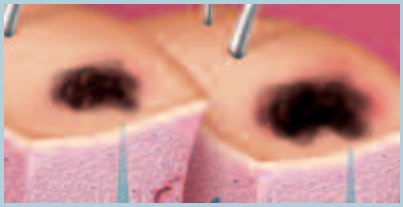
abstract



The incidence of melanoma continues to rise. The clinician needs to be familiar with characteristics of lesions more likely to be melanoma and be able to apply the "ABCDE" criteria. Additional imaging techniques such as digital photography and dermoscopy aid the clinician in deciding which nevi require biopsy. The techniques for biopsying cutaneous lesions vary, and clinicians need to be familiar with the various techniques. Once a cutaneous melanoma is diagnosed, the most important histologic feature of the primary is Breslow thickness.

Key words: *melanoma, pigmented nevi, digital imaging, dermoscopy*

Detection and Diagnosis of Cutaneous Melanoma

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Introduction

In North America, the incidence of melanoma is rising more rapidly than any other tumour,[1] yet the actual number of deaths from melanoma has remained steady since 2000 (approximately 7,700 deaths/year in the United States). In Australia, melanoma is now the second most common tumour in both men and women (Bruce Armstrong, personal communication). Well-documented risk factors for lifetime risk of developing melanoma include blonde or red hair, blue eyes, pale complexion, and the skin's reaction to sun exposure.[2] In population-based studies, melanoma patients demonstrate little or no association with occupational sun exposure (i.e., individuals who work outside); however, there is a consistent correlation with recreational sun exposure.[3] Clearly, the rising incidence of melanoma is multifactorial, and the key to treating this deadly disease is early detection. Detection and diagnosis will be the focus of this review of cutaneous melanoma. Part 2 of this series will address the surgical management for patients diagnosed with cutaneous melanoma.

Evaluation of Pigmented Nevi

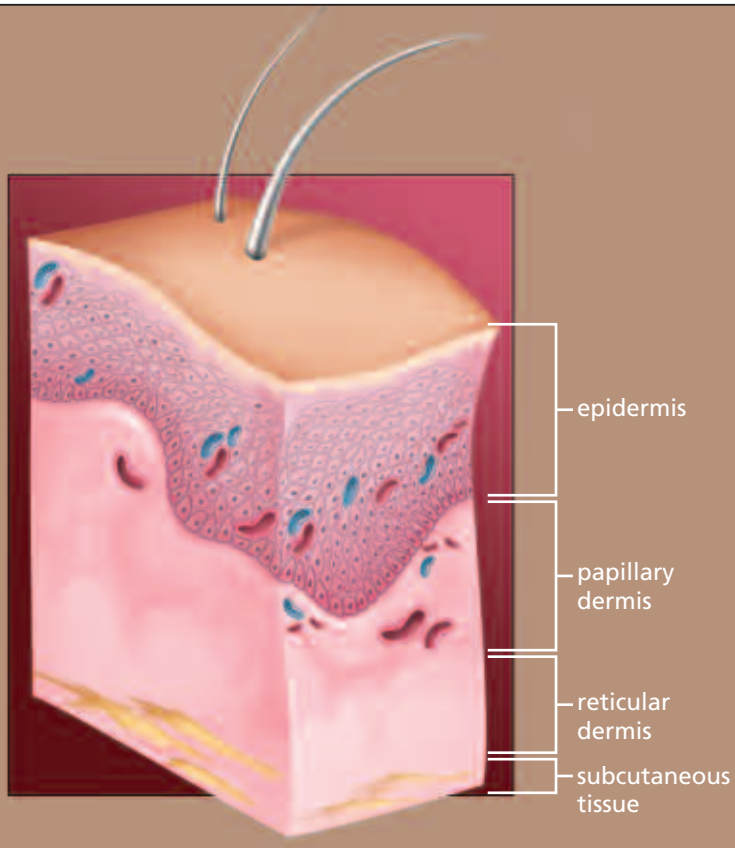
The early detection of cutaneous malignancies is a very important function of the dermatologist and/or primary care physician. The vast majority of the lesions identified will either be benign, premalignant conditions (dysplastic nevi), or malignancies with very little (squamous cell carcinoma) or no metastatic potential (basal cell carcinomas). These malignancies were thoroughly reviewed in the October 2005 issue of *Geriatrics and & Aging*.

Since it was first described in 1985, clinicians have relied heavily on the mnemonic ABCD for assessing pigmented nevi and skin lesions.[4] In the assessment of pigmented nevi, the parameters to be cognizant of are: Asymmetry, Border, Colour, and Diameter. Nevi that are asymmetrical, have irregular borders, varying colour, and are larger than 6 mm classically have been concerning to clinicians for potential malignancy. This now well-known mnemonic has been expanded to include E for Evolving or change.[5] A nevus that changes in shape, size, colour, or begins to itch or bleed is a red flag to the clinician. A lesion that is uneven in shape or size, has ragged irregular borders, multiple shades of colour (brown, black, red), and is larger in size (6 mm or greater) should strongly be considered for biopsy. It is the combination of ABCDE criteria that drives the decision to obtain a biopsy.[5] If two criteria are met, the sensitivity and specificity of correctly diagnosing a melanoma with a biopsy are 89.3% and 65.3%, respectively. If three criteria are met in the assessment of a nevus, then the sensitivity and specificity of diagnostic biopsy for melanoma are 65.5% and 81% respectively. Thus, if three criteria are used to trigger a biopsy then the sensitivity decreases at roughly the same percentage that the specificity increases.[6]

Another method used for surveillance of skin lesions, usually reserved for patients with a high risk (i.e., multiple dysplastic nevi, multiple nevi, prior

Figure 1:

Classification of Cutaneous Melanoma
The Clark Level and Breslow Thickness

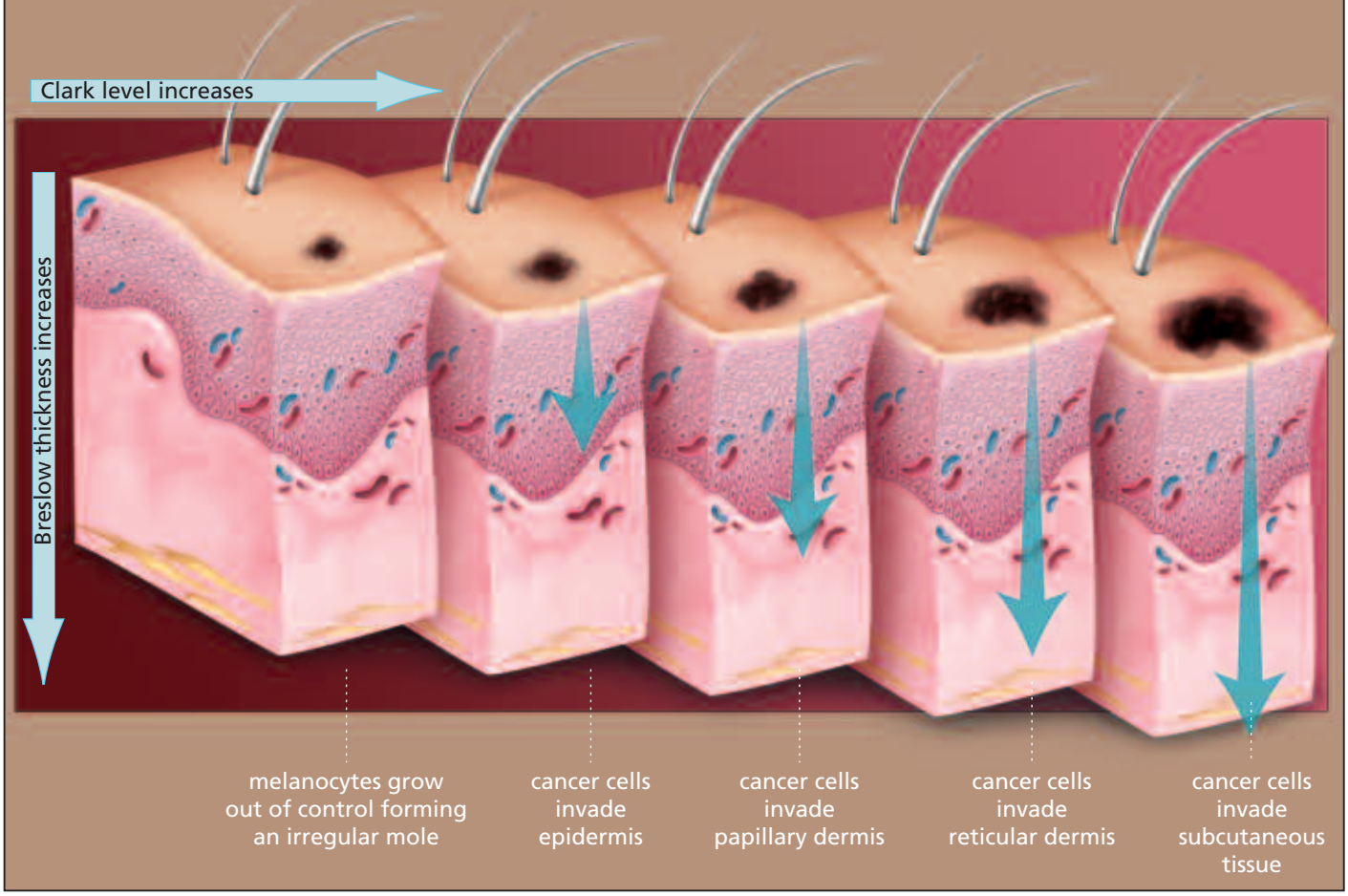


cutaneous melanoma thickness In general, as the thickness of the melanoma increases, there is a proportional reduction in overall survival. There are two standard measures of thickness.

clark level The Clark level is based on the depth of invasion of the melanoma related to the standard skin components: epidermis, papillary dermis, reticular dermis, and subcutaneous tissue.

breslow thickness The Breslow thickness is determined by using an ocular micrometer under the microscope to measure in millimetres the thickness of the melanoma.

Increasing Clark level and increasing Breslow thickness are associated with an increased likelihood of metastasis and reduced survival.



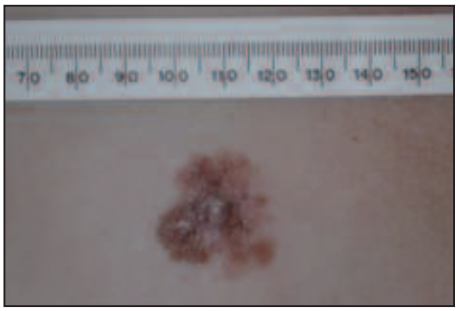


Figure 2: Superficial Spreading Melanoma

melanoma, or family history of melanoma)[7] for development of malignant lesions is total body photography (TBP).

TBP documents a patient's entire clinical skin examination at a concrete point in time and allows for comparison of the current clinical examination, providing tangible documentation of a changing or evolving nevus. Historically, clinicians have relied on the patient's self-reporting or the patient's medical record to provide this information. With technological advances, common practice is to have images obtained digitally and copied onto a compact disc. Computer programs are utilized for contrast and comparison of skin lesions on subsequent visits to the clinician.[7]

Science has continued to progress, from relying on the naked eye of the clinician for determination of potential malignant skin lesions, to the development of dermoscopy (also known as skin surface microscopy or epiluminescence microscopy). Dermoscopy was developed for use in conjunction with the ABCDE criteria.[8] Dermoscopy utilizes a handheld instrument to provide a magnified (commonly 10x) illuminated view of the skin. The addition of a liquid (i.e., mineral oil or ultrasound gel) under the scope renders the epidermis transparent. This allows the clinician to view morphology and colour not visible with the naked eye at the epidermis, dermal-epidermal junction, and papillary dermis.[7,9]

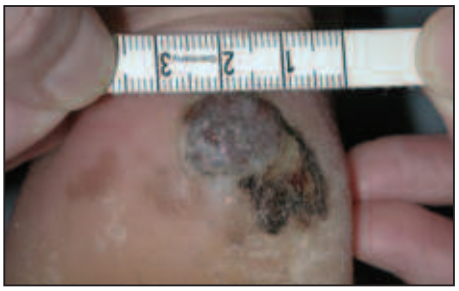


Figure 3: Nodular Melanoma

European clinicians have embraced dermoscopy; however, in the United States, it has not been widely adopted. There is a learning curve on the technique based on the degree of experience of the clinician.[10] Used correctly, dermoscopy has been shown to increase diagnostic accuracy 5–30% over visual examination.[11,12]

Cutaneous Biopsy Techniques

Using all or some of the above techniques to assess a suspicious nevus leads the clinician to determine whether a lesion is potentially malignant. To confirm a malignant diagnosis, tissue must be obtained for histopathologic evaluation. This can be accomplished through a variety of biopsy techniques.

There are three basic techniques for a diagnostic biopsy. The first is a shave biopsy. This is performed using a razor blade or scalpel by shaving the lesion off at its base. The disadvantage of a shave biopsy is that the base of the lesion may inadvertently be transected. Thus, the pathologist may not have obtained a true representative histologic section of the lesion, which makes accurate diagnosis of the depth of melanoma extremely difficult. In general, a shave biopsy should be avoided when the clinical suspicion is melanoma. To overcome this problem, some clinicians advocate a deep or "scoop-shave." It involves removal of the complete lesion using a shave technique but including the subcutaneous fat. It holds the same disadvantage of a shave biopsy in that the true depth of the lesion might not be obtained.[12]

The second type is a full-thickness incisional skin biopsy, which samples the most suspicious part of the nevus. There are two variations of an incisional biopsy. The first is a surgical incisional biopsy performed using a scalpel to remove a fusiform ellipse of epidermis, dermis, and subcutaneous fat. The second is a punch biopsy performed using a 4—6 mm diameter circular cutting device that is pushed through the epidermis, dermis, and into the subcutaneous tissue. The advantage of an incisional biopsy is the true depth of the pigmented lesion will be known if the suspicious nevus is indeed a melanoma. The disadvantage of both incisional biopsy techniques is that a sampling error may occur since only a portion of the lesion is sampled, resulting in a false-negative or underestimation of the lesion.[12]

Excisional biopsy involves complete removal of the entire lesion, with a 1–2 mm lateral margin and a deep margin to the subcutaneous fat. The benefit of excising the lesion in its entirety is that it allows for the entire lesion to undergo dermatopathology, eliminating sampling error or a false-negative result.[13]

Histopathology of Cutaneous Melanoma

All tumours, including melanoma, are staged based upon the American Joint Committee on Cancer (AJCC)[14] staging system. This system is based upon the TNM staging of a patient's tumour. T represents the thickness of the primary melanoma, N represents lymph node status, and M denotes distant organ involvement. Recently, the staging system for melanoma has undergone major modifications based on an evolving understanding of the tumour biology. The AJCC issued a revised classification system in 2003[14] based upon the AJCC Melanoma Database that included data on 17,600 patients with all stages of disease, who had received a wide range of therapies. Major revisions from the previous edition include a designation for melanomas with ulceration, a distinction for number of involved lymph nodes as well as microscopically positive versus clinically diagnosed lymph node involvement, and recognition of the variability in metastatic sites.[14–17] This new classification system was then validated by a prospective database involving 13 institutions and cooperative study groups.[18]

In general, as the T or thickness of the melanoma increases, there is a proportional reduction in overall survival. There are two classification systems for determining how thick a melanoma is (Figure 1). The first is Clark level,[19] which is based on the depth of invasion of the melanoma related to the standard skin components: epidermis, papillary dermis, reticular dermis,

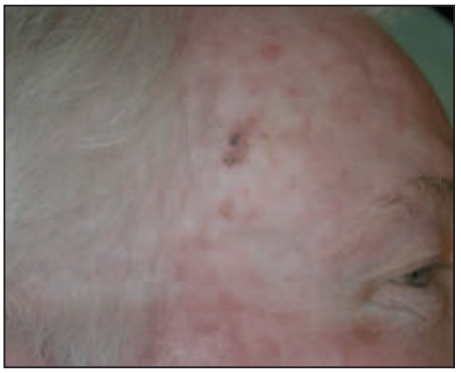


Figure 4: Lentigo Maligna Melanoma

and subcutaneous tissue. The second is Breslow thickness;[20] this is determined by the pathologist using an ocular micrometer under the microscope to measure in millimetres the thickness of the melanoma. Increasing Clark level and increasing Breslow thickness are associated with an increased likelihood of metastasis and reduced survival. The precise thickness of melanoma is a critical factor in the patient's prognosis. It is this factor, rather than histologic subtype of melanoma, that dictates the patient's treatment and further management.

For historical completeness, there are four main pathologic classifications of melanoma based on histologic features. The most common subtype of melanoma, superficial spreading melanoma (SMM), represents about two-thirds of all melanoma (Figure 2). It can be present at any cutaneous site with the trunk of men and the extremities of women being the most common sites.[21,22] The second most common histologic subtype is nodular melanoma (NM), which clinically appear as polypoid lesions on any cutaneous site (Figure 3). They are often brown, red, grey, or black but may be amelanotic (devoid of any color) and constitute about 10% of cutaneous melanoma.[23] The third most common histologic subtype is lentigo maligna melanoma (LMM), which usually arises on sun exposed sites, particularly head, neck, back, and upper extremities of middle-aged and older people (Figure 4). LMM arises in a precursor lesion called lentigo maligna (Hutchinson's melanotic freckle), which is a slow-growing, irregularly shaped, pigmented macule.[24] The last histologic subtype is acral lentiginous melanoma (ALM) which arises on palms, soles, and subungual sites (Figure 5). It is the most common form of melanoma in Asian and African-American populations and accounts for less than 5% of melanomas in white populations.[21]

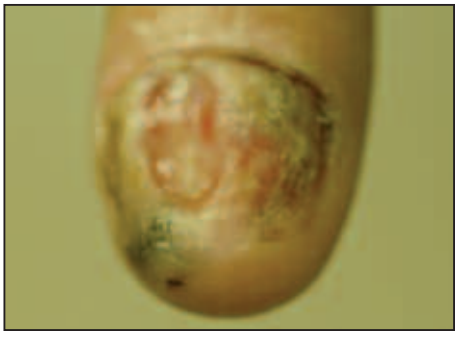


Figure 5: Acral Lentiginous Melanoma

Conclusion

The etiology of cutaneous melanoma is multifactorial. The key to a good prognosis is early detection. Clinicians are aided by the ABCDE mnemonic to determine which lesion should undergo biopsy. There are several biopsy techniques but a full-thickness biopsy is preferred because it gives the pathologist the epidermis, dermis, and subcutaneous fat to make an accurate diagnosis. The true thickness of the melanoma will determine prognosis and appropriate surgical management. Part 2 in this review of Cutaneous Melanoma will address the management of patients with biopsy-proven melanoma.

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