



**FIGURE 103e-1 Gompertzian tumor growth.** The growth fraction of a tumor declines exponentially over time (*top*). The growth rate of a tumor peaks before it is clinically detectable (*middle*). Tumor size increases slowly, goes through an exponential phase, and slows again as the tumor reaches the size at which limitation of nutrients or autoregulatory or host regulatory influences can occur. The maximum growth rate occurs at  $1/e$ , the point at which the tumor is about 37% of its maximum size (*marked with an X*). Tumor becomes detectable at a burden of about  $10^9$  ( $1 \text{ cm}^3$ ) cells and kills the patient at a tumor cell burden of about  $10^{12}$  (1 kg). Efforts to treat the tumor and reduce its size can result in an increase in the growth fraction and an increase in growth rate.

## LOCALIZED CANCER TREATMENTS

### SURGERY

Surgery is unquestionably the most effective means of treating cancer. Today at least 40% of cancer patients are cured by surgery. Unfortunately, a large fraction of patients with solid tumors (perhaps 60%) have metastatic disease that is not accessible for removal. However, even when the disease is not curable by surgery alone, the removal of tumor can obtain important benefits, including local control of tumor, preservation of organ function, debulking that permits subsequent therapy to work better, and staging information on extent of involvement. Cancer surgery aiming for cure is usually planned to excise the tumor completely with an adequate margin of normal tissue (the margin varies with the tumor and the anatomy), touching the tumor as little as possible to prevent vascular and lymphatic spread, and minimizing operative risk. Such a resection is defined as an R0 resection. R1 and R2 resections, in contrast, are imprecisely defined pathologically as having microscopic or macroscopic tumor at resection margins. Such outcomes may be necessitated by proximity of the tumor to vital structures or recognition only in the resected specimen of the extent of tumor involvement, and may be the basis for reoperation to obtain optimal margins if feasible. Extending the procedure to resect draining lymph nodes obtains prognostic information and may, in some anatomic locations, improve survival.

Increasingly, laparoscopic approaches are being used to address primary abdominal and pelvic tumors. Lymph node spread may be assessed using the sentinel node approach, in which the first draining lymph node a spreading tumor would encounter is defined by injecting a dye or radioisotope into the tumor site at operation and then resecting the first node to turn blue or collect label. The sentinel node assessment is continuing to undergo clinical evaluation but appears to provide reliable information without the risks (lymphedema, lymphangiosarcoma) associated with resection of all the regional nodes. Advances in adjuvant chemotherapy (chemotherapy given systemically after removal of all disease by operation and without evidence of active metastatic disease) and radiation therapy following surgery have permitted a substantial decrease in the extent of primary surgery

necessary to obtain the best outcomes. Thus, lumpectomy with radiation therapy is as effective as modified radical mastectomy for breast cancer, and limb-sparing surgery followed by adjuvant radiation therapy and chemotherapy has replaced radical primary surgical procedures involving amputation and disarticulation for childhood rhabdomyosarcomas and osteosarcomas. More limited surgery is also being used to spare organ function, as in larynx and bladder cancer. The magnitude of operations necessary to optimally control and cure cancer has also been diminished by technical advances; for example, the circular anastomotic stapler has allowed narrower (<2 cm) margins in colon cancer without compromise of local control rates, and many patients who would have had colostomies are able to maintain normal anatomy.

In some settings (e.g., bulky testicular cancer or stage III breast cancer), surgery is not the first treatment modality used. After an initial diagnostic biopsy, chemotherapy and/or radiation therapy is delivered to reduce the size of the tumor and clinically control undetected metastatic disease. Such therapy is followed by a surgical procedure to remove residual masses; this is called *neoadjuvant therapy*. Because the sequence of treatment is critical to success and is different from the standard surgery-first approach, coordination among the surgical oncologist, radiation oncologist, and medical oncologist is crucial.

Surgery may be curative in a subset of patients with metastatic disease. Patients with lung metastases from osteosarcoma may be cured by resection of the lung lesions. In patients with colon cancer who have fewer than five liver metastases restricted to one lobe and no extrahepatic metastases, hepatic lobectomy may produce long-term disease-free survival in 25% of selected patients. Surgery can also be associated with systemic antitumor effects. In the setting of hormonally responsive tumors, oophorectomy and/or adrenalectomy may eliminate estrogen production, and orchiectomy may reduce androgen production, hormones that drive certain breast and all prostate cancers, respectively; both procedures can have useful effects on metastatic tumor growth. If resection of the primary lesion takes place in the presence of metastases, acceleration of metastatic growth has also been described in certain cases, perhaps based on the removal of a source of angiogenesis inhibitors and mass-related growth regulators in the tumor.

In selecting a surgeon or center for primary cancer treatment, consideration must be given to the volume of cancer surgeries undertaken by the site. Studies in a variety of cancers have shown that increased annual procedure volume appears to correlate with outcome. In addition, facilities with extensive support systems—e.g., for joint thoracic and abdominal surgical teams with cardiopulmonary bypass, if needed—may allow resection of certain tumors that would otherwise not be possible.

Surgery is used in a number of ways for palliative or supportive care of the cancer patient, not related to the goal of curing the cancer. These include insertion and care of central venous catheters, control of pleural and pericardial effusions and ascites, caval interruption for recurrent pulmonary emboli, stabilization of cancer-weakened weight-bearing bones, and control of hemorrhage, among others. Surgical bypass of gastrointestinal, urinary tract, or biliary tree obstruction can alleviate symptoms and prolong survival. Surgical procedures may provide relief of otherwise intractable pain or reverse neurologic dysfunction (cord decompression). Splenectomy may relieve symptoms and reverse hypersplenism. Intrathecal or intrahepatic therapy relies on surgical placement of appropriate infusion portals. Surgery may correct other treatment-related toxicities such as adhesions or strictures. Surgical procedures are also valuable in rehabilitative efforts to restore health or function. Orthopedic procedures may be necessary to ensure proper ambulation. Breast reconstruction can make an enormous impact on the patient's perception of successful therapy. Plastic and reconstructive surgery can correct the effects of disfiguring primary treatment.

Surgery is also a tool valuable in the prevention of cancers in high-risk populations. Prophylactic mastectomy, colectomy, oophorectomy, and thyroidectomy are mainstays of prevention of genetic cancer syndromes. Resection of premalignant skin and uterine cervix lesions and colonic polyps prevents progression to frank malignancy.