



Figure 7-20 Cancer incidence (A) and mortality (B) by site and sex. Excludes basal cell and squamous cell skin cancers and in situ carcinomas, except urinary bladder. (Adapted from American Cancer Society. Cancer Statistics 2011.)

death rates from lung, prostate, and colorectal cancers; among women, nearly 60% of the decrease is due to reductions in death rates from breast and colorectal cancers. Decreased use of tobacco products is responsible for the reduction in lung cancer deaths, while improved detection and treatment are responsible for the decrease in death rates for colorectal, female breast, and prostate cancer.

The last half-century has also seen a sharp decline in the number of deaths caused by cervical cancer in the United States, which is attributable to the Papanicolaou (Pap) smear test, which enables detection of precursor lesions and early, curable cancers. A downward trend in deaths from stomach cancer in both sexes has been observed that is attributed to a reduction in unknown dietary carcinogens. However, between 1990-1991 and 2004, lung cancer death rates in women, and liver and intrahepatic bile duct cancer death rates in men, increased substantially, offsetting some of the improvement in survival from other cancers. Indeed, although carcinomas of the breast occur about 2.5 times more frequently than those of the lung in women, lung cancer now causes more deaths in women. Deaths due to primary liver cancers, which declined between 1930 and 1970, have approximately doubled over the past 40 years. This number is expected to increase further over the coming decades as a large number of individuals infected with the hepatitis C virus (HCV) begin to develop hepatocellular carcinoma.

Although race is not a clearly defined biological variable, it can define groups at risk for certain cancers. The disparity in cancer mortality rates between white and black Americans persists, but African Americans had the largest decline in cancer mortality during the past decade. Hispanics living in the United States have a lower frequency of the most common tumors seen in the white non-Hispanic population but a higher incidence of tumors of the stomach, liver, uterine cervix, and gallbladder, as well as certain leukemias.

Environmental Factors

Although both genetic and environmental factors contribute to the development of cancer, environmental influences appear to be the dominant risk factors for most cancers. Evidence supporting a central role for environmental factors can be found in the wide geographic variation that exists in the incidence of specific forms of cancer (Fig. 7-21). For example, the most common tumor of men in the United States and most of the developed world is prostate cancer, but in certain countries or regions (most located in the developing world), cancers of the liver, stomach, esophagus, bladder, lung, oropharynx, and the immune system rise to the top of the list. Similarly, the incidence of breast cancer is generally much higher in women in developed countries than in most parts of the developing world. Although racial predispositions cannot be ruled out, it is believed that environmental influences—some known, some not—underlie most of these differences in cancer incidence.

Among the best established environmental factors affecting cancer risk are the following:

- **Infectious agents.** About 15% of all cancers worldwide are believed to be caused directly or indirectly by infectious agents, with the burden of cancers linked to infections being roughly three times higher in the developing world than in the developed world. For example, *human papilloma virus* (HPV), an agent that is spread through sexual contact, is responsible for a large majority of cases of cervical carcinoma and an increasing fraction of head and neck cancers. Specific infectious agents and their associated cancers are discussed later in this chapter.
- **Smoking.** Cigarette smoking has been called the single most important environmental factor contributing to premature death in the United States. Smoking,