

not accounted for by these differences in body size and composition. Sex steroids alter the binding and metabolism of a number of drugs. Further, menstrual cycle phase and pregnancy can alter drug action. Two-thirds of cases of drug-induced torsades des pointes, a rare, life-threatening ventricular arrhythmia, occur in women because they have a longer, more vulnerable QT interval. These drugs, which include certain antihistamines, antibiotics, antiarrhythmics, and antipsychotics, can prolong cardiac repolarization by blocking cardiac voltage-gated potassium channels. Women require lower doses of neuroleptics to control schizophrenia. Women awaken from anesthesia faster than do men given the same doses of anesthetics. Women also take more medications than men, including over-the-counter formulations and supplements. The greater use of medications combined with these biologic differences may account for the reported higher frequency of adverse drug reactions in women than in men.

### PSYCHOLOGICAL DISORDERS

(See also Chap. 466) Depression, anxiety, and affective and eating disorders (bulimia and anorexia nervosa) are more common in women than in men. Epidemiologic studies from both developed and developing nations consistently find major depression to be twice as common in women as in men, with the sex difference becoming evident in early adolescence. Depression occurs in 10% of women during pregnancy and in 10–15% of women during the postpartum period. There is a high likelihood of recurrence of postpartum depression with subsequent pregnancies. The incidence of major depression diminishes after age 45 years and does not increase with the onset of menopause. Depression in women appears to have a worse prognosis than does depression in men; episodes last longer, and there is a lower rate of spontaneous remission. Schizophrenia and bipolar disorders occur at equal rates in men and women, although there may be sex differences in symptoms.

Both biologic and social factors account for the greater prevalence of depressive disorders in women. Men have higher levels of the neurotransmitter serotonin. Sex steroids also affect mood, and fluctuations during the menstrual cycle have been linked to symptoms of premenstrual syndrome. Sex hormones differentially affect the hypothalamic-pituitary-adrenal responses to stress. Testosterone appears to blunt cortisol responses to corticotropin-releasing hormone. Both low and high levels of estrogen can activate the hypothalamic-pituitary-adrenal axis.

### SLEEP DISORDERS

(See also Chap. 38) There are striking sex differences in sleep and its disorders. During sleep, women have an increased amount of slow-wave activity, differences in timing of delta activity, and an increase in the number of sleep spindles. Testosterone modulates neural control of breathing and upper airway mechanics. Men have a higher prevalence of sleep apnea. Testosterone administration to hypogonadal men as well as to women increases apneic episodes during sleep. Women with the hyperandrogenic disorder polycystic ovary syndrome have an increased prevalence of obstructive sleep apnea, and apneic episodes are positively correlated with their circulating testosterone levels. In contrast, progesterone accelerates breathing, and in the past, progestins were used for treatment of sleep apnea.

### SUBSTANCE ABUSE AND TOBACCO

(See also Chaps. 467 and 470) Substance abuse is more common in men than in women. However, one-third of Americans who

suffer from alcoholism are women. Women alcoholics are less likely to be diagnosed than men. A greater proportion of men than women seek help for alcohol and drug abuse. Men are more likely to go to an alcohol or drug treatment facility, whereas women tend to approach a primary care physician or mental health professional for help under the guise of a psychosocial problem. Late-life alcoholism is more common in women than in men. On average, alcoholic women drink less than alcoholic men but exhibit the same degree of impairment. Blood alcohol levels are higher in women than in men after drinking equivalent amounts of alcohol, adjusted for body weight. This greater bioavailability of alcohol in women is due to both the smaller volume of distribution and the slower gastric metabolism of alcohol secondary to lower activity of gastric alcohol dehydrogenase than is the case in men. In addition, alcoholic women are more likely to abuse tranquilizers, sedatives, and amphetamines. Women alcoholics have a higher mortality rate than do nonalcoholic women and alcoholic men. Women also appear to develop alcoholic liver disease and other alcohol-related diseases with shorter drinking histories and lower levels of alcohol consumption. Alcohol abuse also poses special risks to a woman, adversely affecting fertility and the health of the baby (fetal alcohol syndrome). Even moderate alcohol use increases the risk of breast cancer, hypertension, and stroke in women.

More men than women smoke tobacco, but this sex difference continues to decrease. Women have a much larger burden of smoking-related disease. Smoking markedly increases the risk of CVD in premenopausal women and is also associated with a decrease in the age of menopause. Women who smoke are more likely to develop chronic obstructive pulmonary disease and lung cancer than men and at lower levels of tobacco exposure. Postmenopausal women who smoke have lower bone density than women who never smoked. Smoking during pregnancy increases the risk of preterm deliveries and low birth weight infants.

### VIOLENCE AGAINST WOMEN

More than one in three women in the United States have experienced rape, physical violence, and/or stalking by an intimate partner. Adult women are much more likely to be raped by a spouse, ex-spouse, or acquaintance than by a stranger. Domestic or intimate partner violence is a leading cause of death among young women. Domestic violence may be an unrecognized feature of certain clinical presentations, such as chronic abdominal pain, headaches, and eating disorders, in addition to more obvious manifestations such as trauma. Intimate partner violence is an important risk factor for depression, substance abuse, and suicide in women. Screening instruments can accurately identify women experiencing intimate partner violence. Such screening by health care providers is acceptable to women in settings ensuring adequate privacy and safety.

### SUMMARY

Women's health is now a mature discipline, and the importance of sex differences in biologic processes is well recognized. There has been a striking reduction in the excess mortality rate from MI in younger women. Nevertheless, ongoing misperceptions about disease risk, not only among women but also among their physicians, result in inadequate attention to modifiable risk factors. Research into the fundamental mechanisms of sex differences will provide important biologic insights. Further, those insights will have an impact on both women's and men's health.