

506 The mucosal side effects of therapy can lead to malnutrition and dehydration. Many centers address issues of dentition before starting treatment, and some place feeding tubes to ensure control of hydration and nutrition intake. About 50% of patients develop hypothyroidism from the treatment; thus, thyroid function should be monitored.

SALIVARY GLAND TUMORS

Most benign salivary gland tumors are treated with surgical excision, and patients with invasive salivary gland tumors are treated with surgery and radiation therapy. These tumors may recur regionally; adenoid cystic carcinoma has a tendency to recur along the nerve tracks. Distant metastases may occur as late as 10–20 years after the initial diagnosis. For metastatic disease, therapy is given with palliative intent, usually chemotherapy with doxorubicin and/or cisplatin. Identification of novel agents with activity in these tumors is a high priority.

107 Neoplasms of the Lung

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Lung cancer, which was rare prior to 1900 with fewer than 400 cases described in the medical literature, is considered a disease of modern man. By the mid-twentieth century, lung cancer had become epidemic and firmly established as the leading cause of cancer-related death in North America and Europe, killing over three times as many men as prostate cancer and nearly twice as many women as breast cancer. This fact is particularly troubling because lung cancer is one of the most preventable of all of the major malignancies. Tobacco consumption is the primary cause of lung cancer, a reality firmly established in the mid-twentieth century and codified with the release of the U.S. Surgeon General's 1964 report on the health effects of tobacco smoking. Following the report, cigarette use started to decline in North America and parts of Europe, and with it, so did the incidence of lung cancer. To date, the decline in lung cancer is seen most clearly in men; only recently has the decline become apparent among women in the United States. Unfortunately, in many parts of the world, especially in countries with developing economies, cigarette use continues to increase, and along with it, the incidence of lung cancers is also rising. Although tobacco smoking remains the primary cause of lung cancer worldwide, approximately 60% of new lung cancers in the United States occur in former smokers (smoked ≥ 100 cigarettes per lifetime, quit ≥ 1 year), many of whom quit decades ago, or never smokers (smoked < 100 cigarettes per lifetime). Moreover, one in five women and one in 12 men diagnosed with lung cancer have never smoked. Given the magnitude of the problem, it is incumbent that every internist has a general knowledge of lung cancer and its management.

EPIDEMIOLOGY

Lung cancer is the most common cause of cancer death among American men and women. More than 225,000 individuals will be diagnosed with lung cancer in the United States in 2013, and over 150,000 individuals will die from the disease. The incidence of lung cancer peaked among men in the late 1980s and has plateaued in women. Lung cancer is rare below age 40, with rates increasing until age 80, after which the rate tapers off. The projected lifetime probability of developing lung cancer is estimated to be approximately 8% among males and approximately 6% among females. The incidence of lung cancer varies by racial and ethnic group, with the highest age-adjusted incidence rates among African Americans. The excess in age-adjusted rates among African Americans occurs only among men, but examinations of age-specific rates show that below age 50, mortality from lung cancer

is more than 25% higher among African American than Caucasian women. Incidence and mortality rates among Hispanics and Native and Asian Americans are approximately 40–50% those of whites.

RISK FACTORS

Cigarette smokers have a 10-fold or greater increased risk of developing lung cancer compared to those who have never smoked. A deep sequencing study suggested that one genetic mutation is induced for every 15 cigarettes smoked. The risk of lung cancer is lower among persons who quit smoking than among those who continue smoking; former smokers have a ninefold increased risk of developing lung cancer compared to men who have never smoked versus the 20-fold excess in those who continue to smoke. The size of the risk reduction increases with the length of time the person has quit smoking, although generally even long-term former smokers have higher risks of lung cancer than those who never smoked. Cigarette smoking has been shown to increase the risk of all the major lung cancer cell types. Environmental tobacco smoke (ETS) or second-hand smoke is also an established cause of lung cancer. The risk from ETS is less than from active smoking, with about a 20–30% increase in lung cancer observed among never smokers married for many years to smokers, in comparison to the 2000% increase among continuing active smokers.

Although cigarette smoking is the cause of the majority of lung cancers, several other risk factors have been identified, including occupational exposures to asbestos, arsenic, bischloromethyl ether, hexavalent chromium, mustard gas, nickel (as in certain nickel-refining processes), and polycyclic aromatic hydrocarbons. Occupational observations also have provided insight into possible mechanisms of lung cancer induction. For example, the risk of lung cancer among asbestos-exposed workers is increased primarily among those with underlying asbestosis, raising the possibility that the scarring and inflammation produced by this fibrotic nonmalignant lung disease may in many cases (although likely not in all) be the trigger for asbestos-induced lung cancer. Several other occupational exposures have been associated with increased rates of lung cancer, but the causal nature of the association is not as clear.

The risk of lung cancer appears to be higher among individuals with low fruit and vegetable intake during adulthood. This observation led to hypotheses that specific nutrients, in particular retinoids and carotenoids, might have chemopreventative effects for lung cancer. However, randomized trials failed to validate this hypothesis. In fact, studies found the incidence of lung cancer was increased among smokers with supplementation. Ionizing radiation is also an established lung carcinogen, most convincingly demonstrated from studies showing increased rates of lung cancer among survivors of the atom bombs dropped on Hiroshima and Nagasaki and large excesses among workers exposed to alpha irradiation from radon in underground uranium mining. Prolonged exposure to low-level radon in homes might impart a risk of lung cancer equal or greater than that of ETS. Prior lung diseases such as chronic bronchitis, emphysema, and tuberculosis have been linked to increased risks of lung cancer as well.

Smoking Cessation Given the undeniable link between cigarette smoking and lung cancer (not even addressing other tobacco-related illnesses), physicians must promote tobacco abstinence. Physicians also must help their patients who smoke to stop smoking. Smoking cessation, even well into middle age, can minimize an individual's subsequent risk of lung cancer. Stopping tobacco use before middle age avoids more than 90% of the lung cancer risk attributable to tobacco. However, there is little health benefit derived from just "cutting back." Importantly, smoking cessation can even be beneficial in individuals with an established diagnosis of lung cancer, as it is associated with improved survival, fewer side effects from therapy, and an overall improvement in quality of life. Moreover, smoking can alter the metabolism of many chemotherapy drugs, potentially adversely altering the toxicities and therapeutic benefits of the agents. Consequently, it is important to promote smoking cessation even *after* the diagnosis of lung cancer is established.

Physicians need to understand the essential elements of smoking cessation therapy. The individual must want to stop smoking and must be