

clubbing of the digits. Although the osteoarthropathy is seldom seen in noncancer patients, clubbing of the fingertips may be encountered in liver diseases, diffuse lung disease, congenital cyanotic heart disease, ulcerative colitis, and other disorders. The cause of hypertrophic osteoarthropathy is unknown.

Several vascular and hematologic manifestations may appear in association with a variety of forms of cancer. As mentioned in the discussion of thrombosis (Chapter 4), *migratory thrombophlebitis* (Trousseau syndrome) may be encountered in association with deep-seated cancers, most often carcinomas of the pancreas or lung. *Disseminated intravascular coagulation* may complicate a diversity of clinical disorders (Chapter 14); among cancers, it is most commonly associated with acute promyelocytic leukemia and prostatic adenocarcinoma. Bland, small, nonbacterial fibrinous vegetations sometimes form on the cardiac valve leaflets (more often on left-sided valves), particularly in individuals with advanced mucin-secreting adenocarcinomas. These lesions, called *nonbacterial thrombotic endocarditis*, are described further in Chapter 12. The vegetations are potential sources of emboli that can further complicate the course of the cancer.

Grading and Staging of Tumors

Methods to quantify the probable clinical aggressiveness of a given neoplasm and its apparent extent and spread in the individual patient are necessary for making an accurate prognosis and for comparing end results of various treatment protocols. For instance, the results of treating well-differentiated thyroid adenocarcinoma that is localized to the thyroid gland will be different from those obtained from treating highly anaplastic thyroid cancers that have invaded the neck organs. Systems have been developed to express, at least in semiquantitative terms, the level of differentiation, or grade, and extent of spread of a cancer within the patient, or stage, as parameters of the clinical gravity of the disease.

- **Grading.** Grading of a cancer is based on the degree of differentiation of the tumor cells and, in some cancers, the number of mitoses or architectural features. Grading schemes have evolved for each type of malignancy, and generally range from two categories (low grade and high grade) to four categories. Criteria for the individual grades vary in different types of tumors and so are not detailed here, but all attempt, in essence, to judge the extent to which the tumor cells resemble or fail to resemble their normal counterparts. Although histologic grading is useful, the correlation between histologic appearance and biologic behavior is less than perfect. In recognition of this problem and to avoid spurious quantification, it is common practice to characterize a particular neoplasm in descriptive terms, for example, well-differentiated, mucin-secreting adenocarcinoma of the stomach, or poorly differentiated pancreatic adenocarcinoma.
- **Staging.** The staging of solid cancers is based on the size of the primary lesion, its extent of spread to regional lymph nodes, and the presence or absence of blood-borne metastases. The major staging system currently in use is the American Joint Committee on Cancer Staging.

This system uses a classification called the *TNM system*—*T* for primary tumor, *N* for regional lymph node involvement, and *M* for metastases. TNM staging varies for specific forms of cancer, but there are general principles. The primary lesion is characterized as T1 to T4 based on increasing size. T0 is used to indicate an in situ lesion. N0 would mean no nodal involvement, whereas N1 to N3 would denote involvement of an increasing number and range of nodes. M0 signifies no distant metastases, whereas M1 or sometimes M2 indicates the presence of metastases and some judgment as to their number.

KEY CONCEPTS

Clinical Aspects of Tumors

Cachexia: progressive loss of body fat and lean body mass, accompanied by profound weakness, anorexia, and anemia, that is caused by release of factors by the tumor or host immune cells

Paraneoplastic syndromes: symptom complexes in individuals with cancer that cannot be explained by tumor spread or release of hormones that are indigenous to the tumor “cell of origin.” For example:

- Endocrinopathies (Cushing syndrome, hypercalcemia)
- Neuropathic syndromes (polymyopathy, peripheral neuropathies, neural degeneration, myasthenic syndromes)
- Skin disorders (acanthosis nigricans)
- Skeletal and joint abnormalities (hypertrophic osteoarthritis)
- Hypercoagulability (migratory thrombophlebitis, disseminated intravascular coagulation, nonbacterial thrombotic endocarditis)

Grading: determined by cytologic appearance; based on the idea that behavior and differentiation are related, with poorly differentiated tumors having more aggressive behavior

Staging: determined by surgical exploration or imaging, is based on size, local and regional lymph node spread, and distant metastases; of greater clinical value than grading

Laboratory Diagnosis of Cancer

Every year the approach to laboratory diagnosis of cancer becomes more complex, more sophisticated, and more specialized. For virtually every neoplasm mentioned in this text, the experts have characterized several subcategories; we must walk, however, before we can run. Each of the following sections attempts to present the state of the art, avoiding details of technologies.

Histologic and Cytologic Methods. The laboratory diagnosis of cancer is, in most instances, not difficult. The two ends of the benign-malignant spectrum pose no problem; however, in the middle lies a gray zone that novices dread and where experts tread cautiously. The focus here is on the roles of the clinician (often a surgeon) and the pathologist in facilitating the correct diagnosis.

Clinical data are invaluable for accurate pathologic diagnosis, but often clinicians underestimate its value. Radiation changes in the skin or mucosa can be similar to