Precursors of Melanoma

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Introduction

The incidence of melanoma is increasing in many parts of the world. Between the early 1960's and the late 1980's, annual increments of 3% to 7% were observed worldwide in people of European origin.[1] Melanoma is the most rapidly increasing malignant tumour in the white population, except for lung cancer in women. The melanoma epidemic is widely believed to stem from changes in lifestyle with increased recreational sun exposure and changed modes of dressing. The particular frequency of melanoma on the trunk in men and on the limbs in women supports this hypothesis. The sun exposure aetiology theory is, however, difficult to reconcile completely with the typical melanoma sufferer, a young or middle-aged office worker of fairly high socioeconomic status rather than a middle-aged or elderly outdoor worker. Short acute episodes of intense burning exposure to ultraviolet B appear more important than occupational sun exposure. ***(SA Fam Pract 2004;46(9): 11-13)***

Part I: Naevi and melanoma. Which naevi matter?

It has been known for some time that certain melanocytic naevi have pre-melanoma potential. The question arises: Which of these naevi have the potential? Identification and appropriate management of such precursors could markedly
reduce the incidence of and mortality from melanoma.

This article deals with the most common precursors of malignant melanoma – a peculiar subtype of acquired melanocytic naevi, atypical moles (dysplastic naevi), giant congenital melanocytic naevi and lentigo maligna.

Melanocytic naevi are very common, virtually everyone has some. They may be acquired or congenital. The acquired kind are not present at birth and develop mostly in the first twenty years of life, occasionally even later.

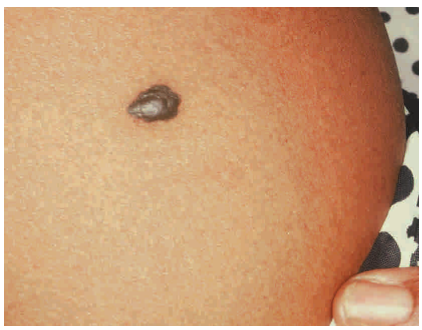
Melanocytic naevi are composed of melanocytes which either did not mature or stopped in their migration towards the basal cell layer of the epidermis during embryonic development (blue naevi).

An acquired melanocytic naevus appears when a group of immature melanocytes starts to proliferate at the dermo-epidermal junction (junctional naevi). After a period of horizontal growth along the dermo-epidermal junction, some melanocytes grow down into the dermis (compound naevi). Finally, all melanocytes come to be located in the dermis (intradermal naevi).

Different melanocytic naevi may be at different phases of their development in the same individual. Junctional naevi are usually flat and uniformly pigmented. Compound naevi are usually slightly elevated, a bit lighter in colour and often mottled or stippled. Intradermal naevi are usually dome-shaped or even pedunculated, pale or very lightly pigmented. Blue naevi (Fig 1) have a characteristic slate-blue colour resulting from the deep intradermal location of pigment producing melanocytes. (Fig 1)

Congenital melanocytic naevi are found in between 1% and 6% of newborn infants. These are usually bigger than acquired naevi. Congenital naevi may vary in size from a few to many

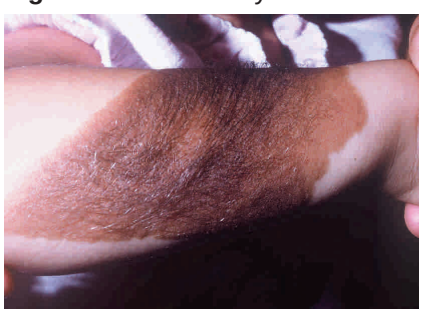
Fig 1: Blue naevus



centimeters.

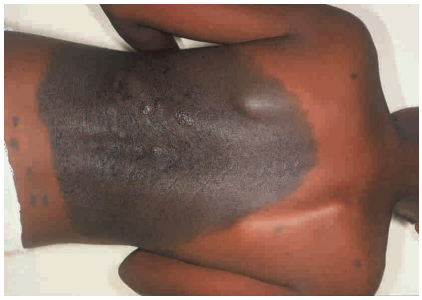
Giant congenital naevi are those greater than 20cm in size or, by another definition, so large that they cannot be removed by simple excision and primary closure using adjacent tissue in a single surgical procedure. (Fig 2)

Fig 2: Giant melanocytic naevus



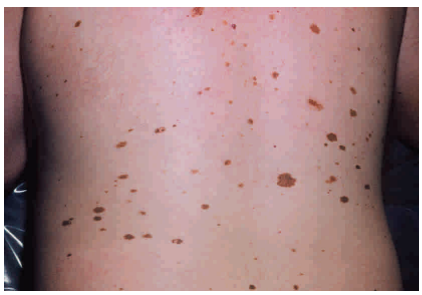
Occasionally, the giant congenital naevi have a "bathing trunk" (or other sort of garment) distribution. (Fig 3)

Fig 3: "Garment" naevus



The importance of acquired melanocytic naevi lies in the fact that 20-50% of malignant melanomas develop within a pre-existing naevus.[2] The greater the number of acquired melanocytic naevi one possesses, the greater the chance to develop melanoma. A group of patients with large numbers of acquired melanocytic naevi greater than 5mm in diameter and with irregular margins, variegated pigmentation and sometimes inflammatory flares appeared to have an increased incidence of malignant transformation of these lesions. (Fig 4)

Fig 4: Patient with numerous acquired melanocytic naevi



In 1978, Clark *et al*[3] described for the first time a clinicopathological entity identifying patients at increased risk for melanoma. They originally used the term B-K syndrome, based on the first initials of the surnames of the probands.

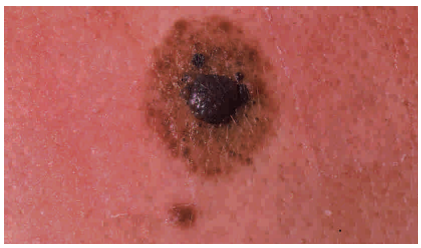
Since then, this syndrome has had several other names have been used for it (dysplastic naevus syndrome, atypical mole syndrome, familial atypical multiple mole-melanoma syndrome).

There are few fields in dermatology that generate as much controversy and discussion as that of the dysplastic naevus. Because of variable definitions for dysplasia, the National Institute of Health issued a Consensus Statement Paper recommending the following: [4] "that the term dysplastic naevus be replaced with atypical mole, and that the syndrome for melanoma-prone families be called familial atypical mole and melanoma syndrome."

A typical mole is defined as a mole with a macular component and showing at least three of five criteria:

1. Ill defined. OR
2. Irregular border.
3. Irregular distributed pigmentation.
4. Background of erythema.
5. Size greater than 5 mm (Fig 5).

Fig 5: Atypical mole



The National Institute of Health Consensus Paper lists the following criteria for diagnosis of familial atypical multiple mole-melanoma syndrome:

1. Occurrence of melanoma in one or more first or second degree relatives.
2. Large number of moles (often greater than 50), several of which are atypical.
3. Moles that demonstrate distinct histological features.

Patients with atypical moles should be seen regularly. The frequency of follow-up depends on the risk for developing melanoma. Patients from melanoma-prone families should have their skin examined initially every 3 to 6 months, until both the patient and the physician are comfortable that the patients's naevi are stable in appearance. If the moles do not appear to change, the frequency of visits can be reduced to every 6 to 12 months. The entire skin surface (including fold areas and the scalp) should be examined.

Regular follow-up is can be facilitated by the use of diagnostic aids for early diagnosis of melanoma (dermoscopy, total body photography and digital imaging devices, eg, Mole-Max system).[5]

It is estimated that between 5% and 10% of melanoma patients have one or more family members with melanoma.

The propensity for developing melanoma is transmitted in an autosomal dominant manner with affected individuals having an 80% to 100% lifetime risk for developing melanoma.[6]

Therefore, if a melanoma is detected, all first degree relatives and selected second degree relatives should be examined. As atypical moles were considered precursors of melanoma it was common, until recently, to recommend their prophylactic removal. Because they, in fact, rarely develop into melanoma they are viewed now primarily as markers of increased risk for developing melanoma. As atypical moles can be diagnosed reliably on clinical grounds, there is no justification to remove them simply to confirm the diagnosis. Removal of all atypical naevi seems to be a futile exercise. Management should include surgical removal and histological assessment of all naevi with clinical features that suggest malignant transformation. Naevi should be removed if they show evidence of growth or change between visits. (Which proves the value of photographic documentation!)

A suspicious naevus should be removed by excision biopsy as this provides the pathologist with optimal tissue for histological assessment. (Fig 6-7)

Fig 6: Malignant melanoma

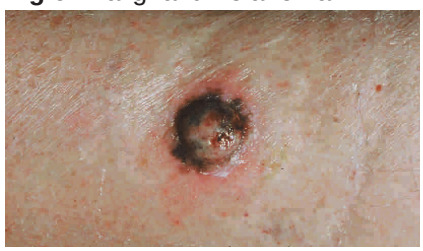
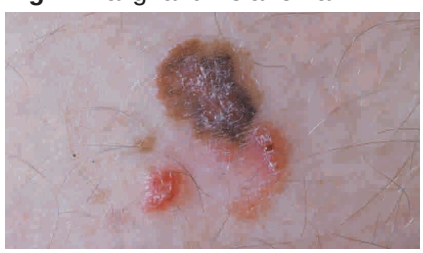


Fig 7: Malignant melanoma



Congenital melanocytic naevi and melanoma

The risk of malignant transformation in congenital naevi is a subject of controversy. The literature tends to give the impression of a very high risk. The majority of reports relates mainly to giant garment or bathing-trunk naevi. It is known that the potential for melanomatous transformation is correlated with size; it is greater in large than in small naevi.

Well-controlled, prospective, long-term studies are rare. The data from one of the more reliable studies[7] estimated lifetime risk for developing malignant melanoma as between 3% and 5%. Individuals with large congenital melanocytic naevi can develop malignant melanoma at any age. However, 70% of malignant melanoma are diagnosed in children less than 10 years old. Current approaches to the management of giant congenital naevi are varied. For those smaller than 1.5cm in diameter, the risk for developing malignant melanoma is considered to below that prophylactic removal may not be warranted.

Early dermabrasion of giant melanocytic naevi within the first 48 hours of life has been recommended.[8] Treatment at such an early age was expected to bring about cosmetic results and to reduce the risk of malignancy by removal of large numbers of melanocytes. The second part of this hypothesis seems still to require long-term study validation. There are at present no sufficient data to recommend prophylactic excision of all congenital naevi. Patients should be examined periodically. If a change is detected, the naevus should be biopsied.

Part II: Lentigo maligna

Lentigo maligna is a pigmented lesion that occurs on the sun-exposed skin, most often on the head and neck in older patients. The lesions slowly increase in size and at some time, usually many years after their onset, may become malignant melanoma (lentigo malignant melanoma).

The frequency of malignant melanoma of the lentigo maligna type is increasing. There is more evidence for ultraviolet light induction of melanoma in lentigo maligna than for other forms of malignant melanoma.

The lentigo malignant form represents 4% to 15% of all malignant melanomas and 10% to 26% of head and neck melanomas.[9]

Clinically, lentigo maligna presents as a flat, brown patch with irregular pigmentation, often with areas of brown, tan and black. (Fig 8-9)

Fig 8: Lentigo maligna

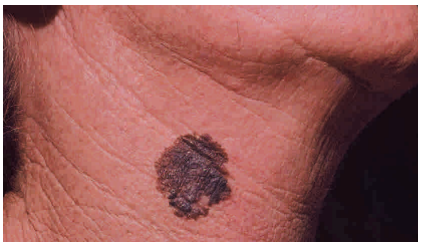
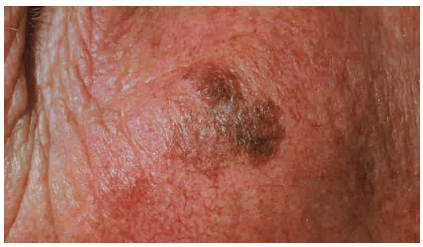


Fig 9: Lentigo maligna

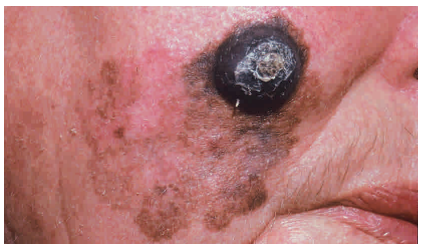


In some patients, the pigmentation is mottled with ill-defined borders, particularly when there is a background of actinic damage and solar lentigines in the adjacent skin.

Lentigo maligna can be difficult to differentiate clinically from flat seborrhoeic warts, pigmented actinic keratosis and solar lentigo. A biopsy is needed to solve the problem.

If lentigo maligna is left untreated, a proportion, after a variable latent period, progresses to invasive lentigo maligna melanoma.(Fig 10)

Fig 10: Melanoma developed in lentigo maligna



Invasion is not, however, an inevitable event.

Because there has never been a longitudinal, prospective study in patients with lentigo maligna (which would require observation and no treatment), the lifetime risk of invasive melanoma is unknown. The anecdotal figures in the literature vary between 2% and 5%.

There are no definite guidelines for the management of lentigo maligna. The importance of establishing the diagnosis by biopsy has been already stressed. The biopsy should be taken from the most likely site of invasion, the area that is most deeply pigmented or evidently raised. When histology confirms the diagnosis of lentigo maligna without invasion, the lesion may either be left untreated (in the very old), carefully observed, excised or treated with cryotherapy. Following cryotherapy, a careful follow-up is mandatory even if there has been a complete clinical clearance, as there may be a few residual lentigo maligna cells left.

Excision is certainly the best therapeutic option. The size of the lesion and its location may make it difficult, though.

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