Why Won't Our Patients Stop Smoking?

The power of nicotine addiction

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Health risks related to tobacco use have been well established for >50 years, with diseases including lung cancer, other malignancies, and cardiovascular diseases linked to smoking and causing early mortality in current and former smokers (1–4). Yet cigarette smoking remains highly prevalent in both the developing and developed worlds (5). Smoking uptake typically occurs in the teenage years, when risk-taking behavior is the norm and peer pressure is a powerful predictor of behavior. The prevalence of chronic diseases, such as hypertension, diabetes, respiratory disease, arthritis, and cardiovascular disease, is low in teenagers and young adults but increases into middle-age and older adulthood (6–9). Conversely, in developed countries like the U.S., smoking prevalence peaks in young adults and decreases as the population ages, because people stop smoking or die (with current smokers dying at a faster rate than former or never smokers) (10). Most of the adult population in the developed world who are current smokers grew up in an environment where the risks of smoking were well established and well known to the public. So why do our adult patients, many of whom have diseases either related to tobacco smoking or complicated by smoking, find it difficult to quit?

This question has been a vexing one to both clinicians and public health practitioners since the adverse affects of smoking became known to us. There are divergent truths. On one hand, in most developed countries, the majority of people who have ever smoked in their lifetime have successfully quit (11). On the other hand, many people with chronic diseases that are clearly worsened by cigarette smoking are unable to quit. So why can some patients quit quickly and easily while other patients smoke right up to their premature death?

The answers to this question are perhaps as varied as our patient population, with a variety of different factors that are important. Tobacco use has many features of a complex chronic illness such as diabetes. For example, in diabetes, the incidence, severity, and outcomes of disease is related to a variety of genetic, environmental, and lifestyle factors (i.e., parental history of disease, exposure to infections, comorbid disease, obesity, etc.). In cigarette smoking, there is evidence that genetic factors, early life exposures, and environmental factors (i.e., living in an area that restricts smoking or heavily taxes cigarettes) influences smoking uptake and cessation (10,12).

One reality is that not all of our patients, even in the face of debilitating disease, want to stop smoking. While a large proportion of current smokers would like to stop smoking, particularly if they have developed a disease due to or worsened by smoking, there remains a significant minority of smokers who have no desire to quit (10,13). The reasons for this are not completely clear and may be, in large part, related to the addictive nature of smoking that will be discussed below. Other potential explanations are that these patients perceive that, at least for them, the "benefits" of smoking outweigh the "risks" (14). Some of these patients are completely aware of the problems related to smoking but have decided that they are so unhappy if not smoking that they decide to continue. In other cases, people may have developed a terminal disease, such as metastatic lung cancer, and the "comfort" of continued smoking outweighs, at least for them, any benefits of stopping.

Among the 60–80% of our adult smoking population who would like to quit, what are the factors that keep them smoking? In the U.S. in 2006, the median prevalence of current daily smokers who quit for at least 1 day was 58.6% (10). Long-term abstinence rates, however, are poor. Among smokers who attempt to quit on their own, 80% relapse within 1 month and 97% relapse within 6 months (15). Smokers typically need four or more quit attempts before they achieve long-term abstinence (16). Even in recent trials using highly motivated patients, validated relapse rates at 12 months ranged from 77% in the active treatment group to 92% in the placebo group (17,18). These and other studies provide strong evidence that the factors that keep smokers smoking are very powerful and that cigarettes are, in fact, addictive (19).

What are the components of this addiction that has many features of a chronic illness? The addiction itself has physiological, psychological, and behavioral components that will be addressed below. Central to addiction to cigarettes is the role of nicotine, the pharmacologic agent that is critical in maintaining smoking. While burning cigarettes emit over 4,000 different agents (2), the evidence that nicotine is the main culprit in maintaining addiction is strong. For example, cigarettes from which nicotine has been removed or those with ultra-low levels of nicotine have never been widely accepted by the smoking public, whereas chewing tobacco and snuff, both of which deliver large amounts of nicotine, are widely used (20). Nicotine meets criteria for drug dependency in that it promotes compulsive use, has psychoactive effects, and reinforces its own use (19,21).

Physiological dependence on nicotine is thought to be related to its action on nicotinic acetylcholine receptors in the brain (20). Activation of these receptors results in the release of neurotransmitters—most importantly, dopamine, but also norepinephrine, acetylcholine, β-en-

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dorphin, and others (22). This then leads to some of the "positive" effects of smoking, such as pleasure, arousal, and the reduction of anxiety and tension. Repeated exposure to nicotine over time, such as occurs in habitual smokers, results in both a desensitization of these receptors to nicotine and an increase in the number of receptors (23). During periods of abstinence, such as while sleeping, it is thought that these desensitized receptors may recover and elicit symptoms of "withdrawal." These acute symptoms include irritability, depressed mood, anxiety, difficulty concentrating, insomnia, and craving for tobacco, among others (24). Thus, the acute changes that occur when a person stops smoking suddenly provide a powerful reinforcement to start smoking again.

The behavioral component of addiction to cigarettes is a powerful reinforcer of the physiological component of this addiction. People smoke in certain situations, such as while driving, while drinking a cup of coffee in the morning, or while out at a bar with friends. They also may smoke in response to certain cues, such as feeling stressed or annoyed (20). In addition, the actual act of inhaling smoke from a cigarette is highly ritualized and repeated hundreds of times per day and thousands of times per year. It is thought that this conditioning may be a major factor in relapses that occur in patients months to years after they stop smoking—an extremely stressful situation and nicotine receptors that have returned to their normal state of sensitization may be enough for the patient to start smoking again.

The psychological component of smoking addiction may be one of the most challenging to deal with (25). People who advance beyond the experimentation stage of smoking may have additional reasons for doing so, such as undiagnosed psychiatric disease, a desire to lose or maintain weight, or other factors (26). The threshold for both initiating and maintain smoking may be different in at-risk individuals. In addition, there may be genetic or early life exposure factors that predispose people to becoming and staying smokers, although this field is controversial (27,28).

While nicotine is the primary substance responsible for addiction in smokers, tobacco smoke also contains thousands of other chemicals that may contribute to this addiction. Some of these, such as acetaldehyde, result from tobacco industry manipulation of sugar levels in tobacco, with the end result being enhancement of nicotine's physiological properties (29,30).

In conclusion, there are a variety of factors that contribute to why our patients are unable to stop smoking. These range from some people believing that the benefits of smoking outweigh the risks, to the very powerful physiological, behavioral, and psychological factors that keep people smoking. Strategies to help our patients stop smoking must address all of these factors.

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