



Clinical Practice Guidelines

The management of cutaneous melanoma



NHMRC

National Health and Medical Research Council

Clinical Practice Guidelines

The Management of cutaneous melanoma

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Disclaimer

This document is a general guide to appropriate practice, to be followed only subject to the clinicians' judgement in each individual case.

The guidelines are designed to provide information to assist decision-making and are based on the best information available at the date of compilation (June 1999).

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Foreword

The Australian Cancer Network (ACN) has been established by the Australian Cancer Society and the Clinical Oncological Society of Australia with the aim, in collaboration with other professional medical groups, of improving cancer management in Australia.

The ACN, following the policy embarked upon by the National Health and Medical Research Council (NHMRC), has developed the following clinical practice guidelines for the management of melanoma. The objective of these guidelines is to assist general practitioners, dermatologists and surgeons to make decisions about appropriate health care for patients with melanoma.

The basic premise for guideline development by the NHMRC, followed by the ACN, is that guidelines should be based on the best available evidence and be developed through a multidisciplinary consensus approach involving surgeons, dermatologists, pathologists, general practitioners, medical and radiation oncologists, palliative care specialists, oncology nurses and advocates for patients and the community. The guidelines are expected to help to improve the quality of care, hopefully making the management of patients with melanoma more cost effective. An expert panel (see Appendix A) recommended these guidelines after consideration of the best available evidence during two consensus development conferences in Sydney in 1995 and 1996 and submissions from other sources. The guidelines were reviewed and revised in 1999 following public consultation and review by NHMRC.

These guidelines are not rigid rules to be followed in every situation. They are based on the best data available at the time of publication. The aim is to provide information on which decisions can be made rather than dictate a specific form of treatment. The guidelines use a four point rating system to identify the evidence base for key decision points. The ratings system is as follows:

- level I Evidence is obtained from a systematic review of all relevant randomised controlled trials.
- level II Evidence obtained from at least one properly-designed randomised controlled trial.
- level III-1 Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).
- level III-2 Evidence obtained from comparative studies with concurrent controls and allocation not randomised (cohort studies), case-control studies, or interrupted time series with a control group.
- level III-3 Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group.
- level IV Evidence obtained from case series, either post-test or pre-test/post-test.

Level I evidence is the best scientific evidence but is not always available. In these circumstances, it is appropriate to base treatment on other levels of evidence. This document details current understanding and is predicated on a plan for review at regular intervals not exceeding five years.

This document is one of a number of clinical reviews of evidence-based practice in cancer. They are titled:

1. Guidelines on Familial Aspects of Cancer
2. Guidelines for the Prevention, Early Detection and Treatment of Colorectal Cancer
3. Guidelines for the Management of Non-Melanocytic Skin Cancer
4. Guidelines for the Management of Localised Prostate Cancer
5. Guidelines for the Management of Epithelial Ovarian Cancer

The ACN and its progenitors are committed to maintaining the quality of the guideline process.

Emeritus Professor Tom Reeve AC CBE

Executive Officer

Australian Cancer Network

Preface

The ACN has as a prime objective—to establish a clearinghouse for relevant educational and contemporary information on cancer management which will be made widely available to promote the tenets of best practice.

The *Guidelines for the Management of cutaneous melanoma* were commissioned by the National Cancer Advisory Committee soon after the ACN was instituted in 1994. Professor William McCarthy AM undertook to initiate the project and was appointed as its convenor.

The process followed in developing these guidelines may prove useful to others undertaking a similar development. For these guidelines, a draft outline and literature search was prepared and circulated three times to the Working Party for additions and amendments. Once agreement in principle of the text was achieved, the Working Party was convened in a face-to-face meeting under the chairmanship of Dr Neville Davis AO. At the first meeting, an important decision was taken to accept the NHMRC *Guidelines for the Development and Implementation of Clinical Practice Guidelines* (October 1995), and to seek NHMRC endorsement of the completed document. It was clear that melanoma met the four basic criteria determining the need for guidelines as sanctioned by the NHMRC.

1. Size of health burden
2. High cost
3. Variations of practice
4. Existence of available evidence.

To achieve endorsement, the Working Party determined to follow the *Standards for Externally Developed Guidelines* issued by the Quality of Care and Health Outcomes Standing Committee (QCHOC) of the NHMRC (October 1995).

Multidisciplinary Panel

A multidisciplinary panel was given the task of developing the guidelines. Following a review of practice and the literature by the convenor, a draft document was circulated to the panel. Specific sections of the document were prepared by the appropriate expert on the consensus panel.

Following the first face-to-face meeting of the multidisciplinary Working Party (detailed in Appendix A), further reviews were sought by mail, and a second meeting took place to fine-tune the document. The document was then referred to each of the 67 special interest groups of the ACN for comment (detailed in Appendix F). Twenty-seven special interest groups contributed to the process, supporting the guidelines and agreeing to their submission to NHMRC. This was done after a final review of comments by a small editorial committee.

In October 1996, the guidelines were submitted to the Quality of Care and Health Outcomes Committee (QCHOC), and a Melanoma Review Panel was established. The comments of this panel were circulated and the document revised accordingly. Dr Mark Ragg assisted in formatting the document.

A final meeting of the editorial panel met under the chairmanship of Dr Neville Davis AO before resubmission to QCHOC.

Scope

The objectives of the Working Party have been to provide a set of guidelines that can be used by general practitioners, dermatologists, surgeons and others in clinical decision-making when managing patients with melanoma. These guidelines are based on the best available evidence and promote best practice in this field.

Identification of Health Outcomes

The trend towards patients presenting with thinner melanomas has already been observed. It is felt that this has been produced in part by increasing community awareness promoted by campaigns for cancer societies and through service clubs (e.g. Lions). Widely-available literature disseminated by cancer societies is seen as important in community education, encouraging earlier consultation so that people present with the very earliest melanoma. This would be a clear way to observe a betterment of process and outcome in this field.

Consultation

The consultation process was widespread, as outlined above. A number of those on the Working Party have consulted widely among their colleagues as well as consulting with especially skilled individuals, clinical colleges and consumers. Consultation with all interested groups making up the ACN (Appendix F) has been carried out and support for the document has been strong.

Systematic Review of Evidence

Searches were made for reviews and studies from library sources and Medline. Attention has been primarily directed to studies on melanoma with some attention to reviews. Only a small number of randomised trials were located and after careful review none were considered to meet the relevant requirement for level I evidence in NHMRC *Guidelines for the Development and Implementation of Clinical Practice Guidelines* (October 1995). The best evidence available has been collated and, while most of it is level IV, there is a substantial component of level III evidence and a small quantum of level II evidence. Where guidelines are not related to effectiveness of treatment, a level of evidence is not provided.

This document summarises evidence and gives clear guidelines for the management of cutaneous melanoma. Among the areas requiring further research are the following:

1. The role of radiotherapy in the management of desmoplastic melanoma is a subject which needs a definitive trial.
2. A controlled trial of observation as against early removal of clinically diagnosed lentigo maligna would be useful in settling an ongoing discussion.
3. Selective lymphadenectomy is currently subject to a worldwide trial. A trial should follow of adjuvant therapies of patients with minimal node involvement as determined by sentinel node localisation and biopsy.
4. Clinical trials aiming to identify the presence of metastases in sentinel lymph nodes i.e. developing and trialing specific antibody labelled imaging products are needed.

Guidelines

The guideline document has been developed to provide a best practice resource for clinicians managing cutaneous melanoma. The quality of evidence has been carefully weighed and prominently placed in the summary and at the end of each section of the document.

A deliberate decision was taken not to develop a separate consumer document, as the excellent educational material that is available through state cancer bodies is consonant with the guideline document.

Flexibility and Adaptability

The multidisciplinary committee has tried to address the clinical settings of the target speciality groups and general practice. It developed the guidelines to allow professionals to have access to best practice information, applicable to a variety of clinical situations, from urban to remote area practice.

Resource Consideration

The cost of diagnosis lies largely within the standard based on the Medical Benefits Schedule.

The current costs are largely related to biopsy, excisional techniques and lymphoscintigraphy, and all are based on the Medical Benefits Schedule. The effectiveness of each type of intervention is outlined in the document.

Adoption of the recommendations proposed in the document should considerably lower resource demands by limiting unnecessary surgery of pigmented lesions, promoting appropriate surgical margins and minimising unnecessary investigative procedures.

Dissemination and Implementation

It is planned to have the associated learned colleges, the executives of which have already made suggestions and given approval to the guidelines, to review and recommend the guidelines to their Fellows in their own publications. The interest groups of the ACN that have commented are those that have involvement or interest in melanoma management and are supportive of the dissemination and implementation processes.

The Australasian College of Dermatologists, the Royal Australasian College of Surgeons, the Melanoma Foundation of the University of Sydney and the Queensland Cancer Fund have all given generous financial support to develop and disseminate this guidelines document. These organisations will disseminate them to their Fellows or members and have already given support for them to be used in clinical practice. Distribution of the document with the imprimatur of these groups is seen as part of the implementation process.

An advance draft of these guidelines was launched at the 4th World Conference on Melanoma by the Convenor (Professor William McCarthy AM) in June 1997. It might also be added that since Professor McCarthy gave a broad overview of the conference at the annual meeting of the Clinical Oncological Society of Australia in Brisbane in November 1996, there have been daily enquiries to the ACN by those wishing to be sent the guidelines.

Evaluation

Evaluation of the impact of the guidelines is to be carried out by monitoring and evaluating national melanoma statistics and statistics on thickness of melanomas on an annual basis, as well as by carefully planned surveys to assess the value of the guidelines to medical practitioners.

Updating

The guidelines will be reviewed and updated by the ACN through its Working Party on Management of Melanoma. It is planned that this should become a standing committee of the ACN. The members of the Working Party come from backgrounds that put them in daily interaction with melanoma patients and health professionals who manage melanoma in its broadest

sense. The core multidisciplinary group and its organisational backers (intellectual not financial) would continue to function with ACN affiliation.

The first review was completed in June 1999. Within three years after the it has been disseminated, all 67 interest groups will be asked for recommendations for the second edition of the guidelines. The responses will be circulated to Working Party members who will return their views to the ACN Executive. After review in this manner and editing of the material, the Working Party will be called together again for final review.

Feedback will also be obtained from an evaluation slip inserted into the guidelines. This contains a questionnaire and space for expressing opinion. (ACN has had a good response to this approach with its *Update on Breast Cancer*.) The guidelines may be completely revised in the process, or an update may be produced, which could be inserted in the original guideline book.

The review of melanoma thickness at presentation and monitoring of mortality rates will continue. This is already done in an efficient manner and provides a sound mechanism for evaluation. Health Insurance Commission (HIC) statistics on excision of pigmented skin tumours are another source of evidence for the document.

The costs of the Working Party have been met to date by donations and by support from the Australian Cancer Society/Clinical Oncological Society of Australia. By the time the need for the second edition is being developed, it should still be possible to fund the activities of the Working Party, but there may be a need to recover some of the costs of the publication. This should represent only a small moiety of the total cost.

Those involved in this process found it a rewarding exercise and agreed that the process established by NHMRC materially assisted their efforts in producing guidelines.

Executive Summary

- Melanoma remains the third most common cancer in Australia (not including non-melanoma skin cancer). Despite the achievement of earlier diagnosis across Australia, it would appear from current statistics (Appendix B) that at least 850 people will continue to die of melanoma each year.
- Many of these deaths will occur at a younger age than for other solid tumours. Thus the number of person years of life lost due to melanoma exceeds that of many other cancers. It is seen as imperative to maximise effective management of melanoma.
- The evidence for *Guidelines for the Management of cutaneous melanoma* have been developed in an attempt to improve management of melanoma through the process of locating the best available evidence on which to base decisions. Since the guidelines are guides, not rules, the document should not in any way be interpreted as prescriptive.
- Prevention of melanoma has not yet been achieved, nor are there conclusive data that current health promotion of sun avoidance has substantially altered the incidence of melanoma. The Working Party has endorsed the hierarchy of protective measures recommended by the Australian Cancer Society-physical protection with protective clothing or shade facilities being more important than the use of sunscreens.
- Early detection is an important factor in melanoma management, with diagnosis based mainly on changes in a skin lesion in colour, diameter, elevation, border (irregularity of outline) or if the lesion is asymmetrical or different from other naevi. People with high risk of melanoma should be offered a surveillance program.
- If there is doubt about a lesion, the patient should be referred for specialist opinion (if readily available) or a limited biopsy undertaken.
- Biopsy of a pigmented lesion should be done only on the basis of suspicion of melanoma. A 2mm margin is adequate. Prophylactic excision of benign naevi is not recommended.
- Most melanomas are treated definitely by excision with a 1cm margin and all excised tissue should be sent for histological examination.
- In general, elective lymph node dissection is not indicated.
- Postoperative Deep X-Ray Therapy (DX-RT) may be helpful in some cases of advanced or recurrent melanoma.
- People with high risk primary melanoma, lymph node involvement and melanoma in unusual sites (e.g. mucosal and disseminated melanoma) should be managed with support from a melanoma centre.

<p>7. BIOPSY OF PIGMENTED LESIONS</p> <p>Biopsy of pigmented lesions should be done only if there are suspicious clinical features. Prophylactic excision of clinically benign lesions is not recommended</p> <p>Where doubt exists about diagnosis, a period of observation based on the history and clinical features of the lesion is acceptable. The period of observation will be short if a high level of suspicion of melanoma is present. However, if the clinician feels the lesion is unlikely to be melanoma and it does not change, it is appropriate to continue observation until evidence of change appears.</p> <p>If melanoma is clinically obvious or strongly suspected, referral for specialist opinion is appropriate, where available, before biopsy is undertaken.</p> <p>Shave and punch biopsies of pigmented lesions should be avoided if excision biopsy with primary skin closure can be achieved.</p> <p>Lesions suspected to be melanoma should be excised with a 2mm lateral margin and to the depth of the upper layer of the fat.</p>		
<p>8. CONGENITAL MELANOCYTIC NAEVI</p> <p>Monitor all congenital lesions >20cm in diameter for the lifetime of the person.</p> <p>Excisional biopsy of suspicious areas in large congenital naevi is recommended.</p> <p>Surgical excision of congenital naevi is appropriate where patient concern is high and where an acceptable cosmetic outcome can be achieved.</p>	III	51–62
<p>9. LENTIGO MALIGNA</p> <p>Biopsy is indicated for changing pigmented lesions on the face.</p> <p>For some patients, treatment by observation for change, with measurement, is an acceptable alternative to immediate excision.</p> <p>Where lentigo maligna is histologically confirmed, complete excision is the preferred management.</p>		

<p>10. HISTOPATHOLOGICAL REPORT</p> <p>Request forms for pathology should include adequate patient identification and clinical details of all lesions removed.</p> <p>Where more than one lesion is excised, separate specimen bottles are essential. The pathologist's report should include all important features of the lesions. Inclusion of tumour thickness, Clark's level and clearance margins is most important.</p> <p>Where clinical and pathological diagnoses do not concur, a second opinion should be sought from a pathologist with expertise in the diagnosis of pigmented tumours.</p>		<p>Appendix D</p> <p>63, 64 Appendix D</p>
<p>11. TREATMENT OF PRIMARY MELANOMA</p> <p>The AJCC/UICC system is recommended as the basis for melanoma therapy.</p> <p>Complete excision with margins determined by tumour thickness measurement should be the basis for management of primary melanoma.</p> <p>A minimum margin of 1cm and a maximum margin of 3cm should be used for invasive melanoma, with the choice of excision margin determined by the tumour thickness.</p> <p>A depth of excision equal to margins is advised but it is not necessary to excise further than the deep fascia.</p> <p>A margin of excision of 5mm is recommended for melanoma in situ.</p> <p>Other pathological features should be used to make an assessment of prognosis and modify management decisions.</p>	<p>II</p> <p>II</p> <p>II</p>	<p>Appendix C</p> <p>66–69</p> <p>66–69</p> <p>63, 64, 71, 72</p>
<p>12. SURVIVAL OUTCOMES OF PRIMARY MELANOMA MANAGEMENT</p>		<p>53,64,4,71–72 Appendix E</p>

<p>17. DISSEMINATED MELANOMA</p> <p>Patients with systemic metastases should be referred to a melanoma centre for consideration of systemic therapies.</p> <p>Clinicians dealing with patients with systemic melanoma should be appropriately skilled in psychological management and palliative care.</p> <p>Surgical resection should be considered for isolated melanoma metastases in lung, brain and peritoneal cavity.</p>	<p>III</p>	<p>110</p>
<p>18. RADIOTHERAPY FOR MELANOMA</p> <p>Post-operative radiotherapy should be considered for cutaneous melanomas likely to recur locally (>4mm thick, satellite nodules or neurotropic spread) or regionally (multiple node involvement or extracapsular spread) and following resection of mucosal melanomas. Primary radiotherapy should be considered for unresectable lentigo maligna melanomas.</p> <p>Radiotherapy is recommended for treatment of extensive cutaneous metastases and for palliative management of cerebral and bone metastases and for other metastases where temporary local control is needed e.g. large nodal or soft tissue masses.</p>	<p>III</p> <p>III</p>	<p>115</p> <p>116–119</p>
<p>19. PALLIATIVE CARE</p> <p>It is recommended that palliative care health professionals be an integral part of the multidisciplinary team in facilities where the patient with melanoma is treated.</p>		
<p>20. FOLLOW-UP</p> <p>A follow-up regimen based on tumour thickness should be arranged for all patients with invasive melanoma.</p> <p>The follow-up examination should include palpation for local recurrence, intransit metastases, lymph node fields and a general examination of the skin for new primary melanomas and other skin cancers.</p>	<p>III</p>	<p>130, 133</p>

<p>21. APPROPRIATE INVESTIGATIONS</p> <p>Investigations such as CT, MRI and PET should be utilised only where specific symptoms suggest the presence of metastases.</p> <p>Extensive investigation for systemic metastases in patients with primary melanoma is not recommended.</p>		
<p>22. SPECIFIC SITES AND TYPES OF MELANOMA</p> <p>a. Mucosal melanoma</p> <p>Patients with mucosal melanoma should be referred to a suitable speciality clinic or clinician.</p> <p>b. Acral lentiginous melanoma (ALM)</p> <p>ALM on the sole of the foot should be referred for specialist excision and appropriate reconstructive procedures.</p> <p>c. Subungual melanoma</p> <p>Subungual melanoma should be considered as a possible cause of any pigmentary changes under the nail. In cases of doubt, removal of the nail and biopsy is recommended. Subungual melanoma should be treated with excision margins which accord to the lesion thickness. This usually involves amputation of the terminal phalanx.</p>		

1. Introduction

Melanoma is one of the commonest cancers in Australia.¹⁻³ According to the Australian Institute of Health and Welfare and the Australasian Association of Cancer Registries³ in 1998, the crude incidence rates of melanoma in 1995 were 45.4 per 100,000 person years in men and 36.5 in women, and the age standardised rates were 36.5 and 28.4 per 100,000 person years, respectively. This compares with an age standardised rate of 96.7 per 100,000 person years for cancer of the prostate, the commonest internal malignancy in men, and 82.9 per 100,000 person years for cancer of the breast, the commonest in women. In 1995, the estimated risk of developing a melanoma before 75 years of age was one in 26 for Australian men and one in 36 for Australian women.³

Survival after diagnosis of melanoma in Australia is high, with 89% relative survival at five years and 86% at both 10 and 15 years.⁴ The latter figures suggest that only about 14% of patients with melanoma ultimately die from this disease. This high survival is attributable to early diagnosis and effective treatment. Behavioural research data show substantial improvement in attitudes to sun protection but recent evidence indicates that further behaviour alterations in the susceptible population may be more difficult to achieve.⁵ The median thickness of melanoma at diagnosis in Australia is now low: 0.75mm in the latest available survey.² However, some 850 people a year still die from this cancer in Australia and there is an annual loss of more than 10,000 person years of life before 75 years of age.^{3,6} As a cause of premature death from cancer, it is exceeded in importance only by cancers of the colon, breast, lung and brain.

These facts, together with its high frequency, make melanoma an important clinical and public health problem in Australia. It is essential, therefore, that the management of melanoma be as effective as possible. These clinical practice guidelines are designed to assist those involved in the management of this very common cancer to provide optimum management for their patients.

2. Prevention

Exposure to sunlight is strongly associated with the development of melanoma. Two thirds of all melanomas can be specifically attributed to solar exposure.⁷ The pattern of exposure is important in the generation of melanoma, with intermittent exposure such as holiday, weekend and recreational exposure being more closely associated with melanoma than the regular patterns of exposure of the outdoor worker.⁷

The action spectrum which is causative for melanoma, in particular the relative roles of UVB and UVA, is as yet unknown. However, in two animal models UVA was found to be a highly significant component in melanoma induction.^{8,9} In addition, the use of sunbeds and tanning booths which deliver mainly UVA radiation may be risk factors for melanoma.¹⁰ A consensus exists that the following recommendations should be adopted by all those exposed to solar radiation. A hierarchy of protection measures is recommended by the Australian Cancer Society, with physical protection being more important than the use of sunscreens.

The Australian Cancer Society recommends:

- 1 Physical protection should be the primary preventive measure. Physical protection involves avoidance of direct sunlight exposure, particularly within two hours on either side of solar noon, the use of shade structures such as protective umbrellas whenever possible and the wearing of sun protective clothing including wide-brimmed hats that offer protection to the sides of the face and ears, together with long-sleeved shirts, particularly during the summer months.

People should be advised to choose dark clothing of closely woven fabrics, which is more protective than light, loosely-woven garments. Some lighter weight garments which offer excellent sunlight protection are available. The Australian Standards Association is introducing a system for the rating of the protection factor of fabrics to help consumers select fabrics with a high protection factor rating.¹¹

2. Sunscreens should be used as an adjunct to physical protection. Only sunscreens with a minimum SPF of 15 are recommended. The Australian Standards Association has determined that the labelling system for sunscreens will now permit labelling of the sun protection factor of a sunscreen up to 30+. This will give people the option to choose products of higher SPF. However, sunscreens should be regarded as filters and not blocks; some sunlight damage to the skin continues despite the use of sunscreens.

The need to reapply sunscreen at recommended intervals should be stressed where the sunscreen may be rubbed off by towelling, water, excessive physical activity or clothing. Reapplication does not completely protect against continuing damage. All recommended sunscreens should be broad spectrum with protection extending as far as possible into the UVA range. For specific circumstances such as swimming, a water-resistant sunscreen should be selected.¹¹

3. Advice should be given regarding the potential risk of UV damage from sunbeds, tanning booths and tanning lamps.

Sun exposure in childhood and adolescence is closely related to the development of naevi. The presence of multiple naevi is a strong risk factor for melanoma.¹²⁻¹⁶ Studies of immigrants to Australia indicate that sun exposure during childhood and early adolescence is very important in causing melanoma.¹⁷ Immigrants arriving before the age of 10 have a similar risk to native-born Australians, whereas those arriving after age 15 years have one-quarter of the native-born rates. This indicates that particular emphasis should be placed on protection from excessive sunlight exposure in childhood and adolescence. (See Appendix B) However, melanoma itself is rare before puberty.

It should be noted that there may be a long latent period, usually many years, from the initiating sun exposure to the time a melanoma becomes clinically apparent.

While childhood sunlight exposure is very important in the development of melanoma, sunlight damage is cumulative and substantially irreversible. It is cumulative in people of all ages. Therefore everyone should be advised to use sun protective measures throughout their life. This is considered advisable despite lack of conclusive evidence of reduced incidence of melanoma resulting from current sun avoidance practice.

Guidelines	Level	Reference
Use sun protective clothing when exposed to direct sunlight for periods greater than 15 minutes. People of fair complexion should be especially careful.	III	5,7,13,17
Advise against the use of sunbeds, tanning booths and tanning lamps.	III	10

Recommendations

- Use broad spectrum sunscreens with a minimum SPF of 15 as an adjunct to sun avoidance and other sun protective measures.
- Use sun protective structures (eg shade structures) whenever possible during daylight hours.
- Avoid direct exposure to sunlight during the two hours either side of solar noon.
- Use sun protective clothing when exposed to direct sunlight for periods greater than 15 minutes. People of fair complexion should be especially careful.
- Provide children with appropriate sun protection for outdoor activities.

3. Classification of Melanoma

A modified version of the current AJCC/UICC (American Joint Committee on Cancer/Union Internationale Contra de Cancer) pTNM classification system for stage I and II melanoma has been recently developed and is now in general use. In this system, 'p' denotes primary and 'T' is tumour.

pTis	Melanoma in situ
pT1	Melanoma ≤ 0.75 mm thick
pT2	Melanoma > 0.75 mm < 1.5 mm thick
pT3a	Melanoma > 1.5 mm < 3.0 mm thick
pT3b	Melanoma > 3.0 mm < 4.0 mm thick
pT4	Melanoma > 4.0 mm thick

These subdivisions are based solely on the most important prognostic variable for patients with stage I and II primary cutaneous melanoma, which is tumour thickness. The current detailed pTNM classification is based on a combination of tumour thickness and level of invasion (see Appendix C). Precedence should be given to tumour thickness for staging patients where there is discordance between tumour thickness and level of invasion.¹⁸

Similarly, a modified version of the current AJCC/UICC pTNM classification system for stage III melanoma (melanoma in lymph nodes) has been recently suggested.¹⁹ This study found that only the number, not the size of positive nodes, was of prognostic significance and as such should take precedence in the staging system.

The detailed currently accepted AJCC/UICC staging and grouping system is shown in Appendix C.

Note: A revised classification system has recently been approved by the AJCC and has been submitted to UICC for discussion and approval. It is likely that this new classification system will be approved. The proposed new system is included in Appendix C.

Recommendation

- Use of the AJCC/UICC classification system (or its revision) is recommended. (Appendix C)

4. Clinical Diagnosis of Melanoma

The diagnosis of melanoma should be considered in all cases of pigmented or changing lesions on the skin. The high prevalence of skin cancer in Australia necessitates that all clinicians should be familiar with the assessment of pigmented skin tumours. Basic requirements for cutaneous diagnosis are good lighting and magnification. The surface microscope (dermatoscope) is an evolving technology which may be helpful to the clinician after appropriate training is undertaken.^{20,21}

The clinical evaluation of patients with a suspected melanoma includes taking a careful history including history of past lesions, family history (defined as melanoma in a direct line family member-grandparent, parent, sibling or child of the patient), an evaluation of the lesion presented, an examination of all the patient's pigmented lesions, palpation of the draining lymph node fields. Skin surface microscopy of the suspected lesion and other suspicious naevi may be helpful. In all cases where there is doubt, referral for a specialist opinion if readily available or biopsy for histopathological confirmation is necessary.

Patients with melanoma will usually present a history of change in size or colour of the lesion, a change in surface characteristics or elevation of part of the lesion. Alternatively, the pigmented lesion may be noted to look different from other naevi, either by the patient, or by relatives or friends, even though there is no history of change. A melanoma may arise from clear skin as well as from a pre-existing mole.

The history of change in a melanoma is usually measured in months. A very short history suggests haemorrhage into the skin or inflammation, while a very long history suggests a benign lesion. The history of change is generally over two to six months, but may be considerably longer or shorter. The change noted is usually minor and is sometimes accompanied by an itch which may be intermittent. Itch in a naevus is not significant in isolation, but in association with other suspicious clinical features is supportive of melanoma diagnosis. Bleeding is rare in early melanomas. Pain is not a feature of primary melanoma.

The key to the clinical diagnosis of a pigmented melanoma is irregularity of the lesion. Irregularity of colour is most important and the presence of a variety of colours in any one lesion is a key feature. While a black or blue/black colour is the most common, many other shades of brown, blue, red, grey or white are often seen. Irregularity of outline is the second most common feature with indentations and outgrowths around the lesion often apparent. Irregularity of the surface is another important sign.

Amelanotic melanoma is clinically difficult to diagnose, usually appearing as an enlarging smooth reddish nodule or patch. Sometimes an area of brown pigment can be discerned in these lesions. Surface microscopy may be helpful.

The ABCDE system of diagnosis of melanoma has gained general support.^{22,23}

A = ASYMMETRY

A lesion is asymmetric if opposite segments of the lesion are appreciably different.

B = BORDER

The border of a melanoma is usually irregular, resembling a coastline with bays and promontories around the edge. All or part of the border is often well defined, in contrast with the dysplastic naevus, whose border is often ill-defined and fades into the background of the surrounding tissues.

C = COLOUR

Variation in colour is an important feature. A narrow red halo is sometimes seen around the edge of a melanoma. It is important to remember that amelanotic melanoma will have little or no distinguishing colour.

D = DIAMETER

Superficial spreading melanomas are often greater than 6mm in diameter when first diagnosed, but it is possible to diagnose smaller melanomas, particularly nodular lesions, which appear not only as small shiny dark nodules but can also be reddish in amelanotic forms.

E = ELEVATION

While E designates elevation, it is important to diagnose melanoma while it is flat or with marginal elevation. At that stage the lesion is more likely to be curable. Thus E should remind the clinician to 'Examine' the patient's other pigmented lesions. A melanoma is usually different from the patient's other moles. Examination of other lesions for comparison is thus an important diagnostic help. Such examinations occasionally detect an unsuspected second primary melanoma.

A feature which may be helpful in diagnosing melanomas is a 'ground glass' amorphous appearance to part of the lesion. Where the skin lines have been destroyed by the tumours, a shiny, glassy appearance is noted. Many melanomas will also have small flakes of keratin on the surface but it is extremely rare for the lesion to be extensively keratinised. The presence of hairs does not exclude a diagnosis of melanoma, but most pigmented lesions with hairs are benign. However, more advanced melanomas will not have hair in the deeply invasive parts of the tumour because the melanoma will destroy the hair follicles as it invades. Thick melanomas are firm to touch and not compressible, unlike haemangiomas, and are rarely waxy to feel, unlike a seborrhoeic keratosis.

The differential diagnosis of pigmented melanoma includes dysplastic naevus, Spitz naevus, pigmented basal cell carcinoma, blue naevus, haemangioma, pigmented seborrhoeic keratosis and some rare adnexal tumours. In children, pigmented Spitz naevus is a likely diagnosis.

The amelanotic or hypomelanotic tumour differential diagnosis includes dermatofibroma, desmoplastic melanoma, basal cell carcinoma and other spindle cell tumours.

Guideline	Level	References
High risk individuals should be advised of the specific changes which suggest melanoma and encouraged to perform self examination.	III	22,28

Recommendations

- Good lighting and magnification is recommended when lesions are being examined.
- All clinicians should be trained in the recognition of early melanoma.
- A good clinical history of the change in the lesion (if any), a past history of skin lesions, and a family history of melanoma should be obtained.
- A family history is defined as melanoma in a direct line family member—grandparent, parent, sibling or child of the patient.
- Lesions which are suspicious or cannot be diagnosed after a period of observation should be biopsied, or the patient referred for a specialist opinion.

5. Surface Microscopy

The diagnosis of melanoma can be enhanced by the use of skin surface microscopy (dermatoscopy, dermoscopy, epiluminescence microscopy). The technique of skin surface microscopy uses an incident light magnification system in combination with immersion oil at the skinmicroscope interface to examine cutaneous lesions. The use of oil removes the normal scattering of light at the stratum corneum, thus allowing the epidermis to become translucent. This permits a detailed examination of the pigmented structures of the epidermis and dermoepidermal junction. The result is the visualisation of a multitude of morphological features, not visible with the naked eye, that enhances the clinical diagnosis of nearly all pigmented lesions, including melanoma.^{24, 25}

A systematic review of dermatoscopy²⁶ revealed that there was significant variation between studies as far as methods, observers and types of pigmented lesions. These factors, together with lack of studies in primary care, limit generalisation of results at the present time.

The development of inexpensive hand-held instruments (Episcope™, Welch Allyn Inc.; Dermatoscope, Heine Ltd) allows a fixed magnification of x10 and is therefore now the favoured magnification. Training and experience in surface microscopy is necessary if the technique is to help in clinical diagnosis.²¹ Excellent atlases on dermatoscopic diagnosis are available.^{20,27} Skin microscopy will not always reveal identifiable characteristics for the diagnosis of melanoma. In particular, early melanomas arising from naevi may be featureless and it is important to remember that some melanomas are only marginally pigmented or non-pigmented (amelanotic). Any changing lesion which is undiagnosed by clinical examination and surface microscopy should be referred for a specialist opinion, if available, or excised for histopathological examination.

Recommendation

- Training and experience with skin surface microscopy is recommended for specialist practice and for all those interested in the diagnosis of skin tumours.

6. Detection and Surveillance of High-Risk Individuals

Surveillance of groups of people at high risk of melanoma has been shown to detect melanoma at an earlier stage than would otherwise occur.²⁸⁻³³ There are no data that show that screening of the general population for melanoma is an effective way of controlling melanoma mortality.^{34, 35}

The presence of large numbers of melanocytic naevi and the presence of clinically determined atypical or dysplastic naevi are very strong risk factors for melanoma.^{13,36-39} Dysplastic naevi are generally larger than normal moles with ill-defined edges and irregular pigmentation, which is mostly shades of brown.⁴⁰ They tend to have a poorly defined edge.⁴⁰ Melanoma risk increases with increasing numbers of total naevi and dysplastic naevi.^{13,36-38} The risk associated with clinical dysplastic naevi has been shown to be independent of that associated with the total numbers of naevi.³⁹ Clinically dysplastic naevi are not always dysplastic on histopathological examination.

There is evidence that numbers of naevi vary with geographical location. In Australia, outside the normal ranges, more than 200 naevi is a high number and more than 10 raised or 20 total naevi on the arms increases the relative risk of melanoma at least tenfold.¹⁶ Ten to 20% of the population have at least one dysplastic naevus.^{36,37,41} It is those with multiple dysplastic naevi who are likely to be at high risk.^{13,36-38} The prevalence of naevi in children has a latitude gradient, with more naevi being apparent on the skin of children in Queensland than in Victoria.⁴²

Other risk factors include a family history of melanoma, fair complexion, a tendency to burn rather than tan, the presence of freckles, the presence of solar lentiginos, light eye colour, light or red hair colour and a past history of non-melanoma skin cancer.³⁶⁻³⁸

All individuals who are at high risk for the development of melanoma should be advised about the changes that might suggest the development of an early melanoma, encouraged to undertake regular self examination and advised regarding appropriate methods of sun protection.

High quality baseline photographs of the skin surface are useful to monitor patients with large numbers of melanocytic naevi or large numbers of dysplastic naevi.^{28,29} Regular follow-up can then be undertaken comparing the patient's pigmented lesions with the baseline photographs in order to detect early changes. The aid of a relative or friend may be helpful in conducting self assessment of pigmented lesions.

Prophylactic excision of dysplastic naevi and other benign naevi is not useful in minimising melanoma risk. A significant proportion of melanomas begin as new lesions rather than developing from pre-existing naevi.⁴³⁻⁴⁵

Changing lesions in high risk patients should be viewed with suspicion and referral or excisional biopsy performed if melanoma cannot be ruled out. Not all changing pigmented lesions are melanomas and skin surface microscopy is helpful in the assessment of changing lesions.

Recent Australian data indicate that 10% of melanoma cases will have at least one (and most only one) confirmed melanoma-affected first degree relative.⁴⁶ Many of these familial clusters will be due to chance, but strict heterogeneity analyses have shown that, at a minimum, one in five (i.e. at least 20% of familial clusters or 2% of all melanoma cases) represent genuine high-risk kindreds, potentially resulting from inheritance of uncommon, major melanoma susceptibility gene(s).⁴⁷ It is as yet unclear what proportion of the remaining familial clusters, or indeed of so-called sporadic cases, represent recent mutations in such genes, or how many are due to weaker, but less uncommon, melanoma susceptibility genes.

Familial melanoma is thus relatively rare. Most patients with melanoma may be reassured that family members are not especially prone to developing melanoma unless there are other obvious

significant risk factors such as the presence of multiple dysplastic naevi. There is a small increase in melanoma incidence in all families where a melanoma has been diagnosed but this increase is not large enough to justify a surveillance program. Families with a strong history of melanoma or families with excessive numbers of naevi may be offered referral to specialised melanoma centres for inclusion in genetic studies.⁴⁸

At present, work is being undertaken to develop tests which may determine melanoma risk, but as yet these tests are not generally clinically applicable. Whether or not these patients are referred to specialist centres, they should be advised to have periodic checks of their skin to seek new or changing lesions. Surveillance of these very high risk groups is not necessary before the early teenage years.

Guidelines	Level	References
People at very high risk of melanoma (e.g those with multiple banal or dysplastic naevi or who have a history of melanoma in first-degree relatives) should be advised of the specific changes which suggest melanoma, encouraged to perform self examination, and offered a surveillance program.	III	13-16, 22, 23
Consider referral of these high risk individuals to a melanoma centre for inclusion in genetic studies.	III	22,28 48

7. Biopsy of Pigmented Lesions

The high level of biopsy excisions of benign pigmented lesions in Australia does not correlate with the age distribution of melanoma, suggesting that biopsy is often used as an alternative to observation, photography or referral for a specialist opinion.⁴⁹ For example, melanoma is extremely rare before puberty and most uncommon in adolescents. Experience and training can lower the rate of excision biopsy. However, where there is doubt about the clinical diagnosis, a period of observation based on the history and clinical features of the lesion is acceptable. Memory can be enhanced by written description, measurement or photograph.⁵⁰ If melanoma is clinically obvious or strongly suspected, referral for a specialist opinion should be considered before biopsy is undertaken.

Punch and shave biopsies are only appropriate where excision biopsy is difficult, e.g. for large macular pigmented lesions on the face. With such limited biopsies, important histopathological features may not be discernible and important areas of the lesion may not be included in the biopsy. For all pigmented lesions where diagnosis rather than therapy is the aim, a 2mm lateral excision biopsy margin is recommended.

In undertaking a biopsy of a pigmented lesion, the line of the excision should follow Langer's (wrinkle) lines, or should point towards the nearest lymph node field if the lesion is one which may subsequently necessitate node dissection in continuity with the primary lesion.

Recommendations

- Biopsy of pigmented lesions should only be done on the basis of suspicious clinical features. Prophylactic excision of clinically benign lesions is not recommended.
- Where doubt exists, a period of observation based on the history and clinical features of the lesion is acceptable. The period of observation will be short if a high level of suspicion of melanoma is present. However, if the clinician feels the lesion is unlikely to be melanoma and it does not change, it is appropriate to continue observation until the evidence of change appears.
- If melanoma is clinically obvious or strongly suspected, referral for specialist opinion is appropriate, where available, before biopsy is undertaken.
- Shave and punch biopsies of pigmented lesions should be avoided if excision biopsy with primary skin closure can be achieved.
- Lesions suspected to be melanoma should be excised with a 2mm lateral margin and to the depth of the upper layer of the fat.

8. Congenital Melanocytic Naevi

Congenital melanocytic naevi are present at birth and are diagnosed from specific histological features⁵¹⁻⁵³ including:

1. Naevus cells present in lower two-thirds dermis
2. Naevus cells between collagen bundles singly or in short files
3. Naevus cells involving appendages.

The lesions are arbitrarily divided into three groups based on diameter: <1.5 cm, 1.5–20 cm and 20+ cm.

SMALL (<1.5 cm) lesions occur in 1% of births.⁵¹⁻⁵³ They are not thought to have an increased malignant potential.

MEDIUM (1.5 – 20 cm) lesions have not been subject to adequate research so the malignant potential of this group is unclear.^{54,55} If excision is undertaken, it should be during the teenage years, since a study of 31 patients with melanomas arising from small congenital naevi (1.5–10cm) found none of these melanomas presenting before puberty. However, at this stage, the body of evidence suggests that observation only is required.

LARGE (>20 cm) lesions. There are only two prospective studies addressing these lesions. These show a crude risk of 3%.⁵⁶⁻⁵⁸ A literature review⁸ has shown that 70% of melanomas in this group develop before puberty.

Superficial removal of the naevus by dermabrasion or tangential excision is not recommended as two-thirds of melanoma develop in non-epidermal sites.^{59,60}

Patients with large congenital naevi of the head and neck are also at risk from neurocutaneous melanosis.⁶¹ An MRI scan should be considered for screening these patients.⁶²

Excision should only be considered on cosmetic grounds. Recent plastic surgery developments such as tissue expansion have improved the cosmetic outcome.

Lifelong surveillance for large and possibly for medium congenital naevi is recommended.

Entry should be considered to an ongoing prospective registry associated with the establishment of a naevus support group.

Guideline	Level	References
Monitor all congenital lesions >20cm in diameter for the lifetime of the person.	III	51-62

Recommendations

- Excisional biopsy of suspicious areas in large congenital naevi is recommended.
- Surgical excision of congenital naevi is appropriate where patient concern is high and where an acceptable cosmetic outcome can be achieved.

9. Lentigo Maligna

Lentigo maligna (Hutchinson's melanotic freckle) is a common pigmented lesion on the exposed skin of the older patient. These lesions are regarded as in-situ melanoma and may progress to invasive melanoma (lentigo maligna melanoma) in many people, and so must be managed carefully. These lesions occur predominantly on the face.

Lentigo maligna is a superficial condition and is one instance where a shave biopsy may be appropriate. However, it should be noted that a shave biopsy from a large lesion may not be representative as it may not include an invasive component which may be clinically inconspicuous. The presence of regression in the superficial dermis in the biopsied area may have obliterated all evidence of melanocytic proliferation. Thus a negative shave biopsy does not obviate the need for careful observation of these lesions if surgical excision is not undertaken. It should be noted that shave biopsy is a technique which requires appropriate training.

Where lentigo maligna is confirmed, complete surgical excision is generally favoured. However, pigmented macules on the face which are not suspicious of invasive melanoma may be measured, photographed and observed for change. A Woods ultraviolet lamp is useful in assessing the extent of the lesion.

There is no evidence to show which of these approaches provides the optimal outcome for patients with lentigo maligna. Certainly if a patient is under observation and a change in size or pigmentation becomes apparent, excisional or shave biopsy is warranted. A margin of 5mm is recommended for removal of lentigo maligna but in some lesions close to the eye, a narrower margin may be acceptable. In very elderly patients, radiotherapy is an acceptable alternative to surgery.

If an invasive melanoma has occurred in the lentigo maligna, the recommendations for margins of excision are those for any melanoma. On the face, a margin of 1cm is not always achievable without compromise to the eye and a lesser margin may have to be accepted.

Recommendations

- Biopsy is indicated for changing pigmented lesions on the face.
- For some patients, treatment by observation for change, with measurement, is an acceptable alternative to immediate excision.
- Where lentigo maligna is histologically confirmed, complete excision is the preferred management.

10. Histopathological Report

An informative and accurate histopathology report is an essential prerequisite for optimal therapy for melanoma. It is important that the clinician provides the appropriate clinical information to assist the pathologist to provide the best possible report. This must include adequate patient identification, the age and sex of the patient and the exact site of the lesion. Other clinical information useful to the pathologist includes the size and colour of the lesion and the duration of symptoms.

A previous history of melanoma is important, as is a family history and the presence of other skin lesions such as multiple dysplastic naevi. A diagram of the excision specimen with markers for orientation may also help. When more than one lesion is excised, it is very important that specimens be carefully placed in separate accurately labelled containers.

The provision of all this information assists the pathologist to supply the clinician with a report on all histopathological features necessary for determining therapy and prognosis. The pathologist's report should include all important features of the lesions (see Appendix D). Tumour thickness, Clark's level and clearance margins are the most important.

It is advisable that the clinician consults with the pathologist if the pathology report does not accord with the clinical diagnosis of the tumour. In cases of doubt, a specialist pathology opinion should be sought.

Recommendations

- Request forms for pathology should include adequate patient identification, and clinical details of all lesions removed. (Appendix D)
- Where more than one lesion is excised, separate specimen bottles are essential.
- The pathologist's report should include important features of the lesions (Appendix D). Inclusion of tumour thickness, Clark's level and clearance margins is most important.^{63,64}
- Where clinical and pathological diagnoses do not concur, a second opinion should be sought from a pathologist with expertise in the diagnosis of pigmented tumours.

11. Treatment of Primary Melanoma

The definitive treatment of primary melanoma depends on its histopathological features, and in particular on the Breslow thickness. Tumour thickness and depth are not exactly the same but pathologists and clinicians use the terms interchangeably. Thickness is the actual measurement used to assess prognosis. Other features such as Clark's level, mitotic rate, the anatomical location of the tumour and particularly the presence of ulceration influence the prognosis of melanoma,⁶³ but do not significantly alter the recommendations for treatment of the primary lesion. Treatment of the primary melanoma may differ for specific types and sites of melanoma such as desmoplastic melanoma, neurotropic melanoma, acral lentiginous melanoma and subungual melanoma, which are dealt with separately elsewhere in these guidelines. Additional prognostic features such as satellitosis and lymphatic invasion may also influence local therapy⁶⁴ and may be important in determining the need for lymph node dissection (see Appendix E).

Complete surgical excision confirmed by comprehensive histological examination of the entire excision specimen is the basis of surgical treatment for primary melanoma. At the present time a case, supported by a National Institutes of Health Consensus Panel⁶⁵ and three randomised clinical trials,⁶⁶⁻⁶⁸ can be made for a minimum margin of 1cm clearance of all invasive melanomas.

Maximum margins are based on non-randomised clinical studies, and the opinion of the panel is:

1. (pTis) Melanoma in situ - margin 5mm
2. (pT1, pT2) Melanoma 0–1.5mm - margin 1cm
3. (pT3) Melanoma 1.54.0mm - minimum margin 1cm and maximum margin 2cm
4. (pT4) Melanoma > 4.0mm - minimum margin 2cm and maximum margin 3cm.

It should be noted there is no evidence that a margin greater than 1cm offers additional benefit for the patient in terms of survival, but it may decrease local recurrence.⁶⁶⁻⁶⁹ Long-term follow-up of the three reported randomised studies on excision margins is not yet available.

The depth of excision should equal the minimum excision margin where possible, but in no instance is it necessary to excise beyond the deep fascia. Lesions excised for biopsy with a margin less than these recommendations should be re-excised to achieve these margins as soon as possible after the preliminary biopsy excision.

Where tissue flexibility is limited (such as face, foot or ankle), a skin graft or a flap repair is sometimes necessary subsequent to an adequate margin of removal. However, in some other areas, flap repair may give a better cosmetic outcome than a free graft. Treatment of most primary melanoma may thus be achieved on an outpatient or day surgery basis unless nodal surgery is required. In most instances, excision can be achieved under local anaesthesia.

Despite these recommendations for relatively narrow excision, it should be stressed that all melanomas have the potential for recurrence or metastases in the local area, in transit to the lymph nodes, in the lymph nodes and internally. A depth of excision equal to margins is advised but it is not necessary to excise further than the deep fascia. Thus, patients with melanoma must be regarded as having a potentially serious condition and treated with particular care and consideration. A follow-up protocol must be developed for every patient.

The patient should be informed that surgical excision may be followed by wound infection, haematoma, failure of skin grafting and possibly an unsightly scar.

Guidelines	Level	References
Complete excision with margins determined by tumour thickness measurement should be the basis for management of primary melanoma.	II	66–69
A minimum margin of 1cm and a maximum margin of 3cm should be used for invasive melanoma, with the choice of excision margin determined by the tumour thickness.	II	66–69
Other pathological features should be used to make an assessment of prognosis and modify management decisions.	II	63, 64, 71, 72

Recommendations

- The AJCC/UICC system is recommended as the basis for melanoma therapy. (Appendix C)
- A depth of excision equal to margins is advised, but it is not necessary to excise further than the deep fascia.
- A margin of excision of 5mm is recommended for melanoma in situ.

12. Survival Outcomes of Primary Melanoma Management

Survival after diagnosis of melanoma falls with increasing tumour thickness.^{63,64} To advise patients on the likely outcome of their primary melanoma management, the following estimates may be given for 10-year survival rates from the South Australian Cancer Registry, 1996.⁴

pTis	Melanoma in situ	100.0% ⁷⁰
pT1	Melanoma ≤ 0.75mm thick	97.9%
pT2	Melanoma > 0.75mm–1.5mm thick	90.7%
pT3a	Melanoma > 1.5mm–3.0mm thick	75.4%
pT3, pT4	Melanoma > 3.0mm – 4.0mm thick	55.0%
pT4	Melanoma > 4mm thick	40.0%

Other prognostic variables influence outcomes. Such factors as a thin melanoma (which reaches Clark's level IV), ulceration, the presence of lymphatic invasion, satellites and high mitotic rate may adversely affect the prognosis for individual patients with melanoma.^{71,72} (see Appendix E)

13. Treatment of Lymph Nodes

All patients with invasive melanoma are at risk for metastases to the lymph nodes. An important part of the follow-up protocol for these patients involves careful examination of the lymph nodes during each follow-up visit. Lymph nodes containing metastatic melanoma often increase in size quickly, apparently appearing overnight according to the patient. An involved node is usually firm to hard in consistency, is often rounded or with a slightly irregular surface and is usually the lymph node closest to the primary lesion.

Metastases to lymph nodes are uncommon for melanomas <1.0mm in tumour thickness. For primary melanomas 1.0mm and greater in thickness, an increasing proportion of patients will develop regional lymph node involvement. At least 25% of melanomas between 1.5mm and 4.0mm thick will have microscopic lymph node involvement at the time of primary diagnosis. Sixty per cent of melanomas thicker than 4.0mm will have nodal involvement,⁷³⁻⁷⁵ but these involved nodes are usually not clinically apparent at the time of primary diagnosis.

a. Lymph node biopsy

Clinical stage III (AJCC/UICC) melanoma patients (i.e. those with clinically suspicious lymph nodes) should have fine needle aspiration biopsy of the suspicious node.⁶³ Open biopsy may increase the risk of tumour spillage and subsequent recurrence of melanoma in the node dissected field. If open biopsy is absolutely necessary, the biopsy excision should be placed so that it can be easily excised in continuity with the lymph node field when radical lymphadenectomy is subsequently performed. Only in centres where cytological diagnosis is unavailable, or if needle biopsy is unhelpful, is open biopsy recommended. A negative needle biopsy is not conclusive and should be repeated if the node remains clinically suspicious after a period of observation of one month.

If open biopsy is performed, it is safest where immediate resection can be undertaken following positive confirmation by frozen section.

b. Elective node dissection

While no final position on the role of elective lymph node dissection has yet been reached from prospective randomised studies, a consensus has emerged that elective lymph node removal should not be recommended for the patients with primary melanoma.⁷⁶⁻⁸⁰ It remains possible that elective lymph node dissection may offer a moderate survival benefit for male patients with melanoma on the trunk between 1.5mm and 4.0mm in tumour thickness.⁸¹⁻⁸⁴ The two large, prospective randomised trials (Intergroup Melanoma Study and WHO Melanoma Group) have yet to provide definitive statements on this matter, although an interim analysis from the Intergroup indicates a survival advantage for younger patients with nonulcerated tumours 1 to 2mm thick.⁸⁴ It is not appropriate at the present time to recommend elective lymph node dissection for any melanoma on a limb, particularly when taking into consideration the morbidity associated with node dissections.

Independent of the tumour thickness measurement, a pathology report of satellitosis or lymphatic invasion demands serious consideration of node dissection. Confirmed lymph node involvement necessitates therapeutic lymph node dissection.

c. Therapeutic dissection—node dissection for clinically positive nodes

Radical lymph node dissections for melanoma are relatively difficult operations and should be undertaken only by surgeons appropriately trained for the operation. There is a substantial risk of recurrence in dissected node fields in patients with clinically positive lymph nodes,⁸⁵ particularly if extranodal spread is detected. Limited dissections do not guarantee adequate excision of melanoma positive lymph nodes and it is not acceptable to undertake 'node picking' operations for such lymph nodes. Thorough formal dissections will substantially lower the risk of recurrence in a dissected node field. Such recurrence is usually fatal.⁸⁶

Adequate node dissection is associated with a reasonably good prognosis, with a 10-year survival of up to 50% where only one node is involved. Even when two or three nodes are involved, 10-year survival rates of up to 30% can be achieved.⁶³ However, extranodal spread is associated with a high fatality rate, and radiotherapy should be considered if this is detected, if the nodes are extensively involved or if tumour spillage occurs during the surgery.

Dissection of the groin nodes below the inguinal ligament, 'superficial' dissection, carries less risk of lymphoedema than does radical dissection of iliac, inguinal and femoral nodes (ilioinguinal dissection), but this complication is relatively common in both types of dissection.⁸⁷⁻⁸⁹

If secondary deposits of melanoma are thought to be in the lymph nodes below the inguinal ligament, a CT scan of the iliac nodes may be helpful in deciding whether or not they are also involved. If only one or two nodes below the inguinal ligament are involved, a subinguinal node dissection is indicated. If there is gross involvement of the subinguinal nodes, the dissection is increased to include the iliac and obturator nodes.

Therapeutic neck dissection in melanoma patients carries a high risk of recurrence in the nodal field.^{90,91} This is a difficult operation, fraught with complications, and specific training is essential to achieve the optimal outcome. Even when this dissection is undertaken by surgeons with specific training, the incidence of recurrence in the neck is considerable (up to 28%).⁹¹

All patients with positive lymph nodes are at high risk (>50%) for systemic dissemination.⁶³ It is thus important to consider consultation with a multidisciplinary melanoma treatment centre if possible. The production of vaccines and other biological adjuvant therapies are facilitated by the availability of living melanoma cells from the resected lymph nodes. Even where minimal involvement of the lymph nodes is found on node dissection, a telephone or fax consultation or a referral of these patients to a melanoma centre may allow their inclusion in adjuvant therapy clinical trials.

d. Lymphatic mapping and sentinel node biopsy

The recent surgical technique of lymphatic mapping, and selective sentinel node biopsy provides an alternative approach to the treatment of melanoma >1mm thick which, if validated by clinical trial, may satisfy both the proponents and the antagonists of elective lymph node dissection.⁹²⁻⁹⁴ Sentinel node biopsy means identification of the first lymph nodes (the sentinel nodes) to take up a radioactive tracer injected around the primary site. These nodes are then marked on the skin and identified at surgery by the injection of patent blue dye around the site of the primary lesion.

The blue stained nodes are selectively biopsied through a small incision and examined by histology and immunohistochemistry. Should they be positive, lymph node dissection is undertaken. This ensures that only patients who have nodal involvement are subjected to full regional

lymphadenectomy with its potential complications. It has been shown that sentinel node status accurately indicates the presence or absence of micrometastases in a node field.⁹⁵ At the present time, the sentinel node biopsy has not been validated by a completed clinical trial and so should be undertaken only in the context of a Multicenter Clinical Lymphadenectomy Trial which is now in progress. Clinicians are encouraged to offer their patients with high risk melanoma entry into the multicentre selective lymphadenectomy trial.

Sentinel node biopsy can be a difficult operation, particularly in the axilla and the head and neck, and should not be undertaken without training in this technique. Failure to correctly identify the sentinel nodes will be counterproductive to good management of the melanoma patient. Selective lymphadenectomy should only be considered for patients with tumours of thickness >1mm or reaching Clark's level IV in the dermis. Expert lymphoscintigraphy is essential if this technique is to be utilised.^{96,97} Lymphatic mapping and sentinel node biopsy should be considered for all melanomas >1mm thick provided it can be done in the context of a controlled clinical trial and by surgeons trained in these procedures.⁹²⁻⁹⁷

If entry into the selective lymphadenectomy trial is not possible and where good lymphoscintigraphy with training in the technique is not available, the consensus recommendation is that in the absence of clinically involved lymph nodes, satellites and/or lymphatic invasion in the primary pathology report, wide excision without any nodal surgery should be practised for all melanoma patients. When therapeutic node dissection is required, it should be undertaken only by surgeons trained in these procedures.⁸⁵⁻⁹¹

Excision biopsy of suspicious nodes should be followed by complete regional node dissection immediately if nodal metastases are detected.

Guidelines	Level	References
Needle aspiration is preferable to excision biopsy of lymph nodes suspicious of metastatic melanoma.	III	75-83
Elective lymph node dissection is not recommended for the majority of melanoma patients.	III	76-80
Elective node dissection may be appropriate for specific subsets of patients.	II	84

Recommendations

- Excision of suspicious nodes should be followed by complete nodal dissection if nodal metastases are detected.
- Therapeutic node dissection should be undertaken only by surgeons trained in these procedures.
- Lymphatic mapping and sentinel node biopsy should be considered for all melanomas >1mm thick provided they can be done in the context of a controlled clinical trial and by surgeons trained in these procedures.

14. Occult Primary Melanoma

Occult primary melanoma comprises 4–12% of clinical presentations of melanoma to major centres.⁹⁸ Occult primary melanoma means that patients usually present with a palpable lymph node, or in rare cases, a systemic metastasis, in the absence of a recognisable coincident primary melanoma and no past history of melanoma. The treatment for cryptogenic metastatic melanoma in lymph nodes is exactly the same as that for lymph node recurrence in patients with previous or existing primary tumour.^{98,99}

There is no difference in survival between those patients with known or unknown primary tumours and the same number of involved lymph nodes.^{100,101}

Guideline	Level	References
Melanoma in lymph nodes or systemic metastases should be treated appropriately regardless of the inability to detect the primary lesion.	III	98,99

15. Locoregional Recurrent Melanoma

A substantial proportion of patients with thick melanomas on the limbs will develop local recurrence, intransit metastases or metastases in the regional lymph nodes. Isolation perfusion or infusion with high dose cytotoxic agents is currently the most effective method for the treatment of multiple local or intransit recurrences.¹⁰²⁻¹⁰⁵ Needle biopsy is the best method to confirm the diagnosis.

The recommended policy is that the first local recurrence or intransit metastases should be widely excised locally, without a skin graft if possible. Patients with any further recurrences should be referred to the nearest melanoma centre, if available, for perfusion or infusion and inclusion in adjuvant therapeutic protocols. Local and intransit recurrences are often due to lymphatic permeation so node dissection should be considered if this has not been previously performed.

Any cutaneous metastases either in the limbs or elsewhere is an indication that the patient is likely to develop multiple systemic metastases. Careful follow up, in association with a melanoma centre, should be implemented.

When more than one cutaneous metastasis has occurred, referral to an appropriate melanoma centre, if available, is advisable. In some patients it is advisable not to resect subsequent cutaneous metastases because they may be useful as an indicator of response to systemic therapies, or for evaluation of new local therapies.

Guideline	Level	References
Patients with multiple local metastases should be referred to a centre specialising in regional therapy, i.e. perfusion or infusion with cytotoxic agents.	III	102-105

16. Adjuvant Therapy

As yet there is no conclusive evidence that adjuvant therapy is beneficial for anyone with melanoma. However, in view of the known poor prognosis for patients with melanomas >4mm in thickness and/or with involved nodes, it may be appropriate to refer these patients to a melanoma centre for inclusion in controlled clinical trials of immunotherapy, chemotherapy or gene therapy. Only in this way will the value of new therapies be established.

Recommendation

- Patients with melanomas >4mm thick or with lymph node metastases should be considered for referral to a melanoma centre for possible adjuvant therapy.

17. Disseminated Melanoma

Systemic metastasis from melanoma carries a poor prognosis. Fewer than 5% of melanoma patients with systemic metastases survive five years.¹⁰⁶ Standard chemotherapy provides complete tumour response rates of less than 5% and partial tumour response rates which rarely exceed 25%. The standard agents for melanoma are DTIC and CCNU, which have partial response rates not exceeding 20%. Multiple agent chemotherapy does not substantially alter this low level of response.

There have been few studies to test whether cytotoxic therapy of metastatic melanoma improves quality of life. In both breast cancer and melanoma, baseline quality of life is predictive of duration of survival.¹⁰⁷⁻¹⁰⁹ Quality of life studies with patients with advanced melanoma are now being undertaken in a variety of centres.

Effective communication with people with advanced malignancy is vital to the wellbeing of the patient and relatives. Breaking bad news requires care and consideration. Appropriate training packages for learning these skills are available from the Australian Cancer Society and State-based cancer councils.

Surgical resection of isolated metastases may provide good palliation, and in a small proportion of cases, long-term survival. Resection should be considered for isolated pulmonary, cerebral, small intestinal and some intraperitoneal recurrences.¹¹⁰

Considerable interest has been generated in the last decade by the possibility of immunotherapy for this moderately immunogenic tumour. To date, response rates for any of the currently available immunotherapeutic modalities do not exceed those of chemotherapy, although some recent studies involving chemotherapy and immunotherapy (biochemotherapy) have suggested higher complete response rates may be achievable.^{110,111}

In the light of this situation, all patients with advanced disease should be considered for referral to a melanoma centre for inclusion in clinical trials of new therapeutic modalities involving both chemotherapeutic and immunotherapeutic regimens. In most instances, once a treatment protocol has been determined in consultation with patients and the selected carers, it can often be undertaken in the patient's own community with assistance from the local medical and surgical oncologists and the patient's general practitioner.

Nursing of patients with metastatic melanoma presents additional challenges and problems because many of the patients are young, with families, jobs and social situations unique to this age group. The involvement of skilled palliative care nurses is a critical part of caring for these patients at home.

Guideline	Level	Reference
Surgical resection should be considered for isolated melanoma metastases in lung, brain and peritoneal cavity.	III	110

Recommendations

- Patients with systemic metastases should be referred to a melanoma centre for consideration of systemic therapies.
- Clinicians dealing with patients with systemic melanoma should be appropriately skilled in psychological management and palliative care.¹⁰⁷⁻¹⁰⁹

18. Radiotherapy for Melanoma

Radiation sensitivity of melanoma

Numerous experimental and clinical studies indicate that melanoma is usually responsive to radiation, in contrast to many early publications stating that melanoma was radioresistant. In general, higher response rates are found when a relatively high daily dose is used.¹¹² The radiation response of melanoma may be increased if adjuvant hyperthermia is used.¹¹³

Primary tumours

Radiation therapy is used rarely as the definitive management of primary melanoma, except for large unresectable lesions (usually mucosal) or for lentigo maligna melanoma in elderly, frail patients. Postoperative treatment reduces local recurrence when surgical margins are close and further resection is not possible, especially if neurotropic histology is reported.

Locoregional extension

Postoperative radiation therapy reduces local recurrence following regional lymph node dissection for positive lymph nodes.¹¹⁴ The indications for postoperative radiation therapy are extensive nodal involvement, extracapsular tumour extension or parotid involvement. Elective irradiation of regional node basins has also been shown to reduce the rate of nodal relapse in high risk patients.¹¹⁴ Radiation is effective in reducing recurrence of multiple cutaneous metastases that occur locoregionally.¹¹⁵

Disseminated melanoma

Radiation therapy provides useful palliation for a range of symptomatic problems due to metastatic melanoma. This includes neurological symptoms from cerebral metastases, bleeding or painful cutaneous lesions, bony metastases, mediastinal masses causing obstruction, and nodal masses causing vascular or neurological compression.^{116–119}

Guidelines	Level	References
Post-operative radiotherapy should be considered for cutaneous melanomas likely to recur locally (>4mm thick, satellite nodules or neurotropic spread) or regionally (multiple node involvement or extracapsular spread) and following resection of mucosal melanomas. Primary radiotherapy should be considered for unresectable lentigo maligna melanomas.	III	115
Radiotherapy is recommended for treatment of extensive cutaneous metastases, and for palliative management of cerebral and bone metastases and for other metastases where temporary local control is needed, e.g. large nodal or soft tissue masses.	III	116–119

19. Palliative Care

Patients with metastatic melanoma and their families are likely to have complex physical, psychosocial and spiritual needs as the disease progresses.¹²⁰⁻¹²¹ The nature and intensity of these needs will vary according to the sites of metastatic involvement (e.g. bone, liver, brain, intraperitoneal), the age and social circumstances of the patients, the speed with which deterioration is occurring, and other factors.

The palliative approach is the application of good symptom control in association with particular attention to the psychological, social and spiritual wellbeing of the person and their family or carers.¹²² Palliative care is the style of care and services offered when it is apparent that the options for further effective anti-cancer treatment are limited.

All people with advanced melanoma should be offered the palliative approach, and some may take up the offer of palliative care.

Palliative care may be provided in a variety of ways. Most palliative care is provided by the existing network of carers, coordinated by either the general practitioner or the treating oncologist. The person coordinating care should draw on the expertise of others already caring for the person and may, where possible, draw on other health professionals as particular expertise is needed.

In some cases, particularly those that are more complex, palliative care is provided by specialist palliative care teams. Specialist palliative care teams should be considered, in particular, when the patient with melanoma has many and complex needs. Although no data are available specifically for patients with melanoma, nor for all types of palliative care services, an idea of the scope of services in Australia can be gleaned from a paper reporting that 56% of people who died of cancer in 1990 year received care from a hospice service.¹²²

Timing of referral

Early referral to a palliative care service will usually be helpful, even though further anti-cancer therapy may be indicated. The precise time at which the services of a palliative care specialist and/or multidisciplinary team are introduced depends on the person's wishes and needs, including, among other factors, the course of the individual illness and its varied symptom complexes, the psychosocial factors involved, and the proximity of the cancer centre or palliative care service to the person's home.¹²³ The transition, when it occurs, is facilitated if the palliative care health professionals are an integral part of the multidisciplinary team at a melanoma unit or treating hospital.^{124, 125}

There are benefits to the patient in establishing contact with a palliative care team, even if he or she is relatively well, at a time when it is becoming clear that specific treatment options are limited. This allows the establishment of access and contacts, with exploration of options for future care without the need for immediate decisions. Palliative care stresses advanced planning rather than crisis intervention.

The concept of parallel care is important to ensure a close and continuing cooperation between oncological and palliative services throughout the often prolonged course of advanced melanoma.

Services and expertise should be available and offered to all patients with melanoma so they can make informed choices about their care and have the opportunity of professional assistance in the home.

Site of palliative care

As the disease progresses, care may be provided in the person's own place of residence—be it their home or another's, a nursing home or hostel, an acute hospital or an inpatient hospice.

Own residence

At all times, the general practitioner will be the local health care provider, working with the palliative care team, visiting in the home, if that assistance has been accepted. Depending on the particular community, the palliative care team will consist of specialist palliative care nurses or generalist community nurses with specialist nurses consulting, and a specialist palliative care physician available to advise the general practitioner. These people are usually available 24 hours a day. Counsellors and pastoral care workers, as well as volunteer help, are available. Links with other community services mean that other help can be accessed as required, including physiotherapy, dietary advice, occupational therapy, home help and so on.

Although home care programs are generally assessed favourably,^{126,128} families undertaking home care experience higher levels of stress and social disruption than those whose relatives are cared for in institutions.¹²⁹

Acute hospital

Situations can arise which will be best treated in the acute hospital. These include the surgical pinning of a pathological fracture, radiotherapy for a painful bone metastasis, thoracocentesis, treatment of hypercalcaemia, pain and symptom control, and respite care.

Inpatient hospices

Occasionally, patients with melanoma require long term admission to a hospice if extensive skeletal metastases or neurological damage from spinal cord compression or brain metastases create heavy nursing requirements, mobility difficulties, and other needs which are not able to be provided in the community indefinitely.

Some patients with melanoma will move between home, hospital and hospice, often many times. It is important that the patients know who bears the primary responsibility for their care at various points in these events, and that there is continuity of care, including the communication of current detailed and accurate information about all aspects of treatment plan and medications.

For further information, clinicians and patients may contact their state-based palliative care organisations. (see Appendix G)

Recommendation

- It is recommended that palliative care health professionals be an integral part of the multidisciplinary team in facilities where patients with melanoma are treated.

20. Follow-up

Follow-up recommendations are based primarily on tumour thickness.¹³⁰ Tumours <1mm thick do not require close and prolonged follow-up unless patients are at high risk for a second primary melanoma due to multiple dysplastic naevi or a history of melanoma in close relatives. Following completion of surgical treatment, two years of follow-up is suggested. After that period, patients should be informed that a remote possibility of recurrence still exists and may present as a spot on the skin, a mass under the skin or a mass in the draining lymph node field. Such masses should be diagnosed by fine needle aspiration biopsy and the patients referred for appropriate management. General practitioners should be encouraged to see patients at least yearly following the first two years of follow-up, to examine the local area, the intransit area and the draining lymph nodes. Follow-up should also include total skin surveillance at every visit. Late recurrence is rare but must be considered a possibility for all melanoma patients.¹³⁰ It is important to remember that for many melanoma patients, the risk of a second primary lesion is higher than the risk of recurrence.¹³¹

Most recurrences are detected by patients themselves even with close follow-up schedules.^{130,132} Follow-up provides additional reassurances and educates patients on the methods used to detect recurrences.

For tumours thicker than 1mm, a suitable protocol is a three to four monthly review for the first two years, a six monthly review until five years and a lifelong yearly review thereafter.¹³³ Patients with tumours >4mm thick or patients with involved nodes have at least a 50% chance of developing further metastases within five years,⁶³ so consultation or networking with a melanoma centre should be considered.

Follow-up examinations should include careful palpation around the primary site, palpation along the draining lymphatic pathways and examination of all nodal fields. It is important that all follow-up visits should include a total body examination looking for suspicious lesions. Second primary melanomas are relatively common in melanoma patients and thus regular skin examinations are appropriate for these patients. After the immediate follow-up period, the general practitioner should be encouraged to continue regular screening for new melanomas at least yearly. These recommendations are particularly pertinent for patients with a large number of naevi, whether or not they are dysplastic. Photography may be helpful in this surveillance program.

Guideline	Level	References
A follow-up regimen based on tumour thickness should be arranged for all patients with invasive melanoma.	III	130, 133

Recommendation

- The follow-up examination should include palpation for local recurrence, intransit metastases, lymph node fields and a general examination of the skin for new primary melanomas and other skin cancers.

21. Appropriate Investigations

The value of extensive investigations for patients with primary melanoma has not been demonstrated to be cost effective.¹³⁴

Baseline investigations such as full blood count, chest X-ray and liver function tests (including LDH) may be undertaken for patients with tumours likely to recur (i.e., >4mm or with nodal involvement) but the effectiveness of extensive investigation even in these patients is as yet unproven.¹³⁴⁻¹³⁶

In some instances, the patient's need for reassurance may be an indication for CT scanning where a high probability of metastases exists. However, there is no evidence at the present time that detection of systemic recurrences of melanoma prior to the development of symptoms offers any survival benefit to the patient. In general, costly investigatory protocols should be undertaken only in response to symptomatology suggestive of recurrent disease, or as part of a research trial protocol.

If investigation is needed, useful imaging modalities include CT and MRI scanning. Positron Emission Tomography (PET) with F18 deoxyglucose has been shown to have a high sensitivity for the detection of recurrent melanoma. However, these imaging techniques should be applied only after appropriate consultation.

Recommendations

- Investigations such as CT, MRI and PET should be utilised only where specific symptoms suggest the presence of metastases.
- Extensive investigation for systemic metastases in patients with primary melanoma is not recommended.

22. Specific Sites and Types of Melanoma

a. Mucosal melanoma

Mucosal melanoma is rare, comprising <1% of all melanoma. It occurs in the mouth, nose, oesophagus, gall bladder, urethra, anus, vulva and vagina, and is usually asymptomatic.^{137,138} For this reason mucosal melanoma is generally detected late and thus has a very poor prognosis.¹³⁹ Apart from amalgam tattoo in the mouth and benign melanosis of the vulva, pigmented lesions of the mucosal surfaces are rare and melanoma should always be considered as a possible diagnosis. Appropriate referral of all pigmented mucosal lesions is recommended.

b. Acral lentiginous melanoma (ALM)

Acral lentiginous melanoma is defined as melanoma of the acral skin, i.e. the thickened skin of the soles and palms. It is the commonest form of subungual melanoma. It is rarely associated with a visible pre-existing benign naevus. The main interest of the ALM classification is that it is the predominant melanoma of non-white individuals. Its prognosis may be marginally worse than other melanomas but this is yet to be conclusively proven.¹⁴⁰⁻¹⁴² Treatment does not differ from the other, more common forms of melanoma. It is often difficult to directly close defects on the sole of the foot. A graft on the sole of the foot tends to hypertrophy and be uncomfortable for patients, so local flap repair or graft from the acral skin of the other instep may be appropriate.

c. Subungual melanoma

Subungual melanoma can be difficult to diagnose early but must be considered for any pigmentation in the nail.¹⁴³ This melanoma has a generally poor prognosis because it is usually deeply invasive at the time of diagnosis.¹⁴⁴⁻¹⁴⁶ The differential diagnosis includes haematoma under the nail and fungal infections. Haemorrhage following trauma may be in the nail substance itself as well as under the nail and a clear margin of normal nail will develop between the nail fold and the nail pigmentation as the nail grows. If this does not develop then the diagnosis remains uncertain and removal of a section of the nail, with or without underlying biopsy, is the preferred initial management.

There are several clinical features that may be helpful in early diagnosis of subungual melanoma, including Hutchinson's sign, which refers to the development of pigmentation in the skin around the nail. Melanoma developing in the nail matrix, under the proximal nail fold, may produce a pigmented band in the nail. In pale skinned individuals, the development of a pigmented band should lead to a biopsy of the nail matrix, after reflection of the proximal nail fold. In darker skinned individuals, such pigmented bands are usually due to benign naevi and warrant biopsy if they are new or have undergone recent change.

Amelanotic melanomas may be very difficult to detect early when they occur under the nail. Any persistent and progressive lesion affecting the nail apparatus should be regarded with suspicion. Subungual melanomas will ultimately cause splitting and loss of the nail plate. The great toenail and the thumbnail are the most common sites for subungual melanoma.

Subungual melanoma of the fingers or toes justifies amputation through the distal interphalangeal joint.¹⁴⁴ A ray amputation of the great toe may provide better cosmesis.¹⁴⁵ This entity has a poor prognosis since it is usually deeply invasive at the time of diagnosis.¹⁴⁶ Because most subungual melanomas are advanced at the time of presentation, elective node dissection may be appropriate for these patients.^{147,148} Selective lymphadenectomy may be an acceptable alternative for nodal management if the technique is validated by the current Multicenter Clinical Lymphadenectomy Trial.

d. Desmoplastic melanoma

Desmoplastic melanoma is an uncommon variant of melanoma characterised by a spindle cell pattern with sclerosis of the dermis (desmoplasia) and may invade nerves (neurotropism). Desmoplasia and neurotropism may occur separately but are often associated. Desmoplastic and neurotropic melanomas are associated with a high risk of local recurrence related to their poorly defined clinical borders, frequent amelanosis and infiltration along nerve sheaths, predisposing to incomplete excision and persistence of the primary tumour.^{149,150} It is therefore reasonable to add at least 1cm to the excision margins recommended for other types of melanoma.

Despite this high risk of local recurrence, even very thick desmoplastic melanomas have not been shown to have a worse prognosis than other histological types of melanoma of equivalent thickness.¹⁵¹ Some centres advocate post-operative radiotherapy for patients with neurotropic melanoma but as yet there is no conclusive evidence of benefit for this modality. It is recommended that these patients be referred to a melanoma centre for consideration of radiotherapy in the context of a clinical trial.

Desmoplastic melanoma is clinically difficult to diagnose as these tumours (commonly on the head and neck) may be non pigmented or present as a subcutaneous nodule.¹⁵² Some develop from lentigo maligna melanoma.¹⁵³ Paraesthesia and cranial nerve symptoms and signs are rare indicators of the presence of neural invasion by this tumour.¹⁵⁴

e. Multiple primary melanoma

Multiple primary melanoma is a relatively common occurrence. Synchronous development of two or more melanomas is quite rare but metachronous new primary melanomas may occur in at least 5% of patients with melanoma.¹⁵⁵⁻¹⁵⁷ Recent data from New South Wales and Victoria indicate that there is a 3-4% risk of a second melanoma in these states although the figure will increase with longer follow-up.¹³¹ These multiple primary melanomas are more common in patients with multiple atypical naevi especially in a familial melanoma setting but can occur in any patient who has had a melanoma.^{158,159} The treatment for multiple primary melanomas is based entirely on the tumour thickness of each specific melanoma.¹⁶⁰ At the present time no systemic therapy has been shown to influence the development of a second or subsequent primary melanoma.

f. Melanoma in childhood

Melanoma is rare in children below the age of 12, but the clinical features are identical to those in the adult.¹⁶¹ The usual differential diagnosis is the pigmented Spitz naevus. Because of the difficulty in distinguishing melanoma from pigmented Spitz naevi, which are benign lesions, excision biopsy is usually warranted.¹⁶² However, parents can be reassured that the large majority of these darkly pigmented, relatively rapidly growing lesions in children will be benign on histopathology. In the

rare event that melanoma is diagnosed, a second histopathology opinion should be sought. Should the diagnosis be confirmed, the recommended treatment of melanoma in childhood is exactly the same as that for the melanoma in the adult.^{163,164}

g. Melanoma during pregnancy

A major review of studies on this subject has found no conclusive evidence that melanoma during or near the time of pregnancy adversely affects the clinical course or prognosis of this disease.^{165,166} A recent large study has indicated that although melanomas detected during pregnancy are thicker than those in non pregnant women, these lesions are not associated with a less favourable prognosis for a given thickness.¹⁶⁷ Where nodal involvement occurs during pregnancy there is a moderately worse prognosis than in the non pregnant patient.¹⁶⁸ Melanoma has been reported to cross the placenta but this appears to occur only in mothers with highly advanced melanoma. Cases have been reported where melanoma metastasis was detected in the surviving baby and the melanoma in the baby has regressed spontaneously shortly after birth.

While there is no specific evidence that pregnancy adversely affects the prognosis, a consensus view is that pregnancy is not advisable for at least two years after the excision of a clinically significant melanoma, i.e. lesions >1.5mm, where the risk of occult metastasis is moderately high. Pregnancy in a woman with occult metastases may promote earlier appearance of metastatic melanoma. Avoiding pregnancy for some years may add reassurance that a subsequent pregnancy will be less likely to be associated with recurrent melanoma. Advice to women with stage III melanoma, i.e. melanoma in lymph nodes, should be that pregnancy is inadvisable for at least five years because of the high risk (exceeding 50%) of systemic disease.

The role of the clinician in these difficult situations is to provide suitable information on risk factors to patients so that an informed decision can be made. Considerations should include the effects of chemotherapy and radiotherapy on the unborn child. Referral to a melanoma centre for advice may be appropriate for those patients contemplating pregnancy.

The question of pregnancy termination is even more difficult for clinicians and patients. There is no evidence that pregnancy decreases the overall survival rate for melanoma patients. The decision to terminate pregnancy in this situation requires detailed consultation on specific risks of individual patients, taking into consideration the risk factors associated with the various stages of melanoma. Consultation with a melanoma referral centre may be helpful for patients and treating clinicians.

The treatment of primary melanoma does not differ because a woman is pregnant. However, in the late stages of pregnancy where node dissection is contemplated, it may be advisable to delay the dissection to allow the pregnancy to be completed or to initiate early delivery to allow the operation to proceed.

h. Hormone replacement therapy and oral contraceptives

There is no conclusive evidence that either hormone replacement therapy or the use of the contraceptive pill play any role in the natural history of melanoma. Indeed, several studies have shown a marginal benefit while others have suggested no association between these hormones and survival.^{169,170}

Guidelines	Level	References
Wider excision than is normal for other histological types of melanoma is	III	149, 150

Guidelines	Level	References
recommended for desmoplastic melanoma.		
Melanoma in children should be treated as appropriate for the same tumour thickness melanoma in the adult.	III	163, 164
Hormone replacement therapy and oral contraceptives are not contraindicated for women who have or have had melanoma.	III	169, 170

Recommendations

- Patients with mucosal melanoma should be referred to a suitable speciality clinic or clinician.
- ALM on the sole of the foot should be referred for specialist excision and appropriate reconstructive procedures.
- Subungual melanoma should be considered as a possible cause of any pigmentary changes under the nail. In cases of doubt, removal of the nail and biopsy is recommended.
- Subungual melanoma should be treated with excision margins which accord to the lesion thickness. This usually involves amputation of the terminal phalanx.
- Post-operative radiotherapy, in consultation with a melanoma centre, should be considered after surgical excision of a recurrent desmoplastic or neurotropic melanoma.
- Multiple primary melanoma should be treated according to the tumour thickness of each lesion.
- Melanoma in a pregnant woman should be treated according to the tumour thickness.¹⁶⁵⁻¹⁶⁷
- Pregnant women with thicker (T3, T4) melanomas and nodal metastases should be treated in consultation with specialised centres.
- Because of the possibility of metastatic recurrence, pregnancy is not advisable for two years after removal of high risk primary melanoma or melanoma in nodes.¹⁶⁸
- Termination of pregnancy should be considered in women with high risk primary or recurrent melanoma only after detailed discussion with the patient and her partner, if the patient wishes her partner to be involved.

23. Conclusion

These Guidelines for the Management of cutaneous melanoma have been developed through a process of review of the best evidence available. We are aware that high level evidence is absent for many of the questions we have addressed. Nonetheless, we believe that the consensus opinions offered will be of value to practitioners in the field pending the availability of higher quality evidence. This relative lack of high level evidence underlines the importance of further research on many of the questions.

Applications of the guidelines should lead to general improvement of the standard of care of malignant melanoma in Australia. The extent to which this is realised, will depend on the guidelines being adopted and implemented. In the process, it is hoped that new questions will be identified which will guide both research and the delineation of questions for updates of guidelines in this area.

Appendix A—Expert Panel Members

Multidisciplinary Working Party Membership

Professor W McCarthy (Convenor)	<i>(Surgery)</i>
Professor R Burton	<i>(Surgery)</i>
A/Professor A Coates	<i>(Medical Oncology)</i>
Dr N Davis (Chairman)	<i>(Surgery)</i>
Professor G Gill	<i>(Surgery)</i>
Professor A Green	<i>(Epidemiology)</i>
Ms K Harfield	<i>(Consumers)</i>
A/Professor P Heenan	<i>(Pathology)</i>
Dr J Kelly	<i>(Dermatology)</i>
Ms M McJannett	<i>(Nursing Oncology)</i>
Professor R McLeod	<i>(Surgery)</i>
Professor R Marks	<i>(Dermatology)</i>
Dr S Menzies	<i>(Dermatological Research)</i>
Emeritus Professor G Milton	<i>(Surgery)</i>
Ms H Moore	<i>(Consumers)</i>
Dr S Porges	<i>(Rural Surgery)</i>
Dr S Precians	<i>(General Practice)</i>
Dr H Shaw	<i>(Epidemiology)</i>
A/Professor M Smithers	<i>(Surgery)</i>
Dr G Stevens	<i>(Radiation Oncology)</i>
Professor J Thompson	<i>(Surgery)</i>

Expert advice was given to the Working Party by:

Professor B Armstrong	<i>(Epidemiology)</i>
Professor M Elwood	<i>(Epidemiology)</i>
Professor L Peters	<i>(Radiation Oncology)</i>
Dr M Quinn	<i>(Plastic & Reconstructive Surgery)</i>
Professor C Silagy	<i>(Cochrane Collaboration)</i>

Ex Officio:

Emeritus Professor T Reeve	<i>(Australian Cancer Network)</i>
Mr T Kober	<i>(Australian Cancer Network)</i>

Appendix B—Epidemiology of Melanoma in Australia

a. Incidence and mortality patterns

According to the Australian Institute of Health and Welfare and the Australasian Association of Cancer Registries,³ the age-standardised incidence rates of cutaneous melanoma in Australia in 1995 were 36.5 per 100,000 person years in men and 28.4 per 100,000 person years in women (standardised to the 'World' population). The crude rates were 45.4 and 36.5 per 100,000 person years, respectively.

Following a dramatic national television program on melanoma late in 1987, the age standardised incidence rate of melanoma peaked at 36.5/100,000 in 1988, then fell to 34 per 100,000 in 1989–90. However, rates began to rise again in 1992 and the rise has continued to at least 1995. The national age-adjusted incidence rates of melanoma increased between 1978 and 1987 by an annual average of 6.5% in men and 4.4% in women.¹⁷¹

With respect to mortality, in 1985–87 the rates were 6.0 and 3.7 per 100,000 person years in men and women respectively, and, since 1930, there has been an average annual increase in age-adjusted rates of 4.4% in men and 3.4% in women. Mortality trends appear to have stabilised recently.^{2,3,6} A well-known gradient of melanoma incidence and mortality inversely associated with latitude is observable.^{6,171}

The latest descriptive data for invasive melanoma across the nation² show that the most commonly specified histological type was superficial spreading melanoma, followed by nodular melanoma and lentigo maligna melanoma, and that 52% of melanomas of known thickness were thinner than 0.76mm. Women had a higher proportion of thin melanomas and men had twice the rate of melanomas thicker than 3mm. The highest rates were seen on the male trunk and female lower limbs, not taking account of surface area.

Analysis of Queensland incidence data for 1987 according to detailed anatomical site, and taking relative surface areas into account, showed the highest incidence of melanoma to be on chronically-sun exposed sites, namely the face and ears of men and the face of women, with the next highest rates on the neck, shoulders and back in men.¹⁷² In contrast, on sites which receive least sun exposure, the buttocks of both sexes and the scalp in women, incidence was negligible. Nevertheless, the association between melanoma site and levels of sun exposure is more complex than previously believed, since a more recent study from Queensland¹⁷³ found similar densities of leg and forearm melanomas, a finding inconsistent with the relative degree of exposure of each.

b. Risk factors for melanoma¹⁷⁴

Genetic factors

It is likely that the increase in risk of cutaneous melanoma due to UV exposure depends on an interaction with genetic factors, which determine level of susceptibility. Melanoma is extremely rare in Aborigines. For a small proportion of the fair-skinned Australian population who have a history of melanoma in close relatives, genetic factors may be particularly important. Linkage analyses are currently being carried out among several large Australian melanoma pedigrees in an attempt to identify the location of genes that predispose these individuals to melanoma, and early findings indicate that familial melanoma may be genetically heterogeneous. In recent studies incorporating

data from some Australian families, a familial melanoma susceptibility locus has been localised to the CDKN2 gene on chromosome 9p21.¹⁷⁵ However, other Australian melanoma kindreds show no linkage to 9p, suggesting other loci may be important.⁴⁸

Epidemiological evidence on risk factors for melanoma in Australia comes from two population-based 'case control' studies carried out in Western Australia¹⁷⁶ and in Queensland¹⁷⁷ in the early 1980s. The strongest predictor of risk of melanoma was the number of benign melanocytic naevi (moles) on the arms. There was a relative risk (RR) of melanoma of 11.3 for 10+ raised naevi on the arms in the Western Australian study, and, in the Queensland study, for any naevi on the arm, flat or raised, the estimated RR was 22.8 compared to people in whom no naevi were counted.

Pigmentary characteristics were also important determinants of melanoma risk in both studies. Melanoma was associated with poor tanning ability, a tendency to sunburn, fair or red hair colour, blue or green eyes and pale skin. However, in a logistic regression model where these factors were included simultaneously, only ability to tan, susceptibility to sunburn and hair colour had independent effects.¹⁷⁷ The number of moles is strongly genetically determined⁴⁶⁷ and is influenced by sun exposure.¹⁷⁸

Environmental factors

Sun exposure was the principal risk factor for melanoma investigated in both the Queensland and the Western Australian populations. The classification of the level of an individual's exposure was mostly a function of that individual's recalled sun exposure at various ages. Given the substantial but unavoidable error inherent in this method of assessing past sun exposure, it is not surprising that findings often varied about the relationship between melanoma and sun exposure. Furthermore, the data in both studies were analysed according to pathological subtype, despite the lack of evidence of an aetiological correlation, which may have reduced the power to identify causal associations with reported sun exposure variables.

To summarise the studies' findings, the indices of high sun exposure, based on recall, which were strongly associated with risk of melanoma were migration to Australia at an early age^{176,177} and history of other skin cancer. More importantly, some objective indicators of higher dose at an early age, namely presence of solar keratoses or other skin cancers on the face¹⁷⁹ and presence of dermal elastosis inferred from the surface pattern of exposed skin on the back of the hand,¹⁷⁶ were strongly and significantly associated with melanoma in Queensland and Western Australian populations.

A range of risk factors other than solar UV were investigated but overall few positive associations with melanoma were found. Other major factors assessed, and for which no relationships with melanoma were found, included hormones, diet and smoking.

Appendix C—AJCC/UICC pTNM Classification System and its Revision

PRIMARY TUMOUR (pT)

- pTX Primary tumour cannot be assessed
- pT0 No evidence of primary tumour
- pTis Melanoma in situ (atypical melanocytic hyperplasia, severe melanotic dysplasia), not an invasive lesion (Clark's level I)
- pT1 Tumour 0.75mm or less in thickness and invades the papillary dermis (Clark's level II)
- pT2 Tumour more than 0.75mm but not more than 1.5mm in thickness and/or invades to papillary-reticular dermal interface (Clark's level III)
- pT3 Tumour more than 1.5mm but not more than 4mm in thickness and/or invades the reticular dermis (Clark's level IV)
 - pT3a Tumour more than 1.5mm but not more than 3mm in thickness
 - pT3b Tumour more than 3mm but not more than 4mm in thickness
- pT4 Tumour more than 4mm in thickness and/or invades the subcutaneous tissue (Clark's level V) and/or satellite(s) within 2cm of the primary tumour
 - pT4a Tumour more than 4mm in thickness and/or invades the subcutaneous tissue
 - pT4b Satellite(s) within 2 cm of the primary tumour

LYMPH NODE (N)

- NX Regional lymph nodes cannot be assessed
- NO No regional lymph node metastasis
- N1 Metastasis 3cm or less in greatest dimension in any regional lymph node(s)
- N2 Metastasis more than 3cm in greatest dimension in any regional lymph node(s) and/or intransit metastasis
 - N2a Metastasis more than 3cm in greatest dimension in any regional lymph node(s)
 - N2b Intransit metastasis
 - N2c Both N2a and N2b

DISTANT METASTASIS (M)

- MX Presence of distant metastasis cannot be assessed
- MO No distant metastasis
- M1 Distant metastasis
 - M1a Metastasis in skin or subcutaneous tissue or lymph node(s) beyond the regional lymph nodes
 - M1b Visceral metastasis

STAGE GROUPING

[I]	pT1	NO	MO
	pT2	NO	MO
[II]	pT3	NO	MO
	pT4	NO	MO
[III]	Any pT	N1	MO
	Any pT	N2	MO
[IV]	Any pT	Any N	M1

Proposed TNM Classification for Cutaneous Melanoma

T classification:

	thickness	ulceration status
T1	≤1.0 mm	a: without ulceration
T1		b: with ulceration
T2	1.1–2.0 mm	a: without ulceration
T2		b: with ulceration
T3	2.1–4.0 mm	a: without ulceration
T3		b: with ulceration
T4	>4.0 mm	a: without ulceration
T4		b: with ulceration

N classification:

	# of nodes	nodal size
N1	one	a: micrometastasis b: macrometastasis
N2	2–4 nodes positive	a: micrometastasis b: macrometastasis c: intransit metastases/satellite(s) without metastatic nodes
N3	5 or more nodes positive matted nodes intransit metastases/satellite(s) and metastatic nodes	

M classification:

	Site	serum LDH
M1a	Distant skin, SQ or nodes	normal
M1b	lung, GI tract	normal
M1c	all other visceral mets. Or any distant metastasis	normal elevated

Proposed Stage Grouping for Cutaneous Melanoma

Clinical Staging ^a				Pathological Staging ^b			
O	Tis	N0	M0	O	Tis	N0	M0
IA	T1a	N0	M0	IA	T1a	N0	M0
IB	T1b	N0	M0	IB	T1b	N0	M0
	T2a	N0	M0		T2a	N0	M0
IIA	T2b	N0	M0	IIA	T2b	N0	M0
	T3a	N0	M0		T3a	N0	M0
IIB	T3b	N0	M0	IIB	T3b	N0	M0
	T4a	N0	M0		T4a	N0	M0
IIIA	T4b	N0	M0	IIIA	T4b	N0	M0
	Any T	N1	M0		Any T	N1	M0
IIIB	Any T	N multiple	M0	IIIB	T4b	N1	M0
	Any T	N satellite(s)	M0		Any T	N2	M0
	Any T	N in transit(s)	M0		Any T	N3	M0
IVA	Any T	Any N	M1a	IVA	Any T	Any N	M1a
IVB	Any T	Any N	M1b	IVB	Any T	Any N	M1b
IVC	Any T	Any N	M1c	IVC	Any T	Any N	M1c

^a clinical staging includes microstaging of the primary melanoma and **clinical/radiological** evaluation for metastases;

^b pathological staging includes microstaging of the primary melanoma and **pathological** information about the regional lymph nodes. (Patients with pathological Stage 0 or Stage 1A do not need pathological evaluation of their lymph nodes.)

Appendix D—Histopathological Reporting

The following recommendations are based, to a large extent, on the 1982 revision of the 1972 Sydney classification,¹⁸⁰ the AFIP fascicle on Melanocytic Tumors of the Skin¹⁸¹, and the WHO *International Histological Classification of Skin Tumors*,¹⁸² with modifications and additions resulting from the ACN consensus conference in Sydney in 1995.

The surgical pathology report should contain the following components:

— the most important components are marked with an asterisk.

Macroscopic Description

- Measured dimensions of excision specimen and the melanoma.
- Description of the melanoma: contour, pigmentation, borders, regression.

Microscopic Description

- Diagnosis of malignant melanoma.*
- Maximum tumour thickness according to the method of Breslow, measured to the nearest 0.1mm.*
- Completeness of excision.*
- Microscopic measurement of margins of excision.*
- Histological classification (see Table 1).
- Level of invasion (Clark's).
- Mitotic rate per square millimetre.
- Ulceration (diameter in mm).
- Regression, presence and extent.
- Vascular invasion.
- Cross-sectional profile.
- Predominant cell type (epithelioid, spindle, naevoid).

Associated benign melanocytic lesion.

- Microsatellites.
- Lymphocytic infiltrate; presence and extent of tumour infiltrating lymphocytes (TIL).
- Growth phase: horizontal growth phase, vertical growth phase.

It is advisable that the clinician consult with a pathologist if the report does not accord with the clinician's diagnosis of the tumour. In cases of doubt, an opinion should be sought from a pathologist with expertise in diagnosis of skin tumours.

Comments

The diagnosis of primary melanoma, the maximum tumour thickness and the assessment of completeness of excision provide the minimum essential information for treatment planning and the assessment of prognosis.

- 1. Cutaneous metastasis.** The possibility of metastatic melanoma must be considered in cases where the tumour is located completely within the dermis and/or subcutis without either attachment to the epidermis or an intraepidermal component of atypical melanocytic proliferation. Epidermotropic metastasis may mimic primary melanoma.
- 2. Histological type.** The most widely accepted histological classification of melanoma is based on Wallace Clark's. The widespread acceptance of this classification is based on its clinicopathological correlations, on the results of epidemiological studies that have indicated possible aetiological differences between some subtypes, and on the didactic value of recognising morphologic variations as an aid to the diagnostic process.

It is likely that nodular melanoma is a variant of the most common form of melanoma, i.e. superficial spreading melanoma, in which expansile growth of the neoplastic cells has produced the characteristic nodule which has overgrown the pre-existing adjacent component.

The epidermal component of lentigo maligna melanoma (Hutchinson's melanotic freckle melanoma) in most cases appears to extend laterally very slowly over a period of many years. When the tumour becomes invasive, however, the prognosis for a given tumour thickness is the same as that of other subtypes of melanoma.

The histological classification has little, if any, prognostic value independent of tumour thickness. This applies to all histological types of melanoma including lentigo maligna melanoma and acral lentiginous melanoma. Further studies on large numbers of desmoplastic melanoma are needed to assess prognostic factors in this tumour but tumour thickness remains the best prognostic index currently available.

- 3. Growth phase.** Assessment of growth phase appears to be of most value in thin tumours. Virtually all tumours in level III and deeper have developed vertical growth phase according to the proposed criteria. The recognition of vertical growth phase in level II tumours is an indication of the possibility of metastasis from thin melanoma.
- 4. Prognostic models** incorporating factors such as ulceration, tumour thickness, satellitosis tumour infiltrating lymphocytes, regression, sex, age and site may provide a more accurate assessment of tumour behaviour than tumour thickness alone.
- 5. Regression.** When regression is present, care must be taken to exclude extension of the regression to the margins of excision.
- 6. Assessment of completeness of excision.** The entire tumour must be embedded. The margins should be carefully examined not only for the presence of invasive melanoma but also for intraepidermal melanoma and other atypical melanocytic proliferation in the epidermis.

In those cases where the borders of the lesion are very poorly defined, as in some cases of lentigo maligna type, the entire periphery of the specimen may be embedded for histopathological examination.

7. **Desmoplasia.** The presence of desmoplasia in the stroma of the tumour itself or ,in the dermis or subcutis, deep to clearly visible invasive melanoma cells should lead to examination for the presence of atypical spindle cells. Extension of desmoplasia to the margins of excision is an indication for wider excision.
8. **Neurotropism.** Infiltration along nerve sheaths is also associated with a higher than expected local recurrence rate. Neurotropism is relatively common in desmoplastic melanoma, but may be found in other forms of melanoma.
9. **Local recurrences, satellites and intransit metastases.** Local recurrence may be due either to persistence of incompletely excised primary melanoma, local lymphatic metastases (satellites), or to cutaneous metastasis. Recurrent melanoma in the scar or graft should be examined carefully for the histological criteria of persistent primary melanoma versus metastatic melanoma, and classified accordingly. Correct classification of these tumours is important for accurate recording by cancer registries and for correlation with the initial method of treatment.
10. **Immunohistochemistry.** S100 protein is expressed by most melanomas. Although not specific for melanocytes, its presence is especially helpful in assessing the extent of inconspicuous infiltration by spindle cell melanomas, especially desmoplastic melanoma. Immunostaining for HMB45 is less likely to be helpful in clarifying problem tumours.

Clinical information recommended to be provided on the request form.

- a) Clinical diagnosis.
- b) History of the present melanoma, i.e. duration, signs of malignancy, size of lesion.
- c) Previous melanoma(s).
- d) History of melanoma in close relatives.
- e) Assessment of skin type for risk of melanoma.
- f) Dysplastic naevus status.
- g) Clinical photograph if possible.
- h) Diagram of excision specimen with markers for orientation.

RECOMMENDED TERMINOLOGY AND SYNONYMS FOR COMMON FORMS OF MALIGNANT MELANOMA ^{180,182}

Recommended Terminology	Synonyms
Superficial spreading melanoma	Malignant melanoma with an adjacent component of superficial spreading type (Pagetoid melanoma).
Lentigo maligna melanoma	Malignant melanoma with an adjacent epidermal component of lentigo maligna melanoma (malignant melanoma of Hutchinson's melanotic freckle type).
Acral lentiginous melanoma	Malignant melanoma with an adjacent epidermal component of acral lentiginous type.
Mucosal lentiginous melanoma	Malignant melanoma with an adjacent component of mucosal lentiginous type
Nodular melanoma	Malignant melanoma with no adjacent component
Unclassified melanoma Desmoplastic melanoma Neurotropic melanoma Uncommon Variants Malignant blue naevus Melanoma in congenital melanocytic naevi Minimal deviation melanoma Clear cell sarcoma Malignant melanocytic schwannoma	Malignant melanoma of unclassifiable histogenetic type.

Appendix E—Prognostic Factors

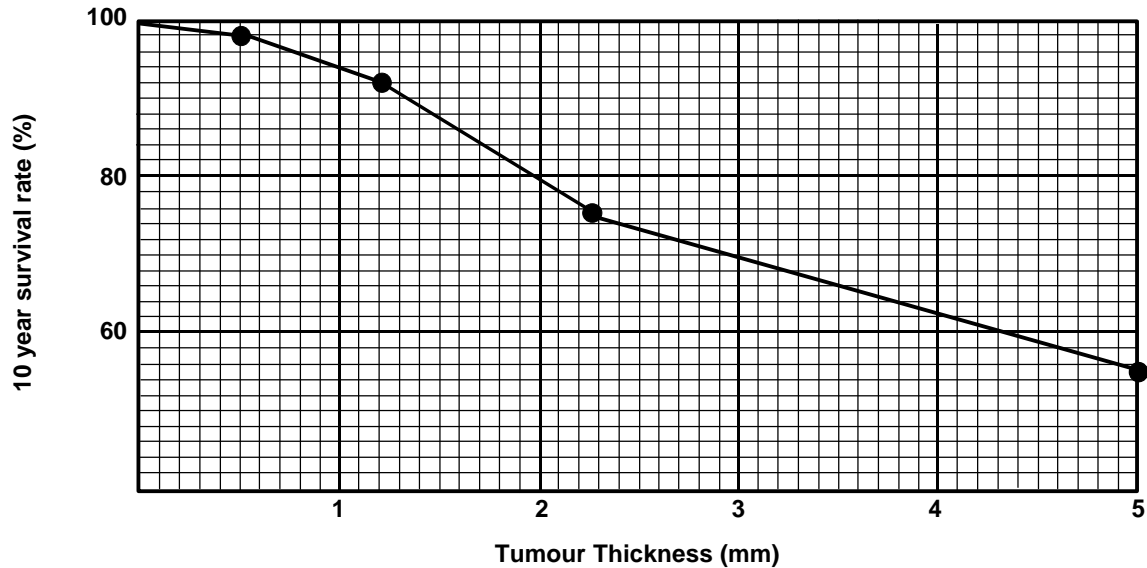
The most important factor influencing treatment of melanoma is the stage of disease at the first presentation.⁶⁴

- Stages I and II, AJCC/UICC pTNM system (disease localised to primary lesion site)
- Stage III (lymphatic metastases)
- Stage IV (distant disease).

1. Stages I and II

- a. Thickness/Clark's levels—thickness is a more objective measure than Clark's level. Occasionally, thickness does not accurately predict prognosis. Very thin tumours may recur, with Clark's level IV tumours being at greatest risk.^{71,72,183} Conversely, very thick tumours may not prove fatal within the expected period.¹⁸⁴
- b. Tumour volume—this may be a more powerful predictor than thickness, but awaits the development of simple methods of estimating volume.
- c. Ulceration—an independent prognostic factor.
- d. Microscopic satellites or lymphatic invasion—both indicate a high possibility of occult regional node metastases.
- e. Mitotic rate—a high rate suggests a worse prognosis, particularly for very thin lesions.
- f. Histological type—e.g. desmoplastic neurotropic and acral lentiginous tumours have a higher risk of local recurrence.
- g. Anatomical site—melanoma on all mucosal sites and those on some cutaneous sites such as the sole, palm, scalp, ear and beneath the nail bed have a poor prognosis. However, delay in diagnosis of these lesions often occurs and worsens the prognosis.
- h. Age of patients—although not proven as an independent prognostic factor, extremes in age must influence extent of surgery. Radical surgery is recommended in children with thick tumours but is not appropriate for old patients with a short life expectancy.
- i. Incomplete or inadequate treatment of the primary lesion.
- j. Miscellaneous factors, the prognostic significance of which has not been clearly demonstrated are gender, skin type, racial origin, and immunological status of patients, psychosocial factors, and tumour features such as regression, lymphocytic response, cellular subtype in the vertical growth phase, association with a naevus, DNA ploidy, nuclear volume, HLA-DR expression, surface gangliosides, growth factor receptors and antibody responses.

Relationship between tumour thickness and 10-year survival rates for patients with stage I and stage II cutaneous melanoma.⁴



2. Stage III

- a. Degree and number of lymph nodes involved—patients with a focus of microscopic involvement in a single lymph node have a 5-year survival rate similar to patients with tumours of comparable thickness and uninvolved lymph nodes. However, those patients with three or more nodes extensively involved with tumour rarely survive five years.
- b. Extranodal extension of tumour—this may warrant adjunctive treatment such as radiotherapy to the dissected field.
- c. Ulceration of primary tumour—an independent prognostic factor indicating a worse prognosis than that determined by thickness alone.

3. Stage IV

Resectability of metastases—if this can be achieved in patients with isolated or small numbers of metastases, prolongation of life exceeds that provided by chemotherapy or other therapeutic modalities.^{110,111}

Appendix F—Interest Groups of the Australian Cancer Network

The draft document was circulated to all interested groups. Those marked with ■ contributed to the development process.

ACT Cancer Society Inc.

■Anti-Cancer Council of Victoria

■Anti-Cancer Foundation of South Australia

Australasian College of Dermatologists

Australasian Faculty of Occupational Medicine

■Australasian Society for Blood Transfusion

Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists

Australasian Society of Clinical Immunology and Allergy

Australia & New Zealand Association of Physicians in Nuclear Medicine

Australian & New Zealand Society of Palliative Medicine

Australian Association of Private Radiation Oncology Practices

■Australian Association of Neurologists

Australian Cancer Society

Australian College of Health Service Executives

Australian Faculty of Public Health Medicine

Australian Faculty of Rehabilitation Medicine

■Australian Health Ethics Committee, NHMRC

Australian Health Insurance Association

Australian Healthcare Association

Australian Institute of Radiography

Australian Institute of Health & Welfare

Australian Leukaemia Study Group

■Australian Medical Association

■Australian Nursing Federation

Australian Private Hospitals Association

Australian Society for Geriatric Medicine

Australian Society for Infectious Diseases

■Australian Society for Medical Research

Australian Society of Gynaecologic Oncologists

Cancer Council of the Northern Territory

Cancer Council of Tasmania

Cancer Foundation of Western Australia

Centre for Health Economics, Research and Evaluation

- Clinical Oncological Society of Australia
- Colorectal Surgical Society of Australia
- Consumers' Health Forum of Australia
- COSA Oncology Nursing Group
- Division of Paediatrics, Royal Australasian College of Physicians
- Endocrine Society of Australia
- Faculty of Radiation Oncology, Royal Australian & New Zealand College of Radiologists
- Gastroenterological Nurses Society of Australia
- Gastroenterological Society of Australia
- Genito-Urinary Oncology Group
- Haematology Society of Australia
- Human Genetics Society of Australasia
- Internal Medical Society of Australia & New Zealand
- Medical Oncology Group of Australia
- National Cancer Control Initiative
- NHMRC National Breast Cancer Centre
- NSW Cancer Council
- NSW College of Nursing
- NSW Nurses Association
- Palliative Care Australia
- Public Health Association of Australia
- Queensland Cancer Fund
- Royal Australasian College of Surgeons
- Royal Australasian College of Physicians
- Royal Australian and New Zealand College of Psychiatrists
- Royal Australian and New Zealand College of Radiologists
- Royal Australian College of General Practitioners
- Royal Australian College of Obstetricians and Gynaecologists
- Royal College of Nursing, Australia
- Royal College of Pathologists of Australasia
- The Australian Academy of Science
- The Australian Society of Plastic Surgeons
- Thoracic Society of Australia and New Zealand
- Urological Society of Australasia

Appendix G—Palliative Care Organisations

ACT Hospice Palliative Care Society Inc.

PO Box 88
Civic Square ACT 2608
Tel: (02) 6247 4511
Fax: (02) 6247 5422

Palliative Care Association of New South Wales

PO Box 55
Allawah NSW 2217
Tel: (02) 9546 2603
Fax: (02) 9546 3482

Northern Territory Hospice and Palliative Care Association

PO Box 42255
Casuarina NT 0811
Tel: (08) 8927 4888
Fax: (08) 8927 4990

Palliative Care Association of Queensland Inc.

PO Box 338
Red Hill QLD 4059
Tel: (07) 3258 2281
Fax: (07) 3258 2281
Email: pcaq@pallcare.org.au
Website: <http://www.pallcare.org.au/qld>.

Tasmania Association for Hospice & Palliative Care

PO Box 517
North Hobart TAS 7002
Tel: (03) 6224 3808
Fax: (03) 6223 5042

Palliative Care Council of South Australia Inc.

202 Greenhill Rd
Eastwood SA 5063
Tel: (08) 8291 4137
Fax: (08) 8290 4122
Email: pcare@pallcare.asn.au
Website: <http://www.pallcare.asn.au>

Palliative Care Victoria Inc.

2nd Floor
182 Victoria Pde
East Melbourne VIC 3002
Tel: (03) 9662 9644
Fax: (03) 9662 9722
Email: info@pallcarevic.asn.au
Website: <http://www.pallcarevic.asn.au>.

WA Hospice Palliative Care Association

Lotteries House
79 Stirling St
Perth WA 6000
Tel: (08) 9228 4084
Fax: (08) 9228 4084

Palliative Care Australia

PO Box 55
Yarralumla ACT 2600
Tel: (02) 6232 4433
Fax: (02) 6232 4434
Email: pcainc@pallcare.org.au
Website: <http://www.pallcare.org.au>.

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