

Smoking and malignant disease: a general practice study

S.J. TYLER, MB, MRCP

R.M. FINCH, MB, MRCP

J. FINCH, MB

B. PATEL, MB

SUMMARY. This study, involving a practice population of 7,200 patients, compared the smoking habits of patients suffering from malignant disease (excluding skin cancer) with the smoking habits of controls matched for age and sex. Patients with malignancies were found to smoke more heavily than their controls; this difference was particularly marked between the younger patients and their controls. Data on the most prevalent malignancies (carcinomata of the breast, cervix, rectum, colon and bladder) revealed that this tendency to heavier smoking was more marked in patients with neoplasia of cervix or bladder than in patients with breast or colorectal neoplasms. The age of these patients at diagnosis was reviewed in relation to smoking habits. Although the numbers were small, it appeared that patients who smoke present at an earlier age than non-smokers, except in cases of neoplasia of the cervix.

These results seem to justify further general practice studies into the links between smoking and malignant disease.

Introduction

IT is now over 30 years since Doll and Hill¹ first reported the now well-accepted relationship between tobacco smoking and carcinoma of the lung, and yet it is a lamentable fact that there are still an estimated 20 million smokers in Britain today, and an estimated 90 per cent of the 40,000 deaths per year from lung cancer are attributable to smoking.

Since 1952, further studies have revealed an association between other malignant disease and smoking.² It is now accepted that smoking can cause oral, laryngeal and oesophageal malignancies, with pipe and cigar smokers especially at risk. There are also less dramatic but nevertheless demonstrable associations between smoking and carcinoma of the pancreas and the urinary tract. Recently, Trevathan and colleagues,³ in a carefully controlled case study, demonstrated an increased risk of carcinoma *in situ*

and dysplasia of the cervix in women smokers, particularly if they had smoked from an early age and for a long time. Thus the list of neoplasms associated with smoking lengthens. In 1981, Doll and Peto⁴ estimated that 30 per cent of all malignancies were associated with smoking. This is a tragically high figure, when one considers that prevention is literally in the patient's own hands.

It may be, however, that it is not just the smoker who is at risk. Evidence has been accumulating for the risks to health of passive smoking—inhalation of the tobacco smoke exhaled into the environment by smokers. In a Japanese study Hirayama showed an increased risk of carcinoma of the lung in the non-smoking wives of smokers.⁵ However, these findings have not been confirmed in other studies.⁶ The potential hazards of passive smoking are emphasized in *Health or smoking?*, the recent publication of the Royal College of Physicians.⁷

This paper reports the results of a general practice enquiry into the smoking habits of patients with malignant disease, including the possible role of passive smoking.

There were two aims to the study: first, to compare the smoking habits of patients with malignant disease with controls from the same practice; secondly, to note the age at diagnosis in the four most prevalent malignancies present in the practice in relation to smoking habits.

Method

Over a two-month period all surviving patients with malignant disease, excluding skin cancer, were identified and their age at diagnosis noted. They were matched for age and sex with controls by taking the next suitable patient named in the age-sex register. Both patient and control were questioned with regard to their tobacco smoking, and the smoking people with whom they were in prolonged contact was also noted so that the significance of passive smoking could be assessed.

Smoking habits were classified as:

1. equivalent to smoking one to nine cigarettes per day;
2. equivalent to smoking 10–20 cigarettes per day;
3. equivalent to smoking 30 or more cigarettes per day.

The authors are all general practitioners. Their practice covers Sandwell and Dudley, West Midlands.

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Passive smoking was regarded as one third of active smoking: for example a non-smoking wife whose husband smoked 20 cigarettes per day would be regarded as smoking the equivalent of six cigarettes per day. Ex-smokers who had ceased to smoke for more than 10 years before the malignancy was diagnosed were regarded as non-smokers. Half an ounce of tobacco was regarded as equivalent to 10 cigarettes.

Initially the results were analysed for all patients with malignant disease and then for each of the four most prevalent malignancies separately—carcinomata of the breast, cervix, rectum, colon and bladder.

Table 1. Prevalence of malignant disease in the study practice.

Site of malignancy	Number of patients
Breast	28
Cervix (grade IV smears and above)	14
Cervix (grade III smears more than once)	5
Rectum and colon	14
Bladder	9
Stomach	5
Bronchus	3
Ovary	3
Uterus	3
Vulva	1
Prostate	1
Larynx	1
Myeloid leukaemia (chronic)	1
Total	88

Results

The prevalence of malignant disease (excluding skin cancer) in the practice of 7,200 patients is shown in Table 1.

The overall percentages of smokers and non-smokers in the malignancy group of patients compared with the control group are shown in Table 2. The passive smokers all 'smoked' the equivalent of 1–9 cigarettes per day. Applying the chi-square test: $\chi^2=15.62$; $df=3$; $0.001 < P < 0.01$. Analyses for the four most prevalent malignancies are shown in Table 3.

Figure 1 illustrates the smoking habits of the malignancy group of patients according to their age at presentation in comparison with the smoking habits of their age-matched controls. The ages at onset of malignancy in relation to the patients' smoking habits for

Table 2. Percentage of smokers and non-smokers in the malignancy and control groups.

	Cigarettes smoked per day			
	0	1–9	10–29	≥30
Malignancy group (n = 88 patients)	34.1	27.3 ^a	28.4	10.2
Control group (n = 88 patients)	42.0	42.0 ^b	15.9	0

^a Passive smokers 10.2 per cent.

^b Passive smokers 21.6 per cent.

Table 3. Percentage of smokers in the malignancy and control groups for the four most prevalent malignancies.

	Site of malignancy	Number of patients	Cigarettes smoked per day			
			0	1–9	10–29	≥30
Malignancy group	Breast	28	35.7	39.3	17.9	7.1
Control group	—	28	57.1	28.6	14.3	0
Malignancy group	Cervix (grade IV and above)	14	21.4	28.6	35.7	14.3
Control group	—	14	21.4	64.3	14.3	0
Malignancy group	Rectum and colon	14	50.0	35.7	14.3	0
Control group	—	14	42.9	50.0	7.1	0
Malignancy group	Bladder	9	22.2	11.1	55.6	11.1
Control group	—	9	33.3	55.6	11.1	0

Table 4. Analyses of the four most prevalent malignancies. Number of patients and mean age at diagnosis.

Site of malignancy	All patients		Non-smokers		All smokers		Heavy smokers (>10/day)	
	No.	Age ^a (yr)	No.	Age ^a (yr)	No.	Age ^a (yr)	No.	Age ^a (yr)
Breast	28	52.8	10	53.4	18	52.5	7	46.7
Cervix (grade IV smear and above)	14	37.3	3	38.0	11	44.6	7	38.9
Rectum and colon	14	64.9	7	71.0	7	61.3	3	57.1
Bladder	9	56.5	2	80.5	7	57.4	5	57.5

^a Mean age at diagnosis.

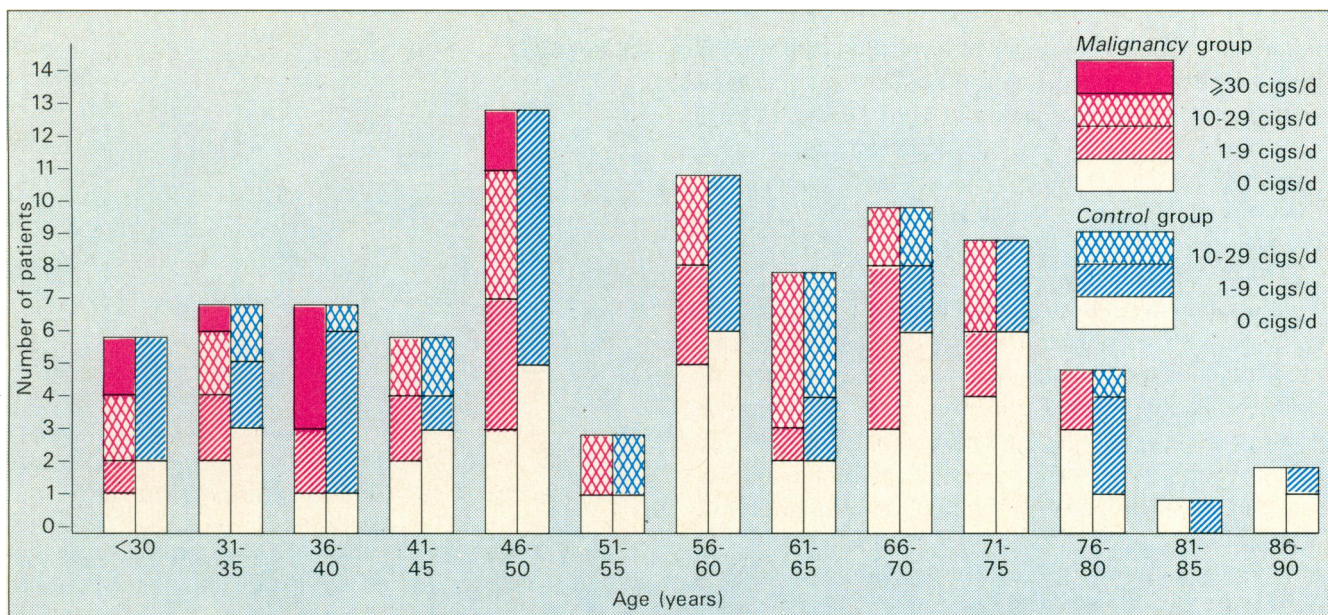


Figure 1. Comparison of smoking habits in malignancy group of patients and their controls by different age groups.

the four most prevalent malignancies are shown graphically in Figures 2 – 5. The mean ages at onset are as shown in Table 4. Since the numbers of patients for each malignant disease are small, statistical testing would not be meaningful.

Discussion

This general practice study, although involving only a relatively small number of patients, shows clearly that, in general, the patients with malignant disease have a significantly higher intake of tobacco smoke than their controls. This difference in tobacco intake between the malignancy group and the control group is particularly marked in those patients who presented with malignant disease at a relatively young age—that is, up to the fifth decade—as illustrated in Figure 1, but is less marked in older patients. The individual results for the four most prevalent malignancies during the study period shows that the association is more marked with certain neoplasms than with others, and confirms the findings that heavy smoking is more common among patients with bladder and cervix neoplasms.^{2,3} The differences between controls and patients with breast or rectal and colonic neoplasms are much less marked—a finding reported previously by Hammond in 1966² and Vessey and colleagues in 1979.⁸

From this study, the higher incidence of smoking among patients with bladder and cervical malignancies cannot be assumed to be causal. Nevertheless, we hope that, as with the original epidemiological study of lung carcinoma by Doll and Hill,¹ the results will promote further investigation and clarify the relationship.

The second part of our study, concerning the age at onset of particular malignancies in relation to smoking,

indicated that in cases of breast, colonic and bladder carcinomata, patients who smoked were more likely to present at an earlier age compared with non-smokers. This finding of earlier age presentation was particularly marked in our patients with carcinoma of the bladder, but this may be a misleading result as it was largely influenced by the one patient who smoked very heavily and presented in her third decade. Even so, the overall results justify the case for further study involving larger numbers of patients.

Patients with neoplasia of the cervix (grade IV smear and above) did not show any trend towards presentation

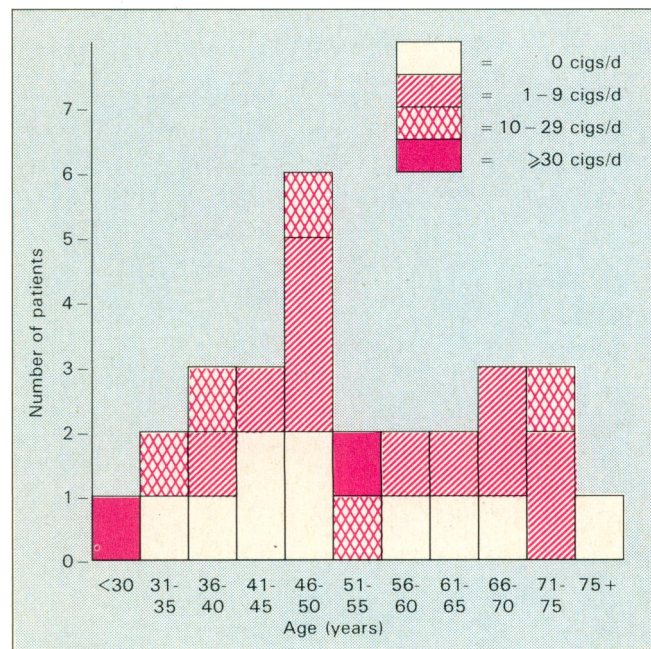


Figure 2. Age of patients at diagnosis of breast malignancy in relation to smoking habits.

at an earlier age with heavier smoking, and this result remained unchanged when patients with dysplasia of the cervix (grade III smear or on more than one occasion) were included. It is interesting to note, however, that 57 per cent of our patients with grade IV smears and above presented before the age of 35 years, and we emphasize that for general practitioners it is worthwhile performing cervical smear tests on all sexually active females regardless of their age.

Analysing the age at presentation of patients with carcinoma of the breast, it would appear that there is a premenopausal and a postmenopausal group; perhaps this reflects two aetiological processes. Another interesting point is that the two patients who smoked over 30 cigarettes per day were both the earliest presenters in these pre- and postmenopausal groupings, as seen most easily in Figure 2.

Unfortunately, the prevalence of other malignancies during the two-month study period was insufficient to

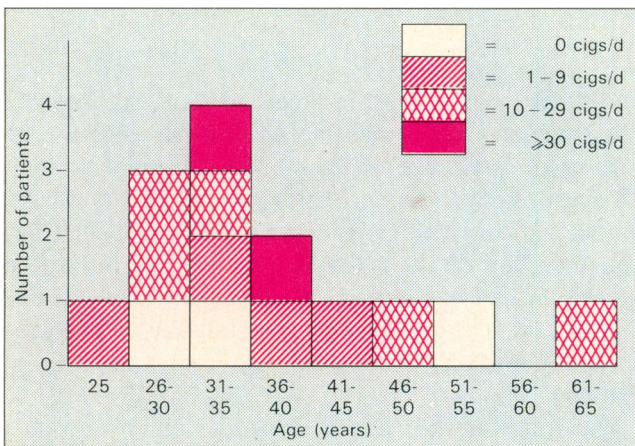


Figure 3. Age of patients at diagnosis of neoplasia of the cervix (grade IV smears and above) in relation to smoking habits.

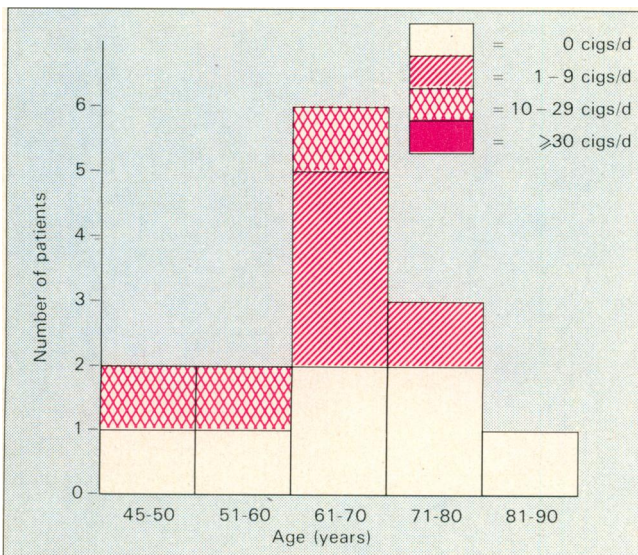


Figure 4. Age of patients at diagnosis of rectum malignancy in relation to smoking habits.

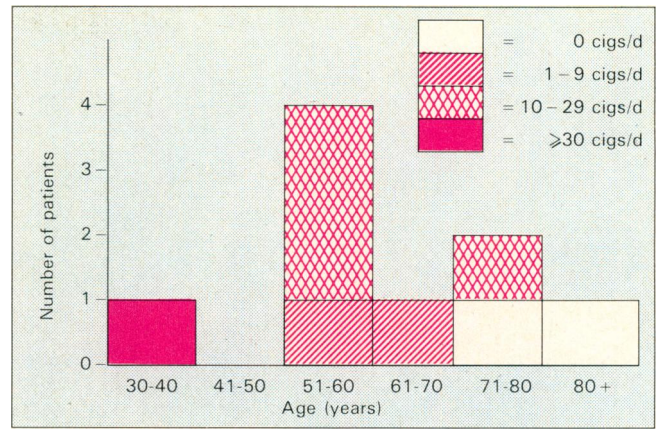


Figure 5. Age of patients at diagnosis of bladder malignancy in relation to smoking habits.

make valid comparisons of age at presentation, either because patients do not survive for long—for example, in cases of stomach and lung neoplasms—or because cases are relatively rare within a general practice population. However, the study is continuing within our practice, so that sufficient numbers of patients with these malignancies might eventually be accumulated and their smoking habits similarly analysed.

The results reported here, however, do provide adequate reason for encouraging patients to discontinue tobacco smoking. As well as its proven role in the pathogenesis of respiratory and cardiovascular disease, there is this mounting evidence that the habit is incriminated in other malignant diseases. As well as being ideally suited to undertake studies on smoking and ill health, general practice is a good starting place for the promotion of primary prevention.

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Address for correspondence

Dr S. J. Tyler, 213 Regent Road, Tividale, Warley, West Midlands B69 1RZ.

COMBINED REPORTS ON PREVENTION

Reports from General Practice 18-21

The College's campaign for health promotion and disease prevention in general practice was signalled by the publication in the years 1981-83 of a series of documents on different aspects of preventive medicine in general practice.

Although at the time these were distributed free of charge with the *Journal* to all Fellows, Members and Associates of the College, the steady demand for these documents has led to several of them going out of print.

Combined Reports on Prevention thus brings together between one set of covers *Reports from General Practice 18, 19, 20 and 21*. These four together can now be obtained from the Publications Sales Office, Royal College of General Practitioners, 8 Queen Street, Edinburgh EH2 1JE, price £4.50 including postage. Payment should be made with order.

CLASSIFICATION OF DISEASES, PROBLEMS AND PROCEDURES 1984

Occasional Paper 26

The new College classification of health problems from the Manchester Research Unit of the Royal College of General Practitioners is a major academic event. This is the first time that the old College classification has been blended thoroughly with the *International Classification of Disease* and that it has been made available in both electronic and printed form.

The printed version, published as *Occasional Paper 26*, describes the background of the classification, offers guidance on its use, and gives the classification in full, first in code order and then in alphabetical groups.

Approved by the Council of the College in 1983, this is likely to be the definitive text on classification in general practice for many years.

Classification of Diseases, Problems and Procedures 1984, Occasional Paper 26, can be obtained from the Publications Sales Office, Royal College of General Practitioners, 8 Queen Street, Edinburgh EH2 1JE, price £4.75 including postage. Payment should be made with order.

Smoking and ulcers

Three hundred and seventy patients with recently healed duodenal ulcers entered into a one-year, double-blind, randomized multicentre trial comparing placebo with three different dose schedules of cimetidine (200 mg twice a day, 300 mg twice a day, and 400 mg at bedtime) for the prevention of recurrent duodenal ulcer. By the end of one year, the cumulative symptomatic recurrence rate as demonstrated by endoscopy was similar for the patients receiving the three dosages of cimetidine (19 per cent, 15 per cent, and 13 per cent, respectively; not significant), whereas the placebo-treated group had a 34.7 per cent symptomatic recurrence rate ($P < 0.001$). The frequency of ulcer recurrence in smokers was significantly reduced by treatment with cimetidine (from 72 per cent to 34 per cent, $P < 0.01$). Smokers who received cimetidine were at least as likely to have a recurrence as were nonsmokers who received placebo (34 per cent vs. 21 per cent, not significant). Thus, smoking appears to be a major factor in recurrence of duodenal ulcer, and in smokers, giving up smoking may be more important in the prevention of ulcer recurrences than administration of cimetidine.

Source: Sontag S, Graham DY, Belsito A, *et al.* Cimetidine, cigarette smoking, and recurrence of duodenal ulcer. *N Engl J Med* 1984; **311**: 689-693.

Chronic ingestion of detergent

It is common practice to leave glasses, crockery, and eating implements to dry with a coating of detergent, and indeed some manufacturers recommend this since the fluorescent additives cause them to 'sparkle'. These compounds are inevitably ingested from such implements. Feeding bottles for babies are often steeped in strong solutions of detergent and not rinsed between feeds.

Synthetic detergents are used in large quantities as household and industrial cleaners. We have calculated that an adult takes in about 1 mg kg⁻¹ detergent a day and babies can be administered between seven and 10 mg kg⁻¹ a day. Rats were fed a dose of 100 mg kg⁻¹ a day in a pilot experiment and gross abnormalities were found in the gastrointestinal tract, the most striking being subtotal villous atrophy of the small bowel mucosa and glandular atrophy in the colon. These changes were not reversible 12 weeks after cessation of detergent administration.

Clearly it would be inappropriate to extrapolate these results to man, nevertheless, the authors would like to draw attention to the potential dosages of between 35 and 50 mg a day in babies weighing about 5 kg and think it possible that early mucosal damage may lead to chronic bowel disease.

Source: Mercurius-Taylor LA, Jayaraj AP, Clark CG. Is chronic detergent ingestion harmful to the gut? *British Journal of Industrial Medicine* 1984; **40**: 279-281.