and function in part to produce and transfer melanin to keratinocytes, thereby determining the color of skin and hair. There are also benign proliferative disorders of melanocytes, including the common acquired nevus (mole).

Melanoma has four major clinicopathologic subtypes. The most common subtype is superficial spreading melanoma, which can occur anywhere on the body but has a predilection for the torso and legs. Lentigo maligna melanoma manifests typically as a tan macule on chronically sun-exposed areas in older individuals. Nodular melanoma is associated with vertical growth into the dermis and manifests as a dark, nodular lesion. Acral lentiginous melanoma is an uncommon variant found on the palmar and plantar surfaces as well as subungual areas. This subtype is the most common form of melanoma in dark-skinned individuals. Other variants have also been described. Although this classification, which dates from the 1960s, captures the clinical heterogeneity of melanoma, it does not provide prognostic information or help determine clinical management.

Pathologic features that have prognostic relevance include the depth of invasion, the presence of ulceration, and the presence and number of mitotic figures. All of these features are incorporated into the AJCC TNM staging system of malignant melanoma. Increasing depth of invasion predicts a poor prognosis. The risk of lymph node metastasis, distant metastasis, and death, exists on a continuum with increasing tumor thickness. Therefore, patients with thin melanomas (≤1 mm thickness) generally have favorable outcomes, whereas patients with thick melanomas (>4 mm thickness), even in the absence of nodal disease, have a 5 year survival rate often less than 50% (Table 60-1).

Clinical Presentation

Most patients with cutaneous melanoma have early-stage disease at presentation. Approximately 15% of patients have clinically apparent regional adenopathy or radiographic evidence for metastatic disease at the time of diagnosis. A number of benign lesions share morphologic features with melanoma, making identification by physical examination challenging. Because survival for patients with limited disease is excellent, early detection is important.

TABLE 60-1 ESTIMATED OVERALL SURVIVAL FOR PATIENTS WITH MELANOMA BASED ON THE DEPTH OF INVASION AND NUMBER OF INVOLVED REGIONAL LYMPH NODES.

DEPTH OF PRIMARY TUMOR INVASION (mm)	AJCC T STAGE	5-YR OVERALL SURVIVAL (%)
≤1	T1	95
1.01-2.0	T2	85
2.01-4.0	T3	70
>4.0	T4	55
NUMBER OF INVOLVED REGIONAL LYMPH NODES	**AJCC N STAGE**	**5-YR OVERALL SURVIVAL (%)**
1	N1	65
2-3	N2	55
≥4	N3	35

Data from Edge S, Byrd DR, Compton CC, et al: AJCC Cancer Staging Manual, ed 7, New York, 2010, Springer.

AJCC, American Joint Committee on Cancer.

Features favoring malignancy are suggested by the *ABCDE* rule: *a*symmetry, irregular *b*orders, variable *c*olor, *d*iameter greater than 6 mm, and *e*volving lesion. A lesion that is changing in shape, size, or color should be considered suspicious.

Melanoma typically disseminates to regional lymph nodes. Regional lymph nodes should be examined. Metastatic disease also occurs in the liver, lung, skin, bone, and brain. Symptoms of advanced disease are highly variable.

In contrast to cutaneous melanoma, mucosal melanoma is often advanced at the time of diagnosis. This disease is rare, and the sites include the head and neck, anorectum, and vulvovaginal areas. Presenting symptoms are similar to those of the more common malignant diseases of these regions.

Diagnosis and Differential Diagnosis

The diagnosis of melanoma requires histologic evaluation of a biopsy specimen. In general, pigmented lesions suspicious for melanoma should undergo an excisional biopsy. This allows adequate assessment of tumor thickness, which informs decisions regarding the need for a sentinel lymph node biopsy and the width of subsequent local excision. If an excisional biopsy cannot be performed, a full-thickness punch biopsy is recommended. So-called shave biopsies of suspicious lesions make subsequent determination of tumor thickness difficult and may provide insufficient material for diagnosis. The histologic diagnosis is based on characteristic morphology and on immunohistochemical staining for markers such as S100, HMB45, and MART1.

In general, imaging investigations for staging purposes are not required for patients with thin or intermediate-thickness melanoma. The likelihood of demonstrating metastatic disease is low. Patients with thick melanomas or lymph node metastasis detected on clinical examination or by sentinel lymph node biopsy are at high risk for disease dissemination and need radiographic staging by CT of the chest, abdomen, and pelvis. Further imaging depends on the clinical context. For example, patients with clinically advanced melanoma and new, diffuse bone pain should undergo a bone scan; those with neurologic symptoms should undergo brain imaging.

Treatment and Prognosis

The prognosis of melanoma can be accurately estimated using the AJCC TNM staging system. Overall survival depends on the thickness of the primary tumor and the presence and number of regional lymph node metastases. Tumor ulceration and high mitotic rate are associated with a poor prognosis. Metastatic disease is incurable, and the clinical course depends on the pattern and extent of dissemination. An elevated serum lactate dehydrogenase (LDH) level is an independent poor prognostic factor for patients with metastases.

Surgery with wide margins is the cornerstone of curative therapy for nonmetastatic disease. The optimal margin depends on the depth of invasion and the location of the primary lesion but is typically between 1 and 2 cm. Patients with tumors larger than 1 mm in thickness and a negative physical examination should also undergo regional lymph node biopsy to evaluate for metastasis. Patients with melanoma in the initial node or nodes merit lymph node dissection for more accurate staging and to remove any residual disease.