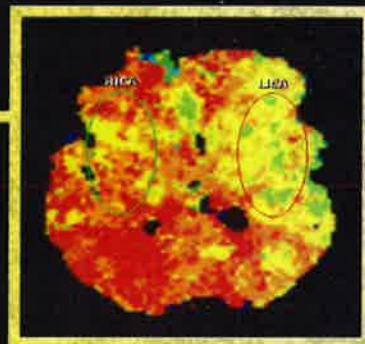


# STROKE

A PRACTICAL APPROACH

James D. Geyer  
Camilo R. Gomez



Wolters Kluwer | Lippincott  
Health Williams & Wilkins

# Tobacco and Stroke

ALAN BLUM AND JAMES D. GEYER

## OBJECTIVES

- What are the vascular risks of smoking?
- How should a treatment plan be designed?
- What is the role of the physician in smoking cessation?

**T**obacco smoking is one of the leading modifiable risk factors for stroke. A truly comprehensive approach to stroke prevention (both primary and secondary) must include an *effective* smoking cessation plan. The approach to the patient is not as easy as handing the patient a prescription. It demands the physician's time and effort. The results of appropriate and aggressive physician counseling cannot be overstated.

## CLINICAL APPLICATIONS

Cigarette smoking is the chief avoidable cause of death in our society. Smoking is responsible for 18% of the total deaths in the United States each year. It is one of the primary modifiable risk factors for stroke. An aggressive approach to smoking cessation is an indispensable component of any stroke treatment or prevention strategy.

Tobacco smoking leads to a dependence on nicotine that is distinguishable from other forms of drug dependence. In such a dependency, the drug is needed to maintain an optimal state of well-being. Nicotine, the habituating constituent of tobacco, meets the criteria for addiction because a typical withdrawal syndrome occurs after smoking cessation.

Although cigarette smoking in adults declined from 42% to 27% in the United States between 1964 and 1992, 28% of men and 24% of women continue to use tobacco daily. Approximately 1.3 million persons per year stop smoking. However, each day approximately 3,000 individuals start smoking. Almost half of all smokers start smoking before 18 years of age. Although 80% of those who smoke say that they would like to stop, only 20% of those who try actually succeed in stopping permanently. The likelihood of success increases with the number of attempts, and those with a college education are twice as likely to break the habit as less-educated smokers.

At present, virtually all life insurance companies now offer significant discounts to persons who do not smoke. Actuarial data leave little doubt that the average life expectancy of a 32-year-old

man who smokes cigarettes is 72 years versus 79 years for someone who does not smoke. The quality of life for those diminished years is frequently complicated by myriad disorders including stroke and chronic obstructive pulmonary disease (COPD).

## HEALTH RISKS ASSOCIATED WITH SMOKING

### Cancer

Forty percent of all cancer deaths are attributable to cigarette smoking. Besides lung cancer, smoking is the major cause of cancer of the larynx, oral cavity, and esophagus (see Table 6.1). It is also a contributory factor in cancer of the pancreas, bladder, kidney, stomach, and uterine cervix. Recent studies have implicated smoking in leukemia, colon cancer, Graves disease, depression, and renal disease in persons with diabetes mellitus. A dose-response relationship exists between smoking and all these diseases. As described in Chapter 8, cancers increase the overall risk of stroke.

### Cardiovascular Disease

#### Heart Disease

Nicotine raises systolic blood pressure, heart rate, and cardiac output and causes vasoconstriction. The relationship between cerebral vasoconstriction and anoxia and the intake of carbon monoxide resulting from cigarette smoking could explain the 50% increase in automobile accidents in smokers. The symptoms associated with carbon monoxide intoxication can be a problem, especially for persons with an already compromised coronary or cerebral circulation. Carbon monoxide has an affinity for hemoglobin that is 245 times stronger than that of oxygen. Thus carbon monoxide reduces oxygen delivery to the myocardium and has a decidedly negative inotropic effect. Carboxyhemoglobin also lowers the threshold for ventricular fibrillation and could help explain the higher incidence of sudden death in those who smoke.

### Diseases or Conditions Influenced by Cigarette Smoking

Cardiovascular	Cancer	Respiratory	Other
Coronary heart disease	Lung	COPD (emphysema)	Infertility
Stroke	Larynx	Bronchitis	Impotence
Subarachnoid hemorrhage	Esophagus	Pneumonia	Osteoporosis
Aortic aneurysm	Pancreas	Asthma	Premature wrinkling
Hypertension	Uterine	Otitis media	Peptic ulcer
Peripheral vascular disease	Cervix		Alzheimer disease
	Ovary		Graves disease
	Colon		Insomnia
	Bladder		Depression
	Kidney		
	Breast		
	Brain		
	Blood (leukemia)		

COPD, chronic obstructive pulmonary disease.

The risk of myocardial infarction is proportional to the number of cigarettes smoked. The trend toward the use of filtered cigarettes does not appear to have reduced the risk of coronary heart disease. Theoretically, filters on cigarettes reduce the amount of tar (the condensate of tobacco smoke that comprises over 3,000 compounds, including more than 40 carcinogens), but they may increase the amount of carbon monoxide, thus contributing to the increased mortality from coronary heart disease. Persons who smoke cigarettes containing low amounts of nicotine have the same degree of risk of myocardial infarction as those who smoke cigarettes containing larger amounts. Smokers of these low-dose cigarettes still have three times the risk of myocardial infarction as nonsmokers. The good news is that the risk of sudden death decreases immediately on stopping, and within a few years of stopping, the risk of myocardial infarction decreases to a level similar to that in people who have never smoked, even in heavy smokers who have a positive family history of coronary heart disease.

Three-fourths of myocardial infarctions in women younger than 50 years have been attributed to smoking. The risk of myocardial infarction increases progressively to as much as 20-fold in persons smoking 35 or more cigarettes per day. There is no safe level of smoking. Women who smoke and use oral contraceptives have a risk of heart attack that is ten times greater than that of women who do neither.

Silent ischemia probably accounts for most of all cardiac ischemic events. Patients with coronary heart disease who smoke have three times as many episodes of silent ischemia as nonsmokers, and the duration of each is 12 times longer. Frequent episodes of myocardial ischemia, even though asymptomatic, damage the heart. Because smoking also increases platelet adhesiveness and lowers high-density lipoprotein cholesterol, the association with a higher incidence of myocardial infarction is no surprise.

Benefits from stopping smoking can be demonstrated at all ages. No decrease in benefits is seen as one gets older, so it is still worthwhile for someone older than 65 to break the addiction. This benefit can be demonstrated in the cerebral as well as the coronary circulation. Older individuals who stop smoking have signifi-

cantly higher cerebral perfusion levels than those who continue to smoke. Even those who have smoked for 30 to 40 years have improved cerebral circulation within a relatively short time after stopping smoking.

### Stroke

Cigarette smoking is one of the most important modifiable risk factors for stroke. The incidence of stroke in smokers is 50% higher than in nonsmokers (40% higher in men and 60% higher in women). The risk of stroke increases in proportion to the amount of smoking; it is twice as great in those who smoke more than 40 cigarettes per day than in those smoking fewer than 10 cigarettes per day.

When compared with women who have never smoked, the risk of stroke increases 2.2-fold in women smoking 1 to 14 cigarettes per day and 3.7-fold in women smoking 25 or more cigarettes daily. Bonita et al. found a threefold increase in the risk of stroke in smokers in comparison to nonsmokers. Cigarette smokers who are also hypertensive have a 20-fold increased risk of stroke.

Sclerosis of the carotid arteries is directly proportional to the amount of smoke exposure. Smoking increases the risk of ischemic heart disease and cerebrovascular disease regardless of the level of serum cholesterol. Jee et al. found that a low cholesterol level did not protect against smoking-related arteriosclerotic cardiovascular disease in patients in South Korea, where the prevalence of smoking is among the highest in the world at 72% of men.

The risk of stroke declines rapidly after cessation of smoking, and after 5 years, is at the level of nonsmokers, which emphasizes that it is never too late to quit no matter how long one has been smoking.

### Subarachnoid Hemorrhage

Habitual smoking also increases the risk of subarachnoid hemorrhage, with an increased relative risk of 3.9 times for men and 3.7 times for women. The risk increases to 22 times that of nonsmokers in women who both smoke and use oral contraceptives.



## Other Diseases and Conditions

### Diabetes Mellitus

The risk of diabetes increases with the number of cigarettes smoked. People smoking more than one pack per day have 1.5 times the risk for diabetes as those who smoke 1 to 14 cigarettes. Albuminuria as a sign of early renal damage and retinopathy is greater in patients with type 1 diabetes mellitus who smoke and can be shown to improve significantly if the person stops smoking.

### Depression

Smokers are more likely to experience major depression than nonsmokers are, and the incidence increases steadily with the number of cigarettes smoked. Conversely, it is estimated that one third of smokers are depressed and self-medicate with tobacco. Kendler et al. suggested that this increased risk could be due to genes that predispose to both conditions.

### Insomnia

Smokers are more likely than nonsmokers to have insomnia, and as a consequence, to feel tired in the morning. Smokers will be more restless during sleep and more likely to awaken tired and then smoke during the day for the stimulation. However, smokers also consume more alcohol and caffeine than nonsmokers do, which will contribute to insomnia.

## PHYSICIAN INVOLVEMENT IN ENDING THE TOBACCO PANDEMIC

A remarkable grassroots antismoking movement that arose in the 1970s has had a major impact on the goal of achieving a smoke-free society and has impelled traditional health organizations such as the American Cancer Society and the American Medical Association to become more outspoken. The first medical organization to develop proven strategies for the clinic, classroom, and community aimed at counteracting tobacco use and promotion was Doctors Ought to Care (DOC), founded in 1977 by a family physician at the University of Miami. During its 25-year existence, DOC was supported by the American Academy of Family Physicians. Tar Wars,

an annual antismoking poster contest for schoolchildren, is a DOC offshoot that has been adopted by numerous state and local family practice organizations.

The *five foci of tobacco control*, the accepted term for this emerging field of public health, included the following: increases in cigarette excise taxes, bans on tobacco advertising and promotion, restrictions on teenagers' access to tobacco products, pharmacologic and behavioral smoking cessation strategies, and legislation to prohibit smoking in public areas and the workplace.

Other tobacco control efforts include regulatory warning labels on cigarette packages, divestment of tobacco stocks, enforcement of laws against cigarette smuggling, an end to tobacco subsidies, and rejection of donations and research grants from the tobacco industry. The American Cancer Society's most visible antismoking effort is an annual day-long event in November, The Great American Smokeout, during which people who smoke are encouraged to quit and use a nicotine-replacement product instead.

## SMOKING CESSATION PROGRAMS

Ideally, the validity of the abstinence rate for a method of smoking cessation should depend on the performance of a controlled, double-blind study with follow-up of at least 6 months duration of all subjects who entered the study. Few published outcome evaluations meet such criteria. Before the introduction of nicotine-replacement products in 1984, smoking cessation techniques in the United States consisted of a hodgepodge of unproven but much-touted chemical remedies, diets, aversive stimuli, hypnotherapy, self-help manuals, special filters, acupuncture, and expensive behavior modification clinics or seminars. Many of these methods are quite costly, but having to pay a high price may well be related to the alleged success of a given method.

When the U.S. Food and Drug Administration (FDA) approved the use of nicotine-containing chewing gum (Nicorette) for smoking cessation, the product gained immediate popularity (see Table 6.2 for a listing of pharmacologic therapies for smoking cessation). However, although the gum was approved for the use as an adjunct to a comprehensive program of behavior modification, most physicians offered few instructions and little follow-up. Moreover, some patients became dependent on the gum and perpetuated their

**Pharmacologic Therapies Used in Smoking Cessation**

Agent	Duration of Therapy	Side Effects	Contraindications
Patch	10 wk	Headache, insomnia,	Recent MI, arrhythmias, TMJ symptoms
Gum	3 mo	site reactions, jaw pain	
Lozenge	3 mo		
Nasal spray	3–6 mo		
Inhaler	3 mo		
Bupropion	3–6 m	Headache, dry mouth, tremor, behavioral changes	Eating disorders, seizures, bipolar disorders
Varenicline	3 mo + 3 mo to enhance cessation	Suicide risk, nausea, insomnia, headache	

MI, myocardial infarction; TMJ, temporomandibular joint.

smoking by using the gum at times and in places where they were not permitted to smoke. The high success rates reported in clinical trials may be attributed in part to the fact that the research was conducted in clinics that specialize in the treatment of smoking cessation. This difference may further explain why placebo groups in some studies fared better than the intervention groups of most other methods.

In 1992, all smoking cessation methods began to take a back seat to use of the transdermal nicotine patch. The theory behind the patch is that controlled, continuous release of nicotine provides partial replacement of the nicotine from smoking, thereby reducing the craving and preventing withdrawal. As with users of nicotine gum, relapse is a problem in patients who use the patch. The most significant problem in clinical practice appears to be a combination of the patient's heightened expectations for the patch (based on word-of-mouth testimonials and advertising in the mass media) and the physician's overeager acquiescence in prescribing it.

Pharmaceutical company claims notwithstanding, smoking is not simply an addiction to nicotine. Social and psychological factors also play determining roles. Promotions for various pharmacological agents for smoking cessation wrongly reinforce the notion that smoking is primarily a medical problem with a simple, prescribable, nonindividualized solution. When a patient requests a drug to help stop smoking, the physician, although not wishing to dash expectations, should emphasize that a drug is an adjunct, not the single solution.

The updated clinical practice guideline *Treating Tobacco Use and Dependence*, published by the U.S. Department of Health and Human Services (DHHS), has added bupropion sustained release (SR) (Zyban), nicotine inhaler (Nicotrol), and nicotine nasal spray to its list of first-line medications that patients should be encouraged to use. All three are available exclusively by prescription. Nicotine gum and transdermal nicotine, the only two recommended medications in the original guideline in 1996, remain on the list. The gum is now available exclusively as an over-the-counter medication in either 2 or 4 mg strengths; the latter is recommended for highly dependent smokers. Clonidine, in doses of 0.1 to 0.75 mg per day delivered either transdermally or orally, is recommended as a second-line agent to treat tobacco dependence. Because of a paucity of data, no other pharmacotherapies are recommended as a second-line agent to treat tobacco dependence. Apart from bupropion SR (which is contraindicated in patients who are at risk for seizures or who have had a previous diagnosis of bulimia or anorexia nervosa), no other antidepressant agent has been documented as effective for smoking cessation or approved by the FDA for this use. Neither benzodiazepines nor  $\beta$ -adrenergic blocking agents have been found to have a beneficial effect in smoking cessation.

Two large multicenter studies have found bupropion SR to be efficacious in doubling long-term abstinence rates when compared with placebo. One advantage of this medication is that it can be instituted a week or two before complete cessation is attempted, unlike nicotine-replacement products, which are based on providing gradually reduced amounts of nicotine without the other toxic components of cigarette smoke. A course of treatment with bupropion SR ranges from 7 to 12 weeks. Treatment with nicotine-replacement products ranges from 6 weeks to 6 months.

Combination therapy appears to be a promising, albeit doubly expensive, approach. A 9-week study combining bupropion SR with transdermal nicotine found much greater efficacy than with

either medication alone. Overall, the guideline found insufficient evidence to recommend combination therapy as a general treatment strategy.

Varenicline (Chantix) is a selective  $\alpha_4\text{-}\beta_2$  neuronal nicotinic acetylcholine receptor partial agonist that was recently approved for smoking cessation therapy. This drug is felt to help decrease the cravings associated with quitting and the withdrawal from nicotine. While this drug may be of benefit, it must be used in concert with behavior modification. Furthermore, concerns have been raised about potential adverse side effects.

The introduction of bupropion SR and newer forms of nicotine-replacement products, backed by intensive advertising campaigns in both medical journals and the mass media, will doubtless stimulate physicians to take a more informed and personal role in smoking cessation. Such active involvement can be extremely crucial in and of itself. In the 1970s, at a time when efforts by physicians to discourage smoking were much less widespread and accepted, Russell et al. (1979) found that just 1 to 2 minutes of simple but unequivocal advice to the patient to stop smoking resulted in a cessation rate of over 5% measured at 1 year as opposed to only 0.3% in the control group. Moreover, when strong advice is given at the time of recovery from a heart attack or other smoking-related disease (combined with a brochure and a promise of follow-up), over 60% stop smoking and stay off cigarettes (measured at 3 years)—more than twice the rate of those who receive less definitive advice. Although most family physicians routinely ask their patients about smoking and advise them to stop smoking, relatively few provide more than advice and actually counsel patients with state-of-the-art techniques.

## ■ OBSTACLES TO CHANGE

Unfortunately, the tobacco pandemic cannot be addressed as though it were a static issue whereby sufficient public health education results in a significant change in societal behavior. Rather, smoking is a dynamic issue, with cigarette advertisers—whose livelihoods depend on maintaining more than 50 million users of tobacco, including 1.25 million teenagers who take up smoking each year—constantly adapting to the challenges brought by the antismoking movement.

Thus, smoking cessation programs for individual patients cannot truly succeed in the long run in the absence of both workplace smoking bans and multimedia counteradvertising strategies that weaken the influence of the tobacco industry and reinforce physician's office-based efforts.

A variety of factors may inhibit physician involvement in smoking cessation, such as a perceived or real lack of time, lack of reimbursement by third-party payers for such counseling, and lack of peer group reinforcement in a technologically oriented, tertiary care-centered, highly intellectualized health care system. Nonetheless, physicians might well find that their increased involvement in efforts to promote smoking cessation among patients, regardless of the minimal enhancement in revenue, becomes a practice-building factor as word spreads about the physicians who care.

## ■ OFFICE-BASED STRATEGIES

Physicians can do a great deal to become better teachers about smoking, in lieu of relegating this role to ancillary personnel, a smoking cessation clinic, or a pamphlet. The physician can develop



an innovative strategy beginning outside the office. A bus bench, billboard, or sign in the parking lot with a straightforward or humorous health promotion message helps establish a thought-provoking and favorable image. In the waiting area, removal of ashtrays and placement of signs noting that "In the interest of comfort, safety, and health, this is a smoke-free environment" further reinforce the message.

Magazines with cigarette advertisements ought not to appear in the physician's office in the absence of prominent stickers or rubber-stamped messages calling patients' attention to the deceptive, absurd nature of such ads. Although responsibility for the office-based smoking cessation strategy should rest with the physician, it is invaluable to include all office staff as positive reinforcement for patients. Labeling each chart with a small "No Smoking" sticker to indicate the need for such reinforcement may be helpful, although care must be taken to avoid stigmatizing the patient as a smoker. One would do well to reconsider using potentially alienating words such as "smoker" or even "quitter."

The key to successful smoking cessation efforts is a positive approach. A discussion about the diseases caused by smoking and the harmful constituents of tobacco smoke is essential—indeed, the physician must not shrink from imparting, through graphic posters, pamphlets, slides, and other audiovisual aids, the gruesome consequences of smoking—but the benefits of not smoking must be emphasized at least as strongly. Moreover, solely educating patients about the facts of smoking in a single office visit is unlikely to result in behavioral change.

In contrast, the physician can, through the use of creative analogies related to the patient's occupation, hobbies, or romantic interest, succeed in changing the patient's entire attitude toward smoking. By noting that cyanide is the substance used in the gas chamber in executions, that formaldehyde is used to preserve cadavers, or that ammonia is the predominant smell in urine, however, the physician is likely to cause the patient to think about smoking a bit differently. No one wishes to have "urine breath." Similarly, it does little good to talk about carcinogens in tobacco in an age when the public believes that "everything causes cancer." Sadly, the concept of relative risk is poorly developed in our society because all too many people who smoke choose to think their million-to-one odds of winning the state lottery are better than their one-in-seven chance of actually getting lung cancer.

### Metaphors that Motivate

A revocabularization on the part of the physician is essential for making progress in office-based smoking cessation. Instead of "pack-year history," a more relevant measure is the "inhalation count." A pack-a-day smoker will breathe in upward of 1 million doses of cyanide, ammonia, carcinogens, and carbon monoxide in fewer than 15 years, not including the inhalation of other people's smoke (calculated at 10 inhalations per cigarette, 20 cigarettes per pack). Another way to emphasize the enormous amount smoked is to state the financial cost: a pack-a-day cigarette buyer will spend in excess of \$1,000 per year (calculated at \$3 a pack). That is well over \$10,000 in a decade that could be put into a savings account. Patients can look forward to the joyful feeling of finding a \$50 bill every 2 weeks—which is what they would indeed find if the money is not spent on cigarettes.

So although patient education in general and smoking cessation in particular depend on the knowledge that both the physician

and the patient have about the deleterious aspects of adverse health behavior, the cognitive component alone is insufficient. Both the physician and the patient must be motivated to succeed. Three keys to office-based smoking cessation are to personalize, individualize, and demythologize.

The physician can learn to personalize approaches to smoking cessation by carefully screening the pamphlets and other audiovisual aids available in the office. (Ideally, physicians should consider producing their own.) It is essential to scrutinize all such materials as one would with a new drug or medical device. Personally handing a brochure to the patient while pointing out and underlining certain passages or illustrations will provide an important reinforcing message. The pamphlets, posters, and signs should be changed or otherwise updated every few weeks or months.

In any event, such dialogue must be practiced over and over again like any medical procedure and individualized to the patient. (Remember that no two construction workers, teenagers, or executives are alike.) The counseling should be designed to call attention not only to the inevitable risks of smoking cigarettes but also to the chemically adulterated tobacco product itself, its inflated price, and the ubiquitous and ludicrous way in which the person's brand is promoted. In effect, the physician can shift the focus away from a resistant or guilt-ridden smoker and onto the product.

### COMMON MYTHS

The most important myth surrounding smoking is that it relieves stress. This myth can be debunked by pointing out that the stress that is relieved is what resulted from being dependent on cigarettes—the essence of addiction. At the same time, it is important to point out that deep breathing in and of itself has a relaxing effect.

The second and saddest myth is that smoking keeps weight off. Aside from pointing to all the obese women who smoke and attempting to correct the misapprehension that being overweight is a greater health risk than smoking is, one can point out that by damaging the taste buds and other digestive tract cells, smoking does inhibit appetite, but it also results in more sedentary behavior through loss of lung capacity and cardiovascular fitness. One need not gain weight on stopping smoking if one will relearn to enjoy walking and running as much as one relearns the taste of food. By no means will all persons who stop smoking gain weight. Even among those who do, the average weight gain is 6 pounds for men and 8 pounds for women. Although smokers may weigh slightly less than nonsmokers, when they stop smoking they simply return to an average weight. Moreover, the slightly lower weight in many who continue to smoke is associated with a higher-risk body fat distribution.

From the physician's standpoint, perhaps the biggest myth that has been encouraged in the medical literature is that the patient must be "ready to quit." Setting a "quit date," the sine qua non of the smoking cessation literature, may rationalize the continuation of an adverse health practice and may strengthen denial. In other words, it is helpful to remind patients that they can stop now. If they do not stop, it does not mean that you will not treat them next time, but it is important to give encouragement and not reinforce excuses. Most authors do believe that a quit date targeted only 1 week or a few weeks into the future is useful for a motivated patient, for whom denial is less of a problem. Its purpose is to let

the individual build up resolve or to permit a gradual reduction in daily cigarette consumption. Giving patients a few written reminders is very helpful (such as lists of the advantages and disadvantages of smoking, the rewards for not smoking and the penalties for lighting up, the situations and environmental influences that encourage one to smoke, and the myths of smoking and smoking cessation). A prescription with a no-smoking symbol signed by the physician and included with the other prescriptions is a thoughtful gesture. The physician should not advise switching to a low-tar cigarette, or changing to a pipe or cigar.

## ■ PRACTICAL RECOMMENDATIONS

A tailored approach to smoking cessation must be developed for each patient who smokes. The approach to a teenage woman should be quite different from the approach to an older man. Counseling is the cornerstone of treatment but medication can play an ancillary role as described in this chapter. The patient should be counseled about the role of the medications—helping to begin the transition to a smoke-free life, although drugs are not a magical treatment with immediate and complete results.

An excellent motivational Web site for all patients who use tobacco products is [www.whyquit.com](http://www.whyquit.com). Patients can also obtain self-help materials from the National Quitline, sponsored by the U.S. Department of Health and Human Services, by dialing 1-800-QUITNOW (1-800-332-8615 for hearing impaired) or online at [www.smokefree.gov](http://www.smokefree.gov).

## SELECTED REFERENCES

- Anda RF, Williamson DF, Escobedo LG, et al. Depression and the dynamics of smoking: A national perspective. *JAMA* 1990;264:1541–1545.
- Blum A. Preventing tobacco-related cancers. In: DeVita VT, Hellman S, Rosenberg SA, eds. *Cancer: Principles and practices of oncology*. 5th ed. Philadelphia, PA: Lippincott; 1997:545–557.
- Blum A. The role of the health professional in ending the tobacco pandemic: clinic, classroom, and community. *J Natl Cancer Inst* 1992;12:37–43.
- Blum AM, Solberg EJ. The tobacco pandemic. In: Mengel MB, Holleman WL, Fields SA, eds. *Fundamentals of clinical practice*. 2nd ed. New York: Plenum; 2002:671–687.
- Cofta-Woerpel L, Wright KL, Wetter DW. Smoking cessation 3: Multicomponent interventions. *Behav Med* 2007;32:135–149.
- Fiore MC, Bailey WC, Cohen SJ, et al. Treating tobacco use and dependence: Clinical practice guideline. Rockville, MD: US Department of Health and Human Services, Public Health Service; 2000.
- Klesges RC, Johnson KC, Somes G. Verenicline for smoking cessation: definite promise, but no panacea. *JAMA* 2006;296:94–95.
- Rakel RE, Blum A. Nicotine addiction. In: Rakel RE, ed. *Textbook of Family Practice*. 6th ed. Philadelphia, PA: WB Saunders; 2002:1523–1538.
- US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. *The Health Consequences of Smoking: A Report of the Surgeon General*. Washington, DC: US Government Printing Office, 2004.
- US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health promotion, Office on Smoking and Health. *The Health Consequences of Involuntary Exposure to Tobacco Smoke. A Report of the Surgeon General*. Washington, DC: US Government Printing Office, 2006.
- US Department of Health and Human Services, National Institutes of Health, National Institute on Alcohol Abuse and Alcoholism. Alcohol and tobacco. In: *Alcohol Alert*. 2007; 71.
- US Department of Health and Human Services, Public Health Service, Centers for Disease Control, Office on Smoking and Health. *The Health Consequences of Smoking: Cardiovascular Disease. A Report of the Surgeon General*. Washington, DC: US Government Printing Office, 1982; DHHS Publication No. (PHS) 82-50179.
- Wannanmehee SG, Shaper AG, Whincup PH, et al. Smoking cessation and the risk of stroke in middle-aged men. *JAMA* 1995;274:155–160.
- Wolf PA, D'Agostino RB, Kannel WB, et al. Cigarette smoking as a risk factor for stroke: The Framingham Study. *JAMA* 1988;259:1025–1029.