**Clinical Aspects of Neoplasia**

Ultimately the importance of neoplasms lies in their effects on patients. Although malignant tumors are of course more threatening than benign tumors, any tumor, even a benign one, may cause morbidity and mortality. Indeed, both malignant and benign tumors may cause problems because of (1) location and impingement on adjacent structures, (2) functional activity such as hormone synthesis or the development of paraneoplastic syndromes, (3) bleeding and infections when the tumor ulcerates through adjacent surfaces, (4) symptoms that result from rupture or infarction, and (5) cachexia or wasting.

**Local and Hormonal Effects**

Location is crucial in both benign and malignant tumors. A small (1-cm) pituitary adenoma, though benign and possibly nonfunctional, can compress and destroy the surrounding normal gland and thus lead to serious hypopituatarism. Cancers arising within or metastatic to an endocrine gland may cause an endocrine insufficiency by destroying the gland. Neoplasms in the gut, both benign and malignant, may cause obstruction as they enlarge.

Hormone production is seen with benign and malignant neoplasms arising in endocrine glands. Such functional activity is more typical of benign than of malignant tumors, which may be sufficiently undifferentiated to have lost such capability. A benign beta-cell adenoma of the pancreatic islets less than 1 cm in diameter may produce sufficient insulin to cause fatal hypoglycemia. The erosive and destructive growth of cancers or the expansile pressure of a benign tumor on any natural surface, such as the skin or mucosa of the gut, may cause ulcerations, secondary infections, and bleeding. Melena (blood in the stool) and hematuria, for example, are characteristic of neoplasms of the gut and urinary tract.

**Cancer Cachexia**

Individuals with cancer commonly suffer progressive loss of body fat and lean body mass accompanied by profound weakness, anorexia, and anemia, referred to as *cachexia*. Unlike starvation, the weight loss seen in cachexia results equally from loss of fat and muscle. There is some correlation between the tumor burden and the severity of the cachexia. However, cachexia is not caused by the nutritional demands of the tumor. In persons with cancer, the basal metabolic rate is increased, despite reduced food intake. This is in contrast to the lower metabolic rate that occurs as an adaptational response in starvation. Although patients with cancer are often anorexic, cachexia probably results from the action of soluble factors such as cytokines produced by the tumor and the host rather than reduced food intake. The basis of these metabolic abnormalities is not fully understood. There is currently no satisfactory treatment for cancer cachexia other than removal of the underlying cause, the tumor. However, cachexia clearly hampers effective chemotherapy, by reducing the dosages that can be given. Furthermore, it has been estimated that a third of deaths of cancer are attributable to cachexia, rather than directly due to the tumor burden itself.

**Paraneoplastic Syndromes**

These defined as elaboration of hormones indigenous to the tissue from which the tumor arose; These occur in about 10% of persons with malignant disease. Despite their relative infrequency, paraneoplastic syndromes are important to recognize, for several reasons:

* They may represent the earliest manifestation of an occult neoplasm.
* In affected patients they may represent significant clinical problems and may even be lethal.
* They may mimic metastatic disease and therefore confound treatment.

The *endocrinopathies* are frequently encountered paraneoplastic syndromes. Because the cancer cells are not of endocrine origin, the functional activity is referred to as *ectopic hormone production*. Cushing syndrome is the most common endocrinopathy. Approximately 50% of individuals with this endocrinopathy have carcinoma of the lung, chiefly the small-cell type. It is caused by excessive production of corticotropin or corticotropin-like peptides.

The *neuromyopathic paraneoplastic syndromes* like *myasthenia gravis symptoms* in bronchogenic carcinoma.

GRADING AND STAGING OF TUMORS

***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, but all attempt, in essence, to judge the extent to which the tumor cells resemble or fail to resemble their normal counterparts.

***The staging of 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. The TNM staging varies for each specific form of cancer, but there are general principles. With increasing size the primary lesion is characterized as T1 to T4. 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.

LABORATORY DIAGNOSIS OF CANCER

**Histologic and Cytologic Methods**

the laboratory evaluation of a lesion can be only as good as the specimen made available for examination. It must be adequate, representative, and properly preserved. Several sampling approaches are available: (1) excision or biopsy, (2) needle aspiration, and (3) cytologic smears.

***Fine-needle aspiration*** of tumors is another approach that is widely used. The procedure involves aspirating cells and attendant fluid with a small-bore needle, followed by cytologic examination of the stained smear. This method is used most commonly for the assessment of readily palpable lesions in sites such as the breast, thyroid, and lymph nodes.

***Cytologic (Pap) smears*** provide yet another method for the detection of cancer ( Chapter 22 ). This approach is widely used to screen for carcinoma of the cervix, often at an in situ stage, but it is also used with many other forms of suspected malignancy, such as endometrial carcinoma, bronchogenic carcinoma, bladder and prostatic tumors, and gastric carcinomas.

**Immunohistochemistry.**

The availability of specific antibodies has greatly facilitated the identification of cell products or surface markers. Some examples of the utility of immunohistochemistry in the diagnosis or management of malignant neoplasms follow.

* *Categorization of undifferentiated malignant tumors:* In many cases malignant tumors of diverse origin resemble each other because of limited differentiation.
* *Determination of site of origin of metastatic tumors.*
* *Detection of molecules that have prognostic or therapeutic significance*.

**Flow Cytometry.**

Flow cytometry can rapidly and quantitatively measure several individual cell characteristics, such as membrane antigens and the DNA content of tumor cells. *Flow cytometry* has also proved useful in the identification and classification of tumors arising from T and B lymphocytes