1
Cigarette Smoking: The Leading Preventable Cause of Pulmonary Disease

Michael C. Fiore, M.D., M.P.H.
Thomas M. Piasecki, M.S.
Linda J. Baker, PH.D.
Susan M. Deeren, R.N., M.S.

See chapters C1, B3, G3, H1, H2, and H4 for related information.

Cigarette smoking is the leading cause of pulmonary illness and death in the United States. Sixty-four thousand deaths from chronic obstructive pulmonary disease (COPD) reported in 1990 were caused directly by cigarette smoking.[15] In addition, 21,000 deaths resulting from asthma, pneumonia, influenza, and other respiratory causes were a direct result of smoking (Fig 1–1). These 85,000 respiratory-related deaths each year caused directly by cigarette smoking are all potentially preventable. They account for approximately 5% of the total deaths in the United States each year.

In this chapter we review the enormous pulmonary burden resulting from cigarette smoking by examining the epidemiology of tobacco use and its relation to respiratory illness, by summarizing the clinical and pathologic impact of tobacco use on the pulmonary system, and finally, by providing guidelines for clinicians to assist their respiratory patients who smoke. Given the tremendous impact of cigarette smoking on pulmonary morbidity and mortality, one might argue that the most effective way to treat pulmonary diseases in the United States would be to eliminate cigarette smoking.

EPIDEMIOLOGY OF CIGARETTE SMOKING

Per Capita Cigarette Consumption

Cigarette smoking, now the leading cause of preventable illness and death in our society, was an extremely uncommon behavior at the beginning of this century.[104] According to per capita consumption data from the United States Department of Agriculture, approximately 50 cigarettes were smoked every year by each adult in the United States in 1900.[118] This modest rate of cigarette use began to increase at an epidemic pace beginning around 1910, a time coincident with the development of machine-made and blended tobacco cigarettes. These new cigarettes were inhaled more easily, thus directly exposing the pulmonary system to a host of toxins and providing a highly effective means of delivering the addictive drug nicotine.

The rate of smoking continued to increase until 1963, when per capita consumption peaked at a rate of 4,300 cigarettes per year for every adult in the United States (Fig 1–2). This event coincided with the release of the first surgeon general's report on the health consequences of cigarette smoking[110] and the first wide-scale dissemination of scientific data linking cigarette smoking to a host of pulmonary, cardiovascular, and neoplastic diseases. Since 1963, cigarette smoking, as measured by per capita consumption, has declined at a steady rate, falling by about one third, to 2,800 cigarettes per year for every adult in the United States in 1989 (see Fig 1–2).

Trends in Cigarette Smoking by Sociodemographic Characteristics

Smoking Among the Overall Population

Although it provides important information regarding overall cigarette use, per capita consumption provides no information on the rates of smoking among the various sociodemographic segments of the U.S. population. Since the release of the first surgeon general's report on smoking and health in 1964, the National Center for Health Statistics has used the National Health Interview Survey (NHIS)[115, 116] to measure smoking prevalence in the United States. The NHIS, using a cross-sectional design, periodically collects health information from a representative sample of the civilian, noninstitutionalized U.S. population.

According to these data, smoking rates in the United States have declined markedly. The prevalence of cigarette smoking among adults decreased from more than 40% in 1965 to 25.5% in 1990.[11, 41] However, the most recent survey data available indicate that this decline has been arrested; in both 1991 and 1992 the prevalence of smoking among adults in the United States has remained at 25.6%.[12, 13] In

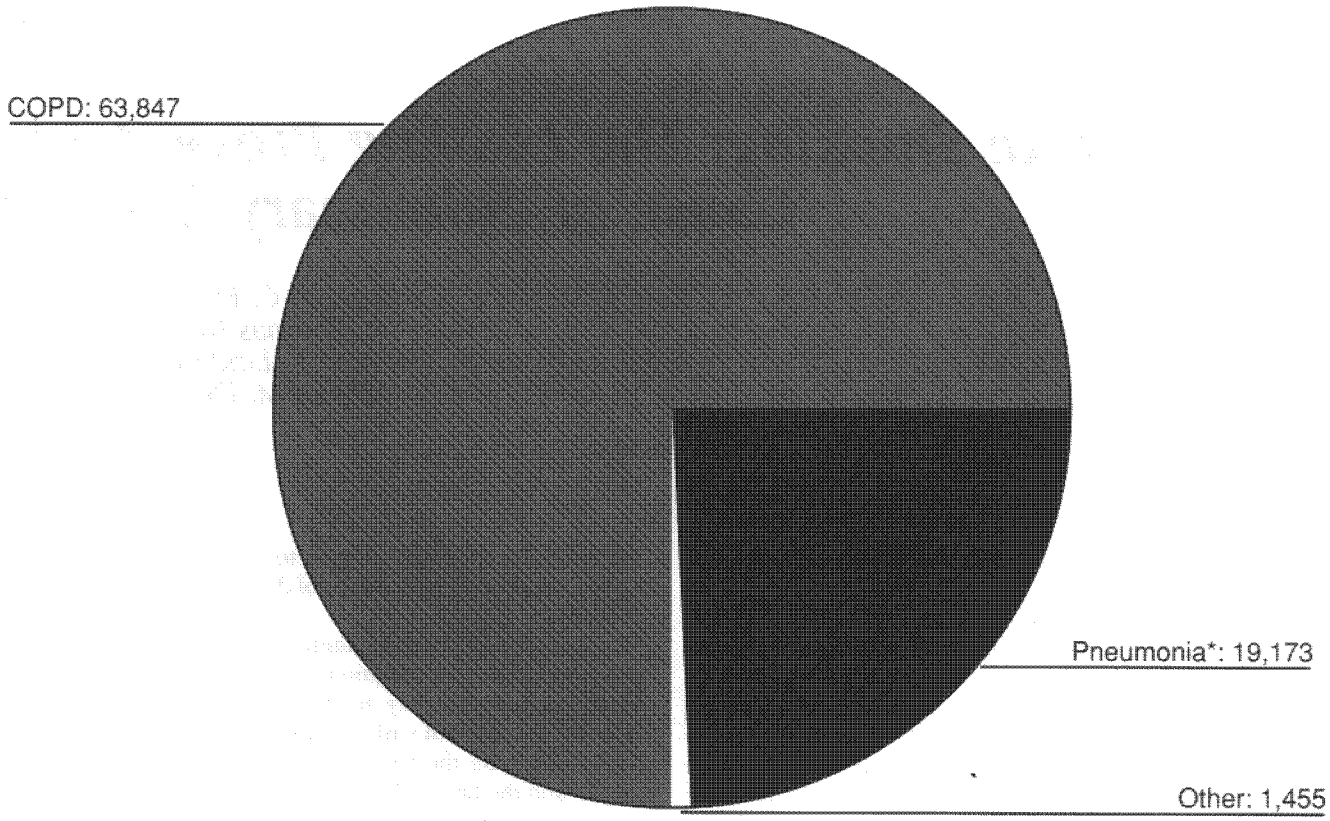

Fig 1–1.—Number of pulmonary deaths resulting from cigarette smoking in the United States in 1990. *COPD* = chronic obstructive pulmonary disease. *Includes deaths caused by influenza. (From Centers for Disease Control: *MMWR* 1993; 43:645–649.)

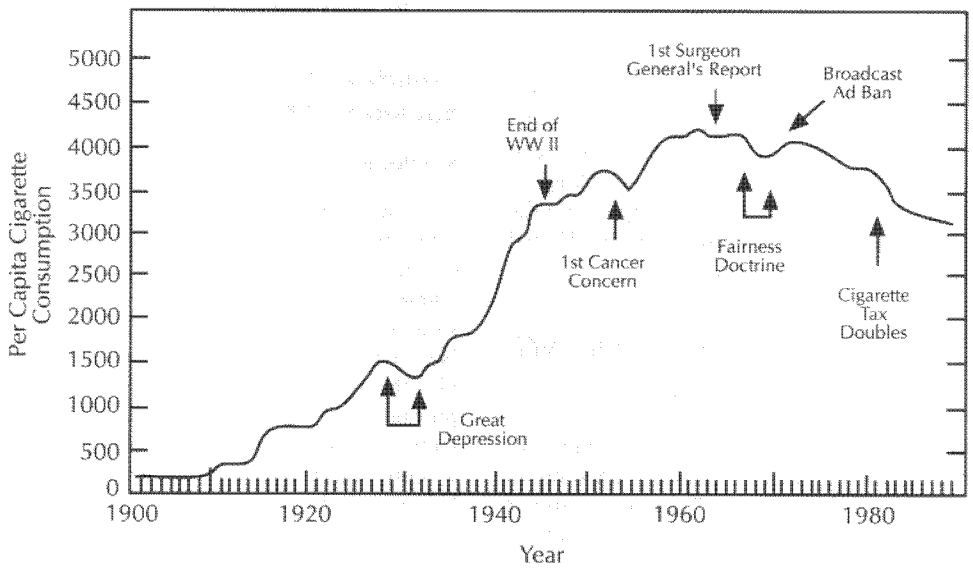

Fig 1–2.—Per capita cigarette consumption among Americans 1900 to 1990.

1993, 25.0% of U.S. adults were smokers.[14] Nonetheless, significant inroads have been made. By 1989, nearly half of all living adults who had ever smoked had quit. Approximately three quarters of a million smoking-related deaths were avoided or postponed between 1964 and 1985 as a result of Americans deciding to quit or never starting to smoke.[108]

Although the decline in smoking prevalence represents significant progress in controlling the epidemic of tobacco-related disease and death, tobacco use continues to pose an enormous public health problem. In particular, the fact that the decline in smoking prevalence has stalled is cause for concern. A recent study estimated that approximately 42 million Americans were smoking in 1992.[13] Clearly, tobacco control efforts will need to be redoubled if our national objective of reducing the prevalence of adult smoking to 15% by the year 2000 is to be achieved.[57] In addition, the decline in cigarette smoking has not occurred equally across all sociodemographic subpopulations in our society. The decline in prevalence has lagged among women,[41] young persons,[41] and the less educated.[85]

Trends in Smoking Rates Based on Gender

In 1989, the U.S. Office of Smoking and Health published analyses of trends in cigarette smoking in this country.[41, 85, 86, 108] The authors noted that the decline in smoking prevalence from 1965 to 1987 was linear across most sociodemographic groups (Table 1–1). Male smoking decreased at a rate of 0.84 percentage points per year, whereas female smoking decreased at a rate of 0.21 percentage points per year from 31.9% to 26.8% over the same period. This slower rate of decline in smoking among women has resulted in a dramatic change in smoking patterns in this country. In the 1950s, cigarette smoking was still a behavior practiced predominantly among men, with males smoking at almost double the rate of females.[54] By 1987, the gap between the sexes had narrowed to less than 4 percentage points. Projections based on trends in the 1987 data predicted that men and women would be smoking at the same rate by the mid-1990s and that women would be smoking at a higher rate than men by the year 2000[41, 86](Fig 1–3). However, survey data from 1992 do not appear to support the predicted trends. In 1992 the gender gap in smoking prevalence remained at 4%: 28.6% of adult U.S. males smoked, whereas 24.6% of adult U.S. females were smokers.[13]

Trends in Smoking Based on Race

Smoking prevalence has declined among both blacks and whites (see Table 1–1). From 1965 to 1987, smoking among blacks declined linearly from 43% to 34% at a rate of 0.39 percentage points per year. Similarly, smoking among whites declined linearly from 40.0% in 1965 to 28.8% in 1987 at a rate of 0.50 percentage points per year. The rates of decline between these races were not significantly different.[41] By 1991, the prevalence of smoking among whites had dropped to 26.0%, and the prevalence of smoking among blacks had dropped to 29.4%.[12] Comparable figures for 1992 were 26.2% and 27.0% for whites and blacks, respectively.[13] Notably, these data indicate that by 1992, blacks were already smoking at a rate lower than the anticipated year 2000 rate (28.9%) extrapolated from the 1965–1989 trends (Fig 1–4).

TABLE 1–1.—*Trends in Smoking Prevalence (%), United States, 1965–1987, Among Adults Aged 20 Years and Older**

		Sex		Race		Educational Level			
Year	Overall Population	Males	Females	Whites	Blacks	Less Than High School Graduate	High School Graduate	Some College	College Graduate
1965†	40.4	50.2	31.9	40.0	43.0				
1966	40.7	50.8	32.0	40.4	42.9	36.5	41.1	42.5	33.7
1970	37.0	44.3	30.8	36.5	41.4	34.8	38.3	36.7	28.1
1974	36.9	43.4	31.4	36.1	44.0	36.5	37.6	36.9	28.3
1976	36.1	42.1	31.3	35.6	41.2	35.8	37.8	36.4	27.4
1977	35.6	40.9	31.4	34.9	41.8	35.8	38.4	35.2	25.6
1978	34.0	39.0	29.6	33.6	38.2	35.3	36.5	32.7	23.8
1979	33.5	38.4	29.2	33.2	36.8	34.9	35.4	33.3	23.4
1980	33.3	38.5	29.0	32.9	37.2	35.5	35.7	31.2	24.6
1983	31.8	35.5	28.7	31.4	36.6	34.7	35.6	30.0	19.9
1985	30.4	33.2	28.0	29.9	36.0	35.7	34.2	28.1	18.4
1987‡	29.1	31.7	26.8	28.8	34.0	35.7	33.1	26.1	16.3
Trend information (1965–1985)									
Change per year§	−0.50	−0.84	−0.21	−0.50	−0.39	−0.06	−0.32	−0.70	−0.76
Standard error	0.03	0.04	0.03	0.03	0.08	0.03	0.05	0.07	0.08
R^2	0.97	0.98	0.81	0.97	0.74	NA¶	0.87	0.94	0.93

*From *Reducing the Health Consequences of Smoking: 25 Years of Progress. A Report of the Surgeon General.* Rockville, Md, US Department of Health and Human Services, Public Health Service, DHHS Publication No (CDC) 89–8411, 1989.
†For 1965, data stratified by education were not available.
‡Provisional data only.
§In percentage points.
¶The slope of the regression line was not significantly different from zero, thus making the R^2 computation inappropriate.

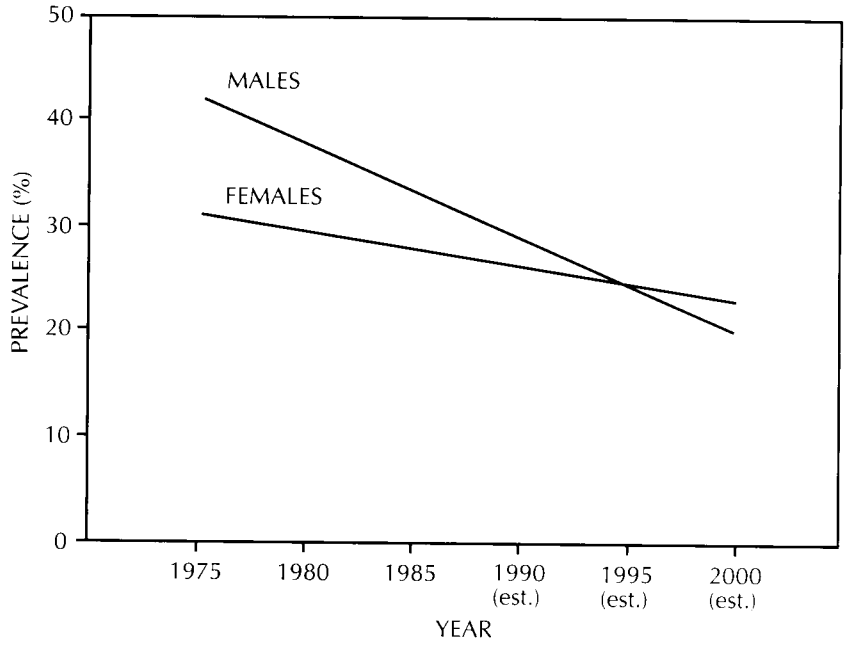

Fig 1–3.—Trends in the prevalence of smoking for men and women aged 20 years and older with projections to the year 2000 in the United States. (From *Reducing the Health Consequences of Smoking: 25 Years of Progress. A Report of the Surgeon General.* Rockville, Md, US Department of Health and Human Services, Public Health Service, DHHS Publication No (CDC) 89–8411, 1989.)

These data also demonstrate that the difference in smoking prevalence between blacks and whites is shrinking; the gap in smoking prevalence was 5.2% in 1987 but only 0.8% in 1992. Both of these observations suggest an acceleration of the decline in smoking prevalence among blacks between 1987 and 1992.

Trends in Smoking Based on Educational Status

Educational status, a marker of socioeconomic status, has become the most important demographic variable in predicting smoking behavior.[85] In the early 1960s, small differences in smoking rates were noted across the various education

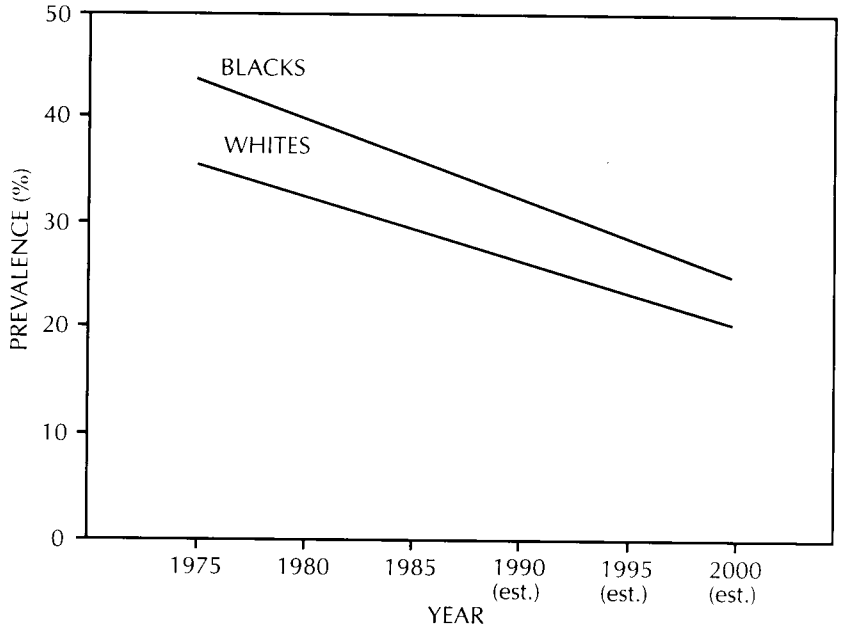

Fig 1–4.—Trends in the prevalence of smoking for blacks and whites aged 20 years and older with projections to the year 2000 in the United States. (From *Reducing the Health Consequences of Smoking: 25 Years of Progress. A Report of the Surgeon General.* Rockville, Md, US Department of Health and Human Services, Public Health Service, DHHS Publication No (CDC) 89–8411, 1989.)

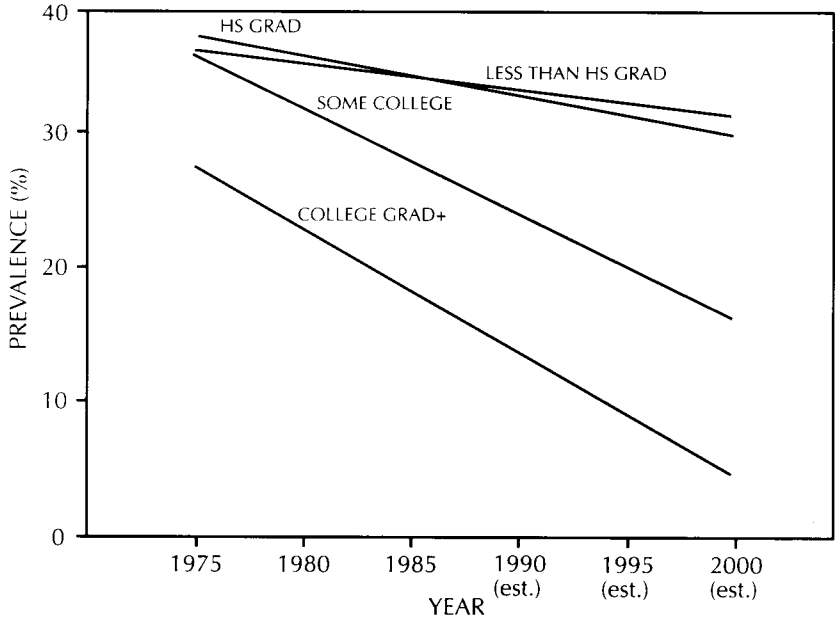

Fig 1–5.—Trends in the prevalence of smoking by educational status among adults aged 20 years and older with projections to the year 2000 in the United States. (From *Reducing the Health Consequences of Smoking: 25 Years of Progress. A Report of the Surgeon General.* Rockville, Md, US Department of Health and Human Services, Public Health Service, DHHS Publication No (CDC) 89-8411, 1989.)

groups; persons with college education smoked at about the same rate as did persons who had not finished high school.[85] In contrast to today, smoking in the early 1960s was viewed widely as a socially acceptable behavior.

By the late 1980s, marked differences in smoking prevalence were noted across education groups. In 1987, 35.7% of high school dropouts smoked, a rate almost double that observed among college graduates (16%) (see Table 1–1). High school graduates and persons with some college education reported intermediate rates of smoking prevalence. These findings suggest that by the late 1980s, smoking was increasingly viewed as a socially unacceptable behavior among the more educated members of our society.

Projections of smoking rates into the next century based on 1965–1987 trends predicted that educational differences in smoking prevalence would continue to grow[85] (Fig 1–5). For example, those trends suggested that only 4.7% of college graduates would be smokers in the year 2000 whereas 31.4% of high school dropouts would smoke.[85] The most recent data, however, indicate that the decline in smoking prevalence has been arrested at all levels of educational attainment. In 1991, 32.0% of high school dropouts were smokers[12]; the comparable figure for 1992 was 32.2%.[13] Among college graduates, 13.6% smoked in 1991,[12] and 13.4% smoked in 1992.[13] High school graduates and persons with some college education had intermediate rates of smoking, and these rates also remained essentially constant from 1991 to 1992.[12, 13]

Total Deaths Attributable to Smoking in the United States

Although the prevalence of smoking in the United States has shown a modest decline over the last 25 years, the toll of illness and death resulting from cigarettes has continued to increase. This finding can be explained by the lag-time effect; exposure to cigarette smoke requires one or more decades to result in clinically apparent illness and even more time to result in death. Although research has documented the deleterious health impact of cigarette smoking on the pulmonary system within a few years of smoking onset,[3–5, 32, 97, 121] the impact of smoking on overall morbidity and mortality data may lag for decades. Thus the current mortality data resulting from cigarette smoking reflect the prevalence in tobacco use in the 1960s and 1970s. Increases in population over the last 30 years also contribute to the observed increases in absolute rates of morbidity and mortality resulting from cigarette smoking.

The most recent data available on the impact of cigarette smoking indicate that as of 1990, approximately 419,000 deaths in the United States were directly attributable to cigarette smoking (Fig 1–6).[15] Smoking is now directly responsible for about 1 of every 5 deaths in this country. In 1990, smoking resulted in about 117,000 lung cancer deaths, 31,000 other cancer deaths, 99,000 heart disease deaths, 23,300 stroke deaths, 64,000 chronic lung disease deaths, and 85,000 deaths from other causes. It is estimated that cigarettes were responsible for the loss of over 5 million years of potential life in 1990.[15]

EPIDEMIOLOGY OF PULMONARY DISEASES AND CIGARETTE SMOKING

Using data from 1990, the U.S. Centers for Disease Control[15] has computed that cigarette smoking was responsible for approximately 85,000 pulmonary-related deaths per year. Thus smoking is responsible for approximately 80% of all deaths

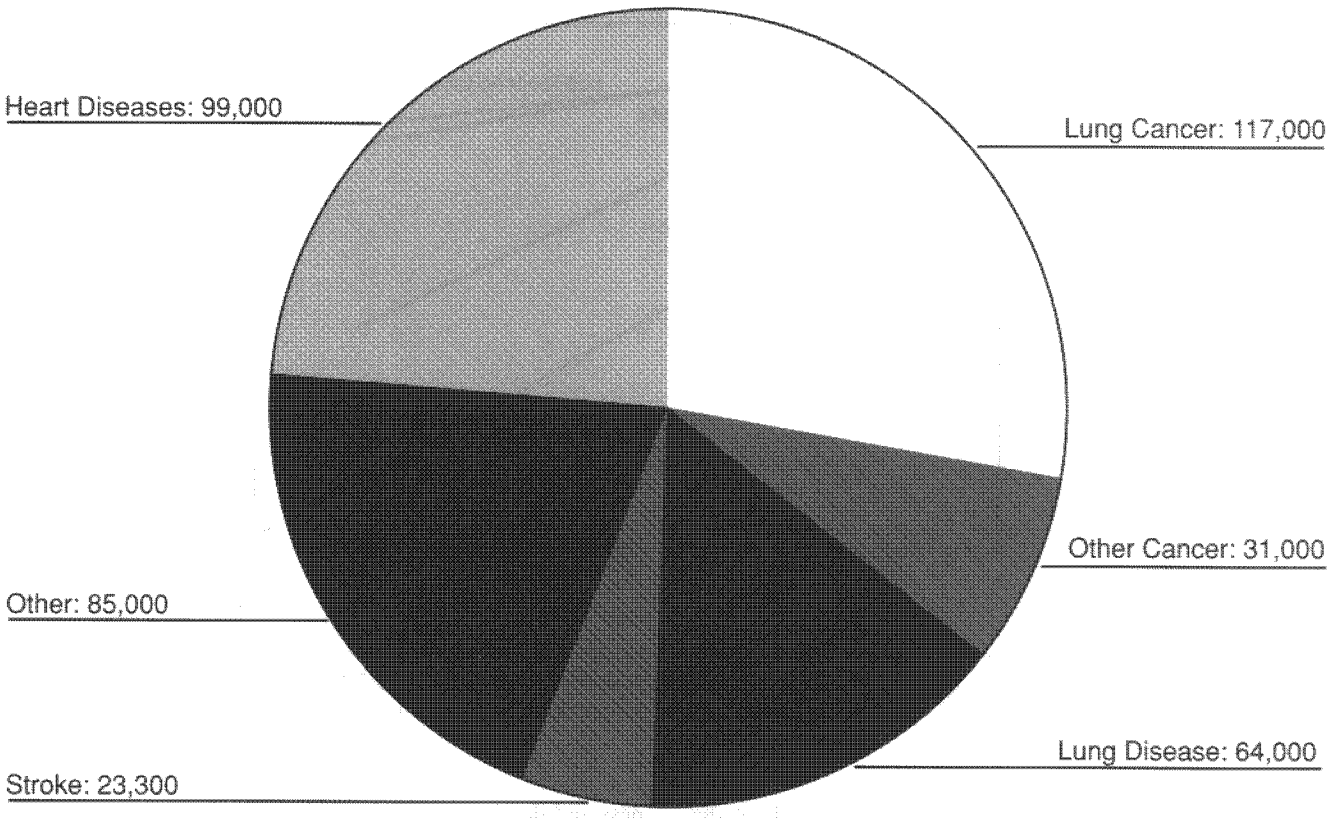

Fig 1–6.—Number of deaths attributable to cigarette smoking per year as compared with various diseases, United States, 1990. (From Centers for Disease Control: *MMWR* 1993; 43:645–649.)

from COPD and 15% of all deaths from pneumonia and influenza each year.

Cigarettes have their most devastating impact on the respiratory system by causing COPD.[19, 28] In 1988, 61,660 persons in the United States died of smoking-attributable COPD, which includes chronic bronchitis (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] 491), emphysema (ICD-9-CM 492), and chronic airway obstruction not otherwise classified (ICD-9-CM 496). Approximately 84% of the COPD-related mortality among men and 79% of that among women in the United States are directly caused by cigarette smoking.[108]

For most of the 85,000 Americans who die of pulmonary diseases caused by cigarette smoking each year, death is preceded by a long period of debilitating morbidity. Approximately 14,786,000 persons, or 6% of the total U.S. population, were estimated to be suffering from clinically obvious COPD in 1986.[16] These 14.8 million patients with COPD require an estimated 743,089 hospitalizations per year.[16] According to another parameter of disease impact, each year COPD-attributable deaths in the United States result in more than 500,000 years of potential life lost before the age of 65 years.[16] This suggests that COPD not only attacks the elderly but is also a killer of individuals during their highly productive middle years. Chronic obstructive pulmonary disease is the fifth leading cause of death in the United States and the most rapidly increasing cause of death among adults older than 65 years of age.[38]

IMPACT OF CIGARETTE SMOKING ON THE PULMONARY SYSTEM

Although it is associated most often with COPD, cigarette smoking has been etiologically associated with the full spectrum of obstructive airway diseases, including emphysema, asthma, chronic bronchitis, and COPD.[82] Despite the fact that they possess distinct clinical features, overlap among these conditions is extremely common and most patients demonstrate clinical evidence of more than one of them.

The development of clinically relevant COPD in smokers has been hypothesized to result from an accelerated rate of decline in lung function among that subsegment of smokers who are predisposed to COPD. Speizer and Tager[104] presented a schematic representation of the changes in lung function among "never-smokers" and smokers in whom COPD will or will not develop (Fig 1–7). In this representation, smokers overall (B) demonstrate an accelerated, although not clinically apparent decline in lung function when compared with nonsmokers (A). Among a subsegment of smokers (C), the decline in lung function is accelerated further, although not yet fulfilling the clinical criteria for COPD. In a smaller segment of smokers (E), clinically apparent COPD will develop and result in disability. In the final group of smokers (G), COPD will develop and rapidly and prematurely result in death. Genetic predisposition and childhood influences such as exposure to environmental tobacco smoke, other toxins, or both may influence an individual's predisposition to COPD.

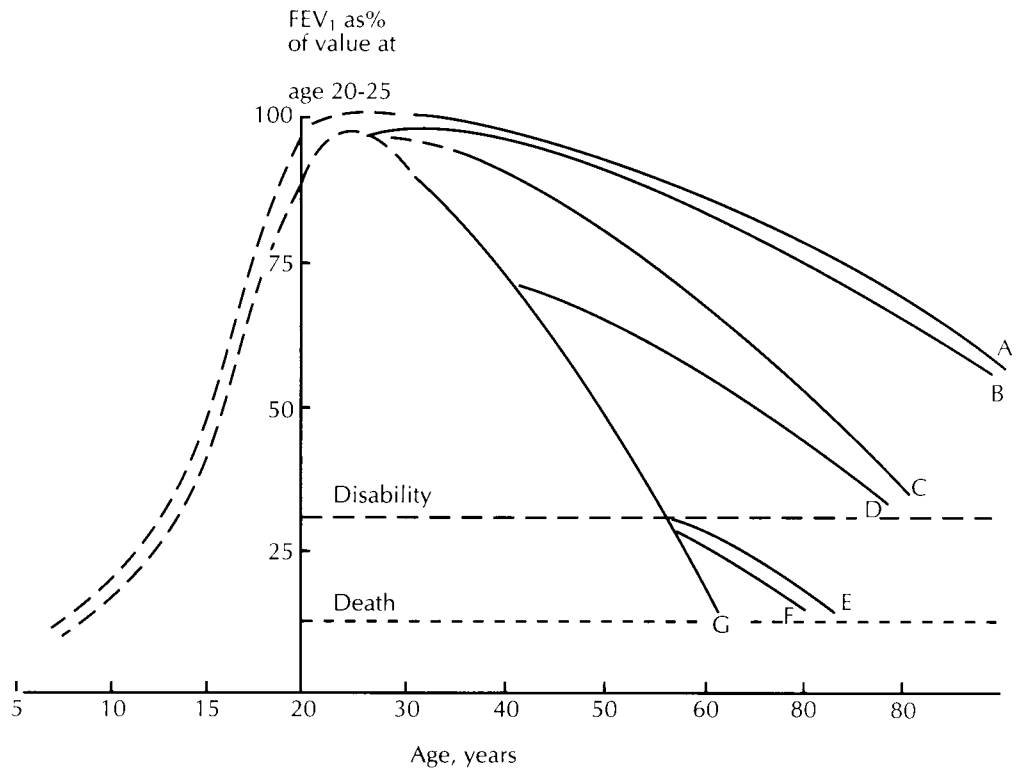

Fig 1–7.—Theoretic curves depicting varying rates of decline in forced expiratory volume in 1 second (FEV_1). *Curves A* and *B* represent never-smokers and smokers, respectively, and are declining at normal rates. *Curve C* shows an increased decline without the development of chronic obstructive pulmonary disease (COPD). Rates of decline for former smokers are represented by *curves D* and *E* for those without and with clinical COPD, respectively. *Curves F* and *G* show the rates of decline with continued smoking after the development of COPD. (From Speizer FE, Tager IB: *Epidemiol Rev* 1979; 1:124–142. Used by permission.)

Cigarette smoking has been shown to cause a number of abnormalities in pulmonary function, including decreased rates of 1-second forced expiratory volume (FEV_1) in cross-sectional studies.[61, 106, 131] In longitudinal studies, continued smoking has been associated with an accelerated rate of decline in FEV_1.[4, 101, 106] These effects increase with the duration and amount of smoking.[106] Specifically, cigarette smoking greatly accelerates the annual volume loss of 20 to 30 mL noted with aging after the fourth decade. Additionally, smoking in adults may shorten the plateau phase between ages 20 and 40 years, a time when lung function in healthy nonsmokers remains relatively constant.[106] Women appear to be more likely than men to display impaired ventilatory function as a result of smoking.[131]

The decline in pulmonary function associated with cigarette smoking also results in clinically apparent disease. Detels and coworkers.[29, 89]studied residents of three southern California communities and found that the prevalence of FEV_1 values less than 75% of predicted was nearly twice as great among current smokers as among those who had never smoked (Fig 1–8). Numerous other studies have demonstrated a strong association among COPD prevalence, COPD-attributable mortality, and smoking.[113] In a study of 1,251 men and women from East Boston, Massachusetts, Tager and colleagues[105] found that lifetime cigarette consumption was the only significant predictor of an FEV_1 less than 65% of predicted (odds ratio, 9.3). Age, respiratory symptoms, and relation to a subject with COPD were not important predictors.

Some recent data suggest that dietary factors may mitigate the deleterious effects of smoking on the respiratory system. Two studies have now shown that high levels of fish consumption may slow the decline in FEV_1[99] in smokers and decrease their risk of clinical COPD.[98]

Pathophysiologic Changes Associated With Cigarette Smoking

The pathologic changes in pulmonary anatomy resulting from cigarette smoking are a sequential development that is initially limited to the small airways but steadily progresses to cause widespread changes involving the small airways, the large airways, and lung parenchyma.[43] Lung injury associated with clinically apparent COPD includes three separate but interconnected processes—chronic mucus hypersecretion (causing cough and sputum production), airway narrowing with expiratory airflow obstruction, and abnormal dilatation of the distal airspaces with destruction of alveolar walls (emphysematous changes). These pathologic changes are accompanied by depression in functional capacity, as measured both by pulmonary function tests and symptomatically. Although some alteration in lung structure or function is detectable in the great majority of long-term smokers, in only a minority of smokers will clinically limiting COPD develop. A recent study

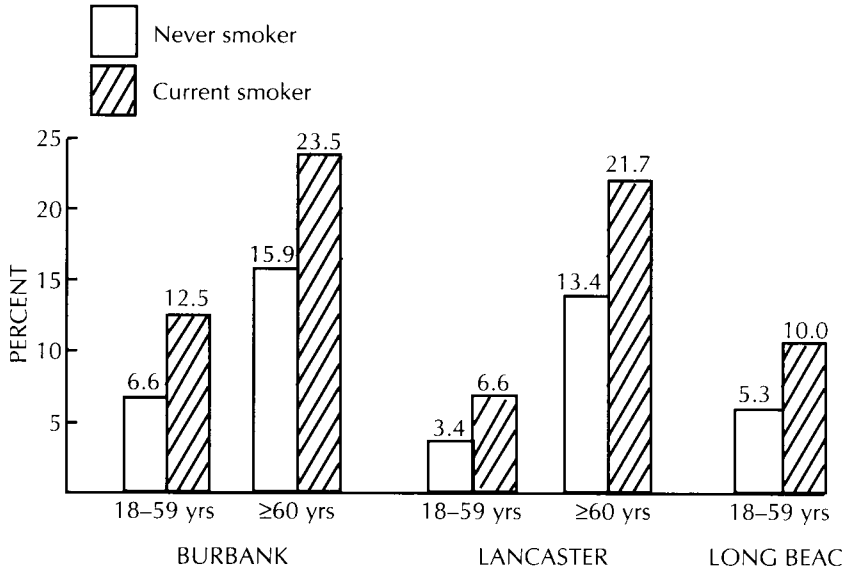

Fig 1–8.—Prevalence of forced expiratory volume in 1 second less than 75% of predicted in three southern California communities by age group and smoking status (prevalence, age, and sex adjusted by using the 1970 white population of the United States as the standard population). (From Rokaw SS, Detels R, Coulson AH, et al: *Chest* 1980; 78:252–262. Used by permission.)

suggests that the decline in FEV_1 in smokers can be partially explained by the loss of lung elastic recoil pressure as a result of microscopic enlargement of the airspaces rather than grossly visible emphysema.[63] Reports have estimated that moderate to severe COPD will develop in approximately 10% to 15% of smokers.[113]

The pathologic changes associated with cigarette smoking that lead to the development of COPD are multiple and interrelated[103, 113, 129] (Table 1–2). Moreover, these changes become clinically apparent in adults only after a long latent period. Impaired lung growth and development in childhood-such as that observed in children exposed to environmental tobacco smoke[106, 112] may predispose or accelerate the development of clinically apparent COPD in adults. Thus far, longitudinal studies have not assessed the various factors in childhood and young adulthood that may predispose adults to either COPD or an acceleration in the decline of lung function that is normally associated with aging. Cigarette smoking is the predominant cause of lung function decline at a greater rate than the annual age-associated changes (volume loss of 20 to 30 mL/yr).[113]

TABLE 1–2.—*Summary of Pathophysiologic Changes Resulting From Cigarette Smoking*

Inflammatory changes
Increase in inflammatory cells (neutrophils and alveolar macrophages)
Elastase release in the lung.
Decrease α_1-antiprotease activity
Altered immune function
Depressed antibody production
Altered cellular immune response
Decreased mitogen responsiveness
Decreased alveolar macrophage responsiveness to lymphokine and macrophage migration inhibitory factor
Depressed phagocytosis and intracellular killing
Higher peripheral leukocyte count
Higher levels of C5, C9, C1 inhibitor, C-reactive proteins, and autoantibodies (antinuclear and rheumatoid factors)
Lower levels of IgG, IgM, IgA
Higher levels of IgE
Blunted immune response to influenza vaccination
Heightened airway responsiveness

Inflammation of both the airways and parenchyma of the lung is a central component of cigarette-induced pulmonary damage.[103, 117, 129] The structural damage resulting from this chronic inflammation has functional consequences that can lead to the development of clinically diagnosed COPD if smoking is continued. Frank parenchymal damage is preceded by an increase in inflammatory cells (both neutrophils and alveolar macrophages) in lung parenchyma at the level of the bronchioli.[79] In sensitive tests of small airway function, it was found that this smoking-induced bronchiolitis is associated with functional abnormalities. Moreover, both macrophages and, probably, neutrophils can release elastase in the lung. Human neutrophil elastase produces emphysema when instilled into animal lungs.[48, 55] Host factors related to the response of the airways and parenchyma to cigarette smoking, as well as the intensity of smoking, are likely to determine the degree of inflammatory response to cigarette smoke and the development of disease. These host factors probably determine in which smokers clinically significant COPD will develop. Even without clinical evidence of emphysema, destruction of peribronchiolar alveoli can be found in the lungs of smokers,[94, 129] in addition to loss of elastic recoil secondary to the loss of alveolar attachments.[129]

A protease-antiprotease hypothesis has been advanced as an additional factor to account for the development of

smoking-related pulmonary damage. This hypothesis is based on the observation that enzymatic digestion of lung parenchyma can occur as a direct consequence of a genetic or acquired imbalance of the protease-antiprotease system and that subsequent repair of connective tissue is compromised. In relation to smoking, the level of functional α_1-antiprotease activity has been shown to be reduced in bronchoalveolar fluid obtained from cigarette smokers.[46, 47]

Cigarette smoking also has a variety of effects on the immune system that may be important in determining the risks of COPD and other respiratory diseases. For example, smoking appears to depress the rate of antibody production in human smokers exposed to a variety of antigens.[40] Additionally, cigarette smoking may have broad effects on the ability of the lung to generate a cellular immune response. Reports have shown that lymphocytes from cigarette smokers respond poorly to mitogens[26] and that the alveolar macrophages of smokers show a decreased response to lymphokine and macrophage migration inhibitory factor.[121] Cigarette smoke also depresses phagocytosis and intracellular killing.

Cigarette smoking produces structural and functional abnormalities in the airway mucociliary system. Long-term exposure to cigarette smoke consistently causes impairment of mucociliary clearance in both patients with chronic bronchitis and apparently healthy smokers (Fig 1–9). Moreover, persistence of mucociliary dysfunction in patients with chronic bronchitis may continue, even after smoking cessation.[10] The consequences of airway mucociliary dysfunction have not been well characterized but may include increased susceptibility to respiratory infections, airflow obstruction by excessive airway secretions, and increased risk of carcinogenesis secondary to prolonged contact between inhaled carcinogens and the respiratory epithelium.

Cigarette smoking may also cause heightened airway responsiveness similar to that induced with histamine or methacholine bronchoprovocation. In an extensive review of these data, O'Connor and colleagues[82] concluded that cigarette smoking may cause heightened airway responsiveness but that this relationship may be evident only among individuals with a sufficiently high cumulative exposure to smoking. Whether this degree of responsiveness is related to the pathogenesis of asthma or COPD remains uncertain. The potential central role of cigarette smoking in parenchymal and airway inflammation is shown in Figure 1–10.

In summary, a variety of host and environmental factors have been hypothesized as etiologic agents in the development of COPD in smokers. These factors may act alone or in combination, depending on an individual smoker's underlying risk of COPD developing. This interaction between host factors and the environmental insult of cigarette smoke probably accounts for the low rate of clinical COPD (about 15%) among long-term smokers.

PULMONARY BENEFITS RESULTING FROM QUITTING SMOKING

Impact of Smoking Cessation on Respiratory Symptoms

Numerous studies have documented the marked increase in respiratory symptoms in smokers of all ages as compared with nonsmokers.[111, 113] Moreover, the number of cigarettes smoked per day is the strongest risk factor for chronic respiratory symptoms, including chronic cough, phlegm production, wheezing, and dyspnea.[113] Recently, the surgeon general summarized the data regarding the impact of smoking cessation on respiratory symptoms.[113]

She reported that quitting smoking results in a rapid and significant decrease in respiratory symptoms, irrespective of the quantity smoked or length of time smoking. This finding has been documented in clinical, cross-sectional, and longitu-

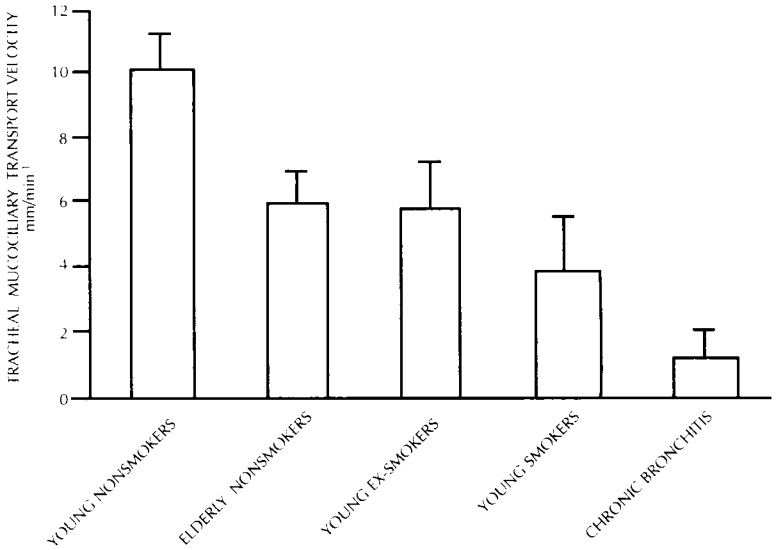

Fig 1–9.—Comparison of mean (SE in *brackets*) tracheal mucociliary transport velocity among young nonsmokers (n = 10), elderly nonsmokers (n = 7), healthy young ex-smokers (n = 9), healthy young smokers (n = 15), and patients with chronic bronchitis (n = 14). (From Goodman RM, Yergin BM, Lamnda JF, et al: *Am Rev Respir Dis* 1978; 117:205–214. Used by permission.)

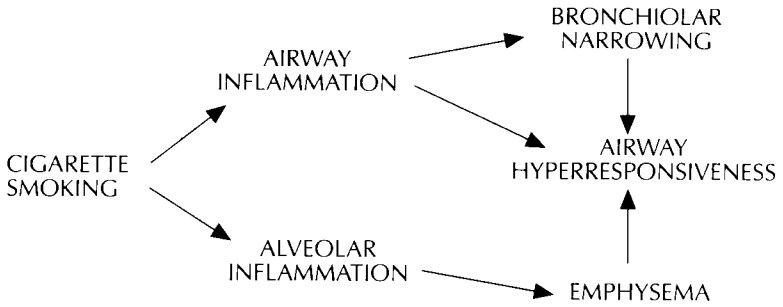

Fig 1–10.—Hypothesized mechanisms by which airway hyperresponsiveness may be associated with developing or established chronic obstructive pulmonary disease without necessarily being a pre-existing risk factor. (From Sparrow D, O'Connor G, Weiss ST: *Epidemiol Rev* 1988; 10:29–47. Used by permission.)

dinal studies that assessed the impact of smoking cessation on respiratory symptoms.

Buist and coworkers[9] reported that smoking cessation was associated with a dramatic reduction in respiratory symptoms (e.g., coughing, expectoration, shortness of breath, and wheezing) within 1 month of cessation. These findings have generally been substantiated in subsequent studies, although sex- and age-specific differences have been noted. In a large study to assess the effect of smoking status on the respiratory symptoms of 5,686 women, Schenker et al.[95] reported that the age-adjusted prevalence rates for chronic cough, chronic sputum production, and wheezing were significantly less among former smokers as compared with current smokers, although grade 3 dyspnea was reported more often by former smokers. Hawthorne and Fry[56] evaluated the association between smoking and respiratory symptoms among 11,295 men and 7,491 women from southwest Scotland. These authors found that the prevalence rates for phlegm production and wheezing were lower among former smokers as compared with current smokers. Male smokers who quit reported decreased rates of dyspnea, whereas female smokers reported increased rates of dyspnea when compared with same-sex current smokers. Studies assessing the impact of smoking cessation on asthmatics who smoke have been limited, although one group[59] reported that asthmatic symptoms decreased after patients stopped smoking.

In addition to the aforementioned cross-sectional studies, numerous longitudinal studies have reported rapid resolution of most respiratory symptoms after smoking cessation.[21, 101, 127] In a study by Woolf and Zamel,[127] 302 female former smokers with a mean cigarette consumption of 15 pack-years had dramatic resolution of respiratory symptoms within 5 years of cessation. Significant decreases in coughing, sputum production, dyspnea, and wheezing were noted in former smokers when compared with women who continued to smoke. Comstock and colleagues[21] reported similar findings in a study of 670 males. Over a 6-year period, the prevalence of symptoms of chronic cough, phlegm production, and wheezing significantly decreased from a level comparable with current smokers at the start of the study to a level comparable to those who had never smoked after 6 years. These authors noted no differences over the 6-year period for the symptom of dyspnea among the successful quitters.

Impact of Smoking Cessation on Respiratory Infections

Alterations in immune function that may contribute to an increased rate of respiratory infections have been noted among cigarette smokers. These alterations include a higher leukocyte count[22]; monocytes that may partially lack the ability to kill intracellular *Candida*[78]; higher levels of C5, C9, and C1 inhibitor[130]; higher levels of C-reactive protein and autoantibodies (antinuclear and rheumatoid factors)[58]; lower levels of specific immunoglobulins (IgG, IgM, IgA)[39]; elevated levels of IgE[58]; reduced immune responses to inhaled antigens among several occupational groups[76, 77]; and a blunted immune response to influenza vaccination[64, 74] (see Table 1–2).

In addition to these alterations in immune function, some studies have assessed the rates of acute respiratory infection among smokers and nonsmokers. For instance, Kark et al.[71] studied an influenza outbreak within a military unit in Israel and found that clinically apparent influenza developed in 68.5% of current smokers as compared with 47.2% of never-smokers or former smokers.

Persons who quit smoking have been shown to have decreased rates of respiratory infections when compared with persons who continue to smoke. In the first American Cancer Society Cancer Prevention Study (ACS-CPS-I) involving more than 1 million Americans from 1959 to 1963, mortality from influenza and pneumonia was 1.3 to 1.9 times more likely among ever-smokers when compared with never-smokers.[53] Other studies have substantiated this finding and have reported a dose-response effect, with an increasing rate of pneumonia deaths correlated to the amount smoked.[30, 88] In the second American Cancer Society Cancer Prevention Study (ACS-CPS-II), age-adjusted mortality from influenza and pneumonia decreased among former smokers when compared with continuing smokers. Male former smokers of fewer than 21 cigarettes per day had mortality rates after 10 years of abstinence that approached the rates of never-smokers. Male former smokers of more than 21 cigarettes per day had mortality rates that approached those of never-smokers after 15 years of abstinence. Female former smokers of any amount had age-adjusted mortality rates that approached those of never-smokers after 3 to 5 years of abstinence. These results provide dramatic evidence of one of the important pulmonary benefits of quitting smoking: the in-

creased rate of influenza and pneumonia deaths observed among smokers rapidly decreases to the lower rate observed among never-smokers.

Impact of Smoking Cessation on Pulmonary Function

Smoking Status and Pulmonary Function

Cigarette smoking is a strong determinant of pulmonary function as measured by FEV_1 and other indicators.[8, 61, 113] Most cross-sectional studies of age-adjusted FEV_1 report that never-smokers have the highest FEV_1 values, current smokers have the lowest FEV_1 values, and former smokers have intermediate FEV_1 values. Higgenbottam and colleagues,[60] in a cross-sectional study of 18,000 male British civil servants, noted a similar gradient for FEV_1 based on smoking history. These authors suggested that the depression of lung function (FEV_1) associated with cigarette smoking has two components—an irreversible component related to lifetime cigarette consumption and a second component that reverses rapidly on smoking cessation. In the 1990 surgeon general's report on the health benefits of smoking cessation,[111] the authors concluded that

> . . . results suggest that permanent loss of FEV_1 occurs with smoking and that the extent of the loss is associated with the cumulative amount smoked (i.e., pack-years). However, before the development of overt COPD, cessation is associated with an average improvement of 75 to 150 mL, implying that smoking also causes reversible decrements of function.

Impact of Smoking Cessation on Overall Pulmonary Function

After smoking cessation, an improvement in pulmonary function is observed in longitudinal studies, particularly among persons who have no evidence of clinical COPD. Although the results vary, most longitudinal studies report that smoking cessation results in a small, but statistically significant improvement in pulmonary function. The U.S. surgeon general, in her 1990 report on the benefits of smoking cessation, summarized these findings with an estimate that forced vital capacity (FVC), vital capacity (VC), and FEV_1 may improve by about 4% or 5% 4 to 8 months after cessation.[111] The absolute value for this improvement is approximately 100 mL of improvement in FEV_1, a value similar to that observed in large cross-sectional studies.

Impact of Smoking Cessation on Small Airway Function

The impact of smoking cessation on small airway function, as measured by single-breath nitrogen testing, is more dramatic. Numerous investigators[6, 9] have used this test to assess changes in closing volume, closing capacity, and the slope of nitrogen concentration during the alveolar plateau (slope of phase III). In summary, these studies concluded that abnormalities in the small airways, as measured by closing volume, closing capacity, and alveolar plateau, are substantially reversible among smokers who do not yet have significant airflow obstruction. Partial recovery of small airway function occurs rapidly and is completed 6 to 12 months after smoking cessation.

Impact of Smoking Cessation on Pulmonary Diffusing Capacity

Pulmonary diffusing capacity has been measured to be 6% to 10% lower among smokers when compared with age-matched nonsmokers in a number of studies.[111] Less information is available, however, regarding the impact of smoking cessation on diffusing capacity. The surgeon general, in her 1990 report on the health benefits of smoking cessation, concluded that the effect of cigarette smoking on pulmonary diffusing capacity includes both irreversible and reversible components. The extent of irreversible change is predicted by cumulative consumption; the reversible component improves quickly after cessation.

Effects of Smoking Cessation on Patients With Clinically Apparent Chronic Obstructive Pulmonary Disease

Numerous longitudinal studies have assessed the impact of smoking cessation on pulmonary function among patients with clinical COPD. These results were summarized in the 1990 surgeon general's report,[111] which concluded that the rate of FEV_1 loss is accelerated after the development of COPD. However, in a finding with important clinical implications, the same authors concluded that after smoking cessation, the rate of decline in FEV_1 returns to the rate observed among never-smokers (approximately 20 mL/yr). This suggests that smoking cessation can arrest the accelerated clinical processes that lead to COPD.

Impact of Smoking Cessation on Chronic Obstructive Pulmonary Disease Mortality

In addition to improving pulmonary function, smoking cessation can reduce the elevated rate of pulmonary mortality observed among patients with COPD. Numerous longitudinal studies have reported that the mortality rates from COPD are approximately ten times higher in current smokers than in never-smokers.[111] The values for former smokers are intermediate and are based on the number of years since cessation. Once COPD is clinically apparent, however, smoking cessation results in an improvement, but not a complete elimination of the increased risk of COPD mortality among former smokers. The 1990 surgeon general's report concluded that "even after 20 years or more of abstinence, the risk of COPD mortality among former smokers remains elevated in comparison with never-smokers."[111] However, in comparison with continued smoking, sustained abstinence after smoking cessation leads to significant improvement in the rate of COPD mortality.[111]

GUIDELINES TO CLINICIANS FOR EFFECTIVE SMOKING CESSATION INTERVENTION

Given the enormous toll of pulmonary morbidity and mortality attributable to smoking, the most effective treatment of pulmonary disease in the United States is the elimination of cigarette smoking among pulmonary patients. This goal will increasingly become an achievable one as clinicians incorporate effective smoking cessation intervention strategies into their clinical practice. Unfortunately, only about half of clinicians assess the smoking status of their patients, and an even smaller percentage provide specific advice on how to quit.

Former Surgeon General C. Everett Koop recently stated that physicians and other health care professionals can significantly reduce the prevalence of smoking in this country if they intervene in smoking cessation.[50] Numerous research studies have supported Dr. Koop's conclusion. Although the efficacy of a physician's advice to quit smoking has varied,[80, 84] Sherin[100] reported that 70% of persons smoking more than one pack a day said that they would quit smoking if urged to do so by a physician. The 1979 surgeon general's report on the health consequences of smoking concluded that 10% to 25% of smokers who are advised to quit by their physicians may quit or reduce the amount they smoke.[109]

Most physicians, however, are not advising their smoking patients to quit. Even fewer physicians go beyond a quit-smoking recommendation and provide their patients with specific advice on cessation.[122] In one study, fewer than 25% of smokers reported ever being advised to stop smoking by their physician.[34] In another recent study, Anda et al.[2] determined that only 44% of smokers who had seen a physician in the previous year reported that they had ever been told to quit smoking by a physician. These findings suggest that physicians have not followed the 1980 American Medical Association Council on Scientific Affairs' recommendation that physicians should "assess routinely the smoking habits of their patients and encourage them to quit smoking by offering them direct assistance or referring them to community cessation clinics."[23]

The physician is strategically placed to have an impact on smokers.[81, 83] In a review of the need to coordinate physician activities against tobacco, Ronald Davis, M.D., former director of the United States Office on Smoking and Health, cited four major reasons why physicians are vital to the anti-smoking campaign.[27] First, physicians are among the most respected and trusted of all professionals who will come into contact with a smoking patient. Second, smokers have frequent contact with physicians; at least 70% of all smokers visit a physician each year,[81] and the average smoker has 4.3 physician visits annually.[124] Third, patients who smoke may be particularly susceptible to receiving quit advice during a visit with a physician. Because patients tend to be maximally perceptive of their own vulnerability during a medical visit, they may be most responsive to a smoking cessation message during this time.[90] Last, Davis cited the body of smoking literature[81, 96] and concluded that even minimal interventions by physicians can result in an increase in the cessation rate of up to five percentage points. A model for such a brief intervention, based on the *Clinical Practice Guideline on Smoking Cessation* by the Agency for Health Care Policy and Research (AHCPR),[20] is presented later in this chapter.

Although many physicians believe that their advice to quit smoking is not worthwhile,[123] the evidence strongly contradicts this belief. Russell et al.,[93] in a large study involving more than 2,000 smokers visiting general practitioners in Great Britain, demonstrated a 5.1% 1-year abstinence rate among smoking patients given a brief stop-smoking message as compared with a 0.3% rate among those not advised to quit. The stop-smoking message took about 1 minute and consisted solely of the physician advising patients to stop smoking, giving patients a booklet to help them quit, and warning them that smoking cessation would be addressed at follow-up visits. Wilson et al.,[125] using a more intense cessation message, demonstrated quit rates of 23% among the intervention group as compared with 12% in the control group. Using a very intensive program in a general practice group involving four physicians, Richmond and Webster[87] noted a 33% 6-month abstinence rate among the smokers who received the intervention, whereas only 3% of the control group continued to abstain from cigarette smoking at 6 months. These Australian physicians designed an intervention program consisting of physician counseling and follow-up, with patients required to see their providers six times during the study period.

Using these and other studies, Kottke et al.[72] conducted a meta-analysis to determine the attributes of successful smoking cessation interventions in medical practice. In their study, 108 cessation interventions in 39 controlled, quit-smoking trials were analyzed. Multivariate analysis revealed that the only significant predictor of sustained smoking cessation was the number of different intervention modalities used; as the number of modalities used increased, so did the probability of long-term success.

The authors commented that successful cessation was not the result of novel or unusual physician interventions; rather, "it is reinforcement—by the types of contacts, and the number of people making the contacts, not a specific intervention or delivery system for the smoking cessation message that produces results." They concluded that smoking cessation programs "will be most fruitful if focused on how the nonsmoking message can be given clearly, repeatedly, and consistently through every feasible delivery system: personalized advice; printed materials; the mass media; and smoke-free medical, work, school, and home environments." Although these roles must be shared equitably among the public health community, physicians can be instrumental in providing these messages clearly, repeatedly, and consistently.

Glynn reviewed the relative effectiveness of physician-initiated smoking cessation programs.[49] He noted a 1-year cessation rate of 3% to 10% among studies using minimal counseling intervention by physicians. Minimal counseling typically consists of a brief, but unequivocal message to stop smoking and usually includes the provision of a self-help booklet. For studies involving more involved physician intervention, cessation rates of 13% to 38% have been reported. These interventions typically include more intensive counseling, frequent and scheduled follow-up visits, ancillary staff in-

volvement, and educational materials. Nicotine replacement therapy has been used in both minimal and intensive intervention programs for physicians.[42, 73, 102, 107]

These findings highlight the enormous potential impact of physician intervention with smoking patients. This is particularly apparent when this success rate is applied to the total population of U.S. smokers. Based on the estimated 48 million adult U.S. smokers in 1987,[86] approximately 2.1 million smokers would quit each year if all physicians adopted a minimal intervention program with their smoking patients. If physicians adopted a more intensive intervention strategy, approximately 7.5 million smokers would quit as a result of these efforts (Table 1–3).

Clinical Guidelines to Promote Smoking Cessation

In an effort to synthesize the enormous body of medical literature on smoking cessation, the AHCPR published its *Clinical Practice Guideline on Smoking Cessation* in 1996.[20] This document provides state-of-the-art recommendations for physicians to promote smoking cessation during a brief intervention with their smoking patients. Another valuable resource for clinical guidelines is the National Cancer Institute's Smoking, Tobacco, and Cancer Program's publication *How to Help Your Patients Stop Smoking.*[50] The booklet is divided into two sections, guidelines for physicians and guidelines for clinic staff. This booklet is available free of charge from the National Cancer Institute by calling (301) 996-6294.

Guidelines for Physicians

The AHCPR guidelines for physicians are shown in Table 1–4. They are based on five principles: ask, advise, identify, assist, and arrange. First, physicians must ask every patient at every office visit whether they smoke. Surprisingly, fewer than 50% of smoking patients report ever being asked whether they smoke,[2] and many smoking patients report that they would try to quit if urged to do so by a physician.[100] The identification of all patients who smoke is the key first step in influencing smoking rates in clinical practice. One simple way to automate this process is to make smoking status assessment one of the vital signs, which are usually assessed by a medical assistant before the physician sees the patient. By making it a vital sign, assessing smoking status will be as automatic as knowing your patient's pulse or blood pressure. A model vital signs stamp including smoking status for clinical practice is shown as part of Table 1–5.

Another part of the physician's role is to advise all patients to quit. This advice must be clear, direct, and unequivocal. Personalizing the message to quit smoking can also help.

The most effective means of assisting patients in quitting is to set a quit date with the patient, usually over the next month. By signing a stop-smoking contract with the patient, the commitment to quit will be reinforced. Self-help materials such as the National Cancer Institute's *Quit for Good* booklet are important additions. Assisting the patient also requires assessing the need for nicotine replacement therapy. Patients with high nicotine dependence characteristics who may particularly benefit from this pharmacologic aid include those who smoke more than one pack per day and those who smoke within 30 minutes of awakening each morning. Fagerstrom has developed a brief scale to measure nicotine dependence that may be clinically useful.[37] For those patients not willing to quit now, ask again on the next visit.

Finally, physicians need to arrange follow-up visits with their patients. A follow-up visit on or around the quit date and another within the month after quitting will emphasize that the patient is accountable to the physician, who will then monitor progress with the quit-smoking commitment.

Clinic Staff Guidelines

The AHCPR guidelines for the clinic staff (Table 1–5) complement those for physicians. These guidelines foster the institutionalization of smoking status assessment and intervention with smoking patients in the clinic while minimizing the time expenditure by physicians and staff. As part of this institutionalization, each clinic should create a smoke-free office environment. This includes the establishment and enforcement of a nonsmoking policy within the clinic, as well as removing ashtrays, displaying smoking cessation materials and posters, and eliminating periodicals that contain tobacco advertisements. Among periodicals that ban tobacco advertisements are *Reader's Digest, National Geographic, The Saturday Evening Post, Scientific American, Good Housekeeping, New Yorker,* and *Seventeen.*

Second, the clinic environment must be institutionalized to identify smoking patients for physician intervention. These institutional changes include using a vital signs stamp that in-

TABLE 1–3.—*Predicted Impact of Universal Smoking Cessation Intervention by Physicians With Their Smoking Patients, United States*†*

Level of Physician Intervention	Median Expected Success Rate	Total Number of U.S. Smokers (Millions)	Proportion Visiting an M.D. per Year	Number of Successful Quitters per Year, Millions
Minimal	.06	49	.70	2.058
Extensive	.22	49	.70	7.546

*From Fiore MC, Remington PL, Pierce JP, et al: *Dis Mon* 1990; 35:218. Used by permission.

†Based on successful cessation rates reported by Schwartz JL: *Review and Evaluation of Smoking Cessation Methods: The United States and Canada, 1978–1985.* US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Cancer Institute, Division of Cancer Prevention and Control, 1987, NIH Publication No 87–2940. Predictions computed by the authors.

TABLE 1–4.—*Guidelines for Physicians in Promoting Smoking Cessation Among Clinic Patients**

Action	Strategies for Implementation
Step 1: *Ask*—Systematically identify all tobacco users at every visit	
Implement an office-wide system that ensures that for *every* patient at *every* clinic visit, tobacco-use status is queried and documented	Expand the vital signs to include tobacco use Data collected by the health care team Can be implemented by using preprinted progress note paper that includes the expanded vital signs, a vital signs stamp, or for computerized records, an item assessing tobacco-use status Alternatives to the vital signs stamp are to place tobacco-use status stickers on all patient charts or to indicate smoking status by using computer reminder systems
Step 2: *Advise*—Strongly urge all smokers to quit	
In a *clear, strong,* and *personalized* manner, urge every smoker to quit	Advice should be *Clear:* "I think it is important for you to quit smoking now and I will help you" "Cutting down while you are ill is not enough" *Strong:* "As your clinician, I need you to know that quitting smoking is the most important thing you can do to protect your current and future health" *Personalized:* Tie smoking to current health/illness and/or social and economic costs of tobacco use, motivation level/readiness to quit, and/or the impact of smoking on children and others in the household Encourage clinic staff to reinforce the cessation message and support the patient's quit attempt
Step 3: *Identify* smokers willing to make a quit attempt	
Ask all smokers if they are willing to make a quit attempt at this time	If a patient is willing to make a quit attempt at this time, provide assistance (see Step 4) If the patient prefers a more intensive treatment, refer to interventions administered by a smoking cessation specialist and follow up with the patient regarding quitting If the patient clearly indicates an unwillingness to make a quit attempt at this time, provide a motivational intervention
Step 4: *Assist*—Aid the patient in quitting	
Help the patient with a quit plan	*Set a quit date:* Ideally, the quit date should be within 2 weeks, with the patient's preference taken into account *A patient's preparations for quitting:* Inform: Family, friends, and coworkers of quitting and request understanding and support Environment: Remove cigarettes from your environment. Before quitting, avoid smoking in places where you spend a lot of time (e.g., home, car) Review: Previous quit attempts. What helped you? What led to relapse? Anticipate: Challenges to planned quit attempt, particularly during the critical first few weeks
Offer nicotine replacement therapy except in special circumstances	*Nicotine patch:* Offer nicotine patch therapy as the primary pharmacotherapy if the patient smokes 15 or more cigarettes per day. Clinical judgment should be used in prescribing the patch for patients who smoke fewer than 15 cigarettes per day *Nicotine gum:* Offer nicotine gum therapy as a pharmacotherapy, particularly if the patient prefers nicotine gum to the nicotine patch or smokes fewer than 15 cigarettes per day
Give key advice on successful quitting	*Abstinence:* Total abstinence is essential. "Not even a single puff after the quit date" *Alcohol:* Drinking alcohol is highly associated with relapse. Those who stop smoking should review their alcohol use and consider limiting/abstaining from alcohol during the quit process *Other smokers in the household:* The presence of other smokers in the household, particularly a spouse, is associated with lower success rates. Patients should consider quitting with their significant others and/or developing specific plans to stay abstinent in a household where others still smoke
Provide supplementary materials	*Sources:* Federal agencies, including AHCPR,† nonprofit agencies, or local/state health departments *Salient characteristics:* Culturally/racially/educationally appropriate for the patient *Location:* Readily available in every clinic office
Step 5: *Arrange*—Schedule follow-up contact	
Schedule follow-up contact either in person or via telephone	*Timing:* First follow-up contact should be within 2 weeks of the quit date, preferably during the first week. A second follow-up contact is recommended within the first month. Schedule further follow-up contacts as indicated *Actions during follow-up visit:* Congratulate success. If a lapse occurred, review circumstances and elicit recommitment to total abstinence. Remind the patient that a lapse can be used as a learning experience and is *not* a sign of failure. Identify problems already encountered and anticipate challenges in the immediate future

*Adapted from Fiore MC, Bailey WC, Cohen SJ, et al: *Smoking Cessation: Clinical Practice Guideline No. 18.* Rockville, Md, US Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research, AHCPR Publication No 96-0692, April 1996.
†AHCPR = Agency for Health Care Policy and Research.

cludes smoking status assessment as one of the vital signs, "flagging" the charts of all smoking patients before their physician visit, and adding a smoking cessation progress note card to the medical charts of all smoking patients.

To supervise implementation of the clinic-wide tobacco control program, each clinic should appoint a smoking cessation coordinator. This individual devotes a small amount of time to these tasks and should be selected from among the current nursing or medical assistant staff. The coordinator is responsible for assisting the physician in tobacco-use assessment and intervention among patients who attend the clinic. The coordinator is responsible for determining whether smoking status is recorded as a vital sign on all patients checking into the clinic. Additionally, this person ensures that the charts of current smokers are flagged as an additional reminder to physicians and that a smoking cessation progress note card is added to these charts. The coordinator assists patients in reviewing smoking cessation plans (including quit dates), self-help materials, and the proper use of nicotine patches or gum. Finally, the smoking cessation coordinator is responsible for ensuring that appropriate follow-up visits are scheduled for patients who are in the process of quitting smoking.

Nicotine Dependence and Smoking Cessation

The Addictive Properties of Nicotine

A paradox in our society today is the finding that almost 50 million Americans continue to smoke even though thousands of medical research studies have implicated cigarettes as the leading cause of preventable death and disease in the United States. A recent report of the surgeon general[114] summarizes the most important reasons for this paradox: (1) cigarettes and other forms of tobacco are highly addictive, (2) nicotine is the drug in tobacco that causes this addiction, and (3) the

TABLE 1–5.—*Guidelines for Clinic Staff in Promoting Smoking Cessation Among Clinic Patients**

Action	Strategies for Implementation
Implement an office-wide system that ensures that for *every* patient at *every* clinic visit, smoking status is queried and/or documented	Expand the vital signs to include tobacco use Data collected by the health care team Can be implemented by using preprinted progress note paper that includes the expanded vital signs, a vital signs stamp, or for computerized records, an item assessing tobacco-use status **VITAL SIGNS** Blood Pressure:_____ Pulse:_____ Weight:_____ Temperature:_____ Respiratory Rate:_____ Tobacco Use: Current Former Never *(circle one)* Alternatives to the vital signs stamp are to place tobacco-use stickers on all clinic patient charts or to indicate smoking status by using computer reminder systems
Health care systems should ensure that clinicians have the knowledge and training to treat smoking, that clinicians and patients have cessation resources, and that clinicians are given feedback about their cessation practices	*Educate*—On a regular basis, offer lectures/seminars/in-services with CME† and other credit for smoking cessation treatment *Resources*—Have patient self-help materials, as well as nicotine replacement "starter kits," readily available in every examination room *Provide feedback*—As part of chart audits, evaluate the degree to which clinicians are identifying, documenting, and treating patients who smoke, and provide feedback to clinicians about their level of intervention
Clinical sites should communicate to staff the importance of intervening with smokers and should designate one staff person (e.g., nurse, medical assistant, or other clinician) to coordinate and deliver smoking cessation treatments	*Communicate* to all staff members (e.g., nurses, medical assistants, or other clinicians) their responsibilities in the delivery of smoking cessation services *Designate* a smoking cessation treatment coordinator for every clinical site *Delineate* the responsibilities of the smoking cessation coordinator, including instructing patients on the effective use of cessation treatments (e.g., nicotine replacement therapy, telephone calls to and from prospective quitters, and scheduled follow-up visits, especially in the immediate postquit period)

(Continued)

TABLE 1–5 (cont.)

Action	Strategies for Implementation
Provide smoking cessation inpatient consultation services to all smokers admitted to a hospital	*Implement* a system to identify and document the tobacco-use status of all hospitalized patients *Offer* cessation treatment to all hospitalized patients who use tobacco *Identify* a clinician to deliver smoking cessation inpatient consultation services for every hospital *Reimburse* providers for smoking cessation inpatient consultation services *Expand* hospital formularies to include effective smoking cessation pharmacotherapy such as the nicotine patch and nicotine gum *Ensure* compliance with JCAHO regulations mandating that all hospitals be entirely smoke free *Educate* all hospital staff regarding nicotine withdrawal, including effective treatments such as nicotine replacement therapy and counseling
Provide all insurance subscribers coverage for *effective* smoking cessation treatments, including pharmacotherapy (nicotine replacement therapy) and counseling	*Cover*—Include effective smoking cessation treatments (both pharmacotherapy and counseling) as part of the basic benefits package for all individual, group, and HMO insurance packages *Evaluate*—Include the provision of smoking cessation treatment as part of "report cards" for managed care organizations and other insurers (e.g., Health Employer, Data, and Information Set [HEDIS]) *Educate*—Inform subscribers of the availability of covered smoking cessation services and encourage patients to use these services
Reimburse fee-for-service clinicians for delivery of effective smoking cessation treatments; include smoking cessation treatments in the defined duties of salaried clinicians	*Include* smoking cessation treatment as a reimbursable activity for fee-for-service providers *Inform* fee-for-service clinicians that they will be reimbursed for using effective smoking cessation treatments with every patient who uses tobacco *Include* smoking cessation intervention in the job description and performance evaluation of salaried clinicians

*Adapted from Fiore MC, Bailey WC, Cohen SJ, et al: *Smoking Cessation: Clinical Practice Guideline No. 18.* Rockville, Md, US Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research, AHCPR Publication No 96-0692, April 1996.
†CME = continuing medical education; JCAHO = Joint Commission on Accreditation of Healthcare Organizations; HMO = health maintenance organization.

pharmacologic and behavioral processes that determine tobacco addiction are similar to those that determine addiction to drugs such as heroin and cocaine.

Tobacco use fulfills all of the established criteria of addiction adopted by various organizations (e.g., the World Health Organization).[68, 128] The American Psychiatric Association now classifies nicotine dependence as a pathologic process similar to other chemical dependencies.[1] Its criteria for addiction include the following: (1) the user's behavior is controlled by a psychoactive substance (nicotine), (2) use of the drug is often compulsive despite damage to the individual, (3) the drug is reinforcing, (4) use of the drug leads to tolerance, (5) physical dependence on the drug can occur, (6) a withdrawal syndrome usually accompanies drug abstinence, and (7) relapse is common after cessation of drug use. Hunt and others demonstrated that the pattern of relapse for cigarette smoking is similar to that observed for persons addicted to heroin and alcohol.[67]

Like other addictions, tobacco use can be treated effectively.[52] The physician must often play a central role in this treatment. Because of the highly addictive nature of tobacco, physicians treating smoking patients must consider therapies that address these dependence properties of nicotine as part of a smoking cessation intervention program. The specific agents and programs available to treat tobacco addiction are described later. These treatments assume that smokers expose themselves to the disease-causing constituents of tobacco at least in part because of the highly addictive nature of nicotine. Finally, the addictive nature of nicotine warrants aggressive public health actions that prevent the initiation of tobacco dependence. Because more than 50% of smokers started using cigarettes regularly by 18 years of age,[120] prevention activities must be directed at young people. These activities should start in the elementary school years, when children begin experimenting with tobacco products.

Effectiveness of Nicotine Replacement Therapy in the Treatment of Tobacco Dependence

Nicotine Gum.—Nicotine replacement in the form of nicotine polacrilex chewing gum has been available in the United Stated in a 2-mg dose (Nicorette, SmithKline-Beecham, Inc.) since 1984 and in a 4-mg dose (Nicorette DS, SmithKline-Beecham, Inc.) since 1993. Since 1984, nicotine replacement therapy has played an increasingly important role in treating tobacco addiction. The basis for this pharmacologic interven-

TABLE 1–6.—*Guidelines for the Use of Nicotine Gum as Part of a Smoking Cessation Progam**

Patient selection	Appropriate pharmacotherapy for smoking cessation for any patient (see precautions). Nicotine gum may be particularly useful for patients who prefer gum over other treatments and smoke fewer than 15 cigarettes per day
Precautions	*Pregnancy:* Pregnant smokers should first be encouraged to attempt cessation without pharmacologic treatment. Nicotine gum should be used during pregnancy only if the increased likelihood of smoking cessation, with its potential benefits, outweighs the risk of nicotine replacement and potential concomitant smoking *Cardiovascular disease:* Although not an independent risk factor for acute myocardial events, nicotine gum should be used only after consideration of risks and benefits among particular cardiovascular patient groups: those in the immediate (within 4 weeks) post–myocardial infarction period, those with serious arrhythmias, and those with serious or worsening angina pectoris *Side effects:* Common side effects of nicotine chewing gum include mouth soreness, hiccups, dyspepsia, and jaw ache. These effects are generally mild and transient and can often be alleviated by correcting the patients' chewing technique (see *"Prescribing instructions"* below)
Dosage	Nicotine gum is available in 2-mg- and 4-mg-per-piece doses. For most patients, the 2-mg gum should be prescribed initially. The 4-mg gum should be prescribed to patients who express a preference for it, have failed with the 2-mg gum but remain motivated to quit, and/or are highly dependent on nicotine. The gum is most commonly prescribed for the first few months of a quit attempt. Clinicians should tailor the duration of therapy to fit the needs of each patient. Patients using the 2-mg strength should use not more than 30 pieces per day, whereas those using the 4-mg strength should not exceed 20 pieces per day
Prescribing instructions	*No smoking* while using the gum *Chewing technique:* Gum should be chewed slowly until a "peppery" taste emerges, then "parked" between the cheek and gum to facilitate nicotine absorption through the buccal mucosa. Gum should be slowly and intermittently "chewed and parked" for about 30 minutes *Absorption:* Acidic beverages (e.g., coffee, juices, soft drinks) interfere with the buccal absorption of nicotine, so eating and drinking anything except water should be avoided for 15 minutes before and during chewing *Scheduling of dose:* A common problem is that patients do not use enough gum to get the maximum benefit: they chew too few pieces per day and they do not use the gum for a sufficient number of weeks. Instructions to chew the gum on a fixed schedule (at least one piece every 1 to 2 hours) for at least 1 month may be more beneficial than ad lib use

*Adapted from Fiore MC, Bailey WC, Cohen SJ, et al: *Smoking Cessation: Clinical Practice Guideline No. 18.* Rockville, Md, US Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research, AHCPR Publication No 96-0692, April 1996.

tion is similar to the general principles of replacement therapy for other addictive drugs: to provide the patient with a safer and therapeutically manageable form of the drug that directly alleviates the signs and symptoms of withdrawal and craving.[68]

Numerous studies have addressed the effectiveness of nicotine chewing gum,* and a number of meta-analyses of the data generated by these trials have appeared in recent years.[17, 73, 102, 107] In general, these analyses suggest that nicotine chewing gum is a highly effective aid to smoking cessation. However, some reports suggest that nicotine gum may not be more effective than placebo gum when it is prescribed in the absence of adjuvant behavioral support.[17, 73] This finding suggests that clinicians must take smoking cessation seriously and should spend time counseling smoking patients when prescribing nicotine gum.

The 1988 surgeon general's report *The Health Consequences of Smoking: Nicotine Addiction*[114] took issue with the conclusion that nicotine gum is no more effective than placebo in the absence of behavioral support. A different interpretation was presented to explain the findings from several studies that noted a positive effect from nicotine gum soon after quitting smoking that decreased by 1 year. The surgeon general's report suggested that "Rather than being interpreted as a failure for nicotine polacrilex gum vs. a placebo, this may mean that what is effective treatment for initial quitting (e.g., relief of withdrawal symptoms) is different from effective long-term relapse prevention."[114]

Improper use of nicotine chewing gum may be another reason for the limited success of this product in the absence of behavioral support. In surveys conducted by the manufacturer of nicotine chewing gum, it was shown that most patients receive the gum with little or no instruction on how to use it and little or no counseling or follow-up about quitting smoking.[65] To assess physician practices in prescribing nicotine gum for smoking cessation, Cummings et al.[25] surveyed randomly selected internists. These authors found that most internists prescribed the gum to fewer than 25% of their patients who try to quit. Nearly half of these internists suggested that patients use the gum to try to cut down on smoking, advice contrary to current recommendations. The authors concluded that "there is a widespread need to train physicians to prescribe nicotine gum more effectively."[25] Guidelines for the effective use of nicotine gum as part of a smoking cessation program are shown in Table 1–6.

Nicotine Patch Therapy

Dosage Requirements.—In late 1991, the Food and Drug Administration (FDA) approved the first nicotine transdermal delivery system (nicotine patch) as a new and effective nicotine replacement therapy to aid smoking cessation. Since then, four different nicotine patches have been approved in the United States: Habitrol by Ciba-Geigy, Nicoderm by Marion

*References 7, 18, 35, 36, 45, 62, 66, 69, 71, 73, 75, 92, 126.

Merrell Dow, Nicotrol by Parke-Davis, and Prostep by Lederle.

Numerous studies have addressed the efficacy of the nicotine patch for smoking cessation. A recent meta-analysis of the data from these trials demonstrated that active patch subjects were 2.6 times more likely to be abstinent than placebo subjects after 6 months and 3 times more likely to be abstinent after 1 year.[42]

Nicotine patches represent a major advance in ease and patient acceptance of nicotine replacement therapy. In general, a person places a new patch on a nonirritated, nonhairy part of the torso or arm each morning. The patch delivers a steady level of nicotine over the course of 24 hours (except Nicotrol, which is designed for 16-hour use). The full-strength patch (15, 21, or 22 mg/day) produces blood levels of nicotine approximately equivalent to "trough" levels in a pack-a-day smoker, the point at which a smoker would feel an urge to light another cigarette. Depending on patient characteristics, patches are recommended for use for 6 to 12 weeks and usually include a tapering of the nicotine dose over the course of treatment. Table 1–7 presents guidelines for effective clinical use of the nicotine patch.

Side Effects.—In contrast to nicotine gum, the patches are something that a person puts on once a day and then forgets about. They also deliver more effective levels of nicotine to the body at a stable rate over a 24-hour period (except Nicotrol, which is designed for 16-hour use). This helps eliminate strong cravings in the early morning resulting from lack of nicotine during sleep, as is the case with smoking or nicotine gum use. However, about 30% of persons using nicotine patches report some form of adverse skin reaction. These are typically minor and can be treated with over-the-counter hydrocortisone cream if necessary. For more serious local skin reactions, triamcinolone cream (0.1%, to the affected area three times daily for 3 days) may be used after the patch is removed. Occasional patients will also require a nonsedating antihistamine agent. Finally, in rare cases, systemic skin reactions may develop; this mandates that patch therapy be stopped immediately. It is important that persons using nicotine patches rotate them (that is, apply the patch to a different location every day) because this helps minimize skin irritation.

The nicotine patch is contraindicated in patients with hypersensitivity or allergy to nicotine or to any of the components of the patch delivery system. Nicotine has the potential to cause fetal harm, so women who are pregnant or likely to become pregnant should be apprised of the potential hazard to the fetus of patch therapy vs. the risks of continued smoking. It would be preferable for such women to first attempt to quit without the use of nicotine replacement therapy.

TABLE 1–7.—*Guidelines for Use of Nicotine Patch as Part of a Smoking Cessation Program**

Patient selection	Appropriate as the primary pharmacotherapy for smoking cessation for any patient who smokes 15 or more cigarettes per day (see Precautions). Clinical judgment should be used in treating those who smoke fewer cigarettes per day
Precautions	*Pregnancy*—Pregnant smokers should first be encouraged to attempt cessation without pharmacologic treatment. The nicotine patch should be used during pregnancy only if the increased likelihood of smoking cessation, with its potential benefits, outweighs the risk of nicotine replacement and potential concomitant smoking
	Cardiovascular diseases—Although not an independent risk factor for acute myocardial events, the nicotine patch should be used only after consideration of risks and benefits among particular cardiovascular patient groups: those in the immediate (within 4 weeks) post–myocardial infarction period, those with serious arrhythmias, and those with severe or worsening angina pectoris
	Skin reactions—Up to 50% of patients using the nicotine patch will have a local skin reaction. Skin reactions are usually mild and self-limiting but may worsen over the course of therapy. Local treatment with hydrocortisone cream (5%) or triamcinolone cream (0.5%) may ameliorate such local reactions. In fewer than 5% of patients do such reactions require discontinuation of nicotine patch treatment
Dosage	Treatment of 8 weeks or less has been shown to be as efficacious as longer treatment periods.[42] Based on this finding, the following treatment schedules are suggested as reasonable for most smokers. Clinicians should consult the package insert for other treatment suggestions. Finally, clinicians should consider individualizing treatment based on specific patient characteristics such as previous experience with the patch, amount smoked, degree of addictiveness, etc.

Brand	Duration	Dose
Nicoderm and Habitrol	4 wk	21 mg/24 hr
	Then 2 wk	14 mg/24 hr
	Then 2 wk	7 mg/24 hr
Prostep	4 wk	22 mg/24 hr
	Then 4 wk	11 mg/24 hr
Nicotrol	4 wk	15 mg/16 hr
	Then 2 wk	10 mg/16 hr
	Then 2 wk	5 mg/16 hr

Prescribing instructions	*No smoking* while using the patch
	Location—At the start of each day, the patient should place a new patch on a relatively hairless location between the neck and waist
	Activities—No restrictions while using the patch

*Adapted from Fiore MC, Bailey WC, Cohen SJ, et al: *Smoking Cessation: Clinical Practice Guideline No. 18.* Rockville, Md, US Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research, AHCPR Publication No 96-0692, April 1996.

Comprehensive Treatment Packages.—Despite all the attention it has garnered, the nicotine patch is not a "magic bullet" for smoking cessation. Providing a patient with a supply of nicotine patches and nothing else is likely to produce little success in quitting. Fortunately, all manufacturers of the nicotine patch have produced high-quality self-help materials to accompany their medication. These can be useful to the patient during the attempt to quit and may be helpful references for clinicians who are not familiar with the process of smoking cessation. Additionally, the National Cancer Institute manual mentioned earlier, *How to Help Your Patients Stop Smoking* (301-996-6294), is an extremely helpful guide to clinicians for brief but effective interventions.

Other Pharmacologic Therapies for Smoking Cessation

There is a long history of generally unsuccessful pharmacologic treatment of smokers dating back to the early 1900s.[33] Many of the over-the-counter aids for smoking cessation (Nikoban, Bantron) include lobeline sulfate as an active ingredient, a product developed to minimize the craving for tobacco.[31] The FDA concluded in 1982 that the data were insufficient to demonstrate the effectiveness of lobeline or other over-the-counter smoking cessation aids.[44]

Currently, nicotine polacrilex gum and nicotine transdermal delivery systems (patches) are the only pharmacologic agents licensed by the FDA for the treatment of tobacco dependence. Many other products, however, are currently undergoing testing. Included among these are a nasal nicotine solution[70] and nicotine aerosols.[91]

Clonidine, both as an oral agent and as a transdermal patch, has received considerable attention as a possible means of treating tobacco withdrawal syndrome. Although clonidine is used primarily to treat hypertension, it has also been shown to diminish symptoms of both opiate and alcohol withdrawal syndrome.[51, 119] It has been proposed that clonidine may also relieve nicotine withdrawal symptoms through its adrenergic effects on the central nervous system.[114] A number of small-scale studies have been conducted to evaluate the efficacy of clonidine for smoking cessation. A meta-analysis of these trials[24] suggests that clonidine may have a beneficial impact, especially among women, but considerably more research is necessary before these conclusions can be advanced with confidence.

SUMMARY AND CONCLUSIONS

In a consistent and relentless manner, cigarette smoking damages the pulmonary system and results in a greatly increased risk of both COPD and pulmonary cancer. The pathophysiologic changes in the pulmonary system caused by smoking are multiple and interrelated. They include inflammatory changes, altered immune function, heightened airway responsiveness, altered airway mucociliary function, and alterations in the protease-antiprotease system. These pathophysiologic changes result in decreased pulmonary function and marked pulmonary symptomatology. Each year, more than 400,000 Americans die as a result of cigarette smoking, including 62,000 deaths from COPD and 112,000 from lung cancer. Approximately 90% of both lung cancer and COPD is a direct consequence of cigarette smoking. Given the tremendous impact of cigarette smoking on pulmonary morbidity and mortality, one might argue that the most effective way to treat pulmonary diseases in the United States would be to eliminate cigarette smoking.

REFERENCES

1. American Psychiatric Association: *Diagnostic and Statistical Manual*, ed 4. Washington, DC, APA Press, 1994.

2. Anda RF, Remington PL, Sienko DG, et al: Are physicians advising smokers to quit? The patient's perspective. *JAMA* 1987; 257:1916–1919.

3. Bates DV: The fate of the chronic bronchititic: A report of the ten-year follow-up in the Canadian Department of Veteran's Affairs Coordinated Study of Chronic Bronchitis. *Am Rev Respir Dis* 1973; 108:1043–1065.

4. Beck GJ, Doyle CA, Schachter EN: A longitudinal study of respiratory health in a rural community. *Am Rev Respir Dis* 1982; 125:375–381.

5. Beck GJ, Doyle CA, Schachter EN: Smoking and lung function. *Am Rev Respir Dis* 1981; 123:149–155.

6. Bode FR, Dosman J, Martin RR, et al: Reversibility of pulmonary function abnormalities in smokers. A prospective study of early diagnostic test of small airways disease. *Am J Med* 1975; 59:43–52.

7. British Thoracic Society: Comparison of four methods of smoking withdrawal in patients with smoking related diseases. *BMJ* 1983; 286:595–597.

8. Buist AS, Ross BB: Predicted values for closing volumes using a modified single-breath nitrogen test. *Am Rev Respir Dis* 1973; 107:744–752.

9. Buist AS, Sexton GJ, Nagy JM, et al: The effect of smoking cessation and modification on lung function. *Am Rev Respir Dis* 1976; 114:115–122.

10. Camner P, Philipson K, Arvidsson T: Withdrawal of cigarette smoking: A study on tracheobronchial clearance. *Arch Environ Health* 1973; 26:90–92.

11. Centers for Disease Control: Cigarette smoking among adults—United States, 1990. *MMWR* 1992; 41:354–362.

12. Centers for Disease Control: Cigarette smoking among adults—United States, 1991. *MMWR* 1993; 42:230–233.

13. Centers for Disease Control: Cigarette smoking among adults—United States, 1992, and changes in the definition of current cigarette smoking. *MMWR* 1994; 43:342–346.

14. Centers for Disease Control: Cigarette smoking among adults—United States, 1993. *MMWR* 1994; 43:925–929.

15. Centers for Disease Control: Cigarette smoking–attributable mortality and years of potential life lost—United States, 1990. *MMWR* 1993; 42:645–649.

16. Centers for Disease Control: Smoking: Attributable mortality and YPLL—U.S., 1988. *MMWR* 1991; 40:62–71.

17. Cepeda-Benito A: Meta-analytical review of the efficacy of nicotine chewing gum in smoking treatment programs. *J Consult Clin Psychol* 1993; 61: 822–830.

18. Christen A, McDonald JL, Olson GL, et al: Efficacy of nicotine chewing gum in facilitating smoking cessation. *JAMA* 1984; 108:594–597.

19. Chronic Disease Reports: *Chronic Obstructive Pulmonary Disease Mortality—United States.* Atlanta, Morbidity and Mortality Weekly Reprints, US Department of Health and Human Services, 1986, p 61.

20. Fiore MC, Bailey WC, Cohen SJ, et al: *Smoking Cessation: Clinical Practice Guideline No. 18.* Rockville, Md, US Department of Health and Human Services, Public Health Service, Agency for Health Care Policy and Research, AHCPR Publication No 96-0692, April 1996.

21. Comstock GW, Brownlow WJ, Stone RW, et al: Cigarette

smoking and changes in respiratory findings. *Arch Environ Health* 1970; 21:55–57.

22. Corre F, Lellouch J, Schwartz D: Smoking and leucocyte counts. Results of an epidemiological survey. *Lancet* 1971; 2:632–634.

23. Council on Scientific Affairs: Smoking and health. *JAMA* 1980; 243:779–781.

24. Covey LS, Glassman AH: A meta-analysis of double-blind placebo-controlled trials of clonidine for smoking cessation. *Br J Addiction* 1991; 86:991–998.

25. Cummings SR, Hanson B, Richard RJ, et al: Internists and nicotine gum. *JAMA* 1988; 260:1565–1569.

26. Daniele RP, Dauber JH, Altose MD, et al: Lymphocyte studies in asymptomatic cigarette smokers. A comparison between lung and peripheral blood. *Am Rev Respir Dis* 1977; 116:997–1005.

27. Davis RM: Uniting physicians against smoking: The need for a coordinated national strategy. *JAMA* 1988; 259:2900–2901.

28. Davis RM, Novotny TE: The epidemiology of cigarette smoking and its impact on chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1989; 140(suppl):82–84.

29. Detels R, Rokow SN, Coulson AH, et al: The UCLA population studies of chronic obstructive respiratory disease. I. Methodology and comparison of lung function in areas of high and low pollution. *Am J Epidemiol* 1979; 109:33–58.

30. Doll R, Peto R: Mortality in relation to smoking: 20 years; observations on male British doctors. *BMJ* 1976; 2:1525–1536.

31. Dorsey JL: Control of the tobacco habit. *Ann Intern Med* 1936; 10:628–631.

32. Dorsman JA, Cotton DJ, Graham BL, et al: Sensitivity and specificity of early diagnostic tests of lung function in smokers. *Chest* 1981; 79:6–11.

33. Edmunds CW: On the action of lobeline. *Am J Physiol* 1904; 11:79.

34. Eraker SA, Becker MH, Streicher VJ, et al: Smoking behavior, cessation techniques, and the health decision model. *Am J Med* 1985; 78:817–823.

35. Fagerstrom K: A comparison of psychological and pharmacological treatment in smoking cessation. *J Behav Med* 1982; 5:343–351.

36. Fagerstrom K: Effects of nicotine chewing gum and follow-up appointments in physician-based smoking cessation. *Prev Med* 1984; 13:517–527.

37. Fagerstrom KO: Measuring degree of physician dependence to tobacco smoking with reference to individualization of treatment. *Addict Behav* 1978; 3:235–241.

38. Feinleib M, Rosenberg HM, Collins JG, et al: Trends in COPD morbidity and mortality in the United States. *Am Rev Respir Dis* 1989; 140(suppl):165–177.

39. Ferson M, Edwards A, Lind A, et al: Low natural killer–cell activity and immunoglobulin levels associated with smoking in human subjects. *Int J Cancer* 1979; 23:603–609.

40. Finlea JF, Hasselblad V, Riggan WB, et al: Cigarette smoking and hemagglutination inhibition response to influenza after natural disease and immunization. *Am Rev Respir Dis* 1979; 104:368–376.

41. Fiore MC, Novotny TE, Pierce JP, et al: Trends in cigarette smoking in the United States: The changing influence of gender and race. *JAMA* 1989; 261:49–55.

42. Fiore MC, Smith SS, Jorenby DE, et al: The effectiveness of the nicotine patch in smoking cessation: A meta-anlysis. *JAMA* 1994; 271:1940–1947.

43. Fletcher CM, Peto R, Tinker C, et al: *The Natural History of Chronic Bronchitis and Emphysema. An Eight-Year Study of Early Chronic Obstructive Lung Disease in Working Men in London.* New York, Oxford University Press, 1976.

44. Food and Drug Administration: Smoking deterrent drug products for over-the-counter human use. *Fed Register* 1982; 47:490–500.

45. Fortmann SP, Killen JD, Telch MJ, et al: Minimal contact treatment for smoking cessation: A placebo-controlled trial of nicotine polacrilex and self-directed relapse prevention: Initial results of the Stanford Stop Smoking Project. *JAMA* 1988; 260:1575–1580.

46. Gadek JE, Fells GA, Crystal RG: Cigarette smoking induces functional antiprotease deficiency in the lower respiratory tract of humans. *Science* 1979; 206:1315–1316.

47. Gadek JE, Fells GA, Zimmerman RL, et al: Antielastases of the human alveolar structures: Implications of the protease-antiprotease theory of emphysema. *J Clin Invest* 1981; 68:889–898.

48. Galdston M, Levytska V, Schwartz MS, et al: Ceruloplasmin. Increased serum concentration and impaired antioxidant activity in cigarette smokers, and ability to prevent suppression of elastase inhibitory capacity of alpha1-proteinase inhibitor. *Am Rev Respir Dis* 1984; 129:258–263.

49. Glynn TJ: Relative effectiveness of physician-initiated smoking cessation programs. *Cancer Bull* 1988; 40:359–364.

50. Glynn TJ, Manley MW: *How to Help Your Patients Stop Smoking: A National Cancer Institute Manual for Physicians.* Bethesda, Md, Department of Health and Human Services, Public Health Service, National Institutes of Health, National Cancer Institute, Division of Cancer Prevention and Control, Smoking, Tobacco, and Cancer Program, NIH Publication No 89-3064, 1989.

51. Gold MS, Redmond DE Jr, Kleber HD: Clonidine in opiate withdrawal. *Lancet* 1978; 1:929–930.

52. Gritz ER, Jarvik ME: Pharmacological aids for the cessation of smoking; in Steinfeld J, Griffiths W, Ball K, et al (eds): *Health Consequences, Education, Cessation Activities, and Governmental Action*, vol 2, *Proceedings of the Third World Conference on Smoking and Health.* Washington, DC, DHEW Publication No (NIH) 77-1413, 1975, pp 575–591.

53. Hammond EC: Evidence on the effects of giving up cigarette smoking. *Am J Public Health* 1965; 55:682–691.

54. Hammond EC, Garfinkel L: Smoking habits of men and women. *J Natl Cancer Inst* 1961; 27:419–442.

55. Harris JO, Olsen GN, Castle JR, et al: Comparison of proteolytic enzyme activity in pulmonary alveolar macrophages and blood leukocytes in smokers and nonsmokers. *Am Rev Respir Dis* 1975; 111:579–586.

56. Hawthorne VM, Fry JS: Smoking and health: The association between smoking behavior, total mortality, and cardiorespiratory disease in west central Scotland. *J Epidemiol Community Health* 1978; 32:260–266.

57. *Healthy People 2000 Review 1994.* Washington, DC, US Department of Health and Human Services Publication No (PHS) 95-1256-1, 1995.

58. Heiskell CL, Miller JN, Aldrich HJ, et al: Smoking and serologic abnormalities. *JAMA* 1962; 181:88–91.

59. Higgenbottam T, Feyeraband C, Clark TJH: Cigarette smoking in asthma. *Br J Dis Chest* 1980; 74:279–284.

60. Higgenbottam T, Shipley MJ, Clark TJH, et al: Lung function and symptoms of cigarette smokers related to tar yield and number of cigarettes smoked. *Lancet* 1980; 1:409–412.

61. Higgins MW, Enright PL, Kronmal RA, et al: Smoking and lung function in elderly men and women: The Cardiovascular Health Study. *JAMA* 1993; 269:2741–2748.

62. Hjalmarson A: Effect of nicotine chewing gum in smoking cessation. *JAMA* 1984; 252:2835–2838.

63. Hogg JC, Wright JL, Wiggs BR, et al: Lung structure and function in cigarette smokers. *Thorax* 1994; 49:47–53–47–58.

64. Holt PG: Immune and inflammatory function in cigarette smokers. *Thorax* 1987; 42:241–249.

65. Hughes JR: Problems of nicotine gum, in Ockene JK (ed): *The Pharmacologic Treatment of Tobacco Dependence; Proceedings of the World Conference.* Cambridge, Mass, Institute for the Study of Smoking Behavior and Policy, 1986, pp 141–147.

66. Hughes JR, Gust SW, Keenan RM, et al: Nicotine vs placebo gum in general medical practice. *JAMA* 1989; 261:1300–1305.

67. Hunt WA, Barnett LW, Branch LG: Relapse rates in addiction programs. *J Clin Psychol* 1971; 27:455–456.

68. Jaffe JH: Drug addiction and drug abuse, in Gilman AG, Goodman LS, Rall TW, et al (eds): *Goodman and Gilman's The Pharmacologic Basis of Therapeutics*, ed 7. New York, MacMillan, 1985, pp 532–581.

69. Jamrozik K, Fowler G, Vessey M, et al: Placebo controlled trial of nicotine chewing gum in general practice. *BMJ* 1984; 289:794–797.

70. Jarvis MJ: Nasal nicotine solution: Its potential in smoking cessation and as a research tool, in Ockene JK (ed): *The Pharmacologic Treatment of Tobacco Dependence: Proceedings of the World Congress.* Cambridge, Mass, Institute for the Study of Smoking Behavior and Policy, 1986, pp 167–173.

71. Kark JD, Lebiush M, Rannon L: Cigarette smoking as a risk factor for epidemic A(H1N1) influenza in young men. *N Engl J Med* 1982; 307:1042–1046.

72. Kottke TE, Battista RN, DeFriese GH, et al: Attributes of successful smoking cessation interventions in medical practice—a meta-analysis of 39 controlled trials. *JAMA* 1988; 259:2882–2889.

73. Lam W, Sze PC, Sacks HS, et al: Meta-analysis of randomized controlled trials of nicotine chewing gum. *Lancet* 1987; 2:27–29.

74. MacKenzie JS, MacKenzie IH, Holt PG: The effects of cigarette smoking on susceptibility to epidemic influenza and on serological response to live attenuated and killed subunit influenza vaccines. *J Hygiene* 1976; 77:409–417.

75. Malcolm RE, Sillett RW, Turner M, et al: The use of nicotine chewing gum as an aid to stopping smoking. *Psychopharmacology* 1980; 70:295–296.

76. McSharry C, Banham SW, Lych PP, et al: Antibody measurements in extrinsic allergic alveolitis. *Eur J Respir Dis* 1984; 65:259–265.

77. Morgan DC, Smyth JT, Lister RW, et al: Chest symptoms and farmer's lung: A community survey. *Br J Med* 1975; 30:259–265.

78. Nielsen H: A quantitative and qualitative study of blood monocytes in smokers. *Eur J Respir Dis* 1985; 66:327–332.

79. Niewoihner DE, Kleinerman J, Rice DB: Pathologic changes in the peripheral airways of young cigarette smokers. *N Engl J Med* 1974; 291:755–758.

80. Ockene JK: Physician-delivered interventions for smoking cessation: Strategies for increasing effectiveness. *Prev Med* 1987; 16:723–737.

81. Ockene JK: Smoking intervention: The expanding role of the physician. *Am J Public Health* 1987; 77:782–783.

82. O'Connor GT, Sparrow D, Weiss ST: The role of allergy and nonspecific airway hyperresponsiveness in the pathogenesis of chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1989; 140:225–252.

83. Orleans CT: Understanding and promoting smoking cessation: Overview and guidelines for physician intervention. *Annu Rev Med* 1985; 36:51–61.

84. Pederson LL: Compliance with physician advice to quit smoking: A review of the literature. *Prev Med* 1982; 11:71–84.

85. Pierce JP, Fiore MC, Novotny TE, et al: Trends in cigarette smoking in the United States: Educational differences are increasing. *JAMA* 1989; 261:56–60.

86. Pierce JP, Fiore MC, Novotny TE, et al: Trends in cigarette smoking in the United States: Projections to the year 2000. *JAMA* 1989; 261:61–65.

87. Richmond R, Webster I: Evaluation of general practitioners use of a smoking intervention programme. *Int J Epidemiol* 1985; 14:396–401.

88. Rogot E, Murray JL: Smoking and causes of death among U.S. veterans: 16 years of observation. *Public Health Rep* 1980; 95:213–222.

89. Rokaw SN, Detels R, Coulson AH, et al: The UCLA population studies of chronic obstructive respiratory disease 3. Comparison of pulmonary function in three communities exposed to photochemical oxidants, multiple primary pollutants, or minimal pollutants. *Chest* 1980; 78:252–262.

90. Russell MAH: Cigarette dependence: II. Doctor's role in management. *BMJ* 1971; 2:393–395.

91. Russell MAH, Jarvis MJ, Sutherland G, et al: Nicotine replacement in smoking cessation: Absorption of nicotine vapor from smoke-free cigarettes. *JAMA* 1987; 257:3262–3265.

92. Russell MAH, Merriman R, Stapleton J, et al: Effect of nicotine chewing gum as an adjunct to general practitioners advice against smoking. *BMJ* 1983; 287:1782–1785.

93. Russell MAH, Wilson C, Taylor C, et al: Effect of general practitioners advice against smoking. *BMJ* 1979; 2:231–235.

94. Saetta M, Ghezzo H, Kim B, et al: Loss of alveolar attachments in smokers: A morphometric correlation of lung function impairment. *Am Rev Respir Dis* 1985; 132:894–900.

95. Schenker MB, Samet JM, Spiezer FE: Effect of cigarette tar content and smoking habits on respiratory symptoms in women. *Am Rev Respir Dis* 1982; 125:684–690.

96. Schwartz JL: *Review and Evaluation of Smoking Cessation Methods: The United States and Canada, 1978–1985.* Philadelphia, US Department of Health and Human Services, Public Health Service, National Institutes of Health, National Cancer Institute, Division of Cancer Prevention and Control, NIH Publication No 87-2940, 1987.

97. Seeley JE, Zuskin E, Bouhyus A: Cigarette smoking: Objective evidence for lung damage in teenagers. *Science* 1971; 172:741–743.

98. Shahar E, Folsom AR, Melnick SL, et al: Dietary n-3 polyunsaturated fatty acids and smoking-related chronic obstructive pulmonary disease. *N Engl J Med* 1994; 331:228–233.

99. Sharp DS, Rodriguez BL, Shahar E, et al: Fish consumption may limit the damage of smoking on the lung. *Am J Respir Crit Care Med* 1994; 150:983–987.

100. Sherin K: Smoking cessation: The physician's role. *Postgrad Med* 1982; 71:99–106.

101. Sherrill DL, Holberg CJ, Enright PL, et al: Longitudinal analysis of the effects of smoking onset and cessation on pulmonary function. *Am J Respir Crit Care Med* 1994; 149:591–597.

102. Silagy C, Mant D, Fowler G, et al: The effectiveness of nicotine replacement therapies in smoking cessation. *Online J Curr Clin Trials* 1994; Document 113.

103. Snider GL: Chronic obstructive pulmonary disease: A definition and implication of structural determinants of airflow obstruction for epidemiology. *Am Rev Respir Dis* 1989; 140(suppl):3–8.

104. Speizer FE, Tager IB: Epidemiology of chronic mucus hypersecretion and obstructive airways disease. *Epidemiol Rev* 1979; 1:124–142.

105. Tager I, Tishler PV, Rosner B, et al: Studies of the familial aggregation of chronic bronchitis and obstructive airways disease. *Int J Epidemiol* 1978; 7:55–62.

106. Tager IB, Segal MR, Speizer FE, et al: The natural history of forced expiratory volumes—effect of cigarette smoking and respiratory symptoms. *Am Rev Respir Dis* 1988; 138:837–838.

107. Tang JL, Law M, Wald N: How effective is nicotine replacement therapy in helping people to stop smoking? *BMJ* 1994; 308:21–26.

108. *Reducing the Health Consequences of Smoking: 25 Years of Progress—A Report of the Surgeon General.* Rockville, Md, US Department of Health and Human Services, Public Health Service, DHHS Publication No (CDC) 89-8411, 1989.

109. *Smoking and Health. A Report of the Surgeon General.* Washington, DC, Office of the Assistant Secretary for Health, Office on Smoking and Health, US Department of Health, Education, and Welfare Publication No (PHS) 79-50066, 1979.

110. *Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service.* Washington, DC, US Department of Health, Education, and Welfare, Centers for Disease Control, PHS Publication No 1103, 1964.

111. *The Health Benefits of Smoking Cessation. (A Report of the Surgeon General.)* Washington, DC, US Department of Health and Human Services, DHHS Publication No (CDC) 90-8416, 1990.

112. *The Health Consequences of Involuntary Smoking: A Report of the Surgeon General.* Rockville, Md, Centers for Disease Control, US Department of Health and Human Services Publication No (CDC) 87-8398, 1986.

113. *The Health Consequences of Smoking: Chronic Obstructive Lung Disease. A Report of the Surgeon General.* Rockville, Md, Office on Smoking and Health, US Department of Health and Human Services Publication No (PHS) 84-50205, 1984.

114. *The Health Consequences of Smoking: Nicotine Addiction. A Report of the Surgeon General.* Washington, DC, US Department of Health and Human Services Office of Smoking and Health, DHSS Publication No (CDC) 88-8406, 1988.

115. *The National Health Interview Survey Design, 1973–84, and Procedures, 1975–83,* Hyattsville, Md, National Center for

Health Statistics, US Department of Health and Human Services Publication No (PHS) 85-1320, 1985.

116. *The Statistical Design of the Health Household Interview Survey by Staff of the U.S. National Health Survey and the Bureau of the Census.* Hyattsville, Md, National Center for Health Statistics, US Department of Health, Education and Welfare Publication No (PHS) 583-4-A2, 1958.

117. Thurlbeck WM: Chronic airflow obstruction in lung disease, in Bennington JL (ed): *Major Problems in Pathology,* vol 5. Philadelphia, WB Saunders, 1976, pp 235–287.

118. *Tobacco Situation and Outlook Report.* Washington, DC, US Department of Agriculture, Economic Research Service, National Economics Division, Publication No TS-199, June 1987.

119. Walinder J, Balldin J, Bokstrom K, et al: Clonidine in morphine withdrawal. *Drug Alcohol Depend* 1981; 8:345–348.

120. Walter S, Nancy NR, Collier CR: Changes in the forced expiratory spirogram in young male smokers. *Am Rev Respir Dis* 1979; 119:717–724.

121. Warr GA, Martin RR: Immune receptors of human alveolar macrophages: Comparison between cigarette smokers and nonsmokers. *J Reticular Dis Soc* 1977; 22:181–187.

122. Wechsler H, Levine S, Idelson RK, et al: The physician's role in health promotion—a survey of primary care practitioners. *N Engl J Med* 1983; 308:97–100.

123. Wells KB, Lewis CE, Leuke B, et al: The practices of general and subspecialty internists in counseling about smoking and exercise. *Am J Public Health* 1986; 6:1009–1013.

124. Wetzler HP, Cruess DF: Self-reported physical health practices and health care utilization: Findings from the National Health Interview Survey. *Am J Public Health* 1985; 75:1329–1330.

125. Wilson D, Wood G, Johnston N, et al: Randomized clinical trial of supportive follow-up for cigarette smoking in a family practice. *Can Med J* 1982; 126:127.

126. Wilson DM, Taylor W, Gilbert R, et al: A randomized trial of a family physician intervention for smoking cessation. *JAMA* 1988; 260:1570–1574.

127. Woolf CR, Zamel N: The respiratory effects of regular cigarette smoking in women. A five-year prospective study. *Chest* 1980; 78:707–713.

128. World Health Organization: *Sixth Review of Psychoactive Substances for Intervention Control.* Geneva, World Health Organization, 1982.

129. Wright JL: Small airway disease: Structure and function, in Hensley MJ, Saunders NA (eds): *Clinical Epidemiology of Chronic Obstructive Pulmonary Disease.* New York, Marcel Dekker, 1989, p 55.

130. Wyatt RJ, Bridges RB, Halatek DG: Complement levels in cigarette smokers: Elevations of serum concentration of C5, C9, and C1-inhibitor. *J Clin Lab Immunol* 1981; 6:131–135.

131. Xu X, Li B, Wang L: Gender differences in smoking effects on adult pulmonary function. *Eur Respir J* 1994; 7:477–483.