

Relative intakes of tar, nicotine, and carbon monoxide from cigarettes of different yields

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ABSTRACT The relative intakes of tar, nicotine, and carbon monoxide were estimated in 2455 cigarette smokers, who freely smoked their usual brands of cigarette. The estimates were derived by using an objective index of inhaling based on the measurement of carboxyhaemoglobin divided by the carbon monoxide yield of the cigarettes smoked, after background and carry over carboxyhaemoglobin effects had been allowed for. Separate analyses were performed according to the yield and type (plain, filter, etc) of cigarette smoked. The analyses based on *yield* indicated that the extent of inhaling was adjusted sufficiently to achieve similar intakes of nicotine/carbon monoxide regardless of the nicotine/carbon monoxide yield. It was not, however, sufficiently increased to achieve a similar intake of tar as the tar yield of the cigarette decreased. The analyses based on *type* of cigarette indicated that the extent of inhaling was adjusted to achieve similar intakes of tar and nicotine regardless of the type of cigarette smoked, but that this led to a greater intake of carbon monoxide among filter cigarette smokers than that among smokers of plain cigarettes—more so than would have been expected from their relative carbon monoxide yields. Two conclusions arise from these results. Firstly, any harmful effects of nicotine/carbon monoxide are unlikely to be materially reduced by smoking cigarettes with lower yields of nicotine/carbon monoxide, but the harmful effects of tar are likely to be reduced by smoking cigarettes with lower tar yields. These predictions appear to be borne out by epidemiological observations. Secondly, any harmful effects of carbon monoxide on the cardiovascular system will be greater in smokers of modern filter cigarettes than in smokers of modern plain cigarettes, provided that these two groups of smokers are otherwise similar with respect to risk of cardiovascular disease.

In an earlier paper we described an objective index of inhaled cigarette smoke based on carboxyhaemoglobin concentration and the carbon monoxide yield of the cigarettes smoked.¹ Smokers of ventilated filter cigarettes were found to inhale 82% more than smokers of plain cigarettes and those who smoked unventilated filter cigarettes 36% more than smokers of plain cigarettes (ventilated cigarettes have perforations in the filter admitting air that dilutes the mainstream smoke). These differences encouraged us to investigate the matter further and estimate the relative intakes of tar, nicotine, and carbon monoxide from cigarettes of different yields.

We did this in a preliminary way in our previous paper in respect of tar and nicotine intakes according to type of cigarette. Here we have extended the observations to include estimates of carbon monoxide intake and have in addition estimated the relative intakes of tar, nicotine, and carbon monoxide according to the yields of the cigarettes and regardless of cigarette type.

Methods

The study population consisted of men aged 35–64 years who attended the BUPA Medical Centre in London for a comprehensive health screening examination and has been described previously.¹ The men were asked about their medical history and their usual and recent smoking habits. All information was collected after arrival at the centre, and the

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men were not forewarned about the survey of smoking habits. The time when each cigarette, cigar, or pipe had been smoked that day was recorded, together with the manufacturer's brand. Each man provided a sample of venous blood and the carboxyhaemoglobin saturation was measured as previously described.² The within assay standard deviation of the method was 0.05% carboxyhaemoglobin. The tar and nicotine yields of the cigarettes were obtained from tables published by the Health Departments of the United Kingdom, and carbon monoxide yields were obtained from the Tobacco Advisory Council. All the yields were obtained under the same experimental conditions. Estimates of relative intakes of tar, nicotine and carbon monoxide were derived by multiplying the average inhaling index in a particular group by the average yields from cigarettes smoked by that group.

Our statistical analyses related to men seen from early 1975 to the end of 1979 who usually smoked only manufactured cigarettes. As before, men who smoked brands of cigarettes for which carbon monoxide yields were not available from the Tobacco Advisory Council were excluded; this applied to less than 5% of men in our study population. The analysis was restricted to the 2455 men who had smoked 1–16 cigarettes before the blood test on the day they were seen at the medical centre, and from whom blood was taken between 13.00 and 16.00 hours. On the basis of detailed information about recent smoking habits and the carboxyhaemoglobin estimation, each person's carboxyhaemoglobin inhaling index was estimated and this was standardised for the number of cigarettes

smoked before the test when different smoking groups were compared in our statistical analyses. The derivation of the carboxyhaemoglobin inhaling index is given in the appendix.

Results

Table 1 shows the estimated relative intakes of tar, nicotine, and carbon monoxide according to the tar, nicotine, and carbon monoxide yields of the cigarettes smoked. The relative intake of all three smoke constituents was greater from the low yield cigarettes than would have been expected from the cigarette yields, confirming the phenomenon of compensatory smoking previously demonstrated. Indeed, the intake of nicotine and carbon monoxide remained relatively constant regardless of the cigarette yield. Only the intake of tar declined with declining tar yield.

Table 2 shows the relative cigarette yield and relative intake of tar, nicotine, and carbon monoxide according to type of cigarette (plain, unventilated filter, or ventilated filter).¹ Our results relating to tar and nicotine are similar to those described before, although the extent of compensation in this extended series is somewhat greater than was observed before. The carbon monoxide intake in smokers of filter cigarettes was about 60% higher than in smokers of plain cigarettes, but the intake of tar and nicotine was slightly less.

Discussion

Our present findings confirm the phenomenon of compensatory smoking and indicate that this may be

Table 1 *Inhaling index and estimated relative intake of tar, nicotine and carbon monoxide according to quintile of tar, nicotine, and carbon monoxide yield of cigarette*

<i>Yield</i>		<i>No of men</i>	<i>Standardised inhaling index* (COHb %/mg CO)</i>	<i>Estimated relative intake (average yield × inhaling index)</i>
<i>Quintile</i>	<i>Limits (mg)</i>			
TAR				
1st	1–	511	0.30	2.62
2nd	10–	544	0.21	3.21
3rd	18–	543	0.18	3.33
4th	19–	583	0.19	3.54
5th	20–36	274	0.16	4.59
NICOTINE				
1st	0.3–	551	0.30	0.24
2nd	1.0–	448	0.21	0.24
3rd	1.3–	405	0.19	0.25
4th	1.4–	418	0.19	0.27
5th	1.5–3.6	633	0.17	0.28
CARBON MONOXIDE				
1st	0.8–	473	0.30	3.50
2nd	12.8	553	0.21	3.08
3rd	17.0–	431	0.20	3.45
4th	18.0–	638	0.18	3.49
5th	20.0–28.1	360	0.16	3.59

*See appendix; standardised for number of cigarettes smoked before the test. COHb—carboxyhaemoglobin; CO—carbon monoxide.

Table 2 Relative cigarette yield and estimated relative intakes of tar, nicotine and carbon monoxide by cigarette type

Type of cigarette	No of Men	Tar		Nicotine		Carbon monoxide	
		Relative yield	Relative intake	Relative yield	Relative intake	Relative yield	Relative intake
Plain	185	100	100	100	100	100	100
Unventilated Filter	1666	72	98 (5)	68	92 (4)	119	162 (8)
Ventilated Filter	604	39	80 (5)	47	97 (7)	79	163 (12)

Standard errors are shown in brackets.

greater than has hitherto been appreciated. The results also show that the estimated relative intakes of tar, nicotine, and carbon monoxide do not vary greatly with the yield of the cigarette. Only the relative intake of tar declined with declining tar yields.

The data also demonstrate an important point in connection with the relative intake of carbon monoxide. When our data are analysed according to the yield of the cigarette the relative intake of carbon monoxide remains fairly constant, but when analysed according to the type of cigarette the relative intake of carbon monoxide is about 60% higher in smokers of filter cigarettes than in smokers of plain cigarettes. This arises largely because, apart from some ventilated cigarettes, filter cigarettes tend to have higher carbon monoxide yields than plain cigarettes. In addition, the smoke from such cigarettes is also inhaled more. This finding does not emerge when the data are analysed according to yield because plain cigarettes during the period of the study represented a very small proportion of the cigarettes smoked.

There are two medical and scientific implications which arise from our results. Firstly, if carbon monoxide or nicotine, or some other constituent of tobacco smoke which is correlated with the yield of these substances, is the cause of the excess risk of heart disease among smokers, smokers of relatively low yield cigarettes would be expected to have about the same excess risk of heart disease as people smoking higher yielding cigarettes. In contrast, the risk of a disease such as lung cancer, which is related to the tar yield of a cigarette, is likely to be lower in smokers of low tar than of high tar cigarettes.

These predictions explain the epidemiological observations on the risk of heart disease and lung cancer in relation to yield and type of cigarette reasonably well. With regard to heart disease, there is a notable recent paper on the risk of myocardial infarction in relation to the nicotine and carbon monoxide yields of cigarettes. The paper showed that there was no significant association between yields of either of these two substances and the risk of disease.³ It is apparent from our findings that this result cannot be taken to exclude the possibility that either nicotine or carbon monoxide may be a cause of myocardial infarction. The result can readily be

explained by the fact that in that study smokers of low tar and low nicotine cigarettes compensated for the lower yields by greater inhaling. Other epidemiological studies have shown either no decrease in risk of heart disease^{4,5} with decreasing yields or only a modest decrease.⁶

So far as lung cancer is concerned, several epidemiological studies have shown that the risk is lower in smokers of low tar cigarettes than in smokers of high tar cigarettes,^{4,6-12} and only one did not.¹³ On the basis of the estimated intake of tar the reduction in risk of lung cancer would not be as much as expected from the relative cigarette yields. It is quite plausible, however, that the increase in inhaling results in a tendency for tar to be inhaled beyond the target site, the main bronchi¹⁴; and this in itself may contribute to the reduction in risk of lung cancer associated with smoking low tar cigarettes.

The second implication from our results is that the difference in relative tar and nicotine intakes among smokers of plain and filter cigarettes can be exploited epidemiologically to investigate whether carbon monoxide is a possible cause of coronary heart disease. If carbon monoxide is the principal agent in tobacco smoke responsible for cardiovascular disease the risk of heart disease among smokers of filter cigarettes would be expected to be higher than among smokers of plain cigarettes if the smokers are otherwise similar in respect of factors associated with the risk of heart disease. This is unlikely to be the case, since the sections of the community switching to filter cigarettes first are likely to have been those making other changes in their life style, particularly diet, that may have reduced their risk of heart disease. But it will tend to mask rather than introduce an effect. If therefore smokers of filter cigarettes are indeed found to have a higher risk of heart disease than similar groups of plain cigarette smokers this will provide useful epidemiological evidence for the hypothesis that carbon monoxide is a cause of cardiovascular disease.

An objection to using only one component of tobacco smoke, such as carbon monoxide, as an index of the relative intake of other smoke components, such as tar and nicotine, is that it assumes that all the components are inhaled in roughly the same proportion. That this assumption is not completely

invalid is suggested by the work of Stepney,¹⁵ which shows that various measures of smoke intake such as nicotine and cotinine excretion in urine, the nicotine retained in the cigarette butt, and the rise in "expired air carbon monoxide over smoking" levels yield similar results during a cigarette switching experiment.¹⁵ It has also been shown that carboxyhaemoglobin concentrations are closely associated with plasma nicotine concentrations in subjects who smoke cigarettes using different dilution filters.¹⁶ Benowitz and his colleagues have recently published results similar to our own but with serum, nicotine, and cotinine values instead of carboxyhaemoglobin concentrations.¹⁷ Their results suggested that smokers of low nicotine cigarettes do not consume less nicotine.

Our results relate to cigarettes smoked in Britain from 1975 to 1979, and since the design and yields of cigarettes have changed over the last few decades it cannot be assumed that they apply to cigarettes manufactured at different times. This point is particularly relevant when predicting the risk of specific diseases in relation to the type and yield of cigarettes made at different times.

We thank the Medical Research Council for part of our financial support and the Tobacco Advisory Council for providing the carbon monoxide yields of the different brands of cigarette.

Appendix: Derivation of carboxyhaemoglobin inhaling index¹

Carboxyhaemoglobin concentrations include a contribution from the carboxyhaemoglobin carryover from the previous day's smoking and the background carboxyhaemoglobin from endogenous and atmospheric carbon monoxide. This contribution was taken as the carboxyhaemoglobin level among men who did not smoke on the day of the test but who had smoked a similar number of cigarettes during the previous evening. The measured carboxyhaemoglobin minus this contribution can be regarded as the "excess" carboxyhaemoglobin.

A quantitative index of inhaling by an individual smoker, which takes account of both the background and the carryover carboxyhaemoglobin as well as the carbon monoxide yield of the particular cigarette smoked, is given by the excess carboxyhaemoglobin concentration divided by the carbon monoxide yield of the cigarette. Since this index depends on the number of cigarettes smoked before the carboxyhaemoglobin test, the mean carboxyhaemoglobin inhaling index for each group of smokers considered in this paper was indirectly standardised for the number of cigarettes smoked,

and we call this the standardised carboxyhaemoglobin inhaling index.

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Nedocromil sodium: a new drug for the management of bronchial asthma

SIR,—Such scant information as was provided about the pharmacology of this drug by Dr S Lal and others (November 1984;39:809–12) suggested that it had properties similar to those of sodium cromoglycate. It is thus extremely strange, to say the least, that there was no mention of that drug in their article.

The clinical trial it reported was claimed to show that nedocromil sodium was superior to placebo in the management of asthma. Even that simplistic conclusion is, however, open to question because the numbers of patients in the two trial groups were small (13 on active drug and 17 on placebo), and no attempt seems to have been made to match them for atropic status, which might well have influenced the response to treatment. As for the results, the three tables show *p* values for 28 separate comparisons of the effects of nedocromil sodium and placebo, but in no less than 16 there were no significant differences between the two treatments. In the other 12 the differences in favour of the active drug were no more than marginally significant ($p < 0.05$) in 11, leaving only one with a *p* value of < 0.01 .

My object in inviting you to publish this letter is, however, not only to criticise some very shaky statistics, but also to ask the authors why the study did not incorporate a comparison with sodium cromoglycate as well as with placebo, which could easily have been done by recruiting perhaps 15 more patients. Nedocromil sodium may or may not be more effective than a placebo in the management of asthma. I would submit, however, that the publication in a prestigious journal of a clinical trial which omits comparison with a "reference" drug of a similar type, in this case sodium cromoglycate, could influence medical prescribing by facilitating the promotion of a new and probably expensive drug which has not yet been shown to have any therapeutic advantage over one of proved efficacy.

WB GRANT

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. This letter was sent to Dr Lal, who replies below.

SIR,—Ours was the first clinical trial to be completed on a drug whose therapeutic activity had so far been tested only under the artificial conditions of bronchial challenge, which is not necessarily predictive of activity in clinical asthma. Accordingly, our main objective was to investigate whether or not nedocromil sodium had any therapeutic activity in patients with asthma—hence the comparison with placebo.

Dr Grant comments on the number of comparisons in which nedocromil sodium was not significantly superior to placebo. These have to be taken in the context of the disease and its management. It is perhaps not surprising, for example, that our patients, who used significantly less inhaled bronchodilator when treated with nedocromil sodium, failed to show improvements in peak expiratory flow rate. Despite this, 12 comparisons attained the 5% significance level and, although no attempt was made to stratify the atopic and non-atopic status of the patients, they had an equal chance of receiving each treatment. Dr Grant

will be pleased to know that the two groups were similar and there was no significant difference between them.

To add an active group of, say, 15 patients as Dr Grant suggests would have involved 15 more patients in the clinical trial, before it was known whether or not nedocromil sodium had any therapeutic activity.

Lastly and most importantly, in our paper we concluded that nedocromil sodium is worthy of further consideration in the management of bronchial asthma. As a first report, a journal like *Thorax* is more suitable for a study like ours, and we are gratified to know that it has aroused much interest in other workers. Only further trials will show if the drug has a place in the management of asthma.

S LAL

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Notice

Confidential inquiry into perioperative deaths

The Association of Surgeons of Great Britain and Ireland and the Association of Anaesthetists of Great Britain and Ireland have jointly set up a Confidential Inquiry into Perioperative Deaths. This study has the support of the surgical colleges, the Royal College of Gynaecologists and Obstetricians, and the faculties of anaesthetists. The study is funded by the Nuffield Provincial Hospitals Trust and the King Edward's Hospital Fund. The project is to enumerate death rates within 30 days of operations in all specialties and to identify remediable factors in the practice of anaesthesia and surgery. The study is fully confidential, only the three coordinators having limited access to the identities of patients and clinical staff concerned, to enable the coordinators to process the data. The study is voluntary but has one novel feature—that is, that a system of feedback has been arranged so that participating individual clinicians who desire it can obtain the opinions of the assessors in person. The Association of Surgeons of Great Britain and Ireland discussed this study during the Reckitt and Colman symposium on quality control at the annual meeting in Birmingham on 27 March 1985. The Chairman of the Joint Working Party is Professor MD Vickers; Mr HB Devlin, Professor JSP Lumley, and Dr John Lunn have been appointed clinical coordinators. Further information and copies of the detailed protocol are available from Mr Nigel Buck, administrator of the confidential inquiry, 14 Palace Court, London W2 4HT.

Correction

Relative intakes of tar, nicotine, and carbon monoxide from cigarettes of different yields

There is an error in table 1 of the paper by Professor NJ Wald and others (May 1984;39:361–4). The estimated relative intake of tar in smokers of cigarettes in the fifth quintile should be 3.82 instead of 4.59. The authors regret this error; it does not alter the sense of remarks in the text.