Theoretical Background and Clinical Use of Nicotine Chewing Gum

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If we accept the fact that the use of tobacco in its various preparations is a form of drug addiction, even though a pleasant one not affecting criminal statistics, we can more readily help our patient when he finds that his problem has gotten out of hand.

John L. Dorsey, MD, FACP, Baltimore, Maryland, 1936.

INTRODUCTION

For many years campaigns and treatments to promote smoking cessation have had disappointing results. In our view, this is because for most smokers cigarette smoking is a form of drug dependence and our programmers have failed because they have not taken this sufficiently into account. But the prospects are now brighter for more successful intervention in the future.

Firstly, there is more widespread appreciation of the addictive nature of smoking and, secondly, the development of nicotine chewing gum has provided the first effective aid to overcoming the pharmacological problem of withdrawal. But it is crucial that the pendulum does not swing too far towards over-reliance on pharmacological treatments and neglect of the important social and psychological factors which are a fundamental part of all addictive disorders. It is also important that the labelling of smoking as an addiction does not lead to the belief that permanent cessation is therefore impossible for smokers who are addicted. An addictive state is in no way impossible to overcome, although it is likely to be difficult and therefore to require commitment, planning, and possibly support as well.

Another significant recent advance that gives grounds for expecting more success in the future is the recognition of the value and cost-efficacy of minimal intervention or self-help, and the potential role of physicians in applying this approach. Most
important of all, perhaps, is the possibility that physician advice could be combined synergistically with the use of nicotine gum. Besides enhancing the efficacy of brief advice to stop smoking, it is likely that the availability of nicotine chewing gum will in turn encourage physicians to be more active in advising and helping their patients to give up smoking.

It is our purpose first to discuss briefly the nature of smoking as a form of drug dependence. This provides the theoretical basis for developing pharmacological approaches to cessation. We then focus on nicotine chewing gum as the first pharmacological approach with proven efficacy and discuss the theoretical rationale for its use, its mode of action, and various practical aspects necessary for effective use in different settings. Finally, besides its use as an effective aid to cessation, it has provided a means for advancing knowledge of the role of nicotine in smoking.

SMOKING AS A FORM OF DRUG DEPENDENCE

People smoke cigarettes for many reasons - social, psychological, sensory, behavioural, and pharmacological. But of all these the pharmacological motives are the most powerful and the most fundamental. If tobacco contained no nicotine, there would be no problem. People wouldn't smoke it, nor would they snuff it or chew it.

Although people begin to smoke for social and psychological reasons, pharmacological motives gradually take over as the smoker learns to inhale and a regular dependent smoking pattern becomes established. This escalation to dependence usually takes two or three years but sometimes occurs far more quickly. Other factors such as taste, smell, sensory irritation, and behavioural components such as handling also become important. This is mainly through frequent and close association with the pharmacological effects of nicotine. In other words, they are secondary. Without the presence of nicotine few people would develop a strong taste for tobacco.

Many surveys have shown that at least three out of every four smokers want to stop smoking or have tried to stop - some of them many times. Surveys also show that only about one in three smokers succeeds in stopping permanently before the age of 60. Thus most people smoke not because they really want to, but because they cannot easily stop. In other words, they smoke because they are hooked and dependent on nicotine. Blood nicotine levels of smokers vary widely, from 5 ng/ml to over 70 ng/ml, with an average level for heavy smokers of about 35 ng/ml. The distribution of peak blood nicotine concentrations just after a cigarette is shown in figure 1 for a sample of heavy smokers. Although the curve for smokers in the general population would be somewhat to the left, measurable pharmacological effects are produced with blood nicotine levels of 10 ng/ml or less. It is thus apparent that most regular smokers inhale and absorb sufficient nicotine to produce pharmacological effects.
It is not our brief here to go into all the pharmacological effects of nicotine or into the details of the evidence for its role in smoking and the tobacco withdrawal syndrome. But it should be emphasised that the modern cigarette is a highly efficient device for getting nicotine to the brain. The smoke is mild enough to be inhaled deeply into the alveoli of the lungs from where nicotine is rapidly absorbed into the bloodstream to reach the brain within about 7 seconds. This means that the inhaling cigarette smoker receives a rapid intravenous-like "shot" or bolus of nicotine to the brain after each inhaled puff. This contrasts with the slower steady rate of absorption from chewing tobacco or non-inhaled cigar smoking. Furthermore, the nicotine concentrations in the post-inhalation boli must be many times higher than those measured in mixed venous blood after completion of a cigarette. The pattern of pharmacological effects is no doubt correspondingly different following the different forms of intake.

PHARMACOLOGICAL APPROACHES

The concept of pharmacological approaches to smoking cessation is not new. In 1936, Dorsey suggested the use of lo&line as a
substitute for nicotine because of some putative pharmacological similarities (Dorsey 1936). But the pharmacological effects of lobeline are weak. It does not substitute for nicotine in animal experiments, and clinically it has never proved superior to placebo. The story is similar for other potential substitutes. Amphetamine, for example, increases smoking behaviour rather than diminishing it, and sedatives have no effect in tranquillizing doses. The subtle dual stimulant and sedative actions of nicotine appear to be unique. Animals discriminate these actions from those of all other drugs that have been tested (Hendry and Rosecrans 1982), and there is evidence for its effect on specific nicotine receptors in the brain (Abood et al. 1981) in addition to its classical effects on acetylcholine receptors.

Receptor blockade is another potential pharmacological approach. A drug that blocks the rewarding effects of nicotine could theoretically be used as an agent of extinction. Beta-adrenergic blockade by propranolol has been shown to block the peripheral effects of smoking on heart rate and blood pressure (Carruthers 1976). However it has no effect on reducing subjective satisfaction from smoking and has no potential, therefore, as a means to produce extinction. Mecamylamine, on the other hand, is a blocker of the nicotinic receptors of acetylcholine and appears to effectively block some of the subjective effects of nicotine (Henningfield and Jasinski 1983). Its short-term effect is to increase smoking behaviour (Stolerman et al. 1973), possibly in an attempt on the part of smokers to overcome the receptor blockade. But this is not an appropriate test of its potential as an aid to smoking cessation. More prolonged use would be necessary to test its capacity to produce extinction. It is our view, however, that cognitive factors and the capacity of humans to discriminate between conditions of smoking with and without mecamylamine make it unlikely that an extinction model based on old-fashioned learning theory would work. For similar reasons pharmacological aversion therapy with drugs such as emetine and apomorphine is unlikely to be effective. There is no punishment-model drug for smoking, such as disulfiram for alcohol abuse. There is also no prospect of one, since none of the known metabolites of nicotine are aversive in realistic concentrations. All this leaves nicotine substitution as the only feasible potentially effective pharmacological approach to smoking cessation.

NICOTINE SUBSTITUTION

There are many potential routes for administering nicotine. Besides the rate of absorption and other issues relating to bioavailability, the therapeutic potential of a particular route will also depend on factors such as safety and social acceptability. A number of routes can be excluded immediately. In the case of ingestion, absorption is slow and most of the nicotine is metabolised by the liver to metabolites which are
pharmacologically inert. Nicotine suppositories or pessaries would be inconvenient and unacceptable. Injections would need to be repeated too frequently to be practical, and would not be feasible for widespread use. Transdermal delivery certainly has potential but has not yet been developed in the case of nicotine. This leaves the three routes—lungs, buccal and nasal mucosae—which have been used for tobacco for over 500 years.

Of these three routes, the rate of absorption through the lungs is, as mentioned earlier, far and away the most rapid. This is simply a matter of surface area, that of the lungs being roughly equivalent to the size of a tennis court. Although it is technically possible to produce aerosols with particles small enough to reach the alveoli, to our knowledge no satisfactory nicotine aerosol has yet been developed. We have seen and tested four. They have been either too clumsy or have failed to produce potentially useful blood nicotine concentrations. Irritancy to the throat has been another major problem. A notable exception has been the development of a vaporiser shaped like a cigarette (Jacobson et al. 1982). Inhalation through this device enables nicotine in vapour form to be taken into the lungs. It is not excessively irritating and is capable of producing therapeutically useful blood nicotine concentrations. If a problem of safety can be overcome, such a device would be well worth further study.

The historical fact that tobacco has been chewed and taken as "wet" snuff in the north and "dry" snuff in the nose suggests that absorption of nicotine by either route is sufficient to produce pharmacological effects. Blood nicotine concentrations after "wet" and "dry" snuff have been shown to be equivalent to those produced by cigarette smoking (Gritz et al. 1981; Russell et al. 1981). Various nicotine-containing lozenges and tablets have been produced from time to time for help with smoking cessation, but they have never been systematically tested, and in most cases their nicotine delivery has been inadequate for therapeutic value. Nicotine-containing chewing gum, on the other hand, has been extensively tested (see below). One possible limitation of nicotine gum is that the rate of nicotine absorption is slow compared with inhaled cigarette smoking. Preliminary study with a nasal nicotine solution (NNS) used as a kind of liquid snuff shows that nicotine is absorbed more rapidly and efficiently through the nose than through the lining of the mouth (Russell et al. 1983a, see figure 2). With refinements in flavour and acceptability, it is possible that a form of NNS could be clinically useful for those smokers who get insufficient help from nicotine gum or who have problems with dyspeptic symptoms.

Finally, as a general principle, it is likely that more therapeutic success might be expected from those forms of nicotine substitution which also provide a sensory experience and a socially acceptable behavioural component to act as substrates for conditioning as acquired secondary reinforcers.
Figure 2. Plasma nicotine concentrations before, during, and after chewing a single piece of nicotine chewing gum containing 4 mg (top) and 2 mg nicotine (bottom). The plasma nicotine concentrations produced by smoking a cigarette are also shown as are those produced by the non-inhaled smoking of a large Havana cigar (top) and use of a single 2 mg dose of nasal nicotine solution (NNS) (bottom). (Top is from Russell et al. Brit Med J, 280:1599-1602, 1980, and bottom from Russell et al. Brit Med J, 286:683-684, 1983). Copyright 1980 and 1983, The British Medical Association.
NICOTINE CHEWING GUM

A nicotine-containing chewing gum was first developed more than 10 years ago by Ove Ferno in Sweden for use as an aid to smoking cessation (Ferno et al. 1973). Its purpose is to ease withdrawal symptoms by providing an alternative source of nicotine and, in addition, a substitute oral activity. It enables the smoker to break the habit in two stages. In the first stage, the smoker is able to focus on overcoming the behavioural and psychological components of dependence without at the same time having to cope with nicotine withdrawal. The dependence on nicotine is overcome at a later stage when there is no longer any urge to smoke.

It should be stressed, however, that the slower rate of nicotine absorption through the buccal mucosa and the absence of puff-by-puff high-nicotine boli (see above) make the gum an incomplete nicotine substitute for smokers who inhale. For the same reason cigarette smokers who inhale deeply gain little satisfaction from cigars unless they too are inhaled. The purpose of nicotine gum, therefore, is to relieve nicotine related withdrawal symptoms rather than provide the same positive pleasure as inhaled smoking.

The product

Since the early days of its development the nicotine-containing chewing gum (Nicorette) has been considerably refined and improved. It is available in two strengths, each piece containing either 2 mg or 4 mg of nicotine (only the 2 mg strength is available in the United States). The nicotine is bound to a resin and its release depends on the rate and vigour of chewing. About 90% of the nicotine is released after 30 minutes of normal chewing (Ferno et al. 1973). The gum also contains a buffer to maintain the pH in the mouth at about 8.5, at which the nicotine is well absorbed through the buccal mucosa. Swallowed nicotine is absorbed and rapidly metabolized in its first passage through the liver (Russell and Feyerabend 1978).

Pharmacology

The rate of absorption of nicotine from the gum is relatively slow (see figure 2). The peak plasma concentration is reached 15–30 minutes after starting to chew the gum, compared with 1–2 minutes after completion of a cigarette. However, a 4 mg piece of gum chewed every hour for 2–3 hours produces plasma nicotine concentrations similar to those in heavy cigarette smokers (McNabb et al. 1982; Russell et al. 1976a and 1977; see figure 3). Cardiovascular effects, such as increase in heart rate and blood pressure, produced by 4 mg gum match those after cigarette smoking, but the 2 mg gum has less effect (Fredholm and Sjogren 1979; Nyberg et al. 1982).

Effect on Ad Libitum Smoking Behaviour

In two short-term studies in subjects who were instructed to smoke freely without making any deliberate attempt to reduce their
Figure 3. Plasma nicotine concentrations in the same subject when smoking one cigarette per hour and when chewing a piece of 4 mg nicotine gum every hour. (From Russell et al. Brit Med J, 1:1043-1046, 1976). Copyright 1976, The British Medical Association.
smoking, nicotine chewing gum had a modest inhibitory effect on smoking behaviour (Kozlowski et al. 1974; Russell et al. 1976b). While chewing active gum, the subjects smoked fewer cigarettes, smoked them less intensively, and inhaled less deeply (as measured by COHb) than when chewing a placebo gum.

Effect on Withdrawal Symptoms

In an early short-term crossover study (Russell et al. 1976b), nicotine chewing gum was rated as more satisfying than a placebo. It was also rated as significantly more effective at putting the subjects off cigarettes and as more helpful after stopping smoking. In more recent clinical studies (see below), besides being more effective than placebo in helping smokers to give up cigarettes, active gum was significantly more effective than placebo at relieving irritability, hunger, and sleepiness during the first 6

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n=21)</th>
<th>Active Gum (n=27)</th>
<th>Difference between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressed</td>
<td>.06</td>
<td>NS</td>
<td>.025</td>
</tr>
<tr>
<td>Irritable</td>
<td>.001</td>
<td>NS</td>
<td>.025</td>
</tr>
<tr>
<td>Less sociable</td>
<td>.025</td>
<td>NS</td>
<td>.05</td>
</tr>
<tr>
<td>Less composed in company</td>
<td>.05</td>
<td>NS</td>
<td>.01</td>
</tr>
<tr>
<td>At a loose end</td>
<td>.05</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Restless</td>
<td>.05</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Dizzy</td>
<td>.05</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Reduced concentration</td>
<td>.025</td>
<td>.001</td>
<td>NS</td>
</tr>
<tr>
<td>Hunger</td>
<td>.001</td>
<td>.001</td>
<td>NS</td>
</tr>
</tbody>
</table>

Note: Ratings of all the withdrawal symptoms listed above changed significantly in those on placebo gum. In those on active gum, the only ratings to show significant change were reduced concentration and increase in hunger. Comparison of the changes in the two groups (3rd column) shows that nicotine replacement provided by 2 mg nicotine gum alleviated symptoms of depression, irritability, reduced sociability and composure in company.

weeks of treatment (Jarvis et al. 1982). However, the active and placebo groups differed in abstinence rates during this period, and this may have partially accounted for the differences in withdrawal symptom ratings.

In a study designed specifically to test the effect of partial nicotine replacement on withdrawal symptoms during the first 24 hours of abstinence from smoking, 48 smokers were randomly assigned to chew either active 2 mg nicotine gum or a placebo (West et al. 1984). Subjective ratings were recorded before and during abstinence. The results in table 1 show that those who received placebo gum experienced a number of withdrawal symptoms during abstinence, whereas those given active gum experienced very few. In other words, the active gum was successful in alleviating some but not all the withdrawal symptoms. Similar findings have been reported in other studies (Hughes et al. 1984; Schneider and Jarvik 1984). It is noteworthy that these results were achieved despite the fact that plasma nicotine concentrations on the active 2 mg gum averaged only 8.3 ng/ml compared with base-line smoking concentrations of 31 ng/ml and 25 ng/ml for peaks and troughs respectively (West et al. 1984). More effective nicotine replacement with 4 mg gum and/or more experience of chewing could lead to greater relief of withdrawal symptoms.

In view of the capacity of nicotine chewing gum to produce blood nicotine levels comparable to smoking, albeit more slowly, in view of its capacity to produce some of the pharmacological effects of smoking, to inhibit ad libitum smoking, and to relieve tobacco withdrawal symptoms, in addition to providing an oral substitute, it would be surprising indeed if it were not also to prove a useful aid to cessation.

CLINIC-BASED TREATMENT

Over the past 20 years, many kinds of treatment methods have been tried to help people to give up smoking. These include hypnosis, group treatment, acupuncture, aversion therapy, and other psychological methods. None of these has been shown to give better results than an equivalent amount of simple attention and support which produces success rates ranging from about 10% - 25% abstinent at 1-year follow up. Drugs such as lobeline and tranquilizers are no better than placebos, probably because they are inadequate substitutes for nicotine (see above). In our view, the main obstacle to success is the addictive nature of smoking. This is the root of the problem and, until recently, none of the cessation methods have been applied directly to it. However, since the development of nicotine chewing gum, the situation has changed.

In a comparative study at our clinic (Raw et al. 1980), those treated with nicotine gum had a success rate of 38% at 1-year follow up, compared with only 14% for those who had intensive psychological treatments. More recently, in a double-blind placebo-controlled trial (Jarvis et al. 1982) we obtained a success rate of 47% not smoking at 1-year follow up, compared with 21% for those on placebo gum (see table 2). The active gum was also
significantly more effective than the placebo at relieving withdrawal symptoms. In both these studies abstinence from smoking was confirmed by carbon monoxide measures. Adverse side-effects were limited to gastrointestinal symptoms such as nausea, indigestion, and hiccups. These were minor and transient and in no case warranted discontinuance of gum use. About 7% of the subjects became dependent on active gum (none on placebo). Probably because absorption of nicotine is less rapid than from smoking, the dependence was also less severe and was usually overcome without relapse to smoking. Similar results have been obtained in placebo-controlled trials in Sweden and the U.S.A. (Fagerstrom 1982; Hjalmarson 1984; Schneider et al. 1983).

**TABLE 2**

<table>
<thead>
<tr>
<th>Treatment with nicotine chewing gum (% abstinent)</th>
<th>Placebo Gum (n=58)</th>
<th>Active Gum (n=58)</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abstinent at 1 month</td>
<td>33%</td>
<td>62%</td>
<td>p&lt;.01</td>
</tr>
<tr>
<td>Abstinent at 1 year</td>
<td>21%</td>
<td>47%</td>
<td>P&lt;.01</td>
</tr>
<tr>
<td>Lapse-free abstinence throughout 1 year</td>
<td>14%</td>
<td>31%</td>
<td>P&lt;.025</td>
</tr>
</tbody>
</table>


**LIMITATIONS OF INTENSIVE METHODS**

Intensive treatment and support at specialised smoking withdrawal clinics can achieve 1-year abstinence rates of up to 40%, but the average is nearer 20%. Even if higher success rates could be obtained, the clinic-based approach has two major limitations. Firstly, only a minority of smokers will ever attend a clinic and, secondly, if they did attend, there are simply too many smokers for clinics to cope with. Few clinics in Britain attract as many as 200-300 clients a year, and many of these attend only once and so do not avail themselves of the treatment offered. A relatively busy and effective clinic is unlikely to achieve more than 100 long-term ex-smokers per year and the yield of the average clinic is probably below 50 per year.
THE MINIMAL INTERVENTION STRATEGY

The rationale behind this strategy is that the yield of long-term ex-smokers will be greater if the therapist/counsellor/advisor spends less time with more smokers rather than focusing on intensive effort with a few. A method with a low but proven success rate, achievable with minimal effort and readily applicable to large numbers of smokers, could be more useful in terms of public health than a time-consuming intensive method with a far higher success rate. In this respect we have been impressed by the powerful role that physicians could exercise. In the course of their everyday work physicians have face-to-face access to the majority of the 17 million cigarette smokers in Britain. Some 95% of the British population attend their family physician at least once in a 5-year period, and about 75% attend at least once in a year. Attendance rates in other developed countries are unlikely to be very different.

In a previous study we showed that brief advice against smoking given by family physicians in their own style, together with a leaflet and warning of follow-up, achieved a success rate of 5.1% who stopped smoking within the first month and were still abstinent at 1 year, compared with 0.3% in non-intervention controls (Russell et al. 1979). It is emphasised that these results were based on all cigarette smokers who attended the physicians' offices, irrespective of whether they wanted to stop at the time or whether they had or had not already got a smoking-related disease. Although small, this effect was highly significant statistically, and for the reasons stated above has the potential for creating more ex-smokers than is ever likely to occur via intensive methods.

PHYSICIAN INTERVENTION WITH NICOTINE CHEWING GUM

We have recently completed a further study designed to see whether the offer and prescription of nicotine chewing gum (2 mg Nicorette) would enhance the efficacy of brief routine advice by physicians (Russell et al. 1983b).

The target sample comprised all cigarette smokers, aged 16 or more, who attended the offices of 34 family physicians in six group practices during a 3 1/2-week period. They were assigned by week of attendance (in a balanced design) to one of three groups. Group 1 were non-intervention controls. Group 2 received advice to stop smoking plus a booklet and a warning of follow up. Group 3 received the same as Group 2 but, in addition, were offered nicotine chewing gum. If the offer was accepted, a prescription and instruction booklet were also given, A postal follow-up was done after 4 months and again after 1 year. Expired-air carton monoxide was checked in two-thirds of those claiming abstinence at 1 year. The results are based on the 1,938 (89%) who had not moved to an unknown address or died during the year. Among these 1,938 there were 327 who did not provide adequate data. They were counted as continuing smokers. The main results are shown in table 3.
TABLE 3

Minimal intervention by family physicians

<table>
<thead>
<tr>
<th></th>
<th>No Advice (N=584)</th>
<th>Advice Only (n=675)</th>
<th>Advice and Nicotine Gum (n=679)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tried to stop</td>
<td>36.6</td>
<td>46.1</td>
<td>61.1</td>
</tr>
<tr>
<td>Abstinent at 4 months</td>
<td>10.3</td>
<td>14.1</td>
<td>20.2</td>
</tr>
<tr>
<td>Still abstinent at 1 year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-report</td>
<td>6.0</td>
<td>6.4</td>
<td>11.9</td>
</tr>
<tr>
<td>Adjusted for non-validation</td>
<td>3.9</td>
<td>4.1</td>
<td>8.8</td>
</tr>
</tbody>
</table>

Note: The results are shown as percentages based on all subjects in each group. All comparisons between the nicotine gum and the other groups were significant at the p<.005 level. (Russell et al. Brit Med J, 287:1782-1785, 1983). Copyright 1983, The British Medical Association.

As with the clinic based studies, use of the gum in a family physician setting doubled the success rate achieved by advice alone. Further analyses, which can be found in the full report (Russell et al. 1983b), showed that the offer and availability of the gum achieved its overall effect in three ways. It motivated more smokers to try to give up smoking (p<.001), it increased the success rate among those who tried (p<.05), and reduced the relapse rate among those who had stopped at 4 months (p<.05).

The greater efficacy of Group 3 intervention was achieved despite the fact that the results are based on all subjects and that only 53% actually tried the gum. There was a complex relation between initial cigarette consumption, gum use, and success rate. Heavier smokers tended to use more gum, and heavy gum use was associated with a higher success rate. In particular, the self-selected subgroup (8% of Group 3) who used more than a box of gum (105 pieces) had a long-term success rate of 34.6% (24% after adjustment for failed validation). These successes had had an initial cigarette consumption prior to intervention averaging 23 cigarettes per day compared with 13 and 12 per day for the successes in Groups 1 and 2 respectively and 12 per day for the remaining successes in Group 3.
An 8.8% success rate may at first seem unimpressive compared with rates of 40% obtained with intensive methods at specialised clinics. It may help to get it in perspective. We calculated that if the 34 physicians in this study were to continue the Group 3 procedure routinely, the net yield of long-term ex-smokers (over and above the spontaneous cessation rate in the non-intervention controls) would average about 38 per physician in the first year. Extrapolated to all 28,000 family physicians in Britain, and assuming they could achieve similar results, the initial yield would be around 1 million w-smokers a year, and possibly similar results could be obtained for several ensuing years.

Finally, although higher success rates could undoubtedly be achieved if physicians had the time for more intensive support and follow up, we suggest that the overall yield of ex-smokers would be greater if physicians allocated their time by spending a little of it with many smokers rather than a longer time with a few. Ideally, physicians should know, by enquiring if necessary, the current smoking status of every patient they see, advise all cigarette smokers to stop, and offer nicotine gum and an instruction booklet to all those who want to stop but have little confidence in being able to succeed without help. Such activity by physicians could achieve more than most other approaches to smoking cessation.

PRACTICAL ASPECTS OF GUM USE

Success rates achieved with the use of nicotine chewing gum depend on many factors, including the degree of motivation and dependence of clients, the intensity of psychological support in the short term, and in the longer term the degree of care given to follow-up. However, one factor is essential if the gum is to be used successfully in any setting. This is adequate information on what the gum will and will not do, and careful instruction on its use. As mentioned previously, the gum is at best a partial substitute for cigarettes and does not provide as much positive satisfaction. It follows that it is a treatment aid rather than a complete treatment. Smokers who approach it naively, hoping, as many do, that it will somehow magically stop their smoking without the need for any effort on their own part, are inevitably disappointed and may wrongly conclude that the gum has nothing at all to offer. It is therefore vital that clients be made aware of the positive and negative aspects of the gum in order to gain maximum benefit from its use. The failure of a recent multicentre trial of nicotine chewing gum to achieve even a placebo effect may reflect among other things inadequate attention to the crucial aspects of subject instructions (British Thoracic Society 1983; Jarvis and Russell 1983). We summarise in appendix 1 the main points that we have found helpful to communicate to clients.
Management of treatment with nicotine gum is relatively straightforward. The main issues are firstly whether all patients need the gum, and secondly whether long-term dependence on it is a matter for serious concern. Motivation to give up cigarettes is a prerequisite for success, and it is sensible to seek evidence of this in serious unaided attempts to quit before considering the offer of nicotine chewing gum. Light smokers are more likely than heavy to stop without any formal help, but present evidence suggests that their success rates, like those of heavy smokers, are enhanced by use of the gum. The main point to resolve therefore should be whether the client's history suggests that dependence as opposed to lack of motivation has been the main block to achieving smoking cessation.

Most people do not find it difficult to stop using the gum, but a small minority do become dependent on it and may continue to use it for a year or longer. While long-term use of the gum should be discouraged, both because continuing dependence on nicotine increases the risk of relapse to smoking and because of possible health risks of gum use per se, in our view it is not advisable to refuse to continue to prescribe to a client who is not smoking. This is almost guaranteed to produce relapse to smoking, which is far more harmful to health. We summarize in appendix 2 the main issues of treatment management.

THEORETICAL IMPLICATIONS

Like most new treatments, nicotine chewing gum given with enthusiasm no doubt has a strong placebo effect. Some people dismiss this quality with scorn. In our view, this is mistaken. As a principle, a safe placebo may be turned to better use than an active treatment that carries a risk. Placebo response is a valid and potentially useful psychological effect. It would seem preferable in treatment situations to view it as an asset to be used positively to enhance results rather than negatively as a reason for undermining the value of treatment.

There is no doubt, however, that nicotine chewing gum has an effect over and above that of the attention-placebo response. Besides achieving higher success rates than placebo, it significantly alleviates withdrawal symptoms, as has been discussed already. There is one further point. In our placebo-controlled trial (Jarvis et al. 1982) we found that among those who were abstinent at 1 month, gum consumption (number of pieces per day) correlated with pretreatment blood nicotine concentration in the active group \((r = .48)\) but not in the placebo group \((r = .17)\). Pretreatment cigarette consumption, on the other hand, correlated with gum use in the placebo group \((r = .47)\) but not in the active gum group \((r = .11)\). These findings were statistically significant and point to different processes underlying the use of nicotine gum and placebo gum. The evidence for the specific efficacy of nicotine chewing gum over and above that of attention-placebo factors is summarized in table 4.
TABLE 4

SUMMARY OF EVIDENCE FOR SPECIFIC EFFICACY OF NICOTINE CHEWING GUM

1. Can produce blood nicotine levels similar to cigarette smoking.
2. Produces some pharmacological effects equivalent to smoking.
3. Inhibits ad libitum smoking.
5. Subjectively helpful to smokers.
6. Reduces withdrawal symptoms.
7. Gum use correlates with pretreatment blood nicotine; placebo does not.
8. About 7% become dependent on nicotine gum, none on placebo.

Besides its use as an effective aid to smoking cessation, nicotine chewing gum has already proved a useful tool for research. Firstly, it has stimulated a new wave of clinical trials in which far more rigour has been applied than previously to important methodological issues such as biochemical validation and success criteria. Only recently, for example, has a clear distinction been made between abstinence at 1 year follow-up and lapse-free abstinence throughout the year.

Secondly, and more importantly, its effect compared with placebo in enhancing smoking cessation success rates, in alleviating withdrawal symptoms, and in inhibiting ad libitum smoking has provided new evidence for the role of nicotine in smoking.
SUMMARY AND CONCLUSIONS

In our view, nicotine chewing gum is the most significant single advance achieved so far in the whole field of smoking cessation. It is the only treatment that has yet been shown to have a specific effect over and above that of attention-placebo factors, and this has been demonstrated repeatedly by several research groups in different countries. It is suitable for use as an adjunct both to intensive psychological methods of treatment and to minimal and largely self-help types of intervention. In either case, it approximately doubles the success rates achieved by intervention without the use of gum. It can be administered effectively by psychologists and family physicians and no doubt by other adequately trained health professionals too.

The efficacy of nicotine chewing gum is not limited to the smokers who use it. Its incorporation into a treatment or intervention programme revitalises and maintains the morale of therapists. Until the advent of nicotine gum it has required either a research interest, financial reward, or a degree of masochism to remain for long at the sharp end of the business of helping people to give up smoking. Without a treatment capable of reducing withdrawal symptoms, therapists became drained by having constantly to give out encouragement and support to help their clients to tolerate withdrawal long enough for the difficulties gradually to wane. The rapid and tangible effect of the gum in relieving withdrawal symptoms is a boost to the morale and confidence of client and therapist alike. It is perceived as helpful even by those who fail. This encourages people who relapse to return for further therapy. A discouraging feature with other treatments has been the tendency for those who relapse to avoid contact with their therapists even to the extent of not responding to data collection at long-term follow up.

In view of its efficacy, its potential for use in many settings, its minimal demands on therapists' time, and its synergistic effect in encouraging and boosting the confidence of clients and therapists alike, it is possible that over a period of years nicotine chewing gum could have a significant impact on national smoking prevalence. But to achieve this, it is essential that it be used correctly.
APPENDIX 1

INFORMATION FOR CLIENTS ABOUT NICOTINE CHEWING GUM
AND INSTRUCTIONS ON ITS USE

★ The gum is not a magic cure. Personal commitment and effort are still necessary for success.

★ The gum contains nicotine which is released as it is chewed and absorbed through the lining of the mouth.

★ Absorption of nicotine is slower than from cigarettes; therefore the gum does not give the same positive pleasure as smoking.

★ The gum does not stop the smoker from smoking, but it does make it easier to cope without cigarettes after stopping.

★ The gum reduces craving for cigarettes and makes withdrawal symptoms less severe.

★ Its use should be started after quitting cigarettes.

★ Each piece should be chewed for 20-30 minutes to allow all the nicotine to be released.

★ The gum should be chewed gently, with frequent pauses. Too vigorous chewing causes excessive salivation. Nicotine which is swallowed is destroyed and wasted. It may also cause indigestion.

★ A piece of gum should be chewed whenever the urge to smoke is very strong. On average pack-a-day smokers use about 7 gums per day.

★ The gum may taste unpleasant at first and irritate the throat. Most people adapt to it after persisting for a day or two, but it may take up to a week to get used to it.

★ The gum should be used for up to 3 months before attempting to discontinue its use. Even then it is a good idea to carry a few pieces in case of emergencies.
APPENDIX 2

MANAGEMENT OF TREATMENT WITH NICOTINE CHEWING GUM

★ Offer only to smokers who seriously want to quit, and have tried previously without success or have little confidence in succeeding without help, including light smokers who meet these criteria.

★ Give usual guidelines on quitting – e.g., setting a target day for stopping, avoiding difficult situations, etc. The gum is probably less suitable for gradual cessation, but can be readily incorporated into most other programs.

★ Give verbal and written instructions to all clients, along the lines suggested in appendix 1. In most countries a manufacturer's booklet is available.

★ Discontinue the gum if the client continues to smoke. We usually warn clients who have not quit by 2 weeks that they will get no more if they have not quit by their next visit.

★ Consider 4 mg gum if the client uses more than 15 per day of the 2 mg strength. (4 mg gum is not yet available in the U.S.A.)

★ Encourage gradual withdrawal from gum after 3 months abstinence from smoking. Most will not find this difficult. Longer term dependence develops in a few, but may be preferable to relapse to smoking, which is the probable alternative if the gum is withheld from clients who feel they cannot do without it.

★ Unwanted effects such as sore mouth, hiccups, and gastric symptoms are relatively common initially but are rarely a cause for discontinuance. They are often a sign of excessively vigorous chewing.

★ In our view the following conditions are cause for caution but do not exclude use of the gum: pregnancy, peptic ulcer, coronary heart disease, hypertension, peripheral vascular disease. In all these conditions continued smoking is probably more harmful than moderate gum use.
REFERENCES


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