

CONCISE GUIDANCE TO GOOD PRACTICE

A series of evidence-based guidelines for clinical management

NUMBER 7

The prevention, diagnosis, referral and management of melanoma of the skin

CONCISE GUIDELINES

September 2007



Clinical Standards Department

The purpose of the Clinical Standards Department of the Royal College of Physicians is to improve patient care and healthcare provision by setting clinical standards and monitoring their use. We have expertise in the development of evidence-based guidelines and the organisation and reporting of multicentre comparative performance data. The department has three core strategic objectives: to *define* standards around the clinical work of physicians; to *measure* and evaluate the implementation of standards and its impact on patient care; and to effectively *implement* these standards.

Our programme involves the relevant specialist societies, patient groups and national bodies including the National Institute for Health and Clinical Excellence (NICE), the Healthcare Commission and the Health Foundation.

Concise Guidance to Good Practice series

The concise guidelines in this series are intended to inform those aspects of physicians' clinical practice which may be outside their own specialist area. In many instances the guidance will also be useful for other clinicians including GPs and other healthcare professionals.

The guidelines are designed to allow clinicians to make rapid, informed decisions based wherever possible on synthesis of the best available evidence and expert consensus gathered from practising clinicians and service users. A key feature of the series is to provide both recommendations for best practice, and where possible practical tools with which to implement it.

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These guidelines were developed by a multidisciplinary group to promote the early diagnosis of melanoma of the skin. This increasingly common tumour 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 these guidelines are intended to aid physicians, GPs and other health professionals in their ability to recognise 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 and the mean age of onset is 50 years but a fifth of cases occur in young adults. In the UK population the most common site is 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. These guidelines provide a series of photographs of moles, melanomas and other skin lesions, which may resemble melanomas. The purpose of these guidelines is to provide physicians, GPs and other relevant healthcare professionals with a practical guide to the recognition of melanoma on the skin.

Methodology

These guidelines were developed by a multiprofessional Guideline Development Group including representatives from specialist nursing, general practice, plastic surgery, in addition to dermatology.

A literature search was carried out using the following databases: Medline, Embase, Cochrane Library. The literature was appraised and articles not published in English were excluded. Much of the advice is based on expert opinion and practice because of a lack of other evidence.

The guidelines were prepared in accordance with the principles laid down by the AGREE Collaboration (Appraisal of Guidelines for Research and Evaluation). A summary of the guideline development process is given in [Appendix 1](#).

The system used to grade the evidence and guidance recommendations has been adapted from that used by SIGN ([Appendix 2](#)). These are indicated in bold type throughout the text, such as **[IIB]**.

Summary of the guidelines

| <i>Recommendation</i> | <i>Grade</i> |
|---|--------------|
| 1 Identifying people at risk People should be considered to have higher risk (approximately 10-fold) of malignant melanoma if they have: <ul style="list-style-type: none">• >100 normal moles• atypical moles• two or more cases of melanoma in first degree relatives. Lower (approximately 2- to 3-fold) levels of risk are associated with: <ul style="list-style-type: none">• freckles• red hair or skin which burns in the sun• any family history of malignant melanoma. | B |
| 2 Primary prevention <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 |
| 3 Secondary prevention <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 |
| 4 Urgent referral to dermatologist The following should be regarded as suspicious lesions requiring urgent referral to a dermatologist within two weeks: <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 |

Introduction

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. In the UK, melanoma is diagnosed at a mean age of around 50 years but a fifth of cases occur in young adults. So while it is one of the less common forms of cancer, it has a large impact in terms of years of life lost. These guidelines have been developed to help healthcare professionals recognise early predictors of melanoma, using the series of photographs provided, and thus to help reduce mortality.

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.

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 [11B]. 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 booklet illustrate each type (pp10–12.)

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. |

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}

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 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 here:

- 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.

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

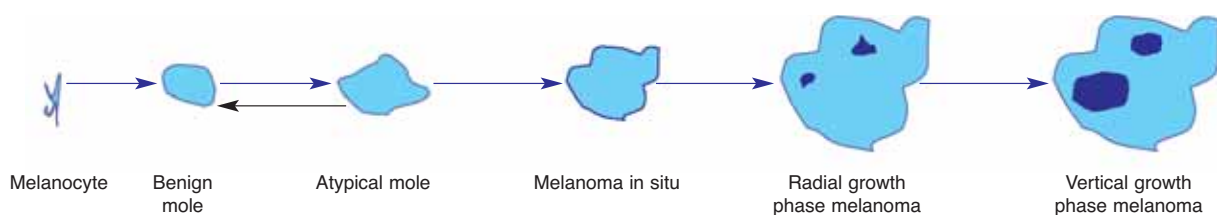


Table 3. Who and when to refer.

| 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 |

An atypical mole which is changing in size, shape or colour should be reviewed by a specialist (see Fig 3).

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 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.

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 |

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.

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

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

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Appendix 1. Guideline development process

The guidelines have been developed in accordance with the principles laid down by the AGREE collaboration (Appraisal of Guidelines for Research and Evaluation).

Scope and purpose

| | |
|-------------------------------------|---|
| Overall objective of the guidelines | To improve the prognosis for melanoma patients by increasing the awareness of melanoma in physicians and therefore by promoting secondary prevention. |
| The patient group covered: | Individuals at risk of melanoma. |
| Target audience | All clinicians, including general physicians, GPs and other health professionals who are involved in examining patients and therefore their skin. |
| Clinical areas covered | How to recognise melanoma; what to do if the diagnosis is suspected. |

Stakeholder involvement

| | |
|---------------------------------|---|
| The Guideline Development Group | A multidisciplinary group comprising: professionals: consultants in dermatology, plastic surgery, a melanoma specialist nurse and a general practitioner user representation: a patient, Tania Mathews. |
| Funding | This guideline was commissioned and edited by the British Association of Dermatologists and the Clinical Standards Department of the Royal College of Physicians. |
| Conflicts of interest | No external funding has been sought or obtained. All authors and group members have declared, and provided details, of any actual or potential conflicts of interest. |

Rigour of development

| | |
|--|---|
| Evidence gathering | Evidence for these guidelines was provided by review of Cochrane Library, Medline, Embase, conference proceedings and other guidelines up to October 2005. Articles not published in English were excluded. Much of the advice is based on expert opinion and practice because of a lack of other evidence. |
| Links between evidence and recommendations | The system used to grade the evidence and guidance recommendations is adapted from that published by the Scottish Intercollegiate Guidelines Network. These are indicated in bold type throughout the text, such as [IIB]. |
| Piloting and peer review. | Not yet piloted. |

Implementation

| | |
|------------------|---|
| Plans for update | Review is planned for 3 years time, and forms part of the work undertaken by the British Association of Dermatologists. |
|------------------|---|

Appendix 2. Grading system for recommendations adapted from the Scottish Intercollegiate Guidelines Network (SIGN) methodology

| <i>Level</i> | <i>Type of evidence</i> | <i>Grade of recommendation</i> |
|--------------|--|--------------------------------|
| IA | Meta-analysis of randomised clinical trials (RCT) or inception cohort studies | A |
| IB | At least one RCT or well-designed cohort studies with good follow-up | A |
| IIA | At least one 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 one non-experimental study (such as descriptive study) | C |
| IV | Expert committee reports or reports by recognised authorities | C |



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.

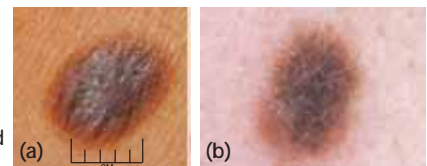


Fig 5. Superficial spreading melanomas progressively become more irregular in shape and colour over time. Two-week rule referral is essential.



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.

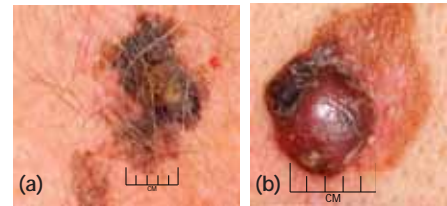


Fig 8. Differential diagnosis dermatofibromas are firm dermal nodules which appear slowly, often on the limbs. Although they may have a pigmented halo as seen in the lesion on the left, they are symmetrical. The symmetry, firm nature and very slow change are reassuring. Such lesions do not require referral.

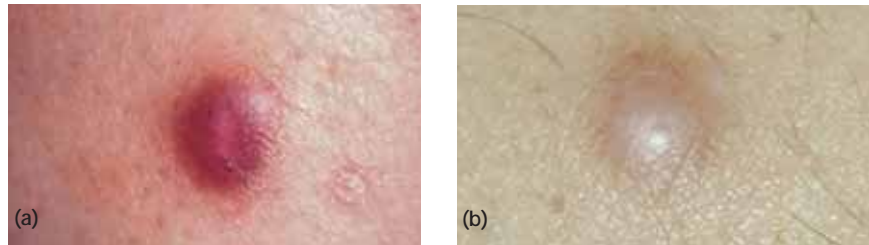


Fig 9. Differential diagnoses: seborrhoeic warts (basal cell papillomas) may be variably pigmented but have a 'stuck on' appearance. Refer if the pigment is variable: rarely nodular melanomas may be difficult to distinguish from warts.

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.

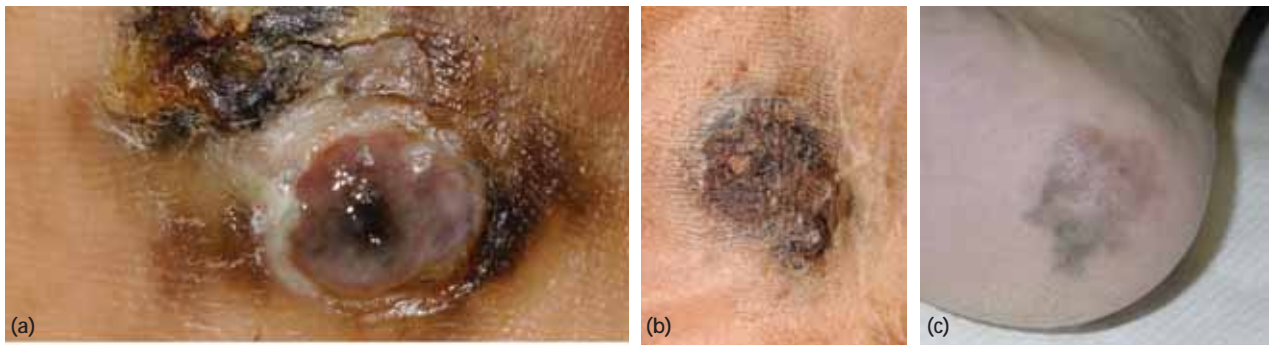
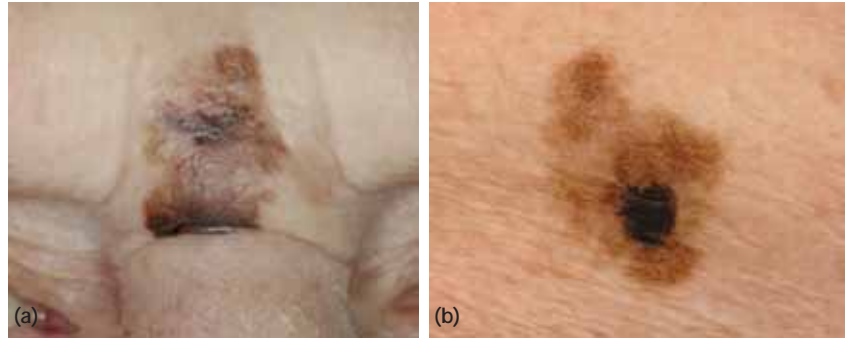


Fig 12. Acral lentiginous melanomas: an early lesion is seen in (c). There is subtle pigmentation which is extensive and irregular. The other two melanomas are much more advanced and there is reactive hyperkeratosis. It is easy to miss these tumours. Beware of scaly lesions or chronic ulcers on the sole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

