# **Treating tobacco dependence**

Jonathan Foulds & Hamid Ghodse

The 1988 US Surgeon General's Report entitled *Nicotine Addiction* reviewed the mass of evidence on the role of nicotine in tobacco consumption and came to three main conclusions, shown in Box 1.

- Box 1. Main conclusions of the 1988 US Surgeon General's Report
- Cigarettes and other forms of tobacco are addicting.
- 2. Nicotine is the drug in tobacco that causes addiction.
- 3. The pharmacologic and behavioural processes that determine tobacco addiction are similar to those that determine addiction to drugs such as heroin and cocaine.

The recognition that smoking is an addiction and that nicotine dependence and nicotine withdrawal are mental disorders (American Psychiatric Association, 1994) clearly places smoking and smoking cessation within the sphere of interest of psychiatry. The main aim of this article is to describe the aspects of treatment of tobacco addiction which are supported in the scientific literature.

### Typical nicotine absorption during smoking

Most cigarettes contain around 10 mg of nicotine, about 1 mg of which is actually absorbed by inhalation of smoke. An average smoker awakens in the morning with blood nicotine levels of less than 5 ng/ml (the half-life of nicotine is about two hours). Afternoon nicotine levels are generally in the range of 15–80 ng/ml. The typical nicotine boost from an afternoon cigarette is 10–15 ng/ml (Foulds *et al*, 1992). When a smoker inhales a puff of smoke and draws it into the lungs, it is transported in one concentrated bolus via the arterial circulation and reaches the brain in unmixed, undiluted form within about ten seconds. Recent studies have found that the nicotine concentration reaching the brain in these boli is around 100 ng/ml (Henningfield *et al*, 1990). A pack-a-day smoker receives about 70 000 of these nicotine hits per year.

The most commonly reported acute subjective, physiological and biochemical effects of smoking a cigarette are summarised in Table 1.

# The nicotine withdrawal syndrome

### Symptoms

On stopping smoking (or markedly reducing nicotine intake of any sort) smokers may experience a number of unpleasant symptoms comprising the nicotine withdrawal syndrome. The diagnostic criteria for nicotine withdrawal listed in DSM–IV (American Psychiatric Association, 1994) are described in Table 2. A number of carefully controlled studies have shown these symptoms are not simply the result of dissatisfaction at having to cease an enjoyable habit, but rather that they are specifically relieved by provision of nicotine (e.g. in the form of nicotine gum or patches) and not by placebo.

The other important symptom which increases on stopping smoking is, of course, craving for a cigarette. A number of other symptoms are commonly reported on stopping smoking, and although they are not thought to be directly attributable to nicotine withdrawal, they may still have some clinical relevance, e.g. newly abstinent

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Table 1. Main	acute* subjective, physiological and neuro	* subjective, physiological and neuroendocrine effects of smoking a cigarette		
Subjective effects	Physiological effects	Neuroendocrine effects		
Increased alertness	EEG stimulation	Release of: acetylcholine		
Increased calmness	Heart rate increase	catecholamines		
Relief of craving	Blood pressure increase	growth hormone		
Dizziness	Peripheral vasoconstriction	ACTH/cortisol		

\*These are effects typically found in a smoker smoking the first cigarette of the day. Many of these effects are subject to acute tolerance and are less apparent after subsequent cigarettes.

smokers often report a difficulty in coughing up sputum, producing an increased feeling of 'chestiness'. This apparent (but transient) worsening of chest symptoms may easily provide an excuse for relapse in someone who is wavering ("I'm supposed to have stopped smoking to improve my health. My chest seems worse since I stopped and so I may as well start smoking again").

Other symptoms may be exacerbated by mechanisms other than nicotine withdrawal. Tobacco smoking induces enzyme production in the liver, increasing the metabolism of many drugs by up to 40%. Stopping smoking may produce an increase in plasma levels of drugs, and therefore also an increase in their side-effects, for example increased palpitations and feelings of anxiety in a heavy coffee drinker.

### Time course

The cluster of symptoms comprising the state of dysphoria which commonly occurs on stopping smoking (irritability, feeling miserable, tense, poor concentration, and so forth) occur within the first 24 hours of abstinence, peaks within the first week of abstinence and then returns to baseline in about 4 weeks.

Craving for a cigarette similarly peaks in the first week, but frequently takes longer to dissipate. Many ex-smokers will report only mild and occasional craving after six months without a cigarette, but stronger craving may continue to be elicited by triggering stimuli (such as stress, or being offered a cigarette in a bar) for over a year. Six months after stopping, 50% of individuals report a desire for a cigarette in the last 24 hours.

Some very dependent ex-smokers report that a cigarette is the first thing they think of on waking for months after quitting. The quality and quantity of craving tends to change over time from being a constant gnawing hunger in the first week (in heavy smokers) to being an occasional nostalgic fond remembrance for an old habit one year later.

Increased appetite and weight gain may continue for at least ten weeks after smoking cessation and

probably last longer. Indeed, the evidence on weight gain is consistent with the view that nicotine is an anorectic drug, and that once it is removed the natural 'set point' body weight increases to a new level (typically about five pounds heavier). This weight gain is thought to be due to a combination of increased food intake and decreased resting energy expenditure (US DHSS, 1990).

# Table 2. DSM–IV diagnostic criteria for nicotine withdrawal

A. Daily use of nicotine for at least several weeks.

B. Abrupt cessation of nicotine use, or reduction in the amount of nicotine used, followed within 24 hours by four (or more) of the following:

- (1) dysphoric or depressed mood
- (2) insomnia
- (3) irritability, frustration or anger
- (4) anxiety
- (5) difficulty concentrating
- (6) restlessness
- (7) decreased heart rate
- (8) increased appetite or weight gain.

C. The symptoms in criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D.The symptoms are not due to a general medical condition and are not better accounted for by another mental disorder.

Associated features: Craving for nicotine

Desire for sweets

Impaired performance on tasks requiring vigilance EEG slowing

Decrease in catecholamine and cortisol levels Decreased metabolism of medications and other substances

### Severity

Most of the individual symptoms described above are rated as mild or moderate over the first week of cessation, with craving tending to be rated as moderate or severe. However, nicotine abstinence occasionally precipitates clinical depression, or such poor concentration that the individual feels unable to drive.

A number of studies have found that severity of craving and depression predict later relapse. In the 1986 US Adult Use of Tobacco Survey, current smokers who had tried to quit were asked to judge the importance of several possible reasons for their return to smoking: 27% reported weight gain as an important reason for their relapse and 39% reported irritability to be an important factor (US Surgeon General, 1990).

# Nicotine dependence and other psychiatric conditions

The prevalence of smoking among psychiatric patients is considerably higher than among the general population, and is particularly high in certain conditions such as schizophrenia and dependence on other substances (Hughes *et al*, 1986). It is generally assumed that psychiatric patients use nicotine to medicate their symptoms. The likelihood of success in stopping smoking is much lower in individuals with a history of poor mental health; and in patients with a history of depression, smoking cessation may precipitate clinical depression.

However, it is also possible that smoking actually exacerbates certain psychiatric conditions. For example, nicotine stimulates mesolimbic dopamine release, and a number of studies have found that schizophrenic patients who smoke exhibit more positive symptoms than patients who do not (Ziedonis *et al*, 1994). The role of nicotine as an appetite suppressant is also frequently ignored in the assessment of patients with eating disorders.

Nicotine use is generally ignored as a factor in assessment, treatment and research on psychiatric disorders, thus relatively little is known about the role of smoking and cessation in psychiatric conditions. Given that many psychiatric hospitals are now implementing 'smoke-free' policies, there is now an urgent need for clinicians to make the assessment of patients' nicotine consumption a routine part of psychiatric evaluation and research.

### Assessment for treatment

As with other addictions, two major factors influence both the type of treatment which is appropriate and the likelihood of success: degree of motivation to quit, and degree of dependence on the drug.

### Assessing motivation

There is little point in spending much time trying to force or persuade a patient to stop smoking if that individual clearly has no desire or intention to do so. There are literally millions of smokers who would appreciate and benefit from help to stop smoking, but even when there is a strong desire to quit, their chance of succeeding is low (about 4% one year success rate for individuals trying to quit on their own (Cohen *et al*, 1989).

Those who actually go to some trouble to obtain smoking cessation treatment (i.e. contact the clinic themselves, complete pre-waiting list questionnaires, attend an assessment appointment and so forth), are generally assumed to be reasonably highly motivated to try to change. Of course this should always be checked at the assessment interview and it is generally not a good sign if the patient suggests cutting down rather than stopping smoking, if they are only there because their partner (or doctor) sent them along, or if they express some half-hearted enthusiasm such as "I'll give it a try and see if it works, doc". Patients exhibiting these signs of lack of motivation should be challenged on this before initiating treatment. The chances of successful abstinence are virtually nil in someone who is unsure of their desire to quit, or who expects some aspect of treatment to remove all the discomfort of stopping smoking.

### Assessing nicotine dependence

The Fagerstrom Tolerance Questionnaire is widely used as a measure of nicotine dependence and has recently been modified to exclude less useful items (Heatherton *et al*, 1991). However, an even further abbreviated set of three questions provides a good measure of nicotine dependence. These are shown in Table 3.

Given that about 50% of daily smokers smoke their first cigarette within 30 minutes of waking in the morning, and that the average number of cigarettes smoked per day is 16, one can see that the vast majority of smokers are at least moderately dependent on cigarettes.

### Treatment

Whatever treatment methods are chosen, a crucial component is the preparation of the client. This includes informing the patient what the treatment involves, and ensuring that they have accurate expectations regarding their role, as well as the effects of any medication they may be taking. Many smokers will have a history of smoking a cigarette during every waking hour throughout the whole of their adult life. For these individuals preparing to stop smoking is like preparing to jump off a cliff with no knowledge about how far it is to the bottom. It is worthwhile spending a little time identifying particular fears and reassuring them that withdrawal symptoms are time-limited and generally of mild to moderate severity.

Very few smoking cessation products or techniques have been adequately evaluated. This section will describe those treatment methods which have some support in the scientific literature.

# Non-pharmacological components of treatment

### Measurement of expired carbon monoxide.

Measurement of end-expired carbon monoxide concentrations (ECO) is now a standard component of smoking cessation treatment. Small portable CO monitors have been available at relatively low cost (around £400 in the UK) for many years. The measurement takes only a minute to perform and provides an immediate and accurate digital estimate of the amount of smoke inhalation in the previous six or more hours (correlation with blood carboxyhaemoglobin, > + 0.95).

This procedure is useful because it quantifies for both the patient and the doctor some of the physical harm caused by smoking and can lead to a discussion and explanation of this. Part of this explanation should include the important fact that smokers' carbon monoxide levels (typically in the range 15–60 parts per million) return to those of nonsmokers (less than 10 parts per million) within 48 hours of quitting, and the monitor can therefore be used to tell whether smokers are telling the truth when they say that they have not smoked (with an accuracy greater than 90%).

Some studies have shown that measuring endexpired carbon monoxide in this way can improve cessation rates, particularly in the lower socioeconomic groups who now make up the majority of smokers (Jamrozik *et al*, 1984).

### **Immediate cessation**

Given that withdrawal symptoms are a major barrier to cessation it would seem sensible to advise on a gradual reduction programme, as is usually the case with benzodiazepines. However, there is good evidence that smokers who cut down the number of cigarettes per day tend to increase the amount they inhale from each cigarette in order to try to attain their usual blood nicotine concentrations (Benowitz *et al*, 1986). Smokers in

Question	Answers	Points
How many cigarettes do you smoke per day?	0–9	0
	10–19	1
	20-29	2
	30+	3
low soon after waking up do you smoke your		
rst cigarette (in minutes)?	0–5	3
	6–30	2
	31–60	1
	61+	0
o you crave for a cigarette in places where smoking		
not permitted, e.g. cinemas, public transport?	Yes	1
	No	0

# A total score of 0 suggests non-dependent, 1–2 mild dependence, 3–4 moderate dependence, and 5–7 high dependence. This scale is intended as a guide for clinical use. Those who wish to use a scale for research purposes are advised to use the longer Fagerstrom Test For Nicotine Dependence (Heatherton *et al*, 1991) which will enable comparability with other studies.

cessation trials who do not succeed in quitting similarly show no signs of being able to cut down in the long term. One of the few studies which randomised smokers to either gradual or abrupt quitting found the latter to produce the greatest reduction in smoking (Flaxman, 1978). A possible explanation is that as the smoker cuts down the number of cigarettes per day, each one becomes more reinforcing and hence the point of total abstinence becomes harder to reach. As long as the smoker is carrying around his or her cigarettes and smoking the occasional one, the old habits and rituals are being maintained.

The sooner these rituals cease to be part of the individual's repertoire, the sooner they will think of themselves as a nonsmoker. One piece of advice which should be emphasised to all patients is that they throw out all their tobacco and other smoking paraphernalia prior to quitting, so as to minimise the temptation later. For these reasons, quitting abruptly on a target 'quit day' has become the standard approach in smokers' clinics.

#### Psychological support in the first month

Those studies which actually randomised patients to receive high or low intensity behavioural support have generally found the benefits of offering numerous long appointments to be very small and generally not statistically significant (Gilbert *et al*, 1992). There is also growing evidence suggesting that those individuals who do not achieve abstinence within the first week or two are extremely unlikely to do so later. These facts suggest that behavioural support should be 'front loaded' (i.e. concentrated in the early stages of abstinence) and need not consist of numerous appointments.

It is also clear that only a small proportion of smokers (5–10% at most) are prepared to attend intensive treatments. This suggests that in a context in which there are many patients with fairly low motivation (for example, in a primary care setting), an appropriate level of support might be an initial appointment and a one week follow-up, with a further follow-up at one month only if they are abstaining at one week.

In a context of a smaller number of highly motivated, dependent smokers (such as at a general hospital smokers clinic), an appropriate level of support would be weekly appointments for the first four weeks (i.e. until most nicotine withdrawal symptoms have returned to baseline).

Intensive treatments are best provided in the context of a group. A particular form of grouporiented treatment has been shown to be particularly helpful. This involves five group meetings over the first four weeks of cessation. All patients quit at the first group meeting and the aim is for the group to provide support during the first few weeks when nicotine withdrawal is at its worst. The therapist limits her role to providing accurate information and encouragement on the use of nicotine replacement medication, ensuring that the group stays focused on the task at hand (i.e. stopping smoking), and encouraging the cohesion of the group (by providing name labels, asking group members to introduce themselves, encouraging contacts outside the group, and encouraging group discussion, for example) and enhancing group pressure to maintain abstinence (possibly by initiating publicly declared commitments to remain abstinent). This type of group has been found to produce higher abstinence rates and better attendance than traditional therapist-oriented groups, and therefore probably contains an 'active ingredient' over and above the usual effects of psychological support (Hajek et al, 1985).

# Pharmacological aids to smoking cessation

A number of drugs have begun to be evaluated as smoking cessation products (including buspirone, clonidine, doxepin, ondansetron and lobeline-based products). However, none of these have particularly impressive results when subject to the rigorous evaluation which is now standard in this field. The only pharmacological treatments which have consistently been shown to be effective are those that provide the smoker with nicotine replacement (collectively known as nicotine replacement therapies, or NRTs). This type of treatment has been subject to numerous reviews and meta-analyses, most of which have concluded that the use of nicotine replacement therapy approximately doubles a motivated smoker's chances of successfully quitting compared with the same level of support plus placebo or no NRT (Foulds, 1993; Silagy et al, 1994).

A combination of nicotine replacement with moderate intensity support typically achieves an initial quit rate in excess of 50%, and a one year abstinence rate of 20–30%.

As the efficacy of NRT is not in doubt, the rest of this section will describe the basic rationale of NRT, and then discuss clinical aspects of the use of NRT products.

#### Rationale of nicotine replacement therapy

NRT is based on the evidence that smokers generally smoke for nicotine, and that the craving for this drug, and the unpleasant withdrawal syndrome which follows cessation, are the major barriers to stopping smoking for many people. The idea is therefore to provide the smoker with pure nicotine via another route during the early stages of abstinence, in order to reduce the severity of craving and withdrawal, and to allow the smoker to focus on kicking the habitual component of their smoking. Once the patient is satisfied with progress and is not unduly troubled by craving or withdrawal symptoms, then nicotine replacement is reduced and eventually stopped. Thus NRT is intended as a temporary substitute for the nicotine provided in tobacco. As it is the tar and carbon monoxide in tobacco (rather than the nicotine) which cause most of the adverse health effects of tobacco (such as cancer and emphysema) the temporary use of nicotine replacement products is considered very safe.

### Nicotine gum

Nicotine gum is available (over the counter from the pharmacist in the UK) in two strengths: 2 and 4 mg. Each piece is chewed intermittently for 30 minutes (with regular resting against the side of the mouth) to facilitate buccal absorption. Nicotine absorption is pH-dependent and so patients using gum should be advised to rinse their mouth with water after consuming acidic beverages such as cola or coffee. Relatively little of the nicotine which is swallowed ever reaches the brain, and hence it is important to advise patients on the proper chewing technique.

Each piece of 2 mg gum produces a boost in blood nicotine of around 5 ng/ml in 20 minutes, and when used properly (that is, at least 10 pieces per day) produces therapeutic afternoon blood nicotine concentrations of 10–20 ng/ml (4 mg gum produces levels about 50% higher). However, as the gum is not pleasant tasting and produces some side-effects (hiccups, sore jaws) the biggest problem is poor compliance. The vast majority of patients who use nicotine gum chew too few pieces for too short a time period to have any therapeutic effect. Therefore an important part of the clinician's role in treating patients with nicotine gum is encouraging adequate gum usage to ensure that the patient receives therapeutic blood levels.

About 6% (25% of long-term quitters) use the gum for at least a year and may require some help to cease use. However, long-term gum use is clearly preferable to relapse to tobacco (Hajek *et al*, 1988).

#### Transdermal nicotine

There are a number of different nicotine patches available (again, over the counter in the UK) in different strengths. The main brand difference is that one brand is intended for daytime (16-hour) use only, whereas the others are intended for 24hour use. The nicotine absorption profiles of these patches are all very similar, the largest size delivering about 1 mg of nicotine per hour, achieving a relatively steady blood nicotine concentration of 10–20 ng/ml in the afternoon.

As yet there is no evidence suggesting that any brand is more effective than another. The patch has the great advantage that it is easy to use, and guarantees the patient a therapeutic dose of nicotine. The disadvantage is that because the speed of absorption is so slow there are no noticeable subjective effects, and the smoker has no opportunity to do something in order to receive more nicotine (at times of stress, for example).

The side-effects (mainly skin irritation) are generally mild. There have been consistent reports of an increased awareness of vivid dreams in patients using 24-hour patches but these are not troublesome (Fiore *et al*, 1992). The course of treatment usually consists of 6–12 weeks of fullsize patches, followed by 4 weeks during which the patient switches onto smaller sized patches in order to gradually wean themselves off nicotine. Patients generally have no problems coming off nicotine patches.

### Nasal nicotine spray (NNS)

Only one placebo-controlled trial of NNS has been published at present (Sutherland *et al*, 1992), but it seems clear that this product will have an important place in the treatment of heavily dependent smokers. The spray delivers a blood nicotine boost of 5–15 ng/ml within ten minutes of each dose (one snort in each nostril), which is capable of providing the smoker with some subjective effects and relief of craving. This advantage is partly offset by the fact that (particularly in the early stages) the spray produces some quite aversive side-effects (such as nasal stinging and watery eyes), not unlike the effect of snorting pepper.

However, in the first trial, patients were allowed to use the spray for 12 months, and 45% of the one year successes did so. This suggests that the spray may have greater dependence potential than gum. For these reasons the spray will probably only be available on prescription, and will be most appropriate in the context of moderately intensive treatment for heavy smokers.

#### **Prospects for NRT**

New forms of nicotine replacement therapy (nicotine inhaler and lozenge) are currently being evaluated and will probably be available in the next few years. At the moment there are no clear indications as to which form of nicotine replaceTable 4. Summary of elements of treatment for tobacco dependence

### Treatment variable

Speed of tobacco withdrawal Timing of psychological support Group or individual treatment Pharmacological aids Additional components

ment would be most helpful to which patients.

Initial signs suggest that the nicotine patch or 2 mg gum are most appropriate for mildly dependent smokers, whereas 4 mg gum or nasal spray (perhaps combined with the patch) would be most helpful to highly dependent smokers. Table 4 summarises the elements of treatment for tobacco dependence which are supported in the smoking cessation literature.

### Conclusion

Nicotine dependence and withdrawal are now recognised mental disorders, and there are a number of smoking cessation treatments of proven efficacy available. It is appropriate for psychiatrists to take a more active role in assessing the effects of smoking on mental health and promoting smoking cessation, both among psychiatric patients and the population as a whole.

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### Method of choice

- Abruptly on quit date
- Concentrated in first four weeks
- Group treatment whenever practical

### Nicotine replacement

- Measurement of expired carbon monoxide before and after cessation
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### Multiple choice questions

- 1 What is the typical half-life of nicotine?
  - a 30 minutes
  - b 1 hour
  - c 2 hours
  - d 6 hours
  - e 20 hours

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- 2 Which of the following is **not** a nicotine withdrawal symptom?
  - a depression
  - b anxiety
  - c insomnia
  - d poor concentration
  - e nausea
- 3 How long after smoking cessation is it before most withdrawal symptoms return to precessation levels?
  - a 2 days
  - b 1 week
  - c 4 weeks
  - d 3 months
  - e 6 months
- 4 Which biochemical measure of smoke intake is most appropriate for routine clinical use?
  - a saliva cotinine
  - b blood nicotine
  - c blood thiocyanate
  - d blood carboxyhaemoglobin
  - e expired carbon monoxide

- 5 Which of the following drugs is most effective in helping smokers to stop smoking?
  - a haloperidol
  - b clonidine
  - c lobeline
  - d diazepam
  - e nicotine

MCQ	answers		
1	2	3	
a F	a F	a F	
bF	bF	bF	
сТ	c F	c T	
d F	d F	d F	
4	5		
a F	a F		
bF	bF		
cF	c F		
dF	d F		
еТ	еT		

## Corrigendum

Advances in Psychiatric Treatment, Vol. 1, pp. 47-56. The footnote to Table 2 on page 53 should read as follows:

Starting levels: 1 = female, unilateral ECT

- 2 = male, unilateral ECT
- 2 = female, bilateral ECT
- 3 = male, bilateral ECT

Start one level higher if patient over 65 years and/or if patient is taking the equivalent of 15mg/

day of diazepam or any anticonvulsant. Increase dose by one level if a stimulation fails to induce a generalised tonic-clonic seizure (maximum 3 stimulations).

Dose levels increase by approximately 50% increments: 25, 50, 75, 125, 200, 275, 400, 550,700, 1000, 1200 (maximum output) milliCoulombs.

In the same article, the answer to the multiple choice question 4c (page 56) should have been False.