weakness of the forehead and eye closure in a unilateral upper motor neurone facial weakness. Dysarthria is a common accompaniment of hemiparesis due to a unilateral cerebral hemisphere vascular lesion in patients who do not have dysphasia and who are not drowsy. Its presence in the absence of dysphasia does not necessarily indicate that there is a lesion within the brain stem or lesions in both cerebral hemispheres. The frequent weakness of sternomastoid contralateral to the hemiparesis is a striking example of the principle that the cerebral hemisphere controls movement of body parts in or towards the contralateral half of the body rather than simply the contralateral muscle groups. That principle is widely accepted but its implications with respect to weakness of head turning in patients with lesions in a cerebral hemisphere have not been emphasised in most of the widely used neurological texts. There has also been little comment about the apparent exception to this principle in people with unilateral supranuclear innervation of the tongue.

References

1 Brodal A. *Neurological anatomy in relation to clinical medicine.* 3rd ed. New York: Oxford University Press, 1981.
2 Members of the Department of Neurology and the Department of Physiology and Biophysics, Mayo Clinic and Mayo Foundation for Medical Education and Research, Graduate School, University of Minnesota, Rochester, Minnesota. *Clinical examinations in neurology.* 3rd ed. Philadelphia: WB Saunders Co, 1971.
3 Chusid JG. *Correlative neuroanatomy and functional neurology.* 18th ed. Los Altos: Lange, 1982.
4 Patten J. *Neurological differential diagnosis.* London: Harold Starke Ltd, 1977.
5 Bickerstaff ER. *Neurological examination in clinical practice.* 4th ed. Oxford: Blackwell Scientific, 1980.
6 Walton JN. *Brain's diseases of the nervous system.* 8th ed. Oxford: Oxford University Press, 1977.
7 De Jong RN. *The neurologic examination.* 3rd ed. New York: Hoeber Medical Division, Harper and Row, 1967.
8 Alpers BJ, Mancall FL. *Clinical neurology.* 6th ed. Philadelphia: F A Davis Co, 1971.
9 Reeves AG. *Disorders of the nervous system. A primer.* Chicago: Year Book Medical Publishers Inc, 1981.
10 Balagura S, Katz RG. Undecussated innervation to the sternocleidomastoid muscle: a reinstatement. *Ann Neurol* 1980;**7**:84-5.
11 Spillane JD, Spillane JA. *An atlas of clinical neurology.* 3rd ed. Oxford: Oxford University Press, 1982.
12 Taverner D. The localisation of isolated cranial nerve lesions. In: Vinken PJ, Bruyn GW, eds. *Handbook of clinical neurology.* Vol 2. *Localization in clinical neurology.* Amsterdam: North-Holland Publishing Company, 1969.
13 Adams RD, Victor M. *Principles of neurology.* 2nd ed. New York: McGraw-Hill, 1981.
14 Gilroy J, Meyer J. *Medical neurology.* 3rd ed. London: MacMillan, 1979.
15 Baker AB, Baker LH, eds. *Clinical neurology.* Hagerstown, Md: Harper and Row, 1976.
16 Basmajian JV. *Muscles alive: their functions revealed by electromyography.* 3rd ed. Baltimore: William and Wilkins, 1974.
17 Geschwind N. Nature of the decussated innervation of the sternocleidomastoid muscle. *Ann Neurol* 1981;**10**:495.

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Placebo controlled trial of nicotine chewing gum in general practice

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Abstract

Of 2110 adult cigarette smokers originally recruited to a study of the effect of antismoking advice in general practice, 429 who reported at follow up after one year that they had tried unsuccessfully to stop smoking were offered "a special antismoking chewing gum," either nicotine gum or a placebo gum, in a double blind study. Of 200 who were willing to try the gum, 101 were randomly allocated to the nicotine gum and 99 to the placebo gum. They were followed up at six months by an unannounced home visit, at which they were interviewed and asked to provide a breath sample for analysis of carbon monoxide. Twenty five claimed that they had stopped smoking, but, of them, seven exhaled levels of carbon monoxide indicative of continued smoking. Of the 18 in whom giving up smoking was validated, 10 had received active gum and eight placebo gum, a difference which was not significant (odds in favour of nicotine gum =1·25, 95% confidence limits 0·47-3·31).

The value of nicotine chewing gum, if any, can be quite small when it is used in general practice.

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Introduction

Nicotine chewing gum became available in Britain as a prescription only aid to giving up smoking in mid-1980. Various trials conducted in clinics for smokers in Britain and Sweden have indicated that nicotine gum gives better results than do either conventional "psychological" methods of giving up smoking[1 2] or placebo gum containing no nicotine.[3 4] The relevance, however, of these studies to everyday medical settings such as hospital outpatients or general practice is not certain because the patients seen at special smokers' clinics are unlikely to be typical of all smokers and the treatment programmes prescribed by the clinics all included intensive contact with patients and follow up by specialist staff. Also, in a large multicentre study investigating 1550 patients seen by British chest physicians nicotine chewing gum was no better than a placebo or simple advice to stop smoking given by the doctor.[5]

More recently, a controlled trial in general practice reported a doubling in the long term incidence of giving up among patients who were offered nicotine gum as well as being advised to stop smoking during a routine consultation compared with patients who received advice alone.[6] Only 53% of the patients who were offered the gum actually tried it, but even the offer of this extra help was associated with both increased numbers of attempts to stop smoking and increased success among those who tried. The "open" nature of this trial, however, meant that the differences in outcome might have been partly or completely due to differences in the way the doctors conducted the consultations.[7] Because of unanswered questions of this kind arising from previous studies we conducted a randomised,

placebo controlled trial of nicotine chewing gum in general practice to examine its effectiveness in this setting when other potential confounding factors were controlled.

Subjects and methods

A controlled trial of nicotine chewing gum was a logical extension of our previous study of the effects of routine advice to stop smoking given by the general practitioner.[8] As the gum is expensive and its use requires careful explanation by the doctor we wished first to identify patients who would respond to simpler, less intensive "treatments." Our earlier study had already served to do this.[8] Smokers were admitted to the trial of nicotine chewing gum if at follow up after one year in the earlier study they reported having made one or more unsuccessful attempts to stop smoking over the preceding 12 months.

All 29 doctors in the six general practices that had participated in the previous study were invited to collaborate in the new project; 24 agreed to do so. After a doctor had confirmed that there were no contraindications to the prescription of nicotine chewing gum, each eligible patient was sent a letter from the trial centre at Oxford University saying that the doctor was pleased that they were trying to give up smoking and was willing to prescribe "a new special chewing gum to help you." The letter also indicated the date and time of an appointment that had been reserved for the patient to discuss this new treatment with the general practitioner.

If the patient kept the appointment the doctor was to complete a brief questionnaire concerning the patient's current smoking habits and outline the study and the principles underlying the use of the gum. He was also to explain why it was an important feature of the project that neither the doctor nor the patient knew if a particular batch of gum contained nicotine (appendix I). The patients were (correctly) assured that both the preparations under study were "specially formulated antismoking chewing gums."

Patients who agreed to try the chewing gum were allocated to the next available of 10 alphabetical codes for treatment from a list kept in each practice. The codes were balanced to give equal numbers of patients receiving either the active gum containing 2 mg buffered nicotine per tablet or a placebo identical in appearance and packaging. The patients were advised that abrupt stopping of smoking was essential and that the gum should be used for at least three months. The practice staff gave each patient two boxes (210 tablets) of gum together with written instructions on how to use it (appendix II) and arranged follow up appointments. No one doctor or member of staff was likely to see sufficient numbers of patients to be able to break the 10 code system.

Patients were asked to attend follow up appointments at the surgery at two, four, and 12 weeks after the index visit. The doctor was to complete a simple data sheet on each of these occasions. Six months after the initial consultation, and regardless of whether the patient had attended the follow up appointments, he or she was paid an unannounced visit at home by KJ, who remained "blind" to the treatment that had been allocated. At this visit patients were questioned about whether they were still smoking and each was asked to provide a sample of exhaled air for analysis by a portable carbon monoxide meter (Ecolyzer, Energetics Science Inc) so that their reported smoking habit could be validated.[9]

TABLE I—*No (%) of eligible patients entering or not entering the trial*

Attended appointment and recruited	200 (42·8)
Attended, not recruited	10 (2·1)
Cancelled appointment	20 (4·3)
Did not attend	199 (42·7)
Already given up smoking	22 (4·7)
Moved from practice	8 (1·7)
Tried gum before	7 (1·5)
Died	1 (0·2)
Total	467 (100)

Results

Four hundred and sixty seven patients were identified as being eligible for the trial, but only 200 (42·8%) of these were eventually studied. Table I gives the reasons for our failure to recruit the remaining 267. In most cases (199 (42·7%)) the reason was that patients simply did not attend the appointment that had been reserved for them.

There were no significant differences in demographic variables or type, quantity, or duration of smoking between the 467 eligible patients and the remaining 1643 cigarette smokers recruited to our previous study of routine antismoking advice from general practitioners.[8] The eligible patients, however, had originally reported more symptoms related to smoking, a greater desire to stop smoking ($p<0·001$), and a stronger intention to stop ($p<0·01$). In addition, more had attempted to stop before the study of the effect of routine advice ($p<0·01$). When the 200 patients enrolled in the trial were compared with the remainder of those who were eligible no major differences were observed.

Ninety nine patients were randomly allocated to receive the placebo and 101 to receive the chewing gum containing nicotine. Internal comparisons showed that the two groups were well matched for all the variables referred to above except that a significantly greater proportion of those allocated to the placebo reported having made more than one attempt to stop smoking over the year preceding recruitment (82 (83%) of those receiving the placebo *v* 54 (53%) of those receiving the active chewing gum; $p<0·001$). Although statistically unlikely, this difference must have arisen by chance.

Table II shows the numbers of patients seen at each follow up investigation and the numbers claiming to have stopped smoking. Less than a quarter of the patients kept the three month follow up appointment with their general practitioner, but data were collected for all the patients, apart from three who had moved house and were untraceable, at the home visit six months after recruitment. One hundred and eighty four patients (91 receiving active chewing gum and 93 receiving placebo) were interviewed in person, and information about the smoking habits of the 13 others was obtained by interviewing an adult relative; seven of these 13 patients also later returned a completed questionnaire by post.

Assuming that patients who were not seen had continued to smoke, the proportion claiming to have given up smoking fell steadily from almost 30% at the follow up after two weeks to 12% after six months. After six months seven (28%) of those describing themselves as ex-smokers had exhaled carbon monoxide levels exceeding 12 parts per million, indicating that they were probably still smoking.[9] A significant difference in incidence of either claimed or carbon monoxide validated stopping of smoking was not seen between the two groups at any stage, and this was also the case after stratification for number of attempts made to stop smoking over the 12 months before entry to the chewing gum trial.

Table III shows other data obtained at follow up. The information collected at the visit after six months was probably the most useful as complete data were collected for all but nine of the patients and by the same person, whereas at the earlier follow up investigations many patients were omitted and the structured interviews conducted by

TABLE II—*Results of controlled trial of nicotine chewing gum in patients receiving either active (2 mg buffered nicotine/piece) chewing gum or a placebo. Values represent numbers of patients*

	Time of follow up investigation							
	Two weeks*		Four weeks*		Three months*		Six months†	
End point	Active gum	Placebo	Active gum	Placebo	Active gum	Placebo	Active gum	Placebo
Allocated	101	99	101	99	101	99	101	99
Attended	73	74	62	48	26	20	100	97
"Not smoking"‡	31	28	29	24	15	7	14	11
Smoking pipe or cigars only	1	1	2	1			7	3
Validated as not smoking							10	8

* General practitioner's surgery. † Home visit by KJ. ‡ Self reported not smoking.

TABLE III—*Minor end points in controlled trial of nicotine chewing gum, with patients receiving either active (2 mg buffered nicotine/piece) chewing gum or a placebo. Values represent numbers of patients*

	Time of follow up investigation							
	Two weeks*		Four weeks*		Three months*		Six months†	
End point	Active gum	Placebo	Active gum	Placebo	Active gum	Placebo	Active gum	Placebo
Allocated	101	99	101	99	101	99	101	99
Attended	73	74	62	48	26	20	100	97
Tried gum	71	73	58	46				
Using gum regularly	51	58	36	35	10	5	9	10
Found gum:								
Helpful	50	42	43	29	18	11	48	40
Unhelpful	15	21	21	12	3	7	30	42
Not sure	7	11	8	9	2	2	14	13
Other comments:								
Sore mouth, nausea, heartburn	33	13	12	4	5	2	19	9
Disliked taste	19	10	11	1	2		33	25
No flavour	6	18	2	14		1	22	39
Less craving	8	9	8	6	2	1	34	22

* General practitioner's surgery. † Home visit by KJ.

several different doctors. Almost all the patients who attended appointments with their doctor tried the gum, and there were differences between the groups receiving active and placebo gums in the pattern of results. More of those using the active gum claimed not to be smoking and considered the gum to be helpful at each of the follow up points. After two weeks, patients using the active gum were more likely to keep follow up appointments and to report that they were using the gum regularly. Patients using the placebo described the gum as having little flavour and giving inadequate satisfaction. Conversely, those using the active preparation were more likely to complain of mouth soreness, heartburn, or nausea and of the gum having an unpleasant taste but were also more likely to state that the gum reduced the craving for a cigarette. Self reported use of the gum was significantly lower in the active group only at follow up after four weeks, and roughly 10% of each group was still using some gum after six months.

TABLE IV—*Odds ratios in favour of nicotine gum in controlled trials*

Reference	No of subjects	Ratio of success rate with active gum to success rate with placebo	95% Confidence limits
Placebo controlled studies			
Axelsson and Brantmark[11]	812	0·90	0·66-1·23
Puska *et al*[12]	229	1·42	0·82-2·46
Malcolm *et al*[13]	136	4·92	1·53-15·88
Fagerstrom[4]	100	2·17	0·95-4·91
Fee and Stewart[14]	352	1·53	0·77-3·05
Jarvis *et al*[10]	116	3·34	1·47-7·57
British Thoracic Society[5]	802	0·84	0·53-1·31
Schneider *et al*[15]	60	1·71	0·52-5·62
Hjalmarson[2]	206	2·14	1·09-4·20
Present study	200	1·25	0·47-3·31
Studies using counselled patients as controls			
Malcolm *et al*[13]	137	1·83	0·74-4·47
British Thoracic Society[5]	777	1·16	0·71-1·90
Russell *et al*[6]	1354	2·24	1·41-3·55

Discussion

Considerable interest in nicotine chewing gum was shown by the general practitioners who took part in our previous study of routine antismoking advice[8]; many were already prescribing it to selected patients when we began the present trial. Apart from considerations of the patient's ability to pay for a private prescription, the doctors themselves recognised the new treatment as being a potentially valuable resource that was not to be squandered. We were pleased therefore that our decision to limit eligibility for the study to patients who reported having recently made an unsuccessful attempt to stop smoking defined a group that appeared to have a higher prevalence of early disease associated with smoking and stronger motivation to stop than the average cigarette smoker drawn from the same population. Moreover, the anecdotal evidence suggested that the general practitioners were already using similar criteria in prescribing the gum. Thus the trial as a whole probably reflected the established patterns of practice.

Only 200 (47%) of the 429 patients who were still on the practice lists and who had not already given up smoking or tried nicotine chewing gum previously were actually willing to enter the trial. In a recent London study 53% of smokers seen during routine general practice consultations accepted an offer of a (free) prescription of nicotine chewing gum.[6] Interestingly, although population surveys have repeatedly found that at least 70% of smokers say that they want to give up the habit, in our experience only 50% are willing to accept an offer of tangible help at a given moment. This difference in proportions may reflect scepticism about the effectiveness of the gum, the patients' unwillingness to divert their energies from other matters (especially at the invitation of an outside party), increasing social pressure against smoking, or a combination of these factors.

Although the number of patients enrolled in our study was smaller than we had expected and could not be increased because of the criteria for eligibility, the trial still had a greater than 95% likelihood of detecting a difference, significant at the 5% level, of the same order of magnitude as that reported from a double blind controlled trial conducted at the Maudsley Hospital smokers' clinic—27 (47%) of those allocated to nicotine chewing gum gave up compared with 12 (21%) controls.[10] We, however, observed nothing like these incidences of giving up smoking and certainly no significant difference in outcome between our active and placebo groups.

Our study is the 11th controlled trial of nicotine chewing gum conducted to date and the first in general practice to include a placebo group. Of the 10 previous studies, seven employed a placebo controlled design, one compared nicotine gum with a counselling intervention, and two included both types of control group. Of the total of 13 possible experimental comparisons, investigating over 5200 patients, 11 have suggested that the gum is of some benefit, but in only four has a significant difference from the control group been apparent (table IV). Differences in the types of subjects enrolled, the nature of the intervention regimens used, and the duration of follow up suggest that these studies should not be pooled to obtain an overall estimate of the effectiveness of the gum. The available evidence indicates that nicotine chewing gum may be effective as an aid to giving up smoking when used in special settings such as smokers' clinics. It also supports the role of nicotine as a pharmacological agent contributing to the maintenance of the smoking habit. The effectiveness of the gum when used in general practice is less certain, with a small effect at best, and this may be because of two important differences. Firstly, smokers attending clinics may be more likely than unselected smokers to be helped by the gum. Secondly, effective use of nicotine gum may require careful explanation, supervision, support, and follow up, and these are more likely to be provided in a special smokers' clinic than in general practice.

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advised on the design of the trial, and Elizabeth Dimmock provided clerical help. The cooperation of the doctors, staff, and patients of the participating practices made the study possible.

Appendix I

Information provided for general practitioners—If a patient accepts the offer to discuss the gum, the doctor will describe the study and outline the principles underlying the use of the gum, during the consultation. Should the patient ask, "Does this gum contain nicotine?" the doctor will explain why it is an important feature of the study that neither the doctor nor the patient should know this but that both preparations under study are "specially formulated antismoking chewing gums." Details of name, address, and current smoking habit will be recorded by the general practitioner on the enrolment sheet for all patients. A written summary of the study accompanies each set of patient records. If the patient agrees to try the "antismoking gum" the reception staff will allocate him or her the next available treatment code, A to J. The codes are balanced with respect to placebo and active chewing gum. The patient will then be given: further information concerning use of the gum; advice that stopping smoking abruptly is essential and that the gum should be used for three months; and details of the follow up schedule. Further written advice accompanies each batch of gum. Finally, the patient will collect an appropriately coded two weeks' supply of gum from the receptionist. When appropriate, reasons for refusal to enter the study will be recorded.

Appendix II

Information for patients: instructions for use of the chewing gum—You are taking part in a study to compare two types of antismoking chewing gum. It is important that neither your doctor nor you should know which gum you are using until the end of the study. You should stop smoking completely from the first day and continue with the gum for at least three months. Most people who stay off cigarettes that long stay off for good. The gum will reduce your desire to smoke and make it easier for you to resist cigarettes, but you must not expect it to be as satisfying as smoking. You will need willpower too. You should chew a fresh piece of the gum when you feel a strong desire to smoke. Chew it slowly for about 30 minutes. Too vigorous chewing causes salivation and, sometimes, uncomfortable symptoms. Swallowing the saliva makes the antismoking substance ineffective. It is sufficient to chew occasionally and leave the gum under the lip or in the corner of the mouth between chews. Until the way you chew becomes automatic you should use the first sign of throat irritation as a sign to stop chewing. Start chewing slowly again when the irritation disappears. Dispose of the used gum neatly. For example, you can replace it in the empty bubble of the strip pack. You should chew as much gum as you need but try not to chew more than 20 pieces a day. Most people manage on about 10 pieces a day. Once you have completely overcome your desire for cigarettes, gradually reduce the number of gums chewed per day. This reduction should be possible after three or four months' use of the gum. Aim to stop using the gum altogether by six months, although it may be a good idea to keep a small supply with you for emergencies. If you develop any side effects from the gum, like nausea, hiccups, or a sore mouth, try chewing more slowly. You may dislike the gum at first and you may take several days to get used to it. If this happens do not worry. Persevere until you get used to it.

References

1 Raw M, Jarvis MJ, Feyerabend C, Russell MAH. Comparison of nicotine chewing-gum and psychological treatments for dependent smokers. *Br Med J* 1980;**281**:481-2.
2 Hjalmarson A. The effect of nicotine chewing-gum in smoking cessation: a randomised double-blind study. In: *Proceedings of the fifth world conference on smoking and health*. Washington: US DHEW (in preparation).
3 Russell MAH, Wilson C, Feyerabend C, Cole PV. Effect of nicotine chewing gum on smoking behaviour and as an aid to cigarette withdrawal. *Br Med J* 1976;ii: 391-3.
4 Fagerstrom K-O. A comparison of psychological and pharmacological treatment in smoking cessation. *J Behav Med* 1982;**5**:343-51.
5 Research Committee of the British Thoracic Society. Comparison of four methods of smoking withdrawal in patients with smoking related diseases. *Br Med J* 1983;**286**:595-7.
6 Russell MAH, Merriman R, Stapleton J, Taylor W. Effect of nicotine chewing gum as an adjunct to general practitioners' advice against smoking. *Br Med J* 1983;**287**:1782-5.
7 Fowler GH. Effect of nicotine chewing gum as an adjunct to general practitioners' advice against smoking. *Br Med J* 1984;**288**:145.
8 Jamrozik K, Vessey M, Fowler G, Wald N, Parker G, Van Vunakis H. Controlled trial of three different anti-smoking interventions in general practice. *Br Med J* 1984;**288**:1499-503.
9 Wald NJ, Idle MS, Boreham J, Bailey A. Carbon monoxide in breath in relation to smoking and carboxyhaemoglobin levels. *Thorax* 1981;**36**:366-9.
10 Jarvis MJ, Raw M, Russell MAH, Feyerabend C. Randomised controlled trial of nicotine chewing-gum. *Br Med J* 1982;**285**:537-40.
11 Axelsson A, Brantmark B. The anti-smoking effect of chewing gum with nicotine of high and low availability. In: Steinfeld J, Griffiths W, Ball K, Taylor RM, eds. *Proceedings of the third world conference on smoking and health*. Washington: US DHEW, 1977:549-59. (DHEW Publication number (NIH) 77-1413.)
12 Puska P, Bjorkqvist S, Koskela K. Nicotine-containing chewing-gum in smoking cessation: a double-blind trial with half-year follow-up. *Addict Behav* 1979;**4**: 141-6.
13 Malcolm RE, Sillett RW, Turner JAMcM, Ball KP. The use of nicotine chewing gum as an aid to stopping smoking. *Psychopharmacology* 1980;**70**:295-6.
14 Fee WM, Stewart MJ. A controlled trial of nicotine chewing gum in a smoking withdrawal clinic. *Practitioner* 1982;**266**:148-51.
15 Schneider NG, Jarvik ME, Forsythe AB, Read LL, Elliott ML, Schweiger A. Nicotine gum in smoking cessation: a placebo-controlled trial. *Addict Behav* 1983;**8**:253-61.

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GENTIAN WATER COMPOUND—"Take of Gentian roots sliced, one pound and a half, the leaves and flowers of Centaury the less, of each four ounces, steep them eight days in twelve pounds of white Wine, then distil them in an alembick."

It conduces to preservation from ill air, and pestilential fevers: it opens obstructions of the liver, and helps such as they say are liver-grown; it eases pains in the stomach, helps digestion, and eases such as have pains in their bones by ill lodging abroad in the cold, it provokes appetite, and is exceeding good for the yellow jaundice, as also for prickings or stitches in the sides: it provokes the menses, and expels both birth and placenta: it is naught for pregnant women. If there be no fever, you may take a spoonful by itself; if there be, you may, if you please, mix it with some cooler medicine appropriated to the same use you would give it for. (Nicholas Culpeper (1616-54) *The Complete Herbal*, 1850.)