Why do people continue to smoke?

RENEE BITTOUN

Bittoun says that smokers have a genetic basis for what is a physiological addiction. In practice, if patients who smoke are not responding to behavioural cessation measures, doctors should proceed directly to pharmaceutical approaches.

In the last two decades, there have been dramatic reductions in smoking in adults in Australia. However, there is still a core group of smokers from every socioeconomic group with no identifiable psychosocial factor in common except for smoking behaviour. This problematic group of smokers, seemingly impervious to Quit campaigns, has led researchers to investigate more intensely the origin and treatment of nicotine addiction and tobacco dependence. This article asserts that nicotine dependence is a disease with a probable genetic basis and reviews the available treatments for this addiction.

Smoking is a disease

The word 'habit' has gone from the lexicon of those working in the field of drug addiction. Smoking is not a habit, it is a disease:

- The DSM IV specifically describes addictions and nicotine addiction *per se* as a disease and lists diagnostic criteria (see the box on this page).[1]
- The Royal College of Physicians in London defines smoking as nicotine addiction, classifies it as a disease and recommends that doctors treat it as such.[2]

In Australia, most people habituated to smoking have been able to quit spontaneously and we are now left with an endemic group of smokers who are most probably dependent and show clear signs of addiction – they have a 'progressive, chronic, relapsing disorder'. We have come to understand that the factors that may initiate individuals (usually in adolescence) into tobacco use may not be the same as those factors that promote the continuation and long term use of tobacco. Surprisingly, long term use may be the result of an individual's

Renee Bittoun is Director of the Smoking Research Unit in the Department of Psychological Medicine, University of Sydney, and a Consultant at the St Vincent's Clinic, Darlinghurst, Sydney, NSW.

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AUSTRAL INTERNATIONAL

Nicotine dependence: diagnostic criteria (DSM IV)

Nicotine dependence is diagnosed when there are three or more of the following:

- tolerance to nicotine (the absence of nausea and dizziness despite use of substantial amounts)
- withdrawals upon abstinence or cessation
- continuation of use despite medical consequences
- relapse after unsuccessful quit attempts
- avoidance of or reduction in important social, occupational or recreational activities due to use
- greater tobacco use than originally intended.

inherent physiological response to nicotine rather than psychological factors.

Smoking is in the genes

Advances in the past decade have thrown some light on the genetic risk factors for the addictive, physiological response to nicotine that occurs in some members of the community. Twin studies have also verified the significant inherited nature of nicotine dependence, adding to the biological plausibility of a genetic predisposition.

Cytochrome P450 2A6

The enzyme cytochrome P450 2A6, a nicotine C-oxidase (CYP2A6) – known to break down nicotine to its major metabolite, cotinine – has three distinct genotypes. Carriers of the type 1 allele for the CYP2A6 gene quickly break down nicotine while carriers of types 2 and 3 (null alleles) have impaired nicotine metabolism and are unlikely to be smokers.

Studies have shown that possessing the type 1 allele is related to nicotine dependence, difficulty in quitting and numbers of cigarettes smoked. Ironically, it is also linked to carcinomas of the lung as it activates the metabolism of nicotine to virulently carcinogenic nitrosamines.

Genotyping smokers for enzyme type is commonly carried out in clinical trials for smoking interventions and routine in some smoking clinics overseas.[3] However, more research needs to be done to establish 'normal values' for these genotypes so that a better grasp of distribution in the base population can be made.

Neurotransmitter receptor sites

Inherited neurological factors may predispose an individual to gain significantly positive effects from nicotine.

Neurotransmitter receptor sites, such as the dopamine subtype D2 (DRD2) receptor, may be sensitive to nicotine in neurons where stimulating reinforcement can act on mood, cognition and some areas of memory. Nicotine-sensitive acetylcholine receptors in some individuals (rather than all) can release considerable levels of dopamine, serotonin, beta endorphin, noradrenaline, and acetylcholine. These effects can be utilised in times of distress, when better concentration is needed or for alertness.[4]

It is not understood why the decay of nicotine leads to the opposite effect, that is, withdrawal phenomena such as agitation, anxiety, an inability to concentrate, depression and aggression. However, we do know that these events are cyclical and that smokers often self-medicate, via smoking, to relieve the side effects caused by the decay of nicotine. (Nicotine is a very short acting drug with a half-life ranging from 40 minutes to two hours so many smokers experience withdrawals of a subtle nature even between cigarettes.)

Monoamine oxidase B

Reports have shown that smokers have significantly lower brain monoamine oxidase B levels than nonsmokers, an acute chemical effect of smoking possibly due to carbon monoxide.[5]

Smoking and nicotine *per se* have been shown to have strong antidepressant actions. These findings may explain the high prevalence of smoking in patients with psychiatric disorders. There is now a growing concern regarding: the prevalence of smoking in this group; the fact that smoking may exacerbate or relieve symptoms; and, that smoking may impact on concurrent medications. This group of patients is also, of course, at risk of diseases related to smoking (as are other smokers) and specific guidelines have been recommended to deal with smoking in patients with mental illnesses.[6] However, this still remains a problem often thrown in the 'too hard basket' by many clinicians.

Smoking in practice

The importance of helping smokers to quit should not be underestimated: smoking tobacco is lethal in 50% of all users. The above new findings may begin to explain the often frustrating situation in general practice when a patient continues to smoke despite evident medical complaints they have as a consequence. They may also begin to explain the smoker who, with the best of intentions and a strong commitment to quit, finds it extremely difficult to quit compared with others who seemingly have little or no problems in doing so.

The GP's role

The role of the GP in smoking cessation has changed from that of 'reprimander'. Now, there is a need to provide information and to offer help in the form of pharmacological intervention. Follow up and adjustment of medication where required is needed to affect a long term 'cure'.

An individual approach

Patients, themselves, seem to prefer a more individualised approach to helping them quit,[7] and with the ability to identify certain typologies of smokers we can now determine specific needs that individuals may have in response to treatment. Brief smoking cessation strategies have been commonly and widely implemented; however, smokers with specific problems (including adolescents) who continue to smoke despite the medical consequences, and thus by definition are dependent, may benefit from intensive efforts.

Research has shown that the more intensive (dose-related) the intervention, the higher the rate of effectiveness.[2] This is also cost effective as these smokers are at greatest risk of exacerbating the medical sequelae of their smoking.

Pharmaceutical interventions

Evidence based

The following evidence based interventions have been tested using double-blind placebo-controlled trials with independent validation of smoking status and have shown good long term (12 months) abstinence rates. There is no gender difference in the outcomes of treatment for nicotine addiction.

Nicotine replacement therapy

Nicotine replacement therapy has shown significant cessation rates and all forms (gum, transdermal patch and inhaler) are effective.[8] However, doses of nicotine may be too low for some smokers and may lead to concomitant smoking. Nicotine patches available in Australia deliver sustained doses of around 10 to 15 ng/mL; some smokers readily achieve doses of 40 ng/mL per cigarette. Thus, it is not uncommon for some smokers to be advised to wear two patches during the daytime if they find that one alone reduces but does not eliminate smoking; this is effective and safe. Nicotine gum (4 mg) delivers about 15 ng/mL nicotine.

Erroneously, patients with coronary artery disease have long been denied the use of nicotine replacement therapy for fear of toxicity. Ironically, most smokers with coronary artery disease who continue to smoke invariably have blood levels of nicotine that are far in excess of the blood levels achieved with any nicotine replacement therapy. Many studies to date have shown that it is safe and effective to recommend nicotine replacement therapy in this group.[9]

Antidepressants

Bupropion (Zyban) currently both on trial and available in Australia, is the first nicotine-free treatment to show substantial efficacy in a small number of clinical trials. A noradrenaline and dopamine reuptake inhibitor, bupropion is active as an oral antidepressant and anticraving agent. Like other antidepressants, it is slow to take effect but reduces the urge to smoke and the anxiety associated with quitting. Like nicotine replacement therapies, bupropion is taken for a finite period of time, from seven to 12 weeks.

Nortriptyline (Allegron) has also increased quit rates in a small number of trials.[8]

Combination therapy

Combination therapies – for example, the combination of nicotine patch and gum or nicotine patch and bupropion – are

highly effective and safe in those with higher baseline nicotine blood levels. There is no evidence that the reduction of patch concentration over time is necessary; however, maintenance of patch wearing over seven to eight weeks is mandatory. The chronic delivery of low dose, slow release nicotine is believed to 'desensitise' the nicotine-sensitive receptors.

Non-evidence based

There are many quit smoking treatments that continue to be recommended for which there is limited or no scientific evidence. For example, meta-analyses of studies of hypnotherapy and acupuncture for nicotine addiction have not shown significant impact and the effectiveness of these techniques, as well as aversion therapy, is uncertain; anxiolytics are not effective.[7]

Other 'cures' available in the marketplace seem to have had no scientific scrutiny of their effectiveness. Resorting to the use of these often expensive potions should not be dismissed as harmless as many patients buy them for a 'quick fix', don't succeed, become demoralised and may believe that they, rather than the potion, are at fault.

Low nicotine-tar cigarettes (and 'cutting down') are considered counterproductive and can have a considerable negative impact on health. Smokers may titrate the amount of nicotine available to them by inhaling deeper and longer or smoking more of the actual cigarette, so that more carbon monoxide (and carboxyhaemoglobin) and particulate matter is inhaled.

Behavioural interventions

Quitting

Contrary to, and possibly because, of the advances made in the pharmacological treatment of nicotine addiction, less scientific research has been done in the past few decades in the behavioural aspects of smoking. This may be because prior to the advent of pharmacological treatments in the 1980s a great deal of research had been done with behavioural interventions that were unsuccessful. Patients showed poor response to treatments aimed at stress management, the activity and ritual of smoking, the handling, and oral and visual stimulation, and these factors, now, are not considered the primary problem in smoking.

Relapse

Behavioural treatment of the endemic problem of relapse has, however, shown promise. Relapse is part of nicotine and all other addictions and a patient may require several attempts to quit with various lengths of abstinence before establishing permanent abstinence. We have learnt that any smoking – even a puff – can lead to relapse.

Studies in cue conditioning, lapses and their prevention have enlightened us recently in how better to help smokers 'stay stopped'.

The first fortnight

The risk of relapse dissipates with time and the most critical period is within the first two weeks of quitting where 62% of new quitters are likely to relapse if left unaided. Therefore, we need to follow up patients rather intensively in the first two weeks of quitting. The intensity of follow up can be reduced after this first fortnight.

After the first fortnight

The factors that predict relapse after the first fortnight are related to:

- exposure to other people smoking
- drinking alcohol, often in excess
- poor response to negative affect.

Studies show that relaxation training to cope with negative events has little impact at this time. Avoidance of stressful situations and other situations such as clubs or pubs, and throwing away packets of cigarettes may initially be helpful; however, urges to smoke recur when finally re-exposed to these cues. What can be done and seems to show promise is 'cue exposure' where, as in treatments for alcohol addiction and other addictions and phobias, triggers are not avoided but confronted. This desensitisation-type of program is based on Pavlovian extinguishing of learned conditioned responses to stimuli. Such stimuli may not always be overtly obvious to the smoker – for example, the stimuli of coffee, alcohol or talking on the telephone. They may also be:

- events, such as an argument
- a place, such as a specific room in the home or at work
- another person, with whom they always smoked.

To actively avoid these circumstances for months is unrealistic. 'Unlearning' some of these conditioned responses occurs quickly and spontaneously as long as smoking does not occur.[9]

The risk of relapse diminishes to very little likelihood of relapse after three months of abstinence.

Conclusion

The simple warning from a doctor to a patient that 'smoking is not doing them any good' may have been adequate in the past (and still does impact on a proportion of patients). However, today, this approach compares poorly with the use of well studied pharmacological interventions that – in randomised placebo-controlled trial conditions – have shown excellent long term abstinence rates. Informing smokers as to the nature of nicotine addiction, the effects of the drug on brain function, the possible genetic responses to nicotine and advances in treatment can be a lifesaving medical intervention. MT

A list of references and further reading is available on request to the editorial office of Medicine Today.

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Further reading

1. The Society for Research on Nicotine and Tobacco (SRNT)'s website: http://www.srnt.org/
2. The Virtual Office of the (US) Surgeon General: http://surgeongeneral.gov/tobacco/