TABLE 55-2 COMMONLY USED CHEMOTHERAPY AGENTS

DRUG	CANCERS TREATED	SPECIFIC CLASS OR MECHANISM OF ACTION	COMMON SIDE EFFECTS
CELL CYCLE SPECIFIC			
5-Fluorouracil	Gastrointestinal, head and neck, breast	Antimetabolite, inhibits thymidylate synthase	Myelosuppression, mucositis, diarrhea
Gemcitabine	Pancreas, lung, breast, bladder	Antimetabolite, deoxycytidine analogue	Myelosuppression, nausea, emesis
Methotrexate	ALL, choriocarcinoma, bladder, lymphoma	Antimetabolite, folic acid antagonist	Myelosuppression, mucositis, acute renal failure
Doxorubicin	Breast, lung, NHL	Anthracycline, intercalates into DNA	Myelosuppression, nausea, emesis, cardiomyopathy
Irinotecan	Colorectal, lung	Camptothecin, topoisomerase I inhibitor	Myelosuppression, diarrhea
Paclitaxel	Breast, lung, Kaposi sarcoma, ovarian	Plant alkaloid, inhibits microtubule formation	Myelosuppression, hypersensitivity reaction, neuropathy
Vincristine	ALL, lymphomas, myeloma, sarcoma	Plant alkaloid, disrupts microtubule assembly	Peripheral neuropathy, constipation
CELL CYCLE NONSPECIFIC			
Cyclophosphamide	Breast, NHL, CLL, sarcoma	Alkylating agent, cross-links DNA	Myelosuppression, hemorrhagic cystitis, nausea, emesis
Cisplatin	Lung, bladder, ovarian, testicular, head and neck	Alkylating agent, cross-links DNA	Nephrotoxicity, nausea, emesis, ototoxicity, sensory neuropathy

ALL, Acute lymphoblastic leukemia; CLL, chronic lymphocytic leukemia; NHL, non-Hodgkin's lymphoma.

from neutropenia and life-threatening bleeding from thrombocytopenia. For most drugs, treatment schedules give successive doses every 2 to 4 weeks. This interval between successive doses, the *cycle* of chemotherapy, allows recovery of blood counts and other side effects before administration of the next dose. The concept of *dose intensity* is also important. Cellular killing with chemotherapy follows first-order kinetics: A given dose of drug kills only a fraction of tumor cells. The dose-response curve for chemotherapy drugs is steep. Therefore, the greater the dose administered, the greater the kill: A 2-fold increase in dose can lead to a 10-fold increase in tumor cell kill. This also means that dose reductions may adversely affect the eventual cure rate. Arbitrary reductions in doses of chemotherapy to spare patients toxicity should be avoided. Shortening of the duration of cycles of chemotherapy using growth factor support—a "dose-dense" approach—has been shown to improve survival in selected patients when compared with traditional chemotherapy for breast cancer.

Single chemotherapy agents seldom cure cancer. Combination chemotherapy regimens have therefore been developed for a variety of cancers. Combination therapy provides maximal cell kill and broader coverage of resistant cells; it may also prevent or slow the development of resistant cells. Drugs used in a combination are chosen because they have known efficacy as single agents but have differing mechanisms of action and nonoverlapping toxicity profiles. These regimens are commonly referred to by acronyms, such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) for lymphoma or FOLFOX (5-fluorouracil, leucovorin, and oxaliplatin) for colorectal cancer.

Indications for Chemotherapy

Chemotherapy for localized or advanced cancers is summarized in (Table 55-3). *Adjuvant* chemotherapy refers to its use after the primary tumor has been resected. Here, chemotherapy is directed against presumed systemic micrometastases in patients who are at high risk for recurrence. In the example of stage III colon cancer (described earlier), 6 months of adjuvant chemotherapy after colonic resection can reduce the patient's likelihood of developing recurrent cancer from 50% to 25%. Adjuvant chemotherapy has been shown to increase cure rates in other cancers.

Neoadjuvant or *preoperative* chemotherapy refers to the use of chemotherapy before surgery, sometimes in combination with radiation therapy. If successful, neoadjuvant therapy can reduce the size of the tumor and consequently permit less removal of normal tissue, such as a lumpectomy instead of a mastectomy in breast cancer or limb-sparing surgery instead of amputation in extremity sarcoma. In certain tumor sites, such as the larynx or the anal canal, neoadjuvant therapy can obliterate the tumor and avoid the need for surgery altogether.

TABLE 55-3 EFFICACY OF MEDICAL THERAPY IN SELECTED CANCERS

CURE POSSIBLE IN ADVANCED SETTING
Testicular cancer
Acute leukemia: lymphocytic, promyelocytic, selected myelocytic
Lymphomas: Hodgkin's lymphoma, selected non-Hodgkin's lymphomas
Childhood solid tumors: rhabdomyosarcoma, Ewing's sarcoma, Wilms' tumor
Choriocarcinoma
Small cell lung cancer
CURE POSSIBLE IN ADJUVANT SETTING
Breast cancer
Colorectal cancer
Osteosarcoma
Non–small cell lung cancer
INCREASED SURVIVAL AND PALLIATION IN ADVANCED DISEASE
Colorectal cancer
Breast cancer
Ovarian cancer
Head and neck cancer
Bladder cancer
Small cell lung cancer
Hepatocellular cancer
Renal cancer
Multiple myeloma