

MELANOMA-CUTANEOUS (MALIGNANT MELANOMA — MELANOCARCINOMA)

Melanoma may arise from otherwise normal skin or mucous membrane or it may come from a benign melanocytic lesion. Exposure to ultraviolet radiation is a prime factor in its causation and if a relative has a history of melanoma the patient's risk factor increases two to eight times. At first, melanoma grows radially (horizontally) within the epidermal and superficial dermal layers, often for a long period of time, and at this stage does not metastasize. Later, however, the growth pattern may become vertical and then the tumor grows downward into deeper dermal layers as an expansile mass without cellular maturation. At this point there is apt to be a nodule develop on the epithelial surface which formerly was flat. The probability of metastasis is predicted by measuring in millimeters the depth of invasion of the vertical growth phase from the top of the granular layer to the deepest point of tumor invasion. Clarke's system of measurement uses several levels that measure the deepest anatomical cutaneous area invaded by tumor. Another system, the Breslow, also measures the distance. In addition, patients are also staged clinically in a fashion similar to that used for squamous cell carcinoma.

Malignant melanoma in situ is called lentigo maligna melanoma. This condition develops from a precursor lesion called lentigo maligna. The lentigo maligna presents essentially the same clinical appearance as melanoma. It can be almost any color, tan, brown, black, and even white; patients usually say the lesion has been present for a long time, even 10-15 years. Then when nodularity appears within the lentigo maligna, invasive or vertical growth phase has commenced and the condition is now termed lentigo maligna melanoma.

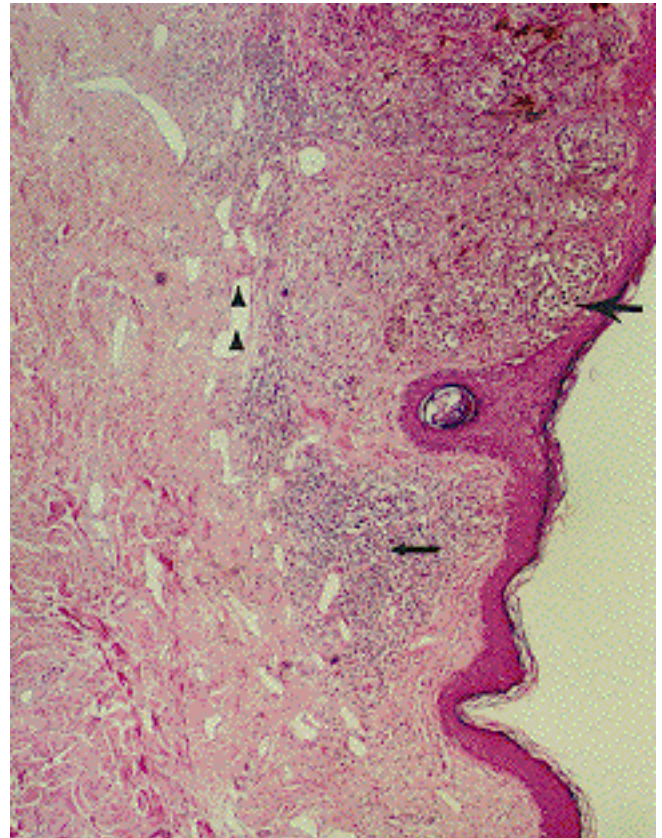
Superficial spreading melanoma is the most common form of melanoma and represents some seventy percent of melanotic skin lesions, and usually is smaller than 3 cm. in greatest diameter but may be much larger. Most lesions are slightly elevated and invasion is indicated by the appearance of surface nodules or induration. Satellite lesions are common.

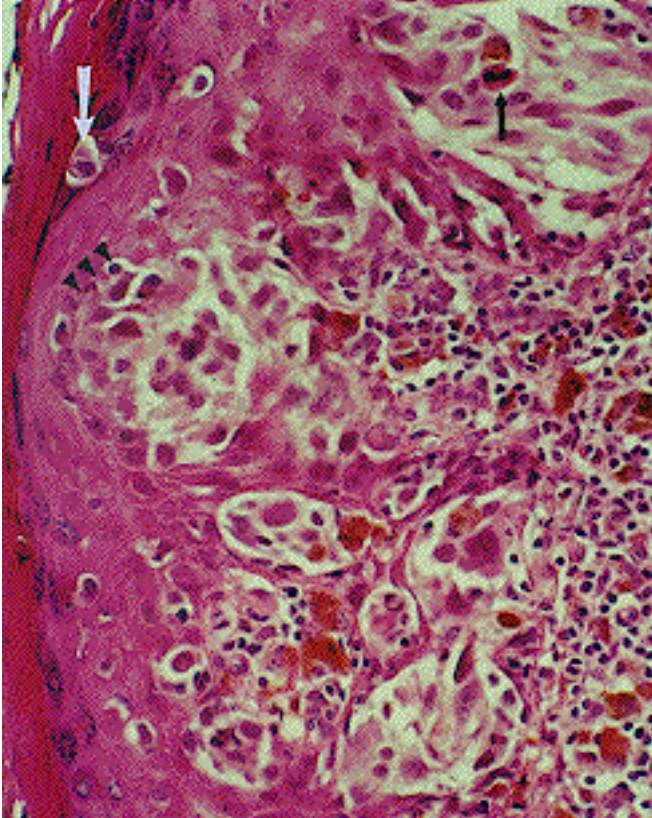
Nodular melanoma does not have a preliminary radial or horizontal phase but begins its vertical growth phase immediately and presents as a nodular elevation as it simultaneously invades the connective tissue. It usually is deeply pigmented and exophytic.

Acral lentiginous melanoma is the most common form of melanoma in blacks and also the most common form of oral melanoma, which is rare. It develops particularly on the palms of the hands and soles and on mucous membranes.

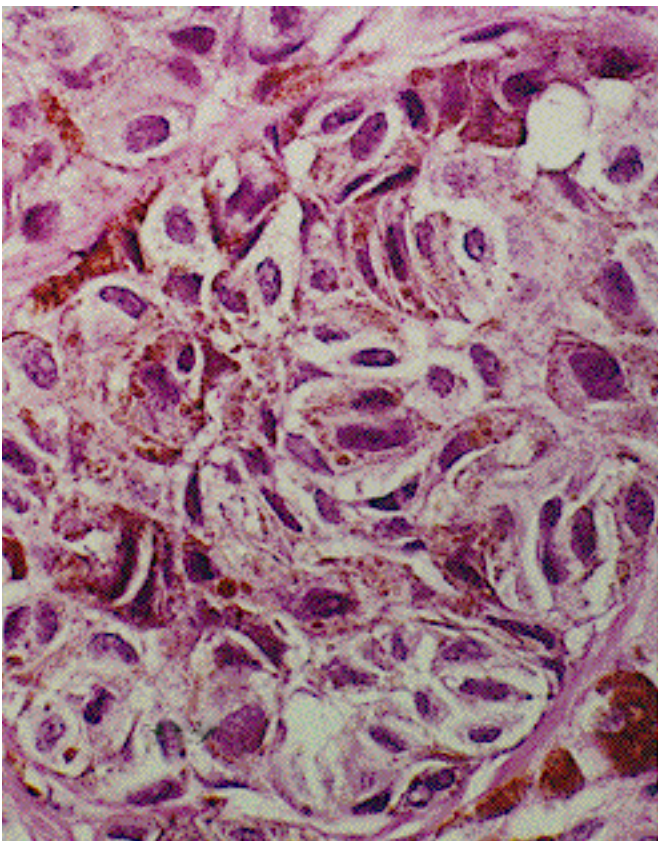
Microscopically, in superficial spreading melanoma in situ, as an example, rounded, large melanocytes with atypical hyperchromatic nuclei are seen. They are often arranged in nests in the lower epidermis with single cells in the upper epidermis. The nests are scattered in pagetoid pattern (resembles an intraepithelial adenocarcinoma known as Paget's disease of the skin). The atypical melanocytes are larger than the normal melanocytes and markedly larger and more pleomorphic than any adjacent nevus cells. The large nuclei have irregular contours with chromatin clumps characteristically at the periphery of the nuclear membrane and there are prominent red nucleoli. Usually, melanoma cells contain melanin granules but sometimes there are none (amelanotic melanoma). Cellular pleomorphism and nuclear hyperchromatism are very common in all types of melanoma although some show vesicular nuclei. Cells may be spindle-shaped or oval and they appear as poorly formed nests or as individual cells at all levels throughout the epidermis and dermis.

Malignant melanoma, high power photo. Arrow indicates a spindled melanocyte and an enlarged melanocyte with large nucleus and abundant cytoplasm. Melanin is present in macrophages and in melanocytes. Cell nests are seen. The spindle cells are relatively few and lie between clusters of epithelioid cells. They have much less cytoplasm than the epithelioid cells and contain less melanin. The clusters of the cells are formed by epithelioid cells. Melanin granules in these cells are fine as compared to the coarser granules in the phagocytes.



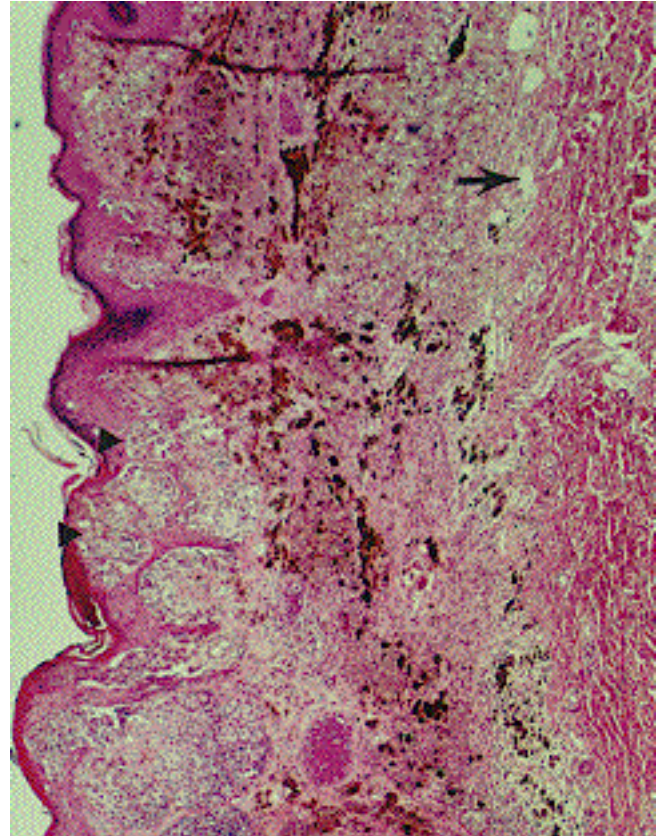


Malignant melanoma, superficial spreading type. There are atypical melanocytes at the dermal epidermal junction and some of these are forming nests (large arrow). The upper or papillary dermis is distended with atypical melanocytes that extend down to the border of the reticular dermis which is just under the telangiectatic vessels marked by two triangles. The small arrow indicates an adjacent area of lymphocytic inflammatory cell infiltrate. In another section, not shown here, there was an intradermal component of the neoplasm.



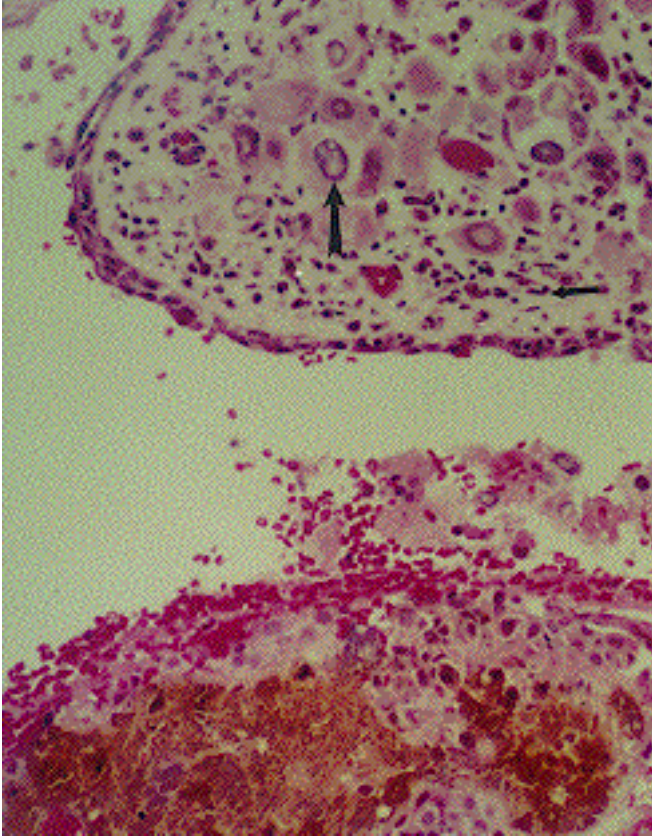
Malignant melanoma, superficial spreading type. Keratin layer of the epidermis and stratum granulosum (large white arrow), and then there are atypical melanocytes forming nests at the dermal-epidermal junction (small triangles) and a scattering of individual melanocytes above the basal layer of the epidermis. Melanin is present in phagocytes and there is lymphocytic inflammatory cell infiltrate. The small arrow points to a mitotic figure. In the case of abnormal melanocytes present only in the epidermis, we speak of in situ melanoma but focal extension into the papillary dermis is the rule. In contrast, tumors that extend into the lower half of the reticular dermis are, by definition, in the vertical growth phase.

Malignant melanoma, superficial spreading type, skin. The heavily pigmented lesion extends under the epidermis in a radial direction, where it involves the papillary dermis but has not yet reached the reticular dermis. There are increased blood vessels just above the reticular dermis and a lymphocytic inflammatory cell infiltrate. Note the cell nests in the upper or papillary dermis and at the dermal-epidermal junction (triangles).

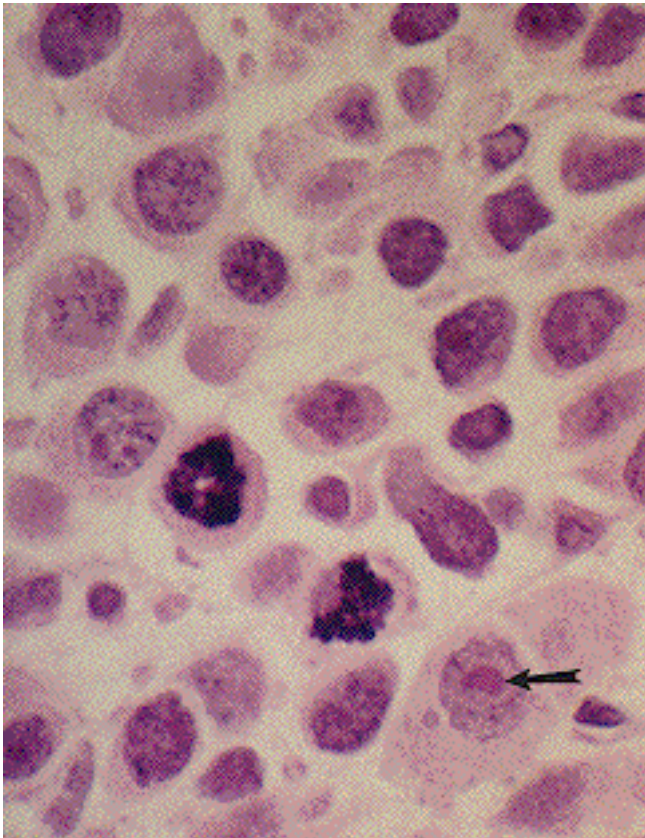


MUCOSAL AND OTHER MALIGNANT MELANOMA

Noncutaneous upper respiratory tract malignant melanoma accounts for a very small percentage of all melanomas. It is seen particularly in the nasal cavity and paranasal sinuses and in the nasopharynx and larynx. Frequently there is surface ulceration. Some tumors show melanin, but most are amelanotic. There are cells with epithelioid features with round, very pleomorphic cells having an increased nuclear-cytoplasmic ratio, large reddish nucleoli, and nuclear pseudo-inclusions. Spindle cell features are also seen with markedly pleomorphic cells and hyperchromatic nuclei and scant cytoplasm.

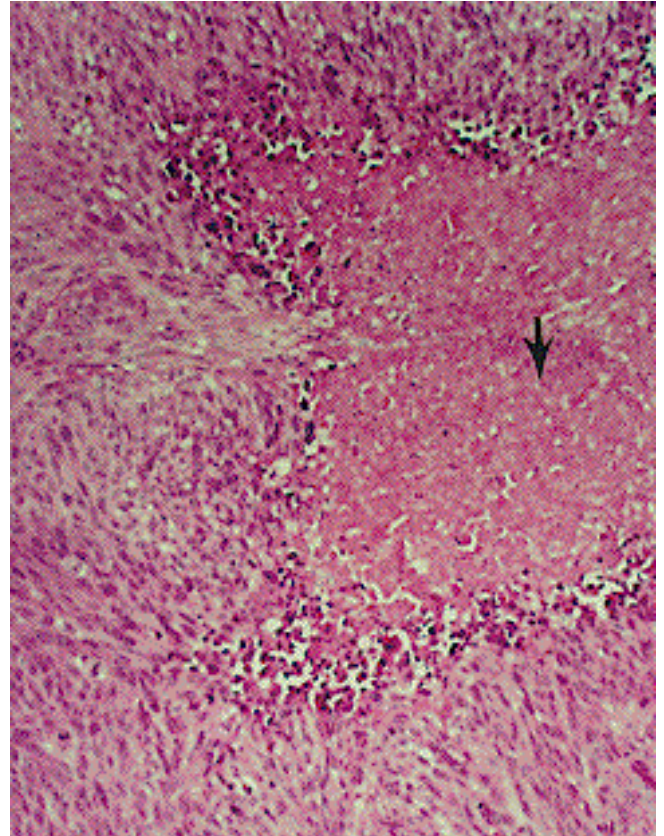


Malignant melanoma, larynx. A dense collection of melanin is seen in one part. The adjacent tissue shows cells with round pleomorphic nuclei and epithelioid features having an increased nuclear-cytoplasmic ratio and prominent nuclear pseudo inclusions (large arrow). Some spindle cells are seen with hyperchromatic nuclei and scant cytoplasm (small arrow).

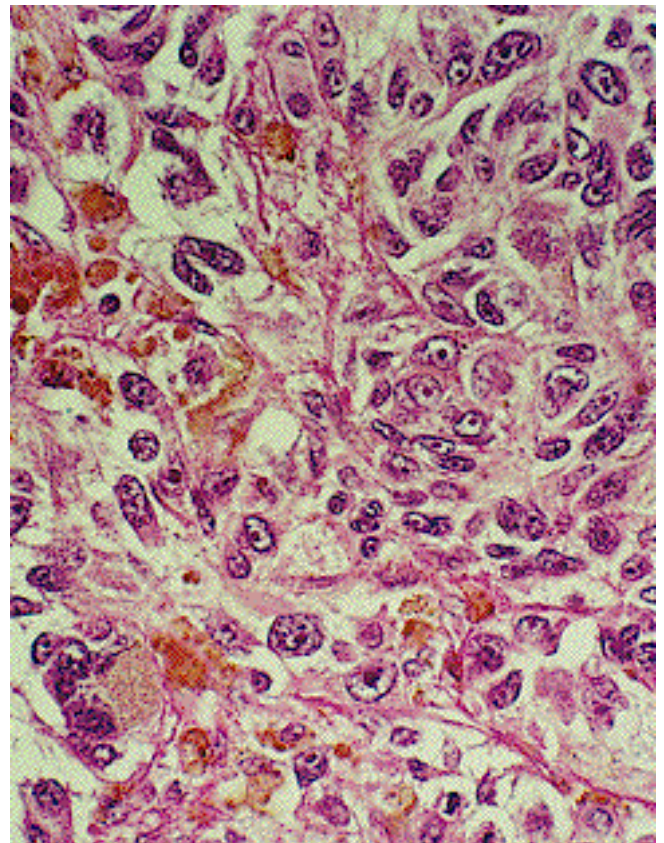


Malignant melanoma, axillary. Two abnormal mitoses stand out and there are large pink nucleoli (arrow).

Malignant melanoma, deep neck tissue. The arrow indicates an area of necrosis. The surrounding tumor cells are spindle shaped.



Malignant melanoma, same tissue. Melanin in phagocytes and in epithelioid-appearing tumor cells with vesicular nuclei. Compare with previous photos showing deeply stained pleomorphic nucleoli.



CLINICAL ASPECTS

It must be emphasized that the extent of the vertical growth phase determines the biologic nature of cutaneous malignant melanoma. Surgical excision is the only curative treatment. In years past, malignant melanoma was considered a most deadly disease, but today most of these cutaneous lesions are cured surgically. There is a ninety percent five year survival rate for cutaneous stage I lesions (no metastasis) and a sixty percent five year survival rate for stage II lesions (local lymphnode metastases). If there is disseminated disease at the time of diagnosis (stage III), the outcome is almost always fatal.

The prognosis in mucosal melanoma is much poorer than for cutaneous melanoma with five year survival rates in the range of ten percent. Treatment is surgical but some patients do receive radiotherapy and chemotherapy. Metastatic disease in the case of cutaneous melanoma is chiefly to regional lymph nodes but in mucosal melanoma, metastasis occurs frequently to the lungs and brain as well as lymph nodes.

Because these tumors bleed frequently, deposits of hemosiderin may be mistaken for melanin so special stains for melanin (Warthin-Starry) and hemosiderin (Prussian blue), should be used to distinguish between the two. Also melanin can be bleached with a solution of potassium permanganate. Melanin demonstrated in tumor cells confirms the diagnosis. Currently, immunohistochemical staining with S-100 and HMB-45 antibodies are used to identify amelanotic melanomas.