other body tissues. These people may have hemolytic anemia when given antimalarial drugs, sulfonamides, analgesics, antipyretics, and other drugs.

Ethnicity

Most drug information has been derived from clinical drug trials using white men; few subjects of other ethnic groups are included. Interethnic variations became evident when drugs and dosages developed for white people produced unexpected responses, including toxicity, when given to other ethnic groups.

One common interethnic variation is that African Americans are less responsive to some antihypertensive drugs than are white people. For example, angiotensin-converting enzyme (ACE) inhibitors and beta-adrenergic blocking drugs are less effective as single-drug therapy. In general, African-American hypertensive clients respond better to diuretics or calcium channel blockers than to ACE inhibitors and beta blockers. Another interethnic variation is that Asians usually require much smaller doses of some commonly used drugs, including beta blockers and several psychotropic drugs (eg, alprazolam, an antianxiety agent, and haloperidol, an antipsychotic). Some documented interethnic variations are included in later chapters.

Gender

Except during pregnancy and lactation, gender has been considered a minor influence on drug action. Most research studies related to drugs have involved men, and clinicians have extrapolated the findings to women. Several reasons have been advanced for excluding women from clinical drug trials, including the risks to a fetus if a woman becomes pregnant and the greater complexity in sample size and data analysis. However, because differences between men and women in responses to drug therapy are being identified, the need to include women in drug studies is evident.

Some gender-related differences in responses to drugs may stem from hormonal fluctuations in women during the menstrual cycle. Although this area has received little attention in research studies and clinical practice, altered responses have been demonstrated in some women taking clonidine, an antihypertensive; lithium, a mood-stabilizing agent; phenytoin, an anticonvulsant; propranolol, a beta-adrenergic blocking drug used in the management of hypertension, angina pectoris, and migraine; and antidepressants. In addition, a significant percentage of women with arthritis, asthma, depression, diabetes mellitus, epilepsy, and migraine experience increased symptoms premenstrually. The increased symptoms may indicate a need for adjustments in their drug therapy regimens. Women with clinical depression, for example, may need higher doses of antidepressant medications premenstrually, if symptoms exacerbate, and lower doses during the rest of the menstrual cycle.

Another example is that women with schizophrenia require lower dosages of antipsychotic medications than men. If given the higher doses required by men, women are likely to have adverse drug reactions.

Pathologic Conditions

Pathologic conditions may alter pharmacokinetic processes (Table 2–1). In general, all pharmacokinetic processes are decreased in cardiovascular disorders characterized by decreased blood flow to tissues, such as heart failure. In addition, the absorption of oral drugs is decreased with various GI disorders. Distribution is altered in liver or kidney disease and other conditions that alter plasma proteins. Metabolism is decreased in malnutrition (eg, inadequate protein to synthesize drug-metabolizing enzymes) and severe liver disease; it may be increased in conditions that generally increase body metabolism, such as hyperthyroidism and fever. Excretion is decreased in kidney disease.

Psychological Considerations

Psychological considerations influence individual responses to drug administration, although specific mechanisms are unknown. An example is the *placebo response.* A placebo is a pharmacologically inactive substance. Placebos are used in clinical drug trials to compare the medication being tested with a "dummy" medication. Interestingly, recipients often report both therapeutic and adverse effects from placebos.

Attitudes and expectations related to drugs in general, a particular drug, or a placebo influence client response. They also influence compliance or the willingness to carry out the prescribed drug regimen, especially with long-term drug therapy.

TOLERANCE AND CROSS-TOLERANCE

Drug *tolerance* occurs when the body becomes accustomed to a particular drug over time so that larger doses must be given to produce the same effects. Tolerance may be acquired to the pharmacologic action of many drugs, especially opioid analgesics, alcohol, and other CNS depressants. Tolerance to pharmacologically related drugs is called *cross-tolerance*. For example, a person who regularly drinks large amounts of alcohol becomes able to ingest even larger amounts before becoming intoxicated—this is tolerance to alcohol. If the person is then given sedative-type drugs or a general anesthetic, larger-than-usual doses are required to produce a pharmacologic effect—this is cross-tolerance.

Tolerance and cross-tolerance are usually attributed to activation of drug-metabolizing enzymes in the liver, which accelerates drug metabolism and excretion. They also are attributed to decreased sensitivity or numbers of receptor sites.

ADVERSE EFFECTS OF DRUGS

As used in this book, the term *adverse effects* refers to any undesired responses to drug administration, as opposed to *therapeutic effects*, which are desired responses. Most drugs produce a mixture of therapeutic and adverse effects; all drugs can produce adverse effects. Adverse effects may produce es-