

# Melanoma



The understanding of melanoma requires an understanding of the skin anatomy, and to this end, the reader is referred to the document on 'Normal Skin Anatomy'. In this talk, it is noticed that the melanocytes, from which melanoma is derived, are cells which migrate from the neural crest in the developing embryo. Because these cells are migratory in nature, it is probably true to say that when they become malignant, this explains their propensity to migrate once again, and metastasize. This is why melanoma is a much more serious skin condition than either basal cell carcinoma or squamous cell carcinoma. Nevertheless, not all melanomas do metastasize, and an understanding of skin anatomy and function will explain why this is the case. Normally, the melanocytes are found along the basal cell layer, scattered amongst these cells, where they produce pigment and transport the pigment into the basal cells, to produce either suntan in Caucasians who tan, freckles in Caucasians who do not, and skin pigmentation in Asians and Africans. Occasionally, melanocytes are found in the dermis in groups. These are cells that have arrested their migratory course during development, and these lesions produce a whole range of benign pigmented skin spots. To the lay person, these are broadly known as "moles", but the histological classification of these lesions is extremely complicated and hundreds of different

types of pigmented skin lesions have been described. These are beyond the scope of this document. There is one condition however, called the dysplastic naevus syndrome, where the moles are slightly larger than normal and they may have an irregular shape and in some cases, mimic melanoma. Dysplastic naevi may in fact turn into melanoma, but usually do not. They are, however, often markers of a propensity to develop melanoma elsewhere in the skin, and the condition may be familial and dysplastic naevus syndrome has been classified according to a number of clinical associations, and this classification may be a useful prognosticator in discussing the development and behaviour of melanoma in some individuals. When the melanocytes become malignant, and melanoma develops, they have two growth phases: One is called the radial growth phase, where the malignant cells spread sideways along the junction of the epidermis and dermis. The other growth phase is called the vertical growth phase. As pointed out in the normal skin anatomy document, there are no lymphatics in the epidermis and no lymphatics in the superficial part of the dermis (papillary dermis), but there are lymphatics and large blood vessels in the deeper parts of the dermis (reticular dermis). To this end, the radial growth phase of melanoma is unimportant and does not affect the prognosis of the disease, as the tumour cells here are not able to metastasize anywhere else in the body. Therefore, the tumour may grow sideways, and yet not be life-threatening. However, when vertical growth phase takes place, the tumour grows down through the epidermis into the papillary dermis and then on into the reticular dermis, and the deeper the tumour grows, the greater the risk of metastatic disease.

The classification of melanoma was simplified in the year 2000, and now the best way to grade melanoma is by measuring the depth of the tumour from the granular cell layer, to the deepest part of the tumour within the dermis. Tumours less than 1mm thick, have a very high cure rate from surgical excision. Tumours 1-2mm thick have cure rates in the order of 85-90%. Tumours 2-3mm thick have cure rates in the order of 60-80%, and tumours greater than 4mm thick have cure rates significantly less than 40% of the time.

The diagnosis of melanoma is not easy. In a melanoma screening clinic, performed in Western

Australia, the accuracy of diagnosing melanoma by specialist surgeons who normally treat this condition on a regular basis, was less than 40% in an unfiltered population (which means, people came off the street to be assessed cold by treating surgeons). These figures line up with similar studies performed in both England and America, where melanoma screening clinics were conducted and run by both dermatologists and/or plastic surgeons, but there were no referring doctors; rather the patients came straight to the clinics. Accuracy rate of diagnosis improved significantly when the patients had been first screened both other practitioners. However, to put it in context, an average GP will see one new case of melanoma every two years in a busy suburban practice, although the new skin magnifying glasses and various light [adjutants] do marginally improve the rate of diagnosing melanoma by simply scanning the skin. The gold standard diagnosis is histological confirmation of the disease. This can be performed by a punch biopsy without compromising the treatment or prognosis of the disease. It can also be performed by using a simple shave biopsy, although this technique may interfere with subsequent prognostication as the depth of the tumour will be altered as a result of the biopsy. (This is really of only academic interest in most instances.)

The treatment of melanoma, once the diagnosis has been established, should always be surgical. Diathermy or curettage does not only inadequately treat the tumour, it also can potentially lead to metastases, and makes subsequent site surveillance almost impossible. The use of creams, such as Imiquimod or Efudex for melanoma, has not been proven, and once again may result in metastatic disease being precipitated.

Surgical treatment of melanoma involves excising the lesion with a reasonable margin and closing the defect in whatever way necessary to produce the best aesthetic and functional outcome. Plastic surgeons undergo rigorous training for usually up to six years to learn the techniques to achieve this aim. The role of sentinel node biopsy is controversial and is currently under debate. This involves injecting of dye into the region of the tumour excision, which is carried up the lymphatics to the nearest node. This node then becomes obvious because it is filled with the dye, and the node is then removed and assessed histologically

to see if it contains any cancer cells. The controversy over this technique exists because there has been no proven benefit from doing this procedure. There is no evidence to show that it reduces the risk of recurrence or loco-regional spread of the disease, it does not increase survival of patients with melanoma and makes subsequent staging of the disease difficult. It also interferes with normal defence mechanisms for the body's handling of tumour cells that may metastasize. Nevertheless, some [centres] believe there is a place for sentinel node biopsy and this technique is therefore employed in those [units]. The follow-up of melanoma depends on the thickness of the primary, and whether or not there is any evidence of secondary spread to either the nodes or other parts of the body. In this practice, the first [adjuvant] test to be ordered is a PET scan. This is a test which involves injecting radioactive glucose into the bloodstream, which is then taken up by tumour cells which avidly incorporate glucose as they are growing quite fast. A PET scan will give an accurate indication as to whether or not any metastatic disease has [taken place] or not. However, it is not a definitive test. Usually this is followed up by various other modalities of imaging, such as CT, MRI scan and/or bone scans.

The treatment of advanced melanoma again is controversial and involves aggressive ablative surgery, radiotherapy, chemotherapy, or alternate therapies. Ablative surgery has a role to play for debulking tumour, which enables the body to fight the disease more effectively. It also has a role to play for immunotherapy. This is a trial that is currently being run out of the United States, where 3g of tumour is flown to a centre in the United States, where it is processed and turns into a vaccine which is subsequently produced and shipped back to Australia where it is administered to the patient. This is still in a trial phase and treatment with the vaccine cannot be guaranteed as there is a double-blind trial going on, in which a percentage of people will receive traditional chemotherapy, and a percentage of people will receive the immunotherapy. The results will be assessed in several years time to see which modality is more effective. Radiotherapy is good for controlling regional disease. It does not affect the spread of subsequent melanoma cells to other areas of the body, but seems to be good in controlling

localized lesions, especially [lithic] lesions in bone which can be painful. It is therefore recommended as an adjunct to surgery.

Chemotherapy has been used for melanoma with very limited success. There are many different regimes, ranging from isolated limb perfusion where extremely toxic chemotherapeutic agents are infused into a limb, which is [exsanguinated] and a tourniquet put on (if the agents were to leak into the general circulation, the dose would be fatal. Usually the limb is [heated] during this process. This obviously is only useful for extensive disease of the arms or the legs. The various systemic chemotherapeutic regimes for melanoma at this stage are extremely toxic, and have many side-effects. The response rates are in the order of about 10%, although some figures vary and it is not clear as to whether they actually improve the length of life.

Various alternate therapies are available for treatment of melanoma, but sadly there is little discourse between alternate therapists and traditional medical practitioners, and to this end, patients wishing to seek alternative therapies are encouraged to research the Internet for themselves.

Finally, a proportion of people with metastatic melanoma go into spontaneous remission and there are some people who co-exist with single metastases of melanoma for many years and remain asymptomatic and healthy. As such, it is a condition which still at times eludes our understanding.



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