

SMOKING AND YOUR HEALTH

How to Quit

(AND WHY YOU SHOULD)

BY NOW, IT IS FIRMLY ESTABLISHED THAT SMOKING IS A MAJOR RISK FACTOR FOR SERIOUS CHRONIC ILLNESSES, INCLUDING CARDIOVASCULAR DISEASE AND CANCER. IN THE EARLY YEARS OF THE EPIDEMIC, MANY PEOPLE WITH HIV/AIDS ASSUMED THERE WAS LITTLE POINT IN WORRYING ABOUT CHRONIC PROGRESSIVE DISEASES, SINCE THEY PROBABLY WOULD NOT LIVE LONG ENOUGH FOR THESE TO DEVELOP.

BUT THIS CHANGED WITH THE ADVENT OF HAART IN THE MID-1990S. WITH LIFE EXPECTANCY DRAMATICALLY EXTENDED BY COMBINATION ANTIRETROVIRAL THERAPY, HIV POSITIVE PEOPLE NOW NEED TO PAY ATTENTION TO THE SAME HEALTH ISSUES THAT AFFECT HIV NEGATIVE PEOPLE AS THEY AGE.

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Studies suggest that HIV positive people are more likely to smoke than HIV negative individuals. Research has yielded conflicting data about the effects of smoking on HIV disease progression, but most studies have shown some harm, and certainly none has demonstrated any benefit. Further, concerns about elevated lipid levels and other complications related to antiretroviral therapy have underlined the importance of changing modifiable risk factors such as smoking, diet, and exercise.

Quitting smoking is not easy, but it can be accomplished. Strategies to assist smoking cessation have evolved over the years as the urgency of the problem has become increasingly evident. A growing body of research shows that people who receive counseling, support, nicotine replacement therapy, and antismoking medications are more likely to quit than those who rely on willpower alone.

No matter how long a person has smoked, quitting can make a big difference in terms of health benefits, some of which begin within days of stopping. According to the U.S. Surgeon General, “Smoking cessation represents the single most important step that smokers can take to enhance the length and quality of their lives”—and this holds true for HIV positive and HIV negative smokers alike.

Smoking as a Public Health Issue

The detrimental effects of smoking are well known, but worth a review. According to the U.S. Centers for Disease Control and Prevention (CDC), cigarette smoking is the nation’s leading preventable cause of death, contributing to both cardiovascular disease and cancer. Smoking causes an estimated 440,000 deaths annually, or about one out of every five; about 10% of these are due to second-hand smoke. Worldwide, the World Health Organization (WHO) estimates that five million deaths per year are attributable to smoking. On average, smok-

ers have a lifespan about 15 years shorter than that of nonsmokers.

Although smoking is much less socially acceptable today than it was half a century ago, the CDC estimates that about 45 million people in the U.S. still smoke, or about 21% of the total population. American women smoke less than men (18% vs 24%), but the gap has narrowed dramatically since the 1960s. Worldwide, the WHO estimates that approximately 1.3 billion people smoke.

Smoking rates vary among racial/ethnic groups in the U.S., being highest among Native Americans (32%). Whites and blacks are about equally likely to smoke (22%), while rates are lower among Latinos (16%) and Asians (13%). Several studies suggest that gay/lesbian/bisexual/transgender people smoke more than the population as a whole; in one survey, the rate of current smoking among gay men was 27%.

Health Hazards of Smoking

Cigarette smoking affects every system of the body. Some harmful effects are caused by nicotine itself, while others are due to the carbon monoxide, tars, and other toxins in cigarette smoke. Many detrimental effects of smoking are related to reduced oxygen levels in body tissues. Smoking also leads to oxidative damage, elevated levels of destructive free radicals, and chronic inflammation.

The immediate effects of smoking include increased blood pressure and elevated heart rate. Over time, breathing capacity diminishes as smoking damages the alveoli (tiny air sacs) in the lungs. But the most serious outcomes of smoking develop over the long term, including cancer, chronic lung disease, and cardiovascular disease.

LUNG CANCER

The disease most commonly associated with tobacco smoking is lung cancer, caused by the tars and other carcinogens in the smoke. In the U.S.,

lung cancer is the leading cause of cancer-related mortality, accounting for about 25% of all cancer deaths. Lung cancer kills more women each year than breast cancer. The high mortality rate is due in part to the fact that lung cancer is difficult to detect early and hard to treat. Smokers are much more likely than nonsmokers to develop lung cancer, with a 13-fold higher risk for women and a 24-fold higher risk for men.

Studies indicate that people with HIV have a higher risk of lung cancer than the general population, and the rate has risen since the advent of HAART. In a study conducted early in the HAART era, British researchers found that HIV positive people were about eight times more likely to develop lung cancer. In a more recent analysis of the large Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study, HIV positive current smokers were three times more likely to die of cancer than nonsmokers, mostly due to lung cancer.

Researchers from Johns Hopkins University reported last year that, overall, HIV positive people (smokers and nonsmokers together) were more than twice as likely as HIV negative individuals to develop lung cancer; however, 85% of those who got lung cancer were smokers. In another recent study, Gregory Kirk and colleagues, also from Johns Hopkins, looked at lung cancer rates among participants in the AIDS Link to the Intravenous Experience (ALIVE) study, a cohort of more than 2,000 HIV positive and at-risk injection drug users in Baltimore. After adjusting for potential confounding factors, including smoking, HIV positive participants had more than three times the risk of death due to lung cancer. While being HIV positive was associated with lung cancer independent of smoking, all but one of the individuals who developed lung cancer were smokers.

Although lung cancer is not known to have an infectious cause like some AIDS-defining malignancies,

a recent meta-analysis by Andrew Grulich and colleagues at the National Centre in HIV Epidemiology and Clinical Research, University of New South Wales, showed that it occurs more often in both HIV positive people and organ transplant recipients who take immunosuppressive drugs, indicating that immune dysfunction plays a role.

CERVICAL AND ANAL CANCER

Women who smoke have a significantly higher risk of cervical cancer, caused by human papillomavirus (HPV), as demonstrated by several studies in HIV negative women. One analysis of 1,812 women, for example, found that those who smoked a pack or more per day had four times the risk of precancerous cell changes (intraepithelial neoplasia) or cervical cancer; even former smokers still had a three-fold increase in risk.

Women with HIV are already at greater risk of infection with cancer-causing strains of HPV, so smoking may be particularly detrimental. Among nearly 1,800 HIV positive and 500 at-risk participants in the Women's Interagency Health Study (WIHS), women with HIV were three times more likely than HIV negative women to be infected with HPV at baseline, more likely to acquire new HPV infection during follow-up, and more likely to have high-risk HPV types 16 and 18. Among the HIV positive women, the risk was significantly higher for smokers. For this reason, HIV positive women who smoke should receive regular Pap smears and HPV tests in order to catch neoplasia at an early, more treatable stage. (See "Women and HIV: Human Papillomavirus" in the Summer 2007 issue of *BETA* for more on HPV prevention and treatment.)

Less is known about whether smoking increases the risk of anal cancer, but since it is caused by the same HPV strains (primarily 16 and 18), it is likely that a similar mechanism is involved. HIV positive men who have sex with men have an elevated risk of anal cancer regardless of

smoking status, but smoking ups the odds.

A study in the pre-HAART era by Joel Palefsky of the University of California at San Francisco and colleagues showed that among 129 HIV positive gay and bisexual men with advanced immune suppression, about 40% had abnormal anal cell changes, and smoking was one of the risk factors. More recently, German researchers studying 267 HIV positive gay and bisexual men found that smokers were significantly more likely than nonsmokers to have high-risk HPV types 16 and 18 (82% vs 69%), had higher HPV-16 and HPV-18 viral loads, and more often had severe intraepithelial neoplasia (18% vs 4%). Experts increasingly recommend that men at risk for anal cancer—which includes HIV positive gay or bisexual men who smoke—should receive regular anal Pap smears.

OTHER CANCERS

Although the increased risk is less dramatic than for lung cancer, smokers are also more likely to develop other types of malignancies, including cancers of the throat, esophagus, stomach, pancreas, liver, kidneys, and bladder, and certain types of leukemia. Evidence is mixed regarding breast and colon cancer, but some studies have demonstrated a link with smoking. People who use chewing tobacco or snuff have an elevated rate of mouth cancers, indicating that tobacco itself—in addition to the tars and other carcinogens in smoke—plays a role in cancer development.

In an analysis of more than 7,300 participants in the Swiss HIV Cohort, people with HIV were three times more likely to develop lip, mouth, and throat cancer, as well as lung cancer; no cases of these cancers were observed in nonsmokers.

LUNG DISEASES AND INFECTIONS

Smoking is the main risk factor for chronic obstructive pulmonary disease (COPD), a degenerative disease that is typically diagnosed in older people

and which encompasses emphysema and chronic bronchitis. Emphysema refers to a loss of elasticity in the walls supporting the bronchioles and alveoli, which can lead to shortness of breath, use of supplemental oxygen, and eventually death.

A study by Philip Diaz of Ohio State University and colleagues, published in 2000, showed that HIV positive individuals were much more likely to develop emphysema than HIV negative people who smoked the same amount (15% vs 2%). Among HIV positive individuals who smoked one pack a day for 12 years or more, 37% developed emphysema, compared with none of the HIV negative participants with similar smoking habits. The average age of HIV positive people in this study was 34 years, indicating an unusually early onset of emphysema.

Cigarette smoking also increases the risk of various types of respiratory infections, which is particularly relevant for HIV positive people with low CD4 cell counts. Research early in the HIV/AIDS epidemic found that smokers were up to three times more likely than nonsmokers or former smokers to develop opportunistic *Pneumocystis* pneumonia (PCP), though this was not observed in all studies. It was later shown that smoking also increased the risk of non-AIDS-defining bacterial pneumonia. In the HIV Epidemiologic Research Study (HERS), which followed 885 HIV positive and 425 at-risk women in four U.S. cities, women with HIV were significantly more likely to contract community-acquired bacterial pneumonia (8.5 vs 0.7 cases 100 person-years), and among the HIV positive women, smoking doubled the risk compared with nonsmokers.

CARDIOVASCULAR DISEASE

Cardiovascular disease is the leading cause of death in the U.S., and smoking is among the major risk factors. It is estimated that smoking a pack or more per day triples the risk of heart attack for men and increases women's

risk six-fold. Smoking also doubles the risk of stroke and increases the likelihood of peripheral vascular disease and aortic aneurysm. Women over age 35 who use oral contraceptives and smoke are at increased risk for heart attack, stroke, and blood clots in the legs.

Cigarette smoking elevates heart disease risk by multiple mechanisms. It increases blood pressure and makes the blood more likely to clot, and the carbon monoxide in smoke can damage the lining of the arteries. Smoking is linked to elevated blood triglyceride levels and lower levels of high-density lipoprotein (HDL or “good”) cholesterol. Further, people who easily become short of breath due to smoking are less likely to exercise.

Along with smoking, traditional cardiovascular risk factors include male sex, older age, family history, obesity, and lack of physical activity. People with high levels of low-density lipoprotein (LDL or “bad”) cholesterol, low levels of protective HDL cholesterol, high blood pressure, and diabetes are more likely to develop coronary heart disease, in which the arteries become clogged and cannot supply enough blood to the heart muscle, potentially leading to angina (chest pain) or heart attack.

Since the advent of HAART, HIV positive people and their care providers have grown increasingly concerned about elevated cardiovascular risk associated with HIV infection and its treatment. In the D:A:D study, which includes more than 23,000 HIV positive participants, use of protease inhibitors (PIs) increased the risk of heart attack by 16% after adjusting for other risk factors. While much has been made of the small increase in cardiovascular risk associated with antiretroviral therapy, many experts emphasize that traditional risk factors play a larger role.

An analysis of the Swiss HIV Cohort found that among more than 8,000 participants, the most common cardiovascular risk factors were smok-

ing (57%), low HDL cholesterol (37%), elevated triglycerides (36%), and high blood pressure (26%). Overall, about 3% of study participants were categorized as having a high 10-year risk for coronary heart disease, while 14% were at moderate risk. When risk was recalculated assuming that all smokers quit, the percentages fell to 0.5% and 6%, respectively.

Some risk factors (such as age and family history) cannot be changed, and many people find it difficult to improve their diet and increase their activity level enough to make much difference. For most people with HIV, the benefits of HAART outweigh the increase in risk associated with antiretroviral drugs. This leaves smoking cessation as a key step toward reducing cardiovascular risk. In an editorial in the April 26, 2007, *New England Journal of Medicine*, James Stein of the University of Wisconsin School of Medicine and Public Health advised, “perhaps more effort should be spent assisting our patients with smoking cessation and the prevention of diabetes, rather than our focusing so intently on the dyslipidemic effects of antiretroviral therapy.”

PREGNANCY AND CHILDREN

Smoking by pregnant or breast-feeding women and parents of young children is particularly harmful. Nicotine passes easily through the placenta, and smoking reduces the delivery of oxygen to the developing fetus. Smoking during pregnancy increases the likelihood of miscarriage, premature delivery, and low birth-weight. Infants whose mothers smoked while pregnant or who are exposed to second-hand smoke are at higher risk of sudden infant death syndrome (SIDS), while children exposed to smoke in the home are more likely to develop asthma, upper respiratory tract infections, and middle-ear infections.

One study done in the pre-HAART era showed that HIV positive women who smoke have a greater chance of transmitting the virus to their babies.

Barbara Turner and colleagues studied HIV positive women who gave birth between 1988 and 1990, before the adoption of antiretroviral therapy to reduce the risk of perinatal transmission. Out of 901 woman-infant pairs, 31% of women who smoked transmitted HIV to their infants, compared with 22% of nonsmokers.

OTHER CONDITIONS

Cigarette smoking can also cause or exacerbate a variety of other conditions, including the following:

- oral candidiasis (thrush)
- oral hairy leukoplakia
- osteoporosis
- kidney disease
- liver fibrosis
- peptic ulcers
- cataracts and macular degeneration
- periodontitis (gum disease)
- slower wound healing
- skin wrinkling
- erectile dysfunction

Some research, especially in the pre-HAART era, showed that HIV positive men who smoked were more likely to develop two opportunistic conditions that affect the mouth: oral candidiasis, also known as thrush (a yeast infection), and oral hairy leukoplakia (a herpesvirus infection). One study found that HIV positive smokers had higher rates of these conditions than nonsmokers, even though they were not more likely to have opportunistic illnesses overall.

Studies have shown that postmenopausal women who smoke have lower bone density and a greater risk of hip fractures than those who never smoked. Though the connection is not fully understood, research suggests that HIV infection itself, as well as certain antiretroviral drugs, are associated with bone loss. Thus, the additional bone loss caused by smoking may be particularly harmful for people with HIV.

Kidney disease is more common in HIV positive than HIV negative people, especially African Americans. A study of more than 500 HIV positive patients at a Miami hospital showed that while the likelihood of kidney dysfunction was not related to HIV viral load or CD4 cell count, long-term smoking (more than 10 years) significantly increased the risk.

Some research indicates that smoking worsens liver inflammation and fibrosis (development of scar tissue) in people with chronic hepatitis B or C, possibly due to the liver's role in metabolizing nicotine and other toxins. In a study reported in the June 2006 issue of *Clinical Gastroenterology & Hepatology*, 21% of smokers with chronic hepatitis C had Metavir fibrosis scores of 3 or 4 (on a scale of 0 to 4), compared with 14% of nonsmokers. In another study, French researchers found that hepatitis C patients' risk of liver inflammation increased in proportion to daily tobacco consumption; 59% of people who never smoked, 67% of light smokers (one to 10 packs per year), and 85% of heavy smokers (more than 20 packs per year) had moderate-to-severe liver inflammation, though there was no observed relationship with fibrosis.

Since HIV positive people coinfectured with hepatitis B or C already tend to experience accelerated liver disease progression, and since certain antiretroviral drugs can cause liver toxicity (indicated by elevated liver enzymes), smoking may be particularly detrimental for such individuals.

Smoking, HIV, and HAART

Several surveys and considerable anecdotal evidence suggest that people with HIV are more likely to smoke compared with the general population. An online survey by the International Association of Physicians in AIDS Care, for example, found that more than half of respondents with HIV/AIDS were smokers—and a third had smoked for 10 or more years—

compared with 21% in the population as a whole.

The connection between cigarette smoking and HIV disease is not fully understood, but there is a growing body of evidence showing that smoking can impair immune response, contribute to disease progression, and increase the risk of death among HIV positive people.

Research looking at the effect of smoking on immune function in HIV

negative people has produced mixed results, and the link has not been extensively studied in people with HIV. In general, smokers tend to have slightly higher CD4 cell counts than nonsmokers, perhaps due to chronic inflammation and immune activation.

Before the advent of HAART, most studies did not show higher rates of disease progression or death among smokers with HIV/AIDS, since smokers and nonsmokers alike often

Benefits of Smoking Cessation Over Time

20 MINUTES

Heart rate and blood pressure drop; temperature of hands and feet increases.

8 TO 12 HOURS

Carbon monoxide level in the blood returns to normal.

24 HOURS

Heart attack and stroke risk begins to decline.

2 WEEKS TO 3 MONTHS

Circulatory and respiratory function improves; lung capacity increases.

1 TO 9 MONTHS

Coughing, shortness of breath, and risk of respiratory infection decrease as cilia, tiny hairs that help filter air in the lungs, regain normal function.

1 YEAR

Risk of coronary heart disease falls to half that of a continuing smoker.

5 TO 15 YEARS

Stroke risk decreases to that of a person who has never smoked; lung cancer risk begins to drop.

10 YEARS

Risk of death from lung cancer falls to half that of a continuing smoker; risk of other types of cancer declines.

15 YEARS

Risk of coronary heart disease falls to that of a lifelong nonsmoker; overall risk of death nearly equals that of a person who has never smoked.

(Adapted from the American Cancer Society and other sources.)

were very ill and died of AIDS-related causes at a relatively young age. British researchers recently reported the results of a systematic review of 15 published studies, mostly pre-HAART, assessing the association between tobacco smoking and HIV seroconversion or disease progression. Taken together, the research found no link between smoking and progression to AIDS, although several studies did show that smokers had a higher risk of becoming infected with HIV.

But this may have changed in the HAART era. In 2005, researchers looking at more than 800 HIV positive U.S. veterans taking combination antiretroviral therapy found that the mortality rate for smokers was twice that of nonsmokers after adjusting for other factors such as age, CD4 cell count, and viral load.

Similarly, a recent analysis involving more than 900 HIV positive women on HAART in the WIHS cohort, conducted by Joseph Feldman of the State University of New York in Brooklyn and colleagues, showed that after controlling for other factors, smokers had a 36% greater likelihood of developing an AIDS-defining condition and a 53% higher risk of dying during the five-year follow-up period. Smoking was also associated with poorer virological and immunological response to antiretroviral therapy, a higher likelihood of viral load rebound, and more frequent immunological failure (lack of CD4 cell recovery). “Some of the benefits provided by HAART are negated in cigarette smokers,” the researchers concluded.

Benefits of Quitting

The benefits of smoking cessation are clear and incontrovertible, producing immediate, short-term, and long-term health benefits.

Experts estimate that men who quit smoking at age 35 can extend their lifespan by as much as nine years, and women by as much as eight years, compared with continuing smokers. But stopping later is still beneficial: people who quit in their

late sixties can add up to four extra years to their life expectancy.

Smoking cessation improves the health even of people who have smoked heavily for decades and those who have already developed lung or heart disease. While much of the lung damage caused by smoking is irreversible, quitting can halt further deterioration. Cardiovascular injury, including atherosclerosis, improves after smoking cessation, especially if other modifiable risk factors are also addressed. Among people with coronary heart disease, the risk of heart attack and sudden cardiac death falls by 50% after quitting.

The benefits of smoking cessation among people with HIV have become increasingly clear in recent years. Researchers from the University of Texas, for example, reported in the September 2007 issue of *AIDS Patient Care and STDs* that among 95 HIV positive individuals enrolled in a smoking cessation study, longer smoke-free periods were associated with fewer HIV-related symptoms and improved quality of life. A recent French study demonstrated that quitting smoking reduced the cardiovascular risk of patients on HAART more than either lipid-lowering medications or switching to a PI-sparing antiretroviral regimen.

Besides improved health, smoking cessation has other benefits, including sharper senses of taste and smell, healthier-looking skin, whiter teeth, improved ability to engage in sports or other strenuous activities, and economic savings in terms of lower health insurance premiums and money not spent on cigarettes. As smoking becomes less socially acceptable and more places ban smoking—even private apartment buildings and outdoor locations such as parks—quitting also can have social benefits.

But most smokers don't need to be reminded of the negative consequences of smoking or the benefits of quitting, which are generally well known. Surveys have found that nearly three-quarters of smokers say

they want to stop. The question is, how?

Kicking the Habit

People derive a variety of perceived benefits from smoking, and understanding these can help determine the best way to quit. A majority of adult smokers started when they were young—usually under age 18—at a time when the immediate advantages of smoking seemed to outweigh potential future health consequences. Once a person starts smoking regularly, he or she typically becomes physically and psychologically addicted to cigarettes.

NICOTINE WITHDRAWAL

Nicotine attaches to acetylcholine receptors in the brain and alters neural signaling. One of its effects is to raise levels of the neurotransmitter dopamine, which accounts for the pleasurable feelings smoking can produce. Over time, people can develop a physical dependence on nicotine. When this happens, they may need higher amounts to produce the desired feelings, and must maintain a stable level just to avoid withdrawal symptoms. Many experts have compared the addictive potential of nicotine to that of heroin or cocaine.

Common symptoms of nicotine withdrawal include anxiety, irritability, mood swings, inability to concentrate, fatigue, insomnia, depression, headaches, dizziness, and increased appetite. People may find it easier to maintain their resolve to quit if they understand in advance what symptoms they may experience and how long these are likely to last. After smoking cessation, withdrawal symptoms typically peak after two to three days, then gradually subside over the next few weeks.

Residual nicotine and its byproducts may remain in the body for up to two weeks. Even after nicotine is eliminated, former smokers often experience cigarette cravings for several months, though these typically become less intense and less frequent over time. Nicotine cravings are typi-

Fagerström Test for Nicotine Dependence

Points for each answer appear in parentheses.

1. How soon after you wake up do you smoke your first cigarette?

- Within 5 minutes (3)
- Within 5 to 30 minutes (2)
- After 31 to 60 minutes (1)
- After 60 minutes (0)

2. Do you find it difficult to refrain from smoking in places where it is prohibited?

- Yes (1)
- No (0)

3. Which cigarette would you most hate to give up?

- The first one in the morning (1)
- Any other one (0)

4. How many cigarettes do you smoke per day?

- 31 or more (3)
- 21 to 30 (2)
- 11 to 20 (1)
- 10 or fewer (0)

5. Do you smoke more frequently during the first hours after waking up than during the rest of the day?

- Yes (1)
- No (0)

6. Do you still smoke if you are so sick that you are in bed most of the day?

- Yes (1)
- No (0)

SCORING:

- 0 to 3: Low nicotine dependence
- 4 to 5: Moderate dependence
- 6 to 7: High dependence
- 8 to 10: Very high dependence

difficult to manage. Most smokers find smoking pleasurable (at least initially), and it becomes a part of their daily routine and even their self-identity. Many smokers find having a cigarette to be relaxing, even as the nicotine boosts alertness and improves concentration. Others smoke primarily to deal with negative feelings such as anxiety, stress, or boredom.

Very often, smoking is associated with triggers such as drinking alcohol or coffee and socializing with other smokers. It may be helpful to keep a journal to identify which emotions and activities arouse the urge to light up. Recognizing such triggers is an important part of the quitting process, and learning to avoid them or deal with them without smoking is key to preventing relapse.

For people who have been at it a long time, smoking often becomes entwined with daily activities such as reading the newspaper, driving, or waiting for the bus. Often, it becomes an integral part of certain social activities. Thus, smoking cessation involves changing habits and essentially retraining oneself to be a nonsmoker. This may involve altering daily routines, finding substitute activities, avoiding places and events associated with smoking, and minimizing contact with smoking friends, family, and coworkers (at least for a while). This has become easier as fewer people smoke and more public places ban smoking, to the point where smoking is often a furtive, solitary activity rather than an indispensable aspect of socializing.

Beyond avoiding situations that arouse the urge to smoke, it is also important to learn new coping skills to deal with stress, anxiety, and other negative feelings. Many people find that exercise and relaxation techniques (such as deep breathing or meditation) help them get through stressful periods without lighting up, and this is supported by clinical trials.

How to Quit

Preparation, both practical and mental, is an important part of a success-

cally brief—10 minutes or less—and will usually dissipate if the person can wait them out.

Individuals may experience variable nicotine withdrawal symptoms depending on a variety of factors, especially how much they smoked. One sign of physical dependence is craving a cigarette first thing in the morning. Some people find it nearly impossible to take a long plane trip or attend a lengthy meeting if they cannot take

smoke breaks. (For a questionnaire to assess nicotine dependence, see sidebar above.) The extent of an individual's nicotine addiction will influence which smoking cessation strategies are most likely to work.

OVERCOMING PSYCHOLOGICAL ADDICTION

The smoking habit has psychological as well as physical aspects, and for some people, the former are more dif-

ful smoking cessation attempt. Most experts recommend setting a “quit date” two to three weeks in the future. This allows time to learn what withdrawal symptoms to expect and plan how to deal with them, figure out ways to avoid smoking triggers, get rid of smoking paraphernalia, and obtain nicotine replacement products or antismoking medication.

Once the quit date arrives, the usual recommendation is to stop “cold turkey”—avoiding all cigarettes—rather than switching to “light” cigarettes or trying to cut down gradually. Research from the National Cancer Institute has shown that smokers who switch to light cigarettes typically compensate by smoking more or inhaling more deeply. While some people do manage to become occasional social smokers, it is more common for smoking frequency to return to the previous level over time.

A recent review of 19 studies found that among smokers who were not yet committed to quitting, cutting down could change smoking routines and increase the likelihood of complete cessation. However, the review authors emphasized that cutting down should be regarded as merely a temporary step toward full cessation, since there is no evidence that smoking fewer cigarettes substantially reduces smoking-related health risks.

On the contrary, a large prospective cohort study of nearly 25,000 men and more than 26,000 women in Norway followed for up to 30 years found that heavy smokers (15 or more cigarettes per day) who cut their daily consumption by more than half did not significantly lower their rates of death due to all causes, cardiovascular disease, or smoking-related cancers compared with continued heavy smokers. The same research team also showed that people who smoked as few as one to four cigarettes per day had three to five times the risk of ischemic heart disease and lung cancer, and a substantially higher mortality rate, compared with nonsmokers. Sim-

ilarly, a Danish study found that women who smoked just three cigarettes per day and men who smoked six cigarettes or one cigar doubled their risk of heart attack.

A Word about Weight Gain

Many smokers are worried about gaining weight when they quit, and this is one of the most commonly cited reasons for continuing to smoke or relapsing, especially among women. A majority of people do gain some weight after they stop smoking. The average gain is around five to 10 pounds, though a small proportion (5% to 10%) will gain more than 30 pounds. Because the antismoking drug bupropion (see page 44) dampens the urge to eat as well as smoke, people who use it typically gain less weight than those who quit using other methods.

Weight gain after smoking cessation is attributable to multiple factors. Nicotine speeds up metabolism; when a smoker stops, the metabolic rate returns to normal and calories are not burned as quickly. Nicotine also suppresses the appetite, which leads smokers to eat less. But much of the weight gain is attributable to people eating more when they stop smoking, in order to satisfy oral cravings or to have something to do with their mouths and hands when they feel the urge to light up.

One way to prevent weight loss is to increase the level of physical activity. Exercise can also reduce cigarette cravings, improve mood, and relieve stress. Plus, it can be a good substitute activity—certainly better than overeating—when one feels the need to smoke. As a bonus, many people find that exercise becomes easier and more enjoyable as their lung capacity improves, which can begin within just a few weeks after quitting.

Because smoking cessation is hard enough, some experts advise against starting a diet at the same time. Better to successfully quit smoking now, the thinking goes, and worry

about losing weight later. On the other hand, some people achieve good results with a complete lifestyle overhaul that involves smoking cessation, a healthier diet, and increased exercise.

While most people don't relish the idea of gaining weight, adding a few pounds is clearly preferable to continued smoking from a health perspective. By one estimate, a person would have to be more than 100 pounds overweight to reach the same level of health risk as smoking one pack of cigarettes per day.

Tools for Quitting

As the negative health consequences of smoking have become more apparent and researchers have learned more about the process of quitting and barriers to success, approaches to smoking cessation have become more sophisticated. Experts recognize that smoking cessation is not simply a matter of willpower. Rather, a majority of smokers will require some form of assistance—and often multiple attempts—before they quit for good.

Two widely used aids for smoking cessation are nicotine replacement therapy and antismoking medications. Current guidelines advise that health-care providers should recommend these for all patients who wish to stop smoking, except for unusual cases where nicotine replacement or medications are contraindicated. Studies have shown that combining these methods with educational materials, counseling, behavior modification techniques, and group support produces the best long-term outcomes.

NICOTINE REPLACEMENT THERAPY

Many smokers find it difficult to change their behavior and break the emotional attachment to smoking while experiencing acute physical withdrawal symptoms. Nicotine replacement therapy is intended to minimize these symptoms, thereby allowing a person to focus on the psychological aspects of the addiction. Once the smoking habit is broken, the

Tips for Smoking Cessation

- Pick a relatively stress-free time to quit (for example, not right before the holidays).
- Tell family, friends, and coworkers that you plan to quit and ask for their support.
- Keep a daily journal to identify smoking routines and triggers.
- Before quitting, change your smoking routine (for example, switch to a brand you don't like and smoke using the opposite hand).
- Stop smoking at home, in the car, and other places where you spend a lot of time.
- Talk to your doctor about nicotine replacement therapy or antismoking medications.
- On or before your quit date, get rid of cigarettes, ashtrays, lighters, and other smoking paraphernalia.
- Make changes to your usual routine and avoid situations and activities (such as drinking coffee or alcohol) that you associate with smoking.
- Eat regular meals, since hunger can trigger the urge to smoke.
- To satisfy oral cravings, chew toothpicks or sugarless gum, suck on hard candy, or eat low-calorie snacks such as raw vegetables.
- When a craving strikes, try to delay smoking for at least 10 minutes, as the urge will often pass.
- Get more exercise.
- Try stress reduction methods such as meditation or deep breathing.
- Find substitute activities or hobbies that keep your hands busy and cannot be done while smoking.
- Reward yourself by spending cigarette money on something you enjoy.

dose of nicotine is gradually tapered off and eventually eliminated.

Nicotine replacement therapy is available in several delivery methods:

- Nicotine transdermal patch (NicoDerm, Nicotrol, Habitrol): 16- and 24-hour patches are available without a prescription. Patches are applied to the arm or torso once daily; the 16-hour patch is taken off at night. Nicotine is absorbed slowly

and continuously through the skin, and takes three to six hours to reach an effective level.

- Nicotine polacrilex gum (Nicorette): 2-mg and 4-mg formulations are available without a prescription; the recommended dose depends on the number of cigarettes smoked. The gum should be chewed until the user senses a peppery flavor or tingling sensation, then “parked”

between the cheek and gums. Nicotine is absorbed through the oral membranes, and takes several minutes to reach the brain.

- Nicotine polacrilex lozenges (Commit): 2-mg and 4-mg doses are available in a hard candy form without a prescription. Lozenges should be sucked slowly, not chewed and swallowed. As with gum, the nicotine is absorbed through the oral membranes and takes about the same length of time to reach the brain.
- Nicotine inhaler: Available by prescription only, the inhaler is a hollow tube the size and shape of a cigarette loaded with replaceable nicotine cartridges. The user puffs on the inhaler, but the nicotine is absorbed through the oral membranes rather than the lungs, taking several minutes to reach the brain.
- Nicotine nasal spray: Available by prescription only. Nicotine is absorbed through the nasal membranes and reaches the brain within a few minutes; this is the fastest nicotine replacement delivery method.

Nicotine replacement therapy should be started the day a person stops smoking. The idea is to maintain a steady level of nicotine in the body in order to prevent cravings. The patch is worn continuously, not applied when a craving arises. Likewise, nicotine gum and lozenges should be chewed or sucked slowly over a period of time, using about one piece per hour. The fast-acting nasal spray most closely approximates the rapid nicotine “hit” from smoking, while the inhaler mimics the action of smoking and helps address the psychological craving.

Studies have shown that nicotine replacement therapy is generally safe, even for people with cardiovascular disease. Pregnant women should try to stop smoking without nicotine replacement therapy, but if this is not possible, nicotine replacement carries

a lower risk to the mother and the developing fetus than continued smoking.

The main hazard of nicotine replacement therapy is excessive nicotine levels, especially if a person continues to smoke. Symptoms of nicotine overdose include dizziness, light-headedness, nausea, and rapid heartbeat. People who wear nicotine patches overnight may experience insomnia or unusual dreams. Patches can cause skin irritation, while the nasal spray and inhaler can irritate the nasal membranes, sinuses, and throat. Nicotine gum and lozenges can cause mouth soreness when used as directed, and can also lead to hiccups, heartburn, and gastrointestinal upset if chewed and swallowed like normal gum or candy.

Nicotine is metabolized by the liver, and replacement therapies can potentially affect the processing of other medications. However, there are no known clinically relevant interactions between nicotine replacement therapy and antiretroviral drugs used to treat HIV.

Numerous controlled trials have shown that nicotine replacement therapy significantly improves the likelihood of sustained smoking cessation, approximately doubling the rate of continued abstinence after one year. There is little evidence that any one delivery method works better than another, so which to use is a matter of personal preference. Methods may also be combined, for example using the patch to maintain a steady level of nicotine and the nasal spray to provide an extra boost to satisfy a craving. Although the usual recommended course of nicotine replacement therapy is three months (and no longer than six months), some experts believe prolonged use may increase the likelihood of long-term abstinence.

Most research on nicotine replacement therapy has been done in HIV negative individuals, but a few recent studies have shown that it is also effective for people with HIV. As reported in the October 2006 issue of *Antiviral*

Therapy, researchers with the Swiss HIV Cohort evaluated a smoking cessation program for HIV positive individuals; 34 participants were randomly assigned to receive nicotine replacement therapy plus counseling, while 383 received no intervention. After one year, half the participants in the intervention group had stopped smoking, compared with just 15% in the control group.

While nicotine replacement helps manage physical withdrawal symptoms, it does not address the psychological aspects of the smoking habit. For this reason, nicotine replacement therapy is most effective when used as part of a comprehensive program that also includes counseling, support, and behavior-change interventions.

ANTI-SMOKING MEDICATIONS

In addition to nicotine replacement therapy, there are two prescription medications approved by the Food and Drug Administration (FDA) to assist smoking cessation: bupropion (Zyban, Wellbutrin) and varenicline (Chantix in the U.S., Champix in Europe). Many other pharmacological therapies have been explored—including several currently undergoing clinical trials—but to date none have demonstrated benefits equaling those of bupropion and varenicline.

BUPROPION

Bupropion is an atypical antidepressant originally marketed as Wellbutrin. Coincidentally, people taking the drug to treat depression also reported a reduced urge to smoke, and in 1997 GlaxoSmithKline relaunched a sustained release formulation as an antismoking medication under the name Zyban (generic bupropion is also available).

It is not clear exactly how bupropion works to dampen the urge to smoke, but it is thought to be related to the drug's effects on dopamine and norepinephrine in the brain, and bupropion appears to influence the brain's pleasure and reward pathways.

Some people find that bupropion also reduces food cravings, and it is being studied as a method for helping people stop using methamphetamine.

Unlike nicotine replacement therapy, bupropion should be started one to two weeks prior to the quit date so it can reach adequate levels in the body. The recommended dose is 150 mg twice daily, and the usual course of treatment is two to three months, although the FDA has approved maintenance therapy lasting six months.

Bupropion seems to work well for some people and have little effect for others. Randomized studies have shown that the drug approximately doubles the likelihood of quitting compared with placebo. In one study, 16% of people randomly assigned to use placebo or nicotine patches alone for two months were still smoke-free after one year, compared with 30% of those taking bupropion alone and 35% taking bupropion plus nicotine replacement.

However, smoking relapse is common after people stop taking the drug. A study comparing bupropion durations of two months and one year found that more people in the longer treatment group sustained smoking cessation at one year, but relapse rates were the same (about 60%) at two years.

Bupropion is generally well tolerated. Potential side effects include insomnia, dry mouth, altered taste perception, nausea, tinnitus (ringing in the ears), and bruxism (jaw clenching and teeth grinding). Insomnia may be lessened by taking the second daily dose in the afternoon rather than at bedtime. The drug should not be used by people with high blood pressure, heavy alcohol consumption, or a history of seizure disorders (e.g., epilepsy), head trauma, or eating disorders (e.g., anorexia or bulimia).

Bupropion can safely be combined with nicotine replacement products, and some studies suggest combination therapy is most effective. Although metabolized by the CYP450

enzyme system in the liver, bupropion goes through a different pathway from antiretroviral drugs, and it has no known clinically relevant interactions with PIs or non-nucleoside reverse transcriptase inhibitors (NNRTIs).

VARENICLINE

Varenicline is a new drug approved by the FDA in 2006. By blocking nicotine receptors in the brain, it both relieves nicotine withdrawal symptoms and reduces the pleasure associated with smoking.

Like bupropion, varenicline should be started about one week prior to smoking cessation. The usual dose is 1 mg twice daily, and it should be taken after a meal with a full glass of water. The recommended course of treatment is three months, but it can be continued as maintenance therapy for an additional three months if a person remains smoke-free up to that point.

Five randomized controlled trials demonstrated that varenicline was significantly more effective than placebo for helping long-term smokers quit, and two trials showed that it worked better than bupropion. In one study, rates of sustained abstinence after three months of therapy and one year of follow-up were 23% with varenicline, 15% with bupropion, and 10% with placebo. A 2007 meta-analysis concluded that 12-month continuous abstinence was more likely with varenicline than with placebo or bupropion.

Varenicline is also generally well tolerated. Potential side effects include headache, nausea, gas, constipation, altered taste perception, insomnia, and abnormal dreams. Taking the drug with food may reduce gastrointestinal side effects. Though uncommon, varenicline may also cause neuropsychiatric side effects including mood swings, depression, and suicidal thoughts. In November, after receiving about 100 reports of mental symptoms, the FDA asked health care providers to monitor patients taking the drug and to report any such problems.

Since varenicline is a new drug, it has not been extensively studied in combination with nicotine replacement therapy or other medications. Varenicline is metabolized by the kidneys and excreted in the urine, and there are no known interactions with antiretroviral drugs. People with impaired kidney function should not use varenicline. Though no interaction studies have been done, varenicline's potential for mental side effects suggests it should be used cautiously by people taking efavirenz (Sustiva), which can cause similar symptoms.

OTHER PHARMACOLOGICAL THERAPIES

A variety of other medications have been studied as smoking cessation aids, with mixed results; none are FDA approved for this indication. These include the anti-anxiety drug buspirone (BuSpar), other antidepressants such as fluoxetine (Prozac) and nortriptyline (Pamelor, Aventyl), the monoamine oxidase B inhibitor selegiline (Eldepryl), the dopamine receptor agonist bromocriptine (Parlodel), the antihypertensive agents clonidine (Catapres) and mecamylamine (Inversine), the antiseizure medication topiramate (Topamax), the lobelia plant derivative lobeline (Bantron), and the plant alkaloid cytosine (from which varenicline is derived). Researchers are also exploring experimental vaccines that stimulate production of antibodies that bind to nicotine.

The opiate antagonist naltrexone (Revia), which is used to manage opiate and alcohol dependence, has not been shown to aid smoking cessation. The cannabinoid receptor antagonist rimonabant (Accomplia) is approved in Europe as a diet aid for treatment of obesity; however, due to concerns about significantly increased rates of depression with long-term use, the FDA has not approved the drug for either obesity or smoking cessation, despite promising trial results.

Some smoking cessation clinics offer injections of the anticholinergic agents atropine and scopolamine

(usually followed by atropine pills and scopolamine patches) to help reduce nicotine withdrawal symptoms. However, this method is not FDA approved, not supported by controlled clinical trials, and can cause dangerous side effects.

COUNSELING AND SUPPORT

While some smokers are able to quit on their own, others find that support and counseling are key components of a smoking cessation program. Education is also crucial, including both health information that may strengthen the resolve to quit and information about what types of withdrawal symptoms and psychological barriers to expect during the quitting process.

Support may come from family or friends concerned about the smoker's well-being, as well as from former smokers who understand from experience what quitting is like. Some people find it helpful to quit with a buddy for the sake of mutual encouragement.

Most cities have organized smoking cessation classes and support groups, often sponsored by local chapters of the American Cancer Society or American Lung Association; some employers and health plans offer similar services. Nicotine Anonymous employs a 12-step program modeled after Alcoholics Anonymous.

Many smokers find professional counseling beneficial. This can range from simple encouragement and education offered by one's regular health care provider, to specialized psychotherapy (for example, cognitive behavioral therapy) focused on strengthening the motivation to quit, modifying habitual behavior, and developing coping and problem-solving skills. Counseling can also help identify and overcome common pitfalls that can lead to relapse. Research indicates that smoking cessation programs involving group or individual counseling and support can significantly improve the likelihood of quitting compared with stopping on one's own.

Because the urge to smoke can strike at any time, telephone counseling and 24-hour hotlines may also be helpful. Many cities and states operate free telephone services, and the American Cancer Society's QuitLine is available nationwide. Studies have demonstrated that telephone counseling can double the likelihood of quitting. In addition, smoking cessation Web sites featuring online support groups are available through the Internet. For a selection of smoking cessation resources, see sidebar at right.

Although there has not been much research on smoking cessation by people with HIV, the recent University of Texas study mentioned previously demonstrated the benefits of a comprehensive program. Damon Vidrine and colleagues studied 95 patients at an inner-city HIV/AIDS clinic who enrolled in a smoking cessation trial. All received a medical consultation about smoking cessation, written educational materials, and nicotine replacement therapy; in addition, some were randomly assigned to also receive more intensive counseling by mobile phone and a hotline. After three months, those who received telephone counseling were more likely to have abstained from smoking for the past 24 hours (37% vs 10%) and had a longer average smoke-free period (31 vs 12 days) compared with the control group.

AVERSION THERAPY, HYPNOSIS, AND ACUPUNCTURE

Other smoking cessation methods may help some individuals quit, but these are not well supported by controlled research.

Aversion therapy involves smoking far more than usual over a short period of time, to the point that it induces nausea and other adverse effects. The idea is that cigarettes will become associated with unpleasant feelings, thus reinforcing the desire to quit. Some people find that excessive smoking immediately prior to their quit date helps them remain smoke-free, but a meta-analysis of aversion

trials did not show a clear relationship between aversive smoking and cessation.

Therapeutic hypnosis, or hypnotherapy, is often promoted as a quick and painless way to quit smoking for good—often at a high cost. Hypnosis aims to induce a state of deep relaxation that renders a person more receptive to suggestion. Hypnosis methods vary widely, which makes it hard to evaluate them in a systematic way. Further, it seems that some people are highly susceptible to hypnosis, while others are not. Some study data suggest that hypnosis works better than nothing, but there is little evidence that it is equal or superior to other smoking cessation methods. However, pulmonary specialist Faysal Hasan and colleagues reported at the October 2007 annual meeting of the American College of Chest Physicians that in a controlled study of patients discharged from the hospital after a cardiac diagnosis, hypnotherapy along with intensive counseling led to a higher rate of smoking cessation after six months than nicotine replacement therapy or no intervention.

Acupuncture for smoking cessation involves placing needles around the outer ear. Many people report that this technique induces relaxation and reduces cravings for nicotine as well as other addictive substances such as cocaine. A related method uses cold lasers rather than needles to stimulate specific acupuncture points. As with hypnotherapy, results from clinical trials of acupuncture and similar techniques have been mixed. A meta-analysis of 22 studies comparing real acupuncture to sham acupuncture or other methods of smoking cessation found no differences in outcomes.

While these methods may be helpful for some people, they do not demonstrate the high level of effectiveness claimed by their practitioners. As a rule, it is wise to be wary of techniques or programs that promise instant results, especially if they are expensive.

SMOKING CESSATION RESOURCES

American Cancer Society

Including Quitline, which offers referrals to local resources
800-ACS-2345
www.cancer.org

American Lung Association

800-LUNG-USA
www.lungusa.org

California Smokers Helpline

1-800-NO-BUTTS (English)
1-800-45-NO-FUME (Spanish)

Centers for Disease Control and Prevention

Office on Smoking & Health
800-CDC-INFO
www.cdc.gov/tobacco

Last Drag

Free smoking cessation classes for lesbian/gay/bisexual/transgender people in the San Francisco and Los Angeles areas
www.lastdrag.org

National Cancer Institute

800-4-CANCER
www.cancer.gov

Nicotine Anonymous

415-750-0328
www.nicotine-anonymous.org

QuitNet

www.quitnet.com

Smokefree.gov

800-QUITNOW
www.smokefree.gov

Preventing Relapse

While many people manage to stop smoking temporarily using various interventions, relapse rates are high with all methods. Research suggests that about 10% of smokers are able to quit cold turkey with no assistance, while 25% to 30% remain smoke-free for six months using nicotine replace-

ment or antismoking medications. But a study with a long follow-up period found that even among people who remained abstinent after one year in a controlled trial of the nicotine patch, only half remained smoke-free at eight years.

Most relapses occur within the first week, while nicotine withdrawal symptoms are at their peak. Among those who make it through this stage, most subsequent relapses happen during the first three months after quitting, since the old smoking habits and triggers have not yet been eliminated or neutralized.

But even after passing the three-month mark, former smokers may continue to experience the urge to light up for months or years, especially in situations that were strongly associated with smoking. One frequent path to relapse is trying to smoke an occasional cigarette, as this often rekindles the addiction. Other common reasons for returning to smoking include stress, weight gain, and lack of confidence in one's ability to quit permanently.

Studies—and the experience of countless smokers—show that most people will make several attempts before they finally quit for good. It is important not to get too discouraged if one slips and has an occasional cigarette during the weeks or months after quitting. One cigarette will not cause physical dependence to return full force. Rather than thinking, “Since I’ve had one, I might as well finish the pack,” the best course is to resolve anew not to smoke any more.

Even if a person experiences complete relapse and returns to the previous level of smoking, this should not be considered a “failure” in the sense that he or she is unable to quit. Rather, each attempt can serve as practice and offers important lessons about specific barriers and which methods work (or don't). People who do not remain smoke-free using one method are advised to try another—or add further interventions—on the next attempt.

Conclusion

People with HIV now have the prospect of a long life thanks to HAART, but this means paying attention to long-term health issues. The attitude of “I’m going to die of AIDS anyway, so why bother to stop smoking?” is no longer justifiable. With rising cancer rates in the HAART era and increasing concern about cardiovascular risk associated with antiretroviral therapy, HIV positive people have more reason than ever to quit.

New techniques to aid smoking cessation, including novel nicotine replacement delivery methods and the recently approved antismoking drug varenicline, give smokers more options. Studies have shown that approved smoking cessation aids are safe and effective compared with no intervention, and there is good evidence that more intensive programs that use a combination of methods—for example, nicotine patches, bupropion, cognitive behavioral therapy, and a peer support group—offer the best chance of success. While little research on these methods has been done in people with HIV, there is no reason to think they will not benefit as much as HIV negative individuals.

Quitting smoking may be one of the hardest things a person will ever do, and staying permanently smoke-free may require several attempts. But, according to the American Cancer Society, more than three million Americans stop smoking each year and more than 46 million have quit for good. As evidence accumulates regarding the detrimental effects of smoking for HIV positive and HIV negative people alike—and as smoking becomes less socially acceptable and subject to ever-expanding restrictions—there's no time like the present to put cigarettes in the past.

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