



EDITORIAL ARTICLE

SMOKING CESSATION: HOW TO MAKE IT A REAL OPTION?

By

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Cigarette smoking is a major preventable cause of disease worldwide. In 1912, Adler first suggested that inhalation of cigarette smoke might be a cause of lung cancer. Since then, knowledge about the adverse health effects of smoking has accumulated. The important causes of mortality are atherosclerotic vascular disease, cancer, and chronic obstructive pulmonary disease (COPD). Smoking also can contribute to other diseases, eg, histiocytosis X, respiratory bronchiolitis, obstructive sleep apnea, idiopathic pneumothorax, low birth weight, and perinatal mortality.

The causal link between smoking and increased morbidity and mortality is now firmly established (USDHHS, 2004). Importantly, there is strong evidence that by stopping smoking, however late in life, smokers can reduce their risk of premature death (Doll et al., 2004) and can improve their current and future health (Royal College of Physician, 2000).

Approximately 4000 chemical compounds have been identified in cigarette smoke, of which over 40 are known to cause cancer. There are three important components of cigarette smoke:

Nicotine is the drug in cigarette which is addictive (it is what keeps smokers smoking), but it does not cause cancer and has, at most, a small effect on

risk of cardiovascular disease.

Tar is the name given to all the other chemicals in the smoke particles, and it is these that are linked to cancer, lung disease, heart disease and the other diseases caused by smoking.

Carbon monoxide is a gas inhaled by smokers from cigarettes; it is linked to heart disease and has adverse effects in pregnancy.

The smoking cessation field has undergone rapid growth over the last few years and there is now an extensive group of health care professionals from many different backgrounds who have become involved in this area. Smoking cessation is an important issue and there is ever increasing pressure to treat more smokers more effectively.

Smoking cessation guidelines recommend that all health professionals should check on the smoking status of their clients at least once a year and advise smoker to stop (West et al., 2000). This brief advice from a health professional should be delivered opportunistically during routine consultations to smokers whether or not they are seeking help with stopping smoking.

Smoking may begin as a voluntary habit, but eventually it becomes an addiction. Health professionals can contribute powerfully to

motivate their patients to attempt and sustain cessation by offering encouragement, advice, and assistance. For patients who are not yet ready to attempt quitting, such advice can move them further toward that point. A willingness to help and to provide assistance is very important in motivating cigarette smokers in attempting to quit. The reassurance that a knowledgeable health professional stands ready to offer guidance and support is immensely beneficial to individuals addicted to nicotine. Understanding the benefits and limitations of the available medications provides an important foundation for such a successful smoking cessation program.

- Assess smoking history, level of addiction, and the health status of the patient. After the assessment, intervene with education and advice.
- Educate patients about the benefits of smoking cessation and the cessation process. Provide a description of the expected withdrawal syndrome. Continue with a discussion of the possible cessation methods, which include physician counseling, nicotine replacement, antidepressant medications, behavioral training, and group therapy.
 - Professional group therapy or counseling achieves a 60-100% initial cessation rate and a 1-year cessation rate of approximately 20%.
 - Hypnosis and acupuncture are popular programs that might encourage renewed attempts by people who failed other techniques, but they are no different from placebo.
 - Verify successful cessation by measuring cotinine or carbon monoxide levels.
- A cigarette delivers 1.2-2.9 mg of nicotine, and the typical one pack-per-day smoker absorbs 20-40 mg of nicotine each day, raising the plasma concentrations to between 23-35 ng/mL. Nicotine produces increased expression of brain nicotine receptors, changes in regional brain glucose metabolism, the

release of catecholamine's tolerance, and physiologic dependence. Nicotine addiction results from positive reinforcement (with the administration of nicotine) and withdrawal symptoms that start within a few hours of the last cigarette. The time to first cigarette and total cigarettes per day are the two strongest predictors of nicotine addiction. The nicotine dependence and nicotine withdrawal could be treated by the following (Henningfield, 2005):

- Other forms of nicotine delivery
- Drugs that selectively target one or more of the underlying mechanisms
- Behavioral treatments, acupuncture, and other therapies
- Nicotine replacement therapy
 - Nicotine replacement therapy works by making it easier to abstain from tobacco by partially replacing the nicotine previously obtained from tobacco. At least 3 mechanisms by which NRT could be effective include (1) reducing either general withdrawal symptoms, thus allowing people to learn without cigarettes; (2) reducing the reinforcing effects of tobacco-delivered nicotine, (3) providing some psychological effects on mood and attention states.
 - Nicotine replacement medications should not be viewed as stand-alone medications that make people stop smoking. Reassurance and guidance from health professionals can be critical to achieve and sustain abstinence.
- Transdermal nicotine patches
 - Nicotine patches deliver nicotine through the skin at a relatively steady rate. Currently, 4 patch formulations are on the market; they vary widely in their design, pharmacokinetics, and duration of wear (ie, 24- and 16-h wear). For some products,

progressively lower doses can be used to provide weaning over a period of several weeks or longer to enable gradual adjustment to lower nicotine levels and ultimately to a nicotine-free state. Smokers who use more than 10 cigarettes per day should use the 21-mg/day patch for the first 6 weeks, move to the 14-mg/day strength for 2 weeks, and then use the 7-mg dose for the final 2 weeks. Nicotine patches have higher compliance than other NRT products but may not adequately protect against craving provoked by smoking-related stimuli. For breakthrough cravings not adequately controlled by transdermal nicotine alone, acute therapies may be added.

- A study tested the efficacy of nicotine patches in combination with behavioral therapy for the treatment of adolescent spit tobacco addiction. The usual care group's spit tobacco cessation rate was 11.4%; placebo patch, 25.0%; and active patch, 17.3%. The cessation rates for active and placebo patch were not significantly different, proving that behavioral intervention is twice as successful and that nicotine patch did not offer additional improvement (Stotts, 2003).

- Nicotine gum

- First available in the 1980s, nicotine polacrilex (nicotine gum) is available without a prescription. The gum is available in doses: 2 mg and 4 mg, delivering approximately 1 mg and 2 mg of nicotine. Users are instructed to use a piece of gum every 1-2 hours for the first 6 weeks, then to reduce use to one piece every 2-4 hours for 3 weeks, and one piece every 4-8 hours for 3 weeks. In highly dependent smokers, the 4-mg gum is superior to the 2-mg gum. Since about 50% of the nicotine in gum is absorbed, a fixed schedule of 10 pieces per day, a smoker receives about 10 mg or 20 mg of nicotine per day using the 2-mg or 4-mg gum, respectively.

- The slow absorption of nicotine from gum doses does not produce the extremely high levels of nicotine. Acidic beverages interfere with buccal absorption of nicotine; patients should avoid acidic beverages (eg, soda, coffee) for 15 minutes before and during chewing gum. Nicotine gum chewing may cause jaw soreness; therefore, the smoker should chew the gum to release nicotine, and then move the gum between the cheek and gum for a minute or so. Gum can also cause a mild burning sensation in the mouth and throat, which may be undesirable.

- **Lozenge:** Available in 2- and 4-mg formulations since 2002, nicotine from the lozenge is absorbed slowly through the buccal mucosa. The lozenge should not be chewed, and the amount of nicotine absorbed per lozenge is somewhat higher than that delivered by gum.

- **Inhaler:**

- Currently marketed as a prescription medication in the United States, the inhaler consists of a mouthpiece and a plastic cartridge containing nicotine. When the inhaler is "puffed," nicotine is drawn into the mouth of the smoker and satisfies the behavioral aspects of smoking, namely, the hand-to-mouth ritual.

- Each inhaler cartridge contains 10 mg nicotine, of which 4 mg can be delivered and 2 mg are absorbed. Nicotine is not delivered to the bronchi or lungs, but rather it is deposited and absorbed in the mouth, like nicotine gum. Most people use between 6 and 16 cartridges a day, the recommended duration of treatment is 3 months, after which patients may be weaned by gradual reduction over the following 6-12 weeks.

- **Nasal spray:** Marketed as a prescription medication, the nasal spray delivers nicotine more rapidly than other NRTs and delivers acute craving relief. The multidose bottle with a pump delivers 0.5 mg of nicotine per 50- μ L

squirt. Each dose consists of 2 squirts, one to each nostril. The dose of nasal spray should be individualized for each patient based on the patient's level of nicotine dependence. Most patients are started with 1 or 2 doses per hour, which may be increased up to the maximum of 40 doses per day.

- **Sublingual tablet:** A small nicotine tablet has been developed. The product is designed to be held under the tongue, where the nicotine in the tablet is absorbed sublingually. The levels of nicotine obtained by use of the 2-mg tablet and 2-mg nicotine gum are similar. It is recommended that smokers use the product for at least 12 weeks, after that the number of tablets used is gradually tapered.
- **Bupropion (Zyban):**
 - Bupropion acts by alleviating some of the symptoms of nicotine withdrawal, which includes depression. One clinical trial demonstrated that highly nicotine-dependent smokers who receive bupropion are more likely to experience a decrease in depressive symptoms during active treatment. Like NRT products, bupropion has been endorsed by the US Clinical Practice Guideline as a first-line therapy (Fiore, 2000).
 - It has a number of actions that are thought to contribute to its ability to help smokers quit. These include inhibition of neuronal re-uptake of dopamine and noradrenalin, non-competitive inhibition of the nicotinic acetylcholine receptor and effects on serotonin re-uptake (Richmond and Zwar, 2003). From a clinical perspective, it helps smokers by reducing the severity of withdrawal symptoms, including the desire or urge to smoke, thereby making the quit attempt easier and success more likely.
 - Combining the results of over twenty studies shows that compared to placebo, bupropion approximately doubles the

chances of remaining abstinent for a year (Hughes et al., 2004). Currently, there is not enough evidence to suggest that combining bupropion with NRT is better than using bupropion alone.

- Bupropion has been shown to approximately double rates of cessation compared with placebo, and the medication is equally effective for men and women. It has also been shown that bupropion combined with nicotine replacement medications may increase cessation rates relative to bupropion alone. The recommended and maximum dose of bupropion is 300 mg/day, given as 150 mg twice daily. Dry mouth and insomnia are the most common adverse events associated with use. A very small risk of seizure exists, which can be reduced by not prescribing the medication to persons with a history of seizure or a predisposition toward seizure.
- Varenicline (Chantix) is a partial agonist selective for alpha4, beta2 nicotinic acetylcholine receptors. Action is thought to result from activity at a nicotinic receptor subtype, where its binding produces agonist activity while simultaneously preventing nicotine binding. Agonistic activity is significantly lower than nicotine. Also elicits moderate affinity for 5-HT3 receptors. Maximum plasma concentrations occur within 3-4 h after oral administration. Following regular dosing, steady state reached within 4 d. Initiate 1 wk before date chosen to stop smoking.

Days 1-3:	0.5	mg	PO	qd	pc
Days 4-7:	0.5	mg	PO	bid	pc
Day 8 to end of treatment: 1 mg PO bid pc					
Continue treatment for 12 w; take pc with full glass of water					
- In two randomized controlled trials to compare the effect of varenicline versus sustained-release bupropion and placebo for smoking cessation, Varenicline was significantly more efficacious than bupropion SR at the end of 12

weeks of drug treatment and at 24 weeks follow-up (David., et al 2006 and Douglas., et al 2006)

- **Other medications:** Besides NRT products and bupropion, nortriptyline and clonidine are endorsed by the US Clinical Practice Guideline as second-line therapies.
- **Nortriptyline:** As a second-line therapy, studies have demonstrated the potential efficacy of nortriptyline for smoking cessation in smokers without history of major depression. Nortriptyline in combination with transdermal nicotine was also shown to enhance the cessation rates above levels seen with transdermal nicotine alone. The tricyclic antidepressant doxepin has also been shown in a small human study to improve cessation rates. The most commonly encountered side effects associated with nortriptyline include fast heart rate, blurred vision, urinary retention, dry mouth, constipation, weight gain or loss, and low blood pressure on standing.
- **Clonidine:** An alpha-2-noradrenergic agonist used to treat hypertension, clonidine has been shown to diminish symptoms of both opiate and alcohol withdrawal symptoms. In one study of heavy smokers who had failed in previous quit attempts found that those treated with clonidine had twice the rate of abstinence as those treated with placebo at the end of the 4-week treatment, and the effect persisted for the 6-month follow-up period. Although clonidine may be efficacious in the treatment of nicotine addiction, the conditions under which it is most appropriately used are not well defined. The most common side effects of clonidine are constipation, dizziness, drowsiness, dryness of mouth, and unusual tiredness or weakness.

Diet: Patients who quit smoking tend to gain weight; therefore, encourage patients to follow a low-calorie diet and exercise regimen during and after cessation.

Further patient Care: Long-term follow-up is recommended because individuals who successfully quit smoking are at high risk for relapse. The health care deliverer should make provisions for support, measurement of progress, and a mechanism to deal with relapse. For motivated patients who have failed smoking cessation, consider referral to an expert for the treatment of a relapse.

Prevention: More than 90% of first-time use of tobacco occurs before high school graduation. Because the average age at first use is 14.5 years, smoking prevention must start early. Approximately 40% of teenagers who smoke eventually become addicted to nicotine. Social attitudes and policies toward smoking can have a major impact on smoking behavior. Physician associations, public health organizations, and consumer groups should lobby for the following:

- Restriction of access to tobacco products for minors
- Restriction of smoking in public places
- Restriction of advertisements
- Increased prices through taxation
- Increased awareness about the harmful health effects of smoking

Medical and Legal Pitfalls:

- Relapse during the first year after achieving smoking cessation occurs in approximately 50% of patients, irrespective of therapeutic regimen.
- The changes in the central nervous system, eg, neurone genetics, cell structure, and cell function, induced by smoking do not reverse with pharmacological therapy.
- Highly nicotine-dependent smokers may require an initial therapy for 6 months or longer. Some individuals may require low-dose maintenance therapy for years.
- Controlled studies are required to help guide management of relapses and prolonged tapering periods. Immediately restarting nicotine medication

might be helpful if a relapse occurs.

- According to Gro Harlem Brundtland, the director of the World Health Organization 2006, "A tax increase is the single most important intervention by governments to curb tobacco consumption." A 10% tax increase worldwide could inspire 42 million people to stop smoking and would prevent approximately 10 million premature deaths.

Special Concerns:

- Smoking and weight gain
 - Concerns about weight gain following smoking cessation are a well-known barrier. Smokers with weight concerns are more likely to relapse. Smoking for weight control reasons has been associated with being female, smoking more cigarettes per day, lower motivation to quit smoking, body image dissatisfaction, and higher Fagerström (Dale, 1998).
 - Interventions designed specifically for weight-concerned smokers such as on-site exercise program improved smoking abstinence rates and delayed weight gain. Cognitive-behavioral therapy to reduce weight concerns improved smoking cessation success and reduced weight gain.
 - NRT can have an additional, positive effect on weight gain as another significant barrier to smoking cessation. NRTs can attenuate post-cessation weight gain, although upon termination of nicotine replacement use, weight continues to increase to the level of ex-smokers who used placebo (Allen, 2005).

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