mastectomy in those with hereditary defects that can lead to breast cancer). Surgery can also make the diagnosis of cancer by biopsy; assist in staging by sampling lymph nodes; provide definitive treatment by removing the primary tumor; reconstruct the limb or organ sacrificed; and provide palliative treatment of cancer (e.g., intestinal bypass for obstruction, spinal cord decompression, or orthopedic procedures to prevent or treat pathologic fractures). Invasive procedures, such as biopsies and the insertion of various access devices, tubes, stents, catheters, and drains, are also performed by interventional specialists, including radiologists, gastroenterologists, and pulmonologists.

When a solid organ cancer is localized, surgery is the most effective curative treatment available. The intent is to completely remove the tumor, regional lymph nodes, and adjacent involved tissue, along with a safe margin of normal tissue. At surgery, the tumor is isolated and is almost never opened during the procedure. Refinements in cancer surgery include increasing use of laparoscopic procedures in selected cancers and the identification of a sentinel lymph node by injection of a dye during surgery, which avoids a full lymph node dissection if the sentinel node is uninvolved by cancer.

PRINCIPLES OF RADIATION THERAPY

Many cancer patients receive radiation therapy at some point during the course of their disease. Radiation therapy can sometimes be used as definitive treatment, either alone or in combination with chemotherapy. Unlike surgery, local or regional treatment with radiation can preserve organ structure and function, improving quality of life for patients. For example, use of radiation with chemotherapy for treatment of localized laryngeal cancer has outcomes similar to those of surgery but allows preservation of the larynx. Radiation therapy is also effective in the palliative setting, where it is used to control various cancer-related problems such as pain, dysphagia, and bleeding.

Ionizing radiation damages cellular DNA directly or indirectly through free radical intermediates. Cells are most susceptible to radiation during the M and G_2 phases of the cell cycle. The aim of radiation therapy is to deliver the highest dose possible to the tumor with minimal toxicity to adjacent normal tissues. Dividing the total planned radiation dose into small daily fractions takes advantage of the difference in repair capability between normal and malignant tissue and improves the tolerance of normal tissue. The biologic effects of radiation can be modified by numerous factors, including the amount of oxygen in the irradiated tissue and the use of chemotherapy for sensitizing tissue to radiation.

The goal of treatment planning for radiation therapy is to precisely define the dose and volume to be irradiated. The dose of radiation is measured in units of absorbed dose, Gray (Gy), which has replaced the older unit, rad (1 Gy = 100 rad). Conventional radiation treatments deliver 1.8 to 2 Gy/day on 5 days per week, over a period of 5 to 6 weeks. For palliative treatment, higher doses per fraction may be used to deliver an effective dose over a shorter period.

Ionizing radiation can be administered as external-beam therapy with the use of a linear accelerator to generate electrons or high-energy x-rays. Electrons have a limited depth of penetration and are useful for superficial tumors. High-energy x-rays deliver the radiation deep into the body while reducing the dose to the skin as they enter. Brachytherapy uses radioactive sources to deliver ionizing radiation (gamma rays) directly to the tumor. An example is the implantation of iodine-125 seeds into the prostate as definitive therapy for early prostate cancer. Current approaches to improving radiation therapy include the use of advanced technology that allows delivery of a higher dose of radiation to specific areas of the tumor and sparing of normal tissue (conformal and intensity-modulated radiation therapy).

TABLE 55-1 ACUTE AND LATE EFFECTS OF RADIATION THERAPY

ORGAN	ACUTE	LATE	DOSE (GY) ASSOCIATED WITH ADVERSE EFFECTS
Bone marrow	Aplasia	Leukemia, myelodysplasia	25
Spinal cord	None	Myelopathy	45
Heart	None	Pericarditis, cardiomyopathy, coronary artery disease	45
Rectum	Diarrhea, tenesmus	Stricture, obstruction	60
Eye	Conjunctivitis	Retinopathy	55
Lung	Pneumonitis	Chronic pneumonitis	25

Injury to normal tissue from radiation therapy can be either acute or late (Table 55-1). Acute effects occur within days to weeks after irradiation and are seen primarily in rapidly proliferating tissues such as skin and gastrointestinal mucosa. The severity depends on the total dose, but the damage can usually be repaired. Late effects, such as necrosis, fibrosis, or organ failure, appear months or years after irradiation and are dependent on fraction size. Another late complication of radiation therapy is the development of secondary malignancies (e.g., after radiation for breast cancer or Hodgkin's disease).

PRINCIPLES OF MEDICAL THERAPY

The term *chemotherapy* refers to the use of cytotoxic agents, singly or in combination, for the systemic treatment of cancer. Most such agents are general antiproliferative agents that are more effective against rapidly growing tumors and have significant adverse effects on normal tissues that also divide rapidly, such as bone marrow and digestive tract mucosa. Newer agents, including monoclonal antibodies and signal transduction inhibitors, are directed against targets that are relatively specific to tumor cells and therefore may have less toxicity. These drugs are classified separately from chemotherapy as *targeted therapy* agents.

Mechanisms of Chemotherapy

Chemotherapeutic agents can be cell cycle specific or cell cycle nonspecific. Cell cycle–nonspecific agents have a greater effect on cells traversing the cell cycle but also affect noncycling cells; cell cycle–specific agents affect only cycling cells. Chemotherapy agents are further classified according to their mechanism of action into alkylating agents, antimetabolites, antitumor antibiotics, and mitotic spindle inhibitors (Table 55-2). Most chemotherapy agents suppress the bone marrow, leading to infections