

# 5 Clinical diagnosis\*

## 5.1 How patients detect melanoma

About half of melanomas are detected by the patient and present with a history of a new and/or changing lesion.<sup>1,2</sup> It is important to pay close attention to any history of change, even if the lesion shows no typical clinical features of melanoma. While most are asymptomatic, there may be sensory changes (most commonly itch) that, if persistent, can be helpful in raising suspicion. Changes that are seen in an early melanoma include changes in size, shape or colour in a macular (flat) lesion and, as the melanoma invades more deeply in the dermis, raising up, bleeding or crusting. The time course of the change in melanoma is generally over months. Aggressive, rapidly growing melanomas are more often detected by patients and often present with a nodule, which may be red in colour or pigmented. Patients find changes more useful than atypical clinical features in distinguishing melanoma from benign lesions.<sup>3</sup> All patients seeking advice about pigmented lesions should be encouraged to regularly check their skin with the aid of a mirror or a partner and advised about the changes to look for in early melanoma.

## 5.2 How doctors detect melanoma

The melanomas detected by doctors may be found opportunistically at health examinations for other purposes or at skin examinations for the purpose of detecting skin cancer. Examination for melanoma detection requires examination of the whole skin surface under good lighting and dermoscopy provides increased diagnostic accuracy in experienced hands.

Most melanomas present with an initial flat phase (superficial spreading melanoma, lentigo maligna melanoma and acral lentiginous melanoma) and the features of these melanomas have been summarised by the ABCD(E) rule (Asymmetry, Border irregularity, Colour variation, large Diameter [and Evolution]).<sup>4</sup> Both ABCD(E) and the 7 point checklist<sup>5</sup> have been recommended for use by trained medical practitioners.

About 15% of melanomas present with a clinically predominant expansile nodule (nodular melanoma) and are symmetric nodules with a single colour that is often pink or red.<sup>6</sup> They are often misdiagnosed as non-melanoma skin cancer. These are generally growing rapidly and surgical excision is urgent. Nodular melanomas account for at least half of thick melanomas and are likely to make a disproportionately high contribution to mortality.<sup>7,8</sup> Greater awareness of this presentation is needed so that urgent therapy is more often instituted. Their appearances can be summarised by the acronym EFG (Elevated, Firm and Growing progressively).<sup>9</sup>

### 5.3 Clinical melanoma subtypes

The clinical subtypes of melanoma mentioned above were originally described by Dr Wallace Clark<sup>10</sup> and describe presentations of melanoma that have distinctive clinical, epidemiological and body site associations. The clinical aspects are summarised here.

**Superficial spreading melanoma (SSM)** is the most common subtype and is characterised by an initial flat phase that shows changes in size, shape or colour. SSM may occur as early as teenage years and mean age for SSM is in the 40s. Large numbers of melanocytic naevi and more than a few dysplastic naevi are strong risk factors. SSM is associated aetiologically with relatively small amounts of ultraviolet light exposure and has been linked to intermittent exposure and sunburns.

**Nodular melanoma (NM)** accounts for about 15% of melanomas overall, but for the majority of thick melanomas. It presents as a symmetrical, raised, firm, often uniformly coloured and frequently non-pigmented nodule that is enlarging and becoming more raised. Bleeding and crusting are common. NM occurs more often in older people, particularly men, and is more commonly seen on the head and neck than elsewhere.<sup>7</sup>

**Lentigo maligna (LM) and lentigo maligna melanoma (LMM, the invasive form of LM)** accounts for 10–15% of melanomas. It has an initial flat phase that may be prolonged. It presents as an atypical pigmented macule that is changing and has to be differentiated from seborrhoeic keratoses, solar lentiginosities and pigmented actinic keratoses. LM has been linked epidemiologically to large cumulative doses of UV light, has a strong predilection for the head and neck, and is more common in outdoor workers, in older people and in association with solar damage and non-melanoma skin cancer.<sup>11</sup>

**Acral lentiginous melanoma (ALM)** accounts for 1–3% of melanomas in Australia and occurs on the acral skin of the palms and soles. It presents with a flat phase with similar appearances and changes to SSM. ALM is more often light-coloured or pink.<sup>12,13</sup> Importantly, melanomas that appear relatively flat on the soles of the feet may have significant depth histologically. Although the epidemiology is not as well understood, this type of melanoma is at least equally common in people with dark skin and may have no relationship with UV exposure.<sup>12</sup>

**Subungual melanoma**, a variant of ALM, arises within the nail matrix and usually presents initially as longitudinal melanonychia (brown to black stripe throughout the full length of the nail). The differential diagnosis of longitudinal melanonychia includes naevi (moles) or lentigo in the nail matrix, ethnic-type pigmentation (seen with dark skin, often familial and affects multiple digits) and drug-induced pigmentation. The skin of the surrounding nail folds may be involved (Hutchinson's sign). Subungual haematoma is the most common differential diagnosis of subungual melanoma, however dermoscopic examination usually allows easy differentiation between these two diagnoses. Like ALM, subungual melanoma appears with a similar incidence in dark skin races and may not be related to sun exposure.<sup>13,14</sup>

**Desmoplastic melanoma** may arise within a lentigo maligna or present *de novo*. The latter presentation is typically as a firm, evenly skin-coloured or pink nodule that is progressively enlarging. The differential diagnosis includes dermatofibroma and hypertrophic scar.

Some melanomas are not easily classified into one of these categories and may have overlapping features.

## 5.4 Good practice points

- Examination for melanoma detection requires examination of the whole skin surface under good lighting
- A careful clinical history of specific changes in the lesion, any symptoms and their time course is critically important in assessing whether a lesion may be melanoma, particularly for melanomas that have absent or unusual clinical features for melanoma
- Where there is a low index of suspicion for early, non-invasive melanoma a short period of observation aided by measurement, a clinical photo or dermoscopic imaging may be appropriate
- All patients seeking advice about pigmented lesions should be encouraged to regularly check their skin with the aid of a mirror or a partner and advised about the changes to look for in early melanoma

## 5.5 Identification of the high-risk patient for prospective surveillance for melanoma

See Chapter 3 *Identification and management of high-risk individuals*.

## 5.6 Evidence-based assessment of aids to the clinical diagnosis of melanoma

### 5.6.1 Dermoscopy

Dermoscopy (surface microscopy, oil epiluminescence microscopy, dermatoscopy) is a technique that uses a hand-held magnifying device combined with either the application of a liquid between the transparent plate of the device and the skin, or the use of cross-polarised light. This technique allows the visualisation of diagnostic features of pigmented skin lesions that are not seen with the naked eye.<sup>15–18</sup> Meta-analyses performed on studies in a variety of clinical and experimental settings have shown that using dermoscopy improves diagnostic accuracy for melanoma.<sup>19,20</sup> From a meta-analysis of nine level II diagnostic studies subject to varying degrees of verification bias performed prospectively in a clinical setting<sup>21–31</sup> the diagnostic accuracy for melanoma, as expressed by the relative diagnostic odds ratio, was 15.6 (95% CI 2.9–83.7) times higher for dermoscopy compared with naked eye examination. Importantly the meta-analysis was restricted to studies that directly compared the two methods within each study. Sensitivity of dermoscopy was 18% (95% CI 9%–27%;  $P=0.002$ ) higher than for eye examination, but there was no evidence of an effect on specificity<sup>31</sup> (see Appendix 4). Specificity can also be examined by its effect on excision rates of benign lesions, which was not addressed in the meta-analysis. Two such studies suggest reduced rates of excision of benign lesions using dermoscopy (reduced benign to malignant ratio of excised lesions and reduction of patients referred to biopsy) and provide indirect evidence for improved specificity in a specialist setting.<sup>22,23</sup>

While there are fewer studies on dermoscopy in general practice, all three that were undertaken in this context (one study with both general practitioners and inexperienced specialists or trainees)<sup>32</sup> show a consistently improved sensitivity for the diagnosis of melanoma or the identification of suspicious lesions requiring biopsy.<sup>21,32,33</sup> It should be noted that all the studies

cited were undertaken by clinicians with some training in dermoscopy (restricted to lectures or reading material in some studies). For this reason, and based on other evidence,<sup>34</sup> some formal training in dermoscopy is required to achieve improvement in diagnostic accuracy.

### 5.6.2 Sequential digital imaging

Sequential digital dermoscopy imaging (SDDI) involves the capture and assessment of successive dermoscopic images, separated by an interval of time, of one or many melanocytic lesions to detect suspicious change. This is performed in two settings: short-term digital monitoring (over a period of 1.5–4.5 months) for suspicious melanocytic lesions, and long-term monitoring for surveillance (usually at intervals of 6–12 months).<sup>35</sup> Four level II studies that were conducted in a specialist setting show consistently that SDDI allows the detection of melanoma that lack dermoscopic evidence of malignancy.<sup>35–38</sup> In one prospective study of melanomas diagnosed by a variety of clinical means, 34% were detected using the changes detected by SDDI exclusively and were without dermoscopic features of melanoma.<sup>36</sup> Long-term digital monitoring is generally used in the surveillance of high-risk patients, usually with multiple dysplastic naevi. In contrast, short-term digital monitoring of individual suspicious naevi can be used in any patient setting. At this time diagnostic accuracy of the technique was not able to be assessed.

### 5.6.3 Automated instruments for the diagnosis of primary melanoma

An automated diagnostic instrument is defined as one that requires minimal or no input from the clinician to achieve a diagnosis. Each automated instrument offers different technology with differing diagnostic ability. Guidelines for assessing such instruments have been published.<sup>39</sup> To date, only three instruments have had their diagnostic accuracy compared with a human diagnosis in the clinical field with a sample size that could allow some assessment of their application to the wider clinical arena.<sup>25,40,41</sup> The instruments showed a significantly inferior<sup>25,41</sup> or equivalent<sup>40</sup> specificity for the diagnosis of melanoma compared with specialists. In all studies sample sizes were not large enough to be able to detect potential differences in the sensitivity for melanoma. Further studies are required to assess the impact of automated instruments against human performance in the clinical field.

## 5.7 Total body photography for early melanoma diagnosis in high-risk subjects

Total body photography (TBP) is widely used in the follow-up of high-risk patients,<sup>42</sup> particularly those with large numbers of melanocytic naevi or dysplastic naevi. TBP has been recommended for the detection of new or changing pigmented lesions. Use of TBP is advocated in the follow-up of high-risk patients by the authors of most studies.<sup>43–50</sup> The technique has been said to reduce the need for unnecessary removal of benign lesions to exclude melanoma<sup>45,46</sup> and to increase the sensitivity and specificity of clinical examination for the detection of melanoma.<sup>46,47</sup> Several authors point out that TBP was the key factor in the detection of most melanomas in their high-risk populations.<sup>44–46,48</sup> Two authors referred to the role of TBP in enabling the detection of clinically subtle or undiagnosable melanoma.<sup>46,47</sup> No appropriately controlled or randomised study has been undertaken to confirm these observations in a high-risk population. Almost all melanomas are new or changing lesions and baseline images are helpful in identifying a new or changing lesion.

Evidence summary	Level	Reference
From a meta-analysis of nine level II studies prospectively performed in a clinical setting, the diagnostic accuracy for melanoma, as expressed by the relative diagnostic odds ratio, was 15.6 times higher for dermoscopy compared with naked eye examination. Sensitivity of dermoscopy was 18% (95% CI 9%–27%; P=0.002) higher than for eye examination, but there was no evidence of an effect on specificity	I	21, 22, 24–31
Dermoscopy has been shown to reduce the benign:malignant ratio of excised melanocytic lesions and reduce the number of patients referred for biopsy in a specialist setting	II	22, 23
Four level II studies show consistently that sequential digital dermoscopic imaging allows the detection of suspicious dermoscopic change in melanomas that lack dermoscopic evidence of melanoma at a particular time	II	35–38
To date only three automated instruments for the diagnosis of primary melanoma have been assessed against clinicians with a reasonable sample size in the clinical field. Here, instrument specificity was either inferior or equivalent to specialist diagnosis, and sample sizes were inadequate to assess differences in sensitivity	II	25, 40, 41
Eight level IV studies and one level III-3 study examined surveillance of high-risk subjects with total body photography but only one included a comparison arm (of lower-risk subjects). All studies on high-risk patients showed early melanoma detection and/or high melanoma incidence. All studies were designed to assess the outcomes of surveillance in high-risk groups rather than the value of TBP	IV	43–51

### Recommendations

	Grade
1. Training and utilisation of dermoscopy is recommended for clinicians routinely examining pigmented skin lesions	<b>A</b>
2. Consider the use of sequential digital dermoscopy imaging to detect melanomas that lack dermoscopic features of melanoma	<b>B</b>
3. Consider the use of baseline total body photography as a tool for the early detection of melanoma in patients who are at high risk for developing primary melanoma	<b>C</b>

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