

GUIDELINES

U.K. guidelines for the management of cutaneous melanoma

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Summary

These guidelines for management of cutaneous melanoma present evidence-based guidance for treatment, with identification of the strength of evidence available at the time of preparation of the guidelines, and a brief overview of epidemiological aspects, diagnosis and investigation. To reflect the collaborative process for the U.K., they are subject to dual publication in the *British Journal of Dermatology* and the *British Journal of Plastic Surgery*.¹

Disclaimer

These guidelines reflect the best published data available at the time the report was prepared. Caution should be exercised in interpreting the data; the results of future studies may require alteration of the conclusions or recommendations in this report. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. Just as adherence to the guidelines may not constitute defence against a claim of negligence, so deviation from them should not necessarily be deemed negligent.

Introduction

These consensus guidelines have been drawn up by a multidisciplinary working party with membership drawn from a variety of groups and co-ordinated by the Melanoma Study Group and the British Association of Dermatologists. The guidelines deal with aspects of the management of melanoma from the prevention of melanoma through the stages of diagnosis and initial treatment to palliation of advanced disease. Levels of evidence to support the guidelines are quoted according to the criteria stated in Table 1.

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Contribution to these guidelines has been made by a large number of clinicians who are members of the Melanoma Study Group and the British Association of Dermatologists. They have also been endorsed by or have had input from representatives of the following groups or organizations: the Royal College of Physicians, London; the Royal College of Pathologists (pathology section only); the Department of Health; the British Association of Plastic Surgeons, London; the Royal College of Radiologists, London; the Specialty Advisory Board in Plastic Surgery of the Royal College of Surgeons of Edinburgh; the Royal College of Surgeons of England; the Royal College of General Practitioners, London.

Members of the British Association of Dermatologists Therapy Guidelines and Audit subcommittee are: N.H.Cox (Chairman), A.V.Anstey, C.B.Bunker, M.J.D.Goodfield, A.S.Highet, D.Mehta, R.H.Meyrick Thomas and J.K.Schofield.

The Multiprofessional Skin Cancer Committee representing the British Association of Dermatologists, the British Association of Plastic Surgeons and members of the Faculty of Clinical Oncology of the Royal College of Radiologists consisted of: N.H.Cox (Chairman), A.Y.Finlay, B.R.Allen, D.Murray, R.W.Griffiths, A.Batchelor, D.Morgan, J.K.Schofield, C.B.Bunker, N.R.Telfer, G.B.Colver, P.W.Bowers and the authors.

¹Because of the dual publication, the style of this paper is not that normally used for official *BJD* guidelines.

Table 1. Levels of evidence on which the guideline is based

Level	Type of evidence
Ia	Evidence obtained from meta-analysis of randomized controlled trials
Ib	Evidence obtained from at least one randomized controlled trial
IIa	Evidence obtained from at least one well-designed controlled study without randomization
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities
Grade of recommendation	
A	There is good evidence to support the use of the procedure
B	There is fair evidence to support the use of the procedure
C	There is poor evidence to support the use of the procedure
D	There is fair evidence to support the rejection of the use of the procedure
E	There is good evidence to support the rejection of the use of the procedure

Due to the process of producing unified guidelines, the quality of evidence grading used in these guidelines differs slightly from that used in other British Association of Dermatologists current guidelines; the strength of recommendations grading is the same as used in other publications.

The consultation process for British Association of Dermatologists guidelines has been published elsewhere.¹ Where no level is quoted the evidence is to be regarded as representing level IV (i.e. a consensus statement). The intention of the working party was to come to a consensus about current best practice for the management of this type of cancer in the belief that the development of such a consensus will promote good standards of care across the whole country. The guidelines are, however, guidelines only. Care should be individualized wherever appropriate.

The guidelines are also intended to promote the integration of care between medical and paramedical specialties for the benefit of the patient. Multidisciplinary care of the patient is held to be the most desirable model as recommended in the report of Calman and Hine.² The guidelines document is concerned with a national consensus but it is hoped that it will assist regional groups in defining local policies.

Caution should be exercised in interpreting the data; the results of future studies may require alteration of the conclusions or recommendations in this report. Possible audit points for melanoma are given in Appendix 1. These guidelines are planned to be updated in 2003.

Prevention of melanoma

Individuals, and particularly children, should not get sunburnt (level III).^{3,4} White-skinned individuals should limit their total cumulative sun exposure through life.^{5,6} Lesions that are not obviously benign, or changing moles, should be seen by family doctors and either removed in their entirety for pathological

examination, or referred and dealt with by appropriately trained specialists (level III).

Clinical diagnosis of melanoma

The seven-point checklist emphasizing a history of change in size, shape and colour of a pre-existing pigmented lesion is recommended for use for both patient and general practitioner education.⁷

Major features are:

- change in size;
- irregular shape;
- irregular colour.

Minor features are:

- largest diameter 7 mm or more;
- inflammation;
- oozing;
- change in sensation.

Lesions with any of the major features or three minor ones are suspicious of melanoma.⁸ Suspicious lesions should ideally be seen by specialists, that is, clinicians routinely treating large numbers of patients with pigmented lesions. Where suspicious lesions are biopsied they should be removed completely and sent for histopathological examination.

Referral

Early recognition of malignant melanoma presents the best opportunity for cure. It is therefore incumbent on dermatologists to provide a service that allows rapid access for diagnosis and management, particularly in view of the Government's suggestion that patients with potential malignant melanoma should be seen within

2 weeks of receipt of a referral letter from the general practitioner. Clearly identified 'pigmented lesion clinics' have been shown to be an effective means of providing rapid access to expert medical services for patients with pigmented lesions, although they may have little impact on melanoma mortality at a population level.^{9,10}

Recommendations for referral

- Patients with lesions suspicious of melanoma should be referred urgently to a dermatologist or surgeon/plastic surgeon with an interest in pigmented lesions.
- These specialists should ensure that a system is in place to enable patients with suspicious lesions to be seen within 2 weeks of receipt of the referral letter.
- All patients who have had lesions removed by their general practitioner that are subsequently reported as melanoma should be referred immediately to specialists.

(Grade C, level III)

Initial assessment and management

Any patient with a pigmented lesion that the specialist feels is clinically suspicious of melanoma should have a full skin examination. The site and size of the pigmented lesion should be documented and a record should be made of other pigmented lesions. Clinical photographs may be helpful. The patient should be carefully examined for lymphadenopathy and hepatomegaly.

Recommendations for record keeping of clinical features

As a minimum, the following should be included:

- History (the presence or absence of these changes should be recorded):
 - Change in size
 - Change in colour
 - Change in shape
 - Symptoms (itching, bleeding etc.)
- Examination
 - Site
 - Size
 - Description (noting irregular margins, irregular pigmentation and ulceration if present)
 - Other pigmented lesions
 - Any regional lymphadenopathy
 - Examination for hepatomegaly

(Grade B, level III)

Screening and surveillance of high-risk individuals

Primary care teams, as well as cancer units and centres, have a responsibility to raise public awareness of skin cancer. The incidence of melanoma in the U.K. is approximately 10 cases per 100 000 per annum.¹¹⁻¹³

There are some individuals at higher risk of melanoma who should be considered for referral to specialist clinics. These individuals can be divided broadly into two groups based upon the degree of risk.

1 Individuals at moderately increased risk (approximately 8–10 times that of the general population) should be counselled about this risk and taught how to self-examine for changing naevi, but very long-term follow-up is not usual. Such patients are those with either a previous primary melanoma¹⁴ or large numbers of moles, some of which are clinically atypical.^{15,16}

2 Those at greatly increased risk of melanoma (at least 100 times that of the general population). Patients with a giant congenital pigmented hairy naevus^{17,18} (definitions include: '20 cm or more in diameter' and '5% of body surface area') should be monitored by an expert for their lifetime because of the risk of malignant change, which is significant but poorly quantified. Excision biopsy of suspicious areas in large congenital naevi may be necessary but requires expert histopathological review. By contrast, surgical excision of small congenital naevi is not considered necessary in the absence of suspicious features.

Patients with a strong family history of melanoma are also at greatly increased risk. Those with three or more cases of melanoma in the extended family should be referred to appropriate clinics managing inherited predisposition to cancer (involving dermatologists and/or clinical geneticists) for counselling. It is the consensus of the Melanoma Genetics Consortium that it is premature to suggest gene testing but this may change as more information regarding the genes predisposing to melanoma becomes available.¹⁹ The risk associated with the presence of two family members affected with melanoma is lower. In these families, if affected individuals also have the atypical mole syndrome, or if there is a history of multiple primary tumours in an individual, then referral should also be made for counselling; otherwise, family members should probably be considered at moderately increased risk.

This group of particularly high-risk individuals should be advised on the specific changes that suggest

melanoma and encouraged to undertake monthly self-examination (level III). Photography may be a useful adjunct to detecting early melanoma in either of these high-risk groups (level III).

Recommendations for screening and surveillance of high-risk individuals

- Patients who have already had a melanoma or who have the atypical mole syndrome are at moderately increased risk of another primary, and should be advised of this and taught how to recognize a melanoma.
- Patients with giant congenital pigmented naevi are at increased risk of melanoma and require long-term follow-up.
- The prophylactic excision of small congenital naevi is not recommended.
- Individuals with a family history of three or more cases of melanoma should be referred to a Department of Clinical Genetics for counselling. Those with two cases in the family may also benefit, especially if one of the cases had multiple primary melanomas or the atypical mole syndrome.

(Grade B, level IIa)

Biopsy of suspected melanoma

Excision of a lesion suspected to be melanoma should be performed as a full-thickness skin biopsy to include the whole tumour with a 2–5-mm clinical margin of normal skin laterally and with a cuff of subdermal fat. This allows confirmation of the diagnosis, such that subsequent definitive treatment can be based on Breslow thickness.

Shave and punch biopsies are not recommended because they will at the very least make the pathological staging of the lesion impossible (level III). Incisional biopsy is occasionally acceptable, for example in the differential diagnosis of lentigo maligna on the face or of acral melanoma, but there is no place for incisional biopsy in primary care (level III). There is little evidence that incisional biopsies of melanoma affect the prognosis^{20,21} although one paper suggests that there may be an adverse effect in lesions situated on the head and neck.²²

Biopsies of possible subungual melanomas should be carried out by surgeons regularly doing such biopsies. The nail should be removed and clinically obvious tumour or, in the absence of a mass, the nail matrix should be adequately sampled.

Prophylactic excision of pigmented lesions or of small congenital naevi in the absence of suspicious features is futile and not to be recommended.

Histopathology

Recommendations for the reporting of tissues removed as part of the surgical treatment of cutaneous melanoma have been published in an international consensus statement supplemented by a proposed final revised staging system for cutaneous melanoma published recently.²³ Table 2 gives the recommended American Joint Committee on Cancer staging system.

Pathology request forms must be accurately completed and give full identification details. The whole lesion should be adequately sampled, probably by serial transverse slicing of the biopsy at approximately 2-mm intervals, processing all of the slices and examining sections cut at three levels. The pathologist's report should include the following minimum data:

- The site of the tumour.
- The type of surgical procedure: excision or re-excision, incision biopsy, punch biopsy, shave biopsy, curettage, other.
- A full description of the macroscopic appearance of the tumour, and the dimensions of the specimen in millimetres.
- When possible, a statement of whether the lesion is primary, locally recurrent or metastatic to the site.
- Whether there is ulceration.
- The Breslow thickness of the tumour, measured from the granular layer of the epidermis to the base of the tumour, to the nearest 0.1 mm. Ulcerated tumours should be measured from the base of the ulcer to the base of the tumour. Tumour forming a sheath around appendages should be excluded when making measurements.
- The depth of penetration of the dermis (Clark's level) may also be stated, although this is a less reliable indicator of prognosis than Breslow thickness in most circumstances.
- The presence of radial growth phase tumour alone or vertical growth phase.
- The frequency of mitotic figures mm^{-2} (vertical growth phase only).
- The presence or absence of tumour regression.
- The presence (and, if present, the degree) or absence of a lymphocytic inflammatory infiltrate in, or in response to, the tumour (level II).
- The presence of any obvious lymphatic or vascular invasion or perineural invasion.

Table 2. The new 2001 American Joint Committee on Cancer (AJCC) staging system

Stage	Primary tumour (pT)	Lymph node (N)	Distant metastases (M)
0	<i>In situ</i> tumours	No nodes	None
IA	< 1.0 mm, no ulceration	No nodes	None
IB	< 1.0 mm with ulceration	No nodes	None
IIA	1.01–2.0 mm, no ulceration	No nodes	None
	1.01–2.0 mm with ulceration	No nodes	None
IIB	2.01–4.0 mm, no ulceration	No nodes	None
	2.01–4.0 mm with ulceration	No nodes	None
IIC	> 4.0 mm with ulceration	No nodes	None
IIIA	Any Breslow thickness, no ulceration	Micrometastases in nodes	None
IIIB	Any Breslow thickness with ulceration	Micrometastases in nodes	None
	Any Breslow thickness, no ulceration	Up to three palpable nodes	None
	Any Breslow thickness ± ulceration	No nodes but in-transit metastases or satellites	None
IIIC	Any Breslow thickness with ulceration	Up to three palpable nodes	None
	Any Breslow thickness ± ulceration	Four or more palpable nodes or matted nodes or in-transit metastases with nodes	None
IV			None M1: skin, subcutaneous or distant lymph nodes M2: lung M3: all other sites or any site with raised lactate dehydrogenase

The AJCC staging system is recommended for general use.⁵⁸

- The histogenetic type of melanoma, including the presence of desmoplasia and/or neurotropism.
- The presence of microsatellites.
- Whether excision is complete, and the minimum margin of excision to peripheral or deep surgical margin, measured in millimetres. If excision is not complete, the residual disease should be identified as *in situ* or invasive.
- Pathological staging (TNM) and coding (e.g. SNOMED code).

Definitive treatment of the primary lesion

Surgical excision margins for invasive melanoma depend on the Breslow thickness as measured by the histopathologist and are based on two randomized clinical trials^{24,25} and a National Institutes of Health Consensus Panel.²⁶ The recommended surgical margins are those measured clinically at the time of surgery, rather than the histopathological margins measured microscopically. The margins suggested may need to be adjusted for cosmetic or functional reasons, for example around the eye.

Lentigo maligna

Initial incisional biopsy is appropriate for changing flat pigmented lesions on the face that may represent lentigo maligna, although sampling problems occa-

sionally mean that biopsies may not be representative of the whole lesion.

Histologically confirmed lentigo maligna is best treated by complete excision because of the risk of invasive change. The risk of progression is, however, poorly established and in the very elderly may be unlikely within their lifespan. Therefore, for some particular clinical situations, treatment by other methods such as radiotherapy, cryotherapy or observation only^{27–30} may be appropriate, although the risk of recurrence is higher than with surgery.^{31–33} If the patient with lentigo maligna is treated by non-surgical means then the reason for this choice should be clearly documented.

Lentigo maligna and other *in situ* melanomas have no potential for metastatic spread and the aim should be to excise the lesion completely with a clear histological margin. No further treatment is then required. Local recurrence of other types of *in situ* melanoma is rare, but recurrence of lentigo maligna is common and is usually attributed to a 'field effect', whereby atypical melanocytes extend laterally along the epidermis but are not clinically detectable.³⁴

Lesions less than 1 mm in depth

The recommended surgical margins are based on the World Health Organization Trial.²⁵ This randomized trial compared 1-cm and 3-cm margins for melanomas

up to 2 mm thick. No local recurrences were seen in patients with melanomas less than 1 mm in depth with either excision margin, and a 1-cm margin was deemed safe and appropriate for these lesions. Thin tumours less than 0.75 mm in Breslow thickness without vertical growth phase are commonly excised with a 0.5-cm margin or even less.^{35,36} It is the consensus view that this margin is probably adequate but there are no data to support this conclusion.

Lesions 1–2 mm in depth

There have been two large randomized studies that have included patients in this category. The World Health Organization Study²⁵ showed no difference in overall patient survival between 1-cm and 3-cm margins in this group. However, there were four patients who developed local recurrences as the first sign of relapse. All these patients had undergone 1-cm excision and each had a primary lesion between 1 and 2 mm thick. The authors were therefore cautious in recommending 1-cm margins for this group and suggested that 2-cm margins may be more appropriate until further follow-up is completed. It is recommended that the decision about margin should be made by the multidisciplinary team after discussion with the patient but that a 1-cm margin should be the minimum where functionally and cosmetically sensible. The Intergroup Melanoma Trial compared 2-cm vs. 4-cm margins of excision for lesions of 1–4 mm in depth.²⁴ No difference was seen between the two groups in either local recurrence or survival. Margins greater than 2 cm are therefore inappropriate in this group.

Lesions 2–4 mm in depth

On the basis of the Intergroup Melanoma Trial it has been shown that there is no difference between 2-cm

and 4-cm margins for this group, in either overall survival or recurrence rates.²⁴ The results of a randomized trial comparing 1-cm with 3-cm margins are awaited. It seems reasonable to suggest, on the basis of published evidence, that 2-cm margins are safe and should be taken where possible.

Lesions greater than 4 mm in depth

Deeper tumours have not been included in any of the randomized studies. The local recurrence rate is high and metastatic spread is common. It would seem reasonable to suggest margins of 2 cm and that there is probably no advantage in margins over 3 cm, but data to confirm this are limited.³⁷

Recommended surgical excision margins

Please see Table 3 for recommendations.

Investigations for patients with melanoma

No investigations are necessary for patients with stage I disease. Stage I and IIA melanoma patients should not be staged by imaging, as the true-positive pick-up rate is low and the false-positive rate is high.^{38,39}

Patients at intermediate or high risk of recurrent disease (stage IIB and over) should have the following staging investigations: chest X-ray; liver ultrasound or computed tomographic (CT) scan with contrast of chest, abdomen ± pelvis; liver function tests/lactate dehydrogenase; and full blood count. In the absence of effective chemotherapy for melanoma, however, it may be reasonable to omit scanning in individual stage IIB patients. There is no place for a bone scan in staging except where symptoms point to possible bone disease.

Table 3. Recommended surgical excision margins

Breslow thickness	Excision margins	Approximate 5-year survival	Grading of evidence
<i>In situ</i>	2–5-mm clinical margins to achieve complete histological excision	95–100% ^a	Level B, grade III
Less than 1 mm	1 cm (narrower margins are probably safe in lesions less than 0.75 mm in depth)	95–100%	Level A, grade I
1–2 mm	1–2 cm	80–96%	Level A, grade I
2.1–4 mm	2–3 cm (2 cm preferred)	60–75%	Level A, grade I
Greater than 4 mm	2–3 cm	50%	Level B, grade III

^aIn theory recurrence should never occur after *in situ* melanoma, but occasional cases do recur.^{59,60} The assumption is that regression at diagnosis obscured a more advanced tumour, or that progression occurred after incomplete removal of the *in situ* disease.

Ideally, patients with stage IIB or more advanced melanoma should be managed in a Cancer Centre by a skin cancer multidisciplinary team, either *in toto* or as shared care with a Cancer Unit. This team should include a dermatologist, surgeon, oncologist, pathologist, radiologist, counsellor, specialist nurse and palliative care specialist. Communication with the primary health care team should be optimized.

Adjuvant therapy

There are no adjuvant therapies of proven benefit for melanoma as yet, but several clinical trials are actively recruiting patients. Patients at intermediate or high risk of relapse should be referred to the multidisciplinary team based at a Cancer Centre, staged (see investigations list above; these may vary according to study protocol) and considered for a trial of adjuvant therapy without delay (stages IIB, IIC or III). Most trials require entry within 8 weeks of completion of surgery and therefore this referral to the Cancer Centre should be prompt.

Patients should be offered entry into clinical trials wherever possible. This is particularly important in the context of adjuvant therapy. Clinicians involved in the care of patients with melanoma should regularly update themselves on the clinical trials available to their patients. This can be done through the local Cancer Centre or the Melanoma Group of the National Cancer Research Institute (tel.: 020 7269 3548). Entry criteria vary but, in general, those with stage IIB or stage III disease can be considered, although this may change with time.

There is currently no standard adjuvant systemic therapy for patients with melanoma. In the U.S.A., following the ECOG 1684 trial the 'Kirkwood' high-dose interferon regimen is regarded as standard therapy for patients at high risk of recurrence⁴⁰ although the ECOG 1690 trial was non-confirmatory.⁴¹ A recent study comparing 1 year's treatment with high-dose interferon with a vaccine to gangliosides (anti-GM2) was closed after interim analysis because of apparently better survival of the interferon-treated group.⁴² Further trials continue to be reported. Views on standard therapy may be modified in light of further information from other trials. Although interferon is now licensed for adjuvant use in the U.K., a second confirmatory trial with mature data is considered necessary before this regimen can be recommended as standard treatment, not least because of the side-effects commonly

experienced. Adjuvant therapies should be delivered by specialists.

The role of vaccines as adjuvant therapies remains to be established.

There is no role for adjuvant isolated limb perfusion (ILP)⁴³ (level Ib), although it may have a role in preoperative reduction of tumour volume.

Recommendations for investigations and adjuvant therapy

- Stage I and IIA melanoma patients should not be staged by imaging as the true-positive pick-up rate is low and the false-positive rate is high. This recommendation would be revised if effective therapy for visceral melanoma were identified (grade A, level II).
- Stage IIB and over patients should be referred to a Cancer Centre service for consideration of trials of adjuvant therapies.
- The role of interferon as an adjuvant therapy remains to be established (grade C, level I).

Management of clinically node-negative patients

There is currently no place for elective lymph node dissection outside a clinical trial (grade A, level I).^{44,45} Sentinel lymph node (SLN) biopsy was developed as a means of identifying the first lymph node draining the skin in which the melanoma arises.⁴⁶ The procedure is carried out at the same time as definitive (wider) excision of the primary tumour. Patients with a positive SLN proceed to excision of nodes in the relevant nodal basin. At the present time SLN biopsy appears to be useful for staging in clinical stage II melanoma, and can be used as part of the staging strategy in those centres that are skilled and experienced in the technique. The procedure is associated with some morbidity. Until there is further evidence that there is an improvement in prognosis as a result of use of this technique to identify patients in whom therapeutic lymph node dissection should be performed, SLN biopsy is not generally recommended for routine use, and preferably should only be performed as part of a clinical study or trial. This is an area where reports of on-going multicentre studies are anticipated and current recommendations may need to be reconsidered.

Recommendations for the management of clinically node-negative patients

- There is no role for elective lymph node dissection (grade E, level I).
- Sentinel node biopsy can be used for staging in stage II melanoma in specialist centres in clinical trials but unless evidence emerges for a role in determining outcome it should not be routine (grade C, level IIa).

Management of patients with clinically or radiologically suspicious lymph nodes

Fine needle aspiration cytology (FNAC) of nodes is recommended when there is clinical doubt about the significance of the nodes. This may need to be repeated if there is a negative result but on-going suspicion. Open biopsy is recommended when there is clinical suspicion even in the presence of negative FNACs in which lymphocytes have been successfully aspirated. If open biopsy is performed, the incision must be such as to allow subsequent complete formal block dissection of the regional nodes without compromise.

Management of patients with confirmed positive lymph node metastasis

Radical lymph node dissections should be performed by those with expertise in the surgery of this condition. Prior to block dissection, staging investigations should be carried out as listed previously. Imaging of the liver by either CT scan or ultrasound should be performed preoperatively. Where preoperative scanning would necessitate delay to surgery that is considered necessary even if widespread disease were to be detected, postoperative scanning may be carried out. The decision as to whether or not surgery should proceed prior to scanning should be made after careful discussion with an informed patient.

The management of regional lymph node metastases is as follows:

- If only one or two involved nodes are present below the inguinal ligament, a subinguinal node dissection of the femoral triangle is indicated.
- If there is gross involvement of the subinguinal nodes, or if the node of Cloquet is involved, then some would recommend extended dissection to include the iliac and obturator nodes to prevent local recurrence (level III).⁴⁷

- Where relapse involves further lymph node basins, these should be treated by block dissection. In the neck, a functional dissection is ideally performed although in more locally advanced disease a radical neck dissection may be appropriate.
- A block dissection specimen should be marked and orientated for the pathologist. The pathologist should be asked to report on the number of nodes in the specimen and the presence of any extracapsular spread.

Locoregional recurrent melanoma: skin and soft tissues

Where possible in the case of single local or regional metastases, surgery is the treatment of choice. Patients with multiple local metastases in a limb should be referred to a centre specializing in regional therapy where the following may be considered: ILP or limb infusion with cytotoxic agents; and carbon dioxide laser ablation for multiple small superficial lesions (level III).⁴⁸ Radiotherapy is not recommended in the first instance (level III).

Recommendations for locoregional recurrent melanoma

- Nodes clinically suspicious of melanoma should be sampled using fine needle aspiration cytology (FNAC) prior to carrying out formal block dissection. If FNAC is negative although lymphocytes were seen, an open biopsy should be performed if suspicion remains (grade B, level III).
- Prior to formal dissection, performed by an expert, staging by scan should be carried out other than where this would mean unnecessary delay (grade B, level III).
- The treatment of locoregional recurrence in a limb is palliative. Initial treatment is usually surgical, followed, where necessary, by carbon dioxide laser treatment and possibly isolated limb perfusion (grade B, level II).

Occult primary melanoma

Patients with occult primary melanoma will present with lymph node disease, a single soft-tissue meta-

stasis or systemic disease in the absence of a recognizable primary. The presenting lymph nodes or systemic metastases should be treated appropriately regardless of the inability to detect the primary lesion (level III).

Metastatic disease

All patients should have access to a palliative care team providing expertise in symptom control and psychosocial support. Links should be made with community cancer support networks as soon as possible.

Consideration of surgical removal of localized metastases should be made (e.g. skin metastases, solitary brain metastases^{49,50} and occasionally those in other sites). Radiotherapy to bone or skin metastases can provide short-term symptomatic control⁵¹ and has a palliative value in patients with brain metastases.^{52,53}

Patients with unresectable metastatic disease should be referred to a specialist oncologist for management advice. Standard chemotherapy outside a clinical trial remains single-agent dacarbazine⁵⁴ but no systemic therapy has yet been shown to prolong significantly the survival of patients with metastatic melanoma. Thus, these patients, wherever possible, should be considered for and then counselled about entry into clinical trials of novel therapies, in addition to being offered standard palliative measures.

Melanoma, hormone replacement therapy and pregnancy

There is no evidence that melanoma at or near the time of pregnancy adversely affects the prognosis, but the data are limited.^{55,56} The Breslow thickness, site and presence of ulceration are still the key determinants (level III).

Advice about continuance of and future pregnancies should be given based on the patient's prognosis and the possible social consequences of it; that is, the relative chance that a mother might die when her child was young, compared with that of a woman of the same age without melanoma. These social or family considerations may also be relevant to a male patient whose partner is pregnant or if he and his partner are considering a pregnancy.

There is no conclusive evidence that either hormone replacement therapy or the use of the oral contracep-

tive pill play any role in the natural history of melanoma (level III).

Recommendations for metastatic disease, hormone replacement therapy and pregnancy

- Consideration of surgically resectable metastases should be made, such as in the skin, brain or gut (grade B, level II).
- Radiotherapy may have a palliative role in the treatment of metastases (grade B, level II).
- The standard chemotherapy of choice is dacarbazine although its role is palliative (grade C, level II).
- There are no data contraindicating the use of the contraceptive pill or hormone replacement therapy after melanoma (grade B, level II).
- The risk of subsequent pregnancy on outcome from melanoma is not known.

Follow-up

All patients should be taught self-examination because many recurrences are found by patients themselves at home rather than by clinicians in the clinic.

Patients with *in situ* melanoma need be reviewed only once after complete excision of the primary lesion.⁵⁷

All patients with invasive melanoma should be followed up 3-monthly for 3 years. In stage I disease some view this frequency of follow-up as excessive; the decision about frequency may be made on an individual basis according to the need to monitor naevi and emotional state. Thereafter, patients with melanomas less than 1.0 mm in depth may be discharged from routine follow-up; other patients should be followed up for a further 2 years at 6-monthly intervals.⁵⁷

The following should be examined and details recorded at each follow-up: site of primary and adjacent skin, for local recurrences and local metastatic disease; the draining lymph node basins, for lymphadenopathy; the remaining skin, for any other suspicious pigmented lesion. Regular radiological imaging is currently not a necessity but clinical photography may be helpful in follow-up, particularly in those with multiple atypical moles.

Recommendations for follow-up

- Patients with *in situ* melanomas do not require follow-up.
- Patients with invasive melanomas should be followed up 3-monthly for 3 years. Where the melanoma thickness was less than 1 mm the patient may be discharged; others should be followed up for a further 2 years at 6-monthly intervals.
(Grade C)

Appendix 1

Possible audit points for melanoma

- What proportion of lesions had incisional rather than excisional biopsy?
- What proportion of melanomas was seen within 2 weeks of referral?

If melanomas have been excised in general practice but not referred:

- Audit completeness of clinical and/or pathology data recording compared with the guidelines dataset
- Audit treatment modalities used for lentigo maligna melanoma
- Have patients had appropriate investigations according to stage of melanoma, and what are the results for each investigation?
- Have eligible patients been counselled about clinical trials, and what proportion has been entered?
- For patients entering clinical trials, have entry criteria been fulfilled (e.g. adequate number of lymph nodes examined pathologically after a block dissection)?

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