

exposure. A strong interaction exists between asbestos exposure and cigarette smoking leading to lung cancer.

A range of medications are associated with increased cancer risk, including the alkylating agents, anthracyclines, and other classes of cancer chemotherapy agents and immunosuppressants. Estrogen use in postmenopausal women increases the risk of endometrial cancer; the rates drop when estrogen is combined with progesterone. Synthetic estrogens, such as diethylstilbestrol (DES), administered to mothers during pregnancy increase the risk of vaginal cancer in offspring. Lifestyle exposures to carcinogenic chemicals include multiple carcinogens in tobacco products and dietary factors, including aflatoxins, in many parts of the world.

## CANCER PREVENTION

Cancer prevention strategies are either primary or secondary based on whether they reduce risk of exposure or detect cancer at an early stage when intervention can change the natural history of the disease. Primary prevention strategies include reductions in lifestyle risks (e.g., smoking cessation; use of sunscreen; adherence to a low-fat, high-fiber diet), avoidance of occupational or environmental risks, and chemoprevention (see Table 54-2).

### Lifestyle Changes

Smoking cessation is unquestionably the most direct and effective cancer prevention strategy available. More than 1 million people die from tobacco-induced cancers globally each year, and tobacco accounts for one third of all cancer diagnoses in the United States. Although tobacco prevention and control programs have resulted in a decline in smoking prevalence in the United States, tobacco use continues to be high and has been increasing in a number of countries. There is also evidence from epidemiologic studies that other lifestyle changes, including regular exercise and dietary modification, may also reduce the risk of cancer. Central adiposity is associated with increased incidence of and mortality from a number of cancers, including breast and endometrial cancers. Sufficient dietary intake of fruits and vegetables appears to reduce the risk for gastric and esophageal cancers. Avoidance of excessive sun exposure and artificial tanning devices may reverse the recent upward trend in cutaneous malignancies. Reduction in exposures to known carcinogenic agents is an important goal in both occupational and domestic settings. Evidence for an association between air pollution and lung cancer incidence illustrates how difficult such reductions may be. However, limiting the use of potentially carcinogenic chemicals and of radiation in the medical setting is sensible.

### Chemoprevention

Chemopreventive agents are drugs, vaccines, or micronutrients (e.g., minerals, vitamins) that prevent the development of cancer. Both randomized trials and epidemiologic studies suggest that a number of strategies can reduce the risk of some common types of cancer. Daily aspirin use may reduce the risks of colon cancer and melanoma. Hepatitis B vaccination may reduce the incidence of hepatocellular cancer. The vaccine directed against specific strains of the human papillomavirus (HPV) promises to prevent cervical cancer.

## CANCER SCREENING

Cancer screening programs should detect premalignant states or early-stage cancers before the onset of symptoms with relatively high sensitivity. For cancer screening to be useful, there must be a treatment available that improves the outcome for patients with premalignant or early-stage disease. Ideally, such screening programs should also be noninvasive, inexpensive, and associated with high specificity (i.e., low rate of false-positive results). Identification of high-risk individuals assists in genetic counseling and testing as well as in cancer screening efforts.

Proper interpretation of the results of cancer screening studies must consider both *lead-time bias* and *length-time bias*. Lead time is the time between detection of disease by screening and the actual appearance of symptomatic disease. If screening leads to early diagnosis, it may appear that the patient lived longer than would have been the case without screening even when the survival of the patient from the onset of disease has not been altered. Length-time bias occurs when subsets of the cancer under study have different growth rates. Screening is more likely to detect cancers that grow slowly because of the greater prevalence of asymptomatic people with slow-growing tumors than those with fast-growing tumors. Patients with cancer that is detected by screening may appear to have longer survival times as a result of screening when in fact the longer course of their disease results from the behavior of the tumor itself. Although randomized controlled trials of cancer screening programs require large numbers of participants and take years to complete, such trials are needed to quantitate the value of screening and to address both lead-time and length-time bias.

Screening tests may also be associated with false-negative and false-positive results. False-negative results fail to identify a proper diagnosis and patients therefore are not provided the opportunity for effective early treatment. False-positive results may also cause harm by leading to unnecessary testing and treatment and by contributing to patient costs and emotional stress.

Currently, recommended cancer screening tests include clinical examination and mammography to detect breast cancer, Papanicolaou smears and HPV DNA tests to detect cervical dysplasia or cancer, colonoscopy to detect polyps or colon cancer, and digital rectal examination and serum prostate-specific antigen (PSA) measurement to detect prostate cancer. Although issues remain to be resolved, low-dose computed tomographic scanning to screen appropriate high-risk individuals for lung cancer has recently been recommended based on results from the National Lung Cancer Screening Trial.

## SUGGESTED READINGS

- Colditz GA, Sellers TA, Trapido E: Epidemiology: identifying the causes and preventability of cancer, *Nat Rev Cancer* 6:75–83, 2006.
- Detterbeck FC, Mazzone PJ, Naidich DP, et al: Screening for lung cancer: diagnosis and management of lung cancer, 3rd ed. American College of Chest Physicians evidence-based clinical practice guidelines, *Chest* 143:e78S–92S, 2013.
- Kushi LH, Doyle C, McCullough M, et al: American Cancer Society guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity, *CA Cancer J Clin* 62:30–67, 2012.

