moles and lesions.

Members of the Guideline Development Group

Julia Newton Bishop, Professor of Dermatology, St James’s University Hospital, Leeds; Veronique Bataille, Consultant Dermatologist, West Herts NHS Trust, Hertfordshire; Alice Gavin, General Practitioner, Bradford; Marko Lens, Consultant Plastic Surgeon, King’s College London, Genetic Epidemiology Unit, London; Jerry Marsden, Consultant Dermatologist, University Hospital, Birmingham; Tania Mathews, Lay Representative; Catherine Wheelhouse, Skin Cancer Nurse Specialist, Bradford Teaching Hospitals Foundation Trust.

References

- 1 Parkin DM, Whelan SL, Ferlay J *et al.* *Cancer incidence in five continents*. IARC Scientific Publications No 143, Lyon: International Agency for Research on Cancer, 1997. II.
- 2 Garland CF, Garland FC, Gorham ED *et al.* The role of vitamin D in cancer prevention. *Am J Public Health*, 2005;96(2);209–10.
- 3 Gandini S, Sera F, Cattaruzza MS *et al.* Meta-analysis of risk factors for cutaneous melanoma: III. Family history, actinic damage and phenotypic factors. *Eur J Cancer* 2005;41(14);2040–59.
- 4 Gandini S, Sera F, Cattaruzza MS *et al.* Meta-analysis of risk factors for cutaneous melanoma: I. Common and atypical naevi. *Eur J Cancer* 2005;41(1);28–44.
- 5 Bertram CG, Gaut RM, Barrett JH *et al.* An assessment of the CDKN2A variant Ala148Thr as a nevus/melanoma susceptibility allele. *J Invest Dermatol* 2002;119(4);961–5.
- 6 Bataille V, Bishop JA, Sasieni P *et al.* Risk of cutaneous melanoma in relation to the numbers, types and sites of naevi: a case-control study. *Br J Cancer* 1996;73(12);1605–11.
- 7 Quinn MJ, Babb P, Brock A *et al.* *Cancer trends in England and Wales 1950–1999*. Office for National Statistics Single Market Programme in Services No 66. London: TSO, 2004.
- 8 Tsao H, Bevona C, Goggins W *et al.* The transformation rate of moles (melanocytic nevi) into cutaneous melanoma: a population-based estimate. *Arch Dermatol* 2003;139(3);282–8.
- 9 Roberts DLL, Anstey AV, Barlow RJ *et al.* UK guidelines for the management of cutaneous melanoma. *Br J Dermatol* 2002;146(1);7–17.

Summary of the guidelines

Recommendation	Grade
<p>1 Identifying people at risk</p> <p>People should be considered to have higher risk (approximately 10-fold) of malignant melanoma if they have:</p> <ul style="list-style-type: none"> ● >100 normal moles ● atypical moles ● two or more cases of melanoma in first degree relatives. <p>Lower (approximately 2- to 3-fold) levels of risk are associated with:</p> <ul style="list-style-type: none"> ● freckles ● red hair or skin which burns in the sun ● any family history of malignant melanoma. 	B
<p>2 Primary prevention</p> <ul style="list-style-type: none"> ● People at risk of skin cancer should protect their skin from the sun by avoidance and clothing primarily. ● They should also use a sun protection factor (SPF) of 20 to 30, and five star ultraviolet A (UVA) protection as an adjunct. 	B
<p>3 Secondary prevention</p> <ul style="list-style-type: none"> ● People who are in any of these higher risk (10-fold) categories above should be referred for risk estimation and education directed towards self examination with a dermatologist specialising in moles and pigmented lesions (routine appointment). ● Base-line photography is a useful aid to monitoring moles. 	C
<p>4 Urgent referral to dermatologist</p> <p>The following should be regarded as suspicious lesions requiring urgent referral to a dermatologist within two weeks:</p> <ul style="list-style-type: none"> ● a new mole which is growing quickly over the age of puberty ● a long-standing mole which is changing progressively in shape or colour regardless of age ● any mole which has three or more colours or has lost its symmetry ● any new nodule which is growing and is pigmented or vascular in appearance ● a new pigmented line in a nail ● something growing under a nail ● a mole which has changed in appearance and which is also itching or bleeding. 	B

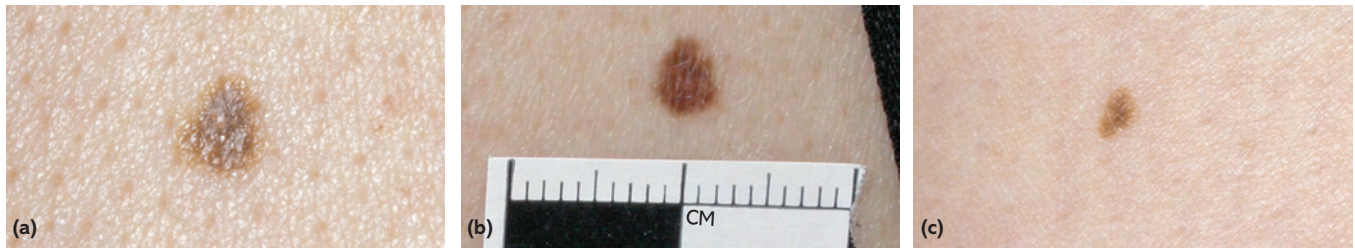


Fig 1. Junctional moles: these are normal moles which develop from early childhood. They are normally less than 5 mm in diameter. The risk of melanoma from any such mole is extremely low but patients should be aware that they should seek advice if there is any change in shape, size or colour.



Fig 2. Mature 'dermal' moles. Over time, particularly on the trunk and face, moles often mature into smooth dome-shaped lesions. This change in shape may cause concern, but the symmetry and slow rate of change is reassuring. These moles have an extremely low risk of change and should be left in situ.



Fig 3. Moderately atypical moles. These are moles which are behaving atypically in that they are becoming irregular in shape, larger (usually over 5 mm in diameter) and may have variable colours. These moles are more likely to evolve into melanoma and should therefore be reviewed at 3 months for change, although the absolute risk of malignant change is very low.

Fig 4. Severely atypical moles/melanoma in situ. These moles are evolving into melanoma and show more marked variation in shape and colour. Early melanomas often look inflamed, as can be seen in both these examples. Lesions like these should be referred urgently (within two weeks) to a dermatologist.

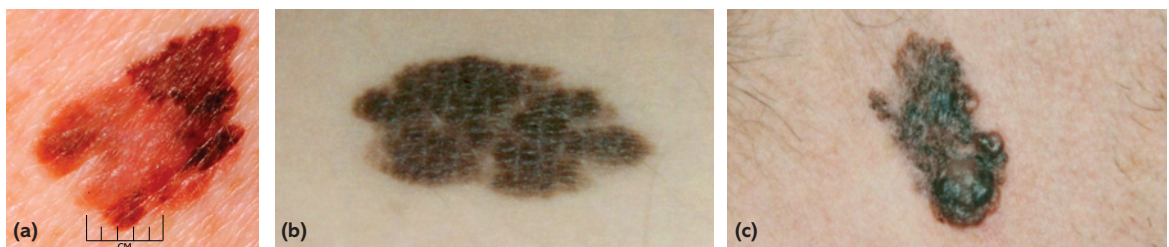
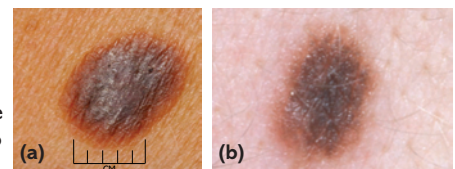


Fig 5. Superficial spreading melanomas progressively become more irregular in shape and colour over time. Two-week rule referral is essential.

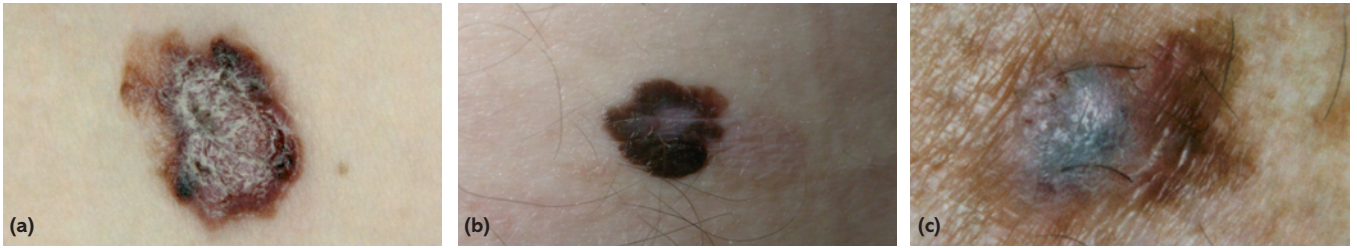


Fig 6. Superficial spreading melanoma: showing irregularity of shape and colour. Melanomas tend to have several different colours: browns, blacks, greys and reds. The continuum of progressive change in appearance is evident.

Fig 7. Superficial spreading melanomas with nodular elements. Superficial spreading melanoma evolves slowly over time: often over many months, if not years. Ultimately, however, nodular elements develop corresponding to a vertical growth phase, associated with much higher risk of metastasis.

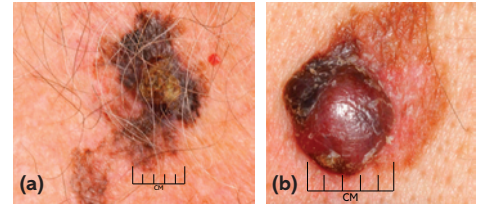


Fig 8. Differential diagnosis dermatofibromas are firm dermal nodules which appear slowly, often on the limbs. Although they may have a pigmented halo as seen in the lesion on the left, they are symmetrical. The symmetry, firm nature and very slow change are reassuring. Such lesions do not require referral.

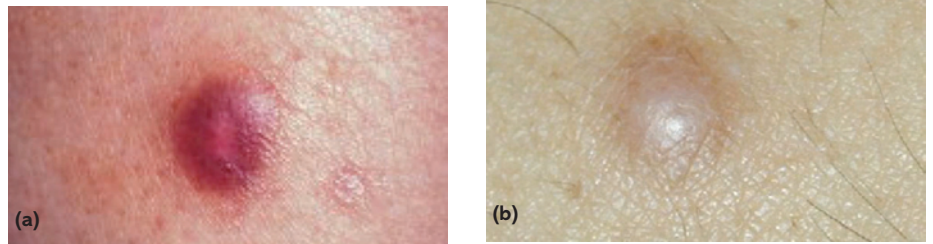


Fig 9. Differential diagnoses: seborrhoeic warts (basal cell papillomas) may be variably pigmented but have a 'stuck on' appearance. Refer if the pigment is variable: rarely nodular melanomas may be difficult to distinguish from warts.

Fig 10. Nodular melanomas: the melanoma on the left is amelanotic. There is no visible pigment. Nodular melanomas exhibit vertical growth phase from the beginning and therefore tend to be thicker and to have a poorer prognosis than superficial spreading melanomas.

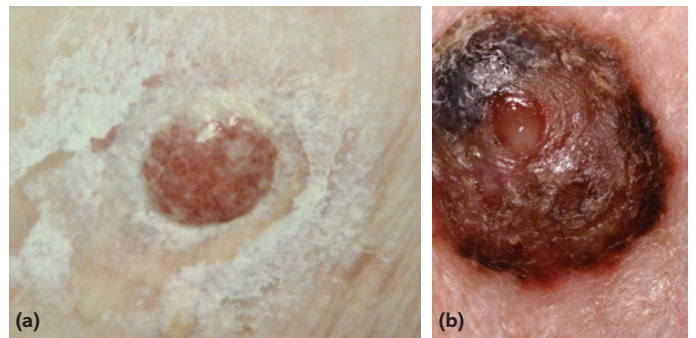


Fig 11. Lentigo maligna melanomas arise in precursor in situ lesions called lentigo maligna or Hutchinson's freckle. The growth rate of the precursor lesion is very slow but once invasive disease develops these melanomas behave prognostically like superficial spreading melanomas.

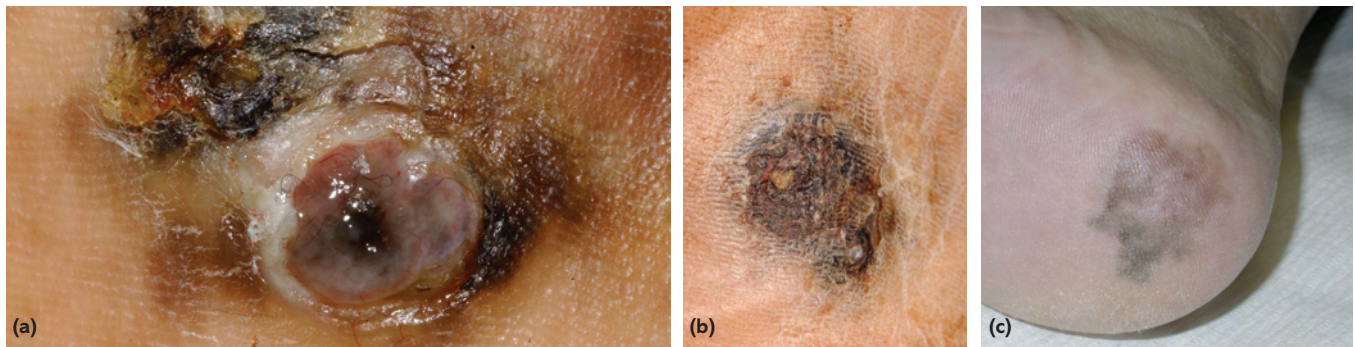
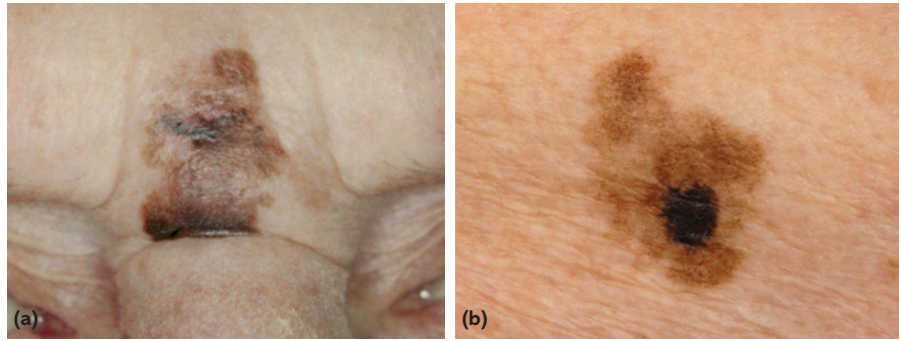


Fig 12. Acral lentiginous melanomas: an early lesion is seen in (c). There is subtle pigmentation which is extensive and irregular. The other two melanomas are much more advanced and there is reactive hyperkeratosis. It is easy to miss these tumours. Beware of scaly lesions or chronic ulcers on the sole of the foot and refer to the dermatologist for advice if in doubt.

Fig 13. Early subungual melanomas are difficult to diagnose. Image (a) shows a melanoma which has disrupted the normal growth of the nail but in which there is no clear pigment. More typically there is a narrow pigmented longitudinal band which gets wider over time. The other two images (b and c) show advanced tumours.

