# Smoking and Crohn's disease

KEVIN W SOMERVILLE, RICHARD F A LOGAN, MARGARET EDMOND, MICHAEL J S LANGMAN

# Abstract

In a case-control study 82 patients with Crohn's disease and matched controls drawn from general practice lists were questioned about their smoking habits. Patients with Crohn's disease were significantly more likely to be smokers than the controls, and the association was stronger for smoking habit before the onset of the disease than for current smoking habit, the relative risks for smokers compared with non-smokers being 4.8 and 3.5 respectively.

Taken in conjunction with earlier data showing an association between non-smoking and ulcerative colitis, these results suggest that smoking habit may be an important determinant of the type of inflammatory bowel disease that develops in predisposed subjects.

# Introduction

Several studies have confirmed the remarkable association of non-smoking and ulcerative colitis first reported by Harries *et al* in 1982, and we have recently shown that the association is particularly strong when smoking habit before the onset of disease is considered.<sup>1-6</sup> In contrast, little information is available about smoking in patients with Crohn's disease. Harries *et al*, who studied both groups of patients, found that patients with Crohn's disease were as likely to be smokers as controls drawn from a fracture clinic. Their results are, however, difficult to interpret as fewer than three quarters of their patients with Crohn's disease replied and the controls were matched with the patients with ulcerative colitis<sup>1</sup>; moreover, patients attending a fracture clinic are not necessarily representative of the ordinary population, from whom patients with Crohn's disease will come.

We carried out a case-control study using the same methods that we used in examining the smoking habits of patients with ulcerative colitis,<sup>6</sup> when we compared the habits of the patients with those of a control group drawn from the general population.

# Patients and methods

The case series consisted of all patients aged 16-80 with Crohn's disease from a defined group of general practices who were attending (76%) or had previously attended (24%) the City Hospital, Nottingham. Table I summarises the clinical details of the 82 patients approached. The site of the disease was confirmed by radiology in 79 (96%) and surgery in 45 (55%). Fifty six (68%) had histological findings typical of Crohn's disease with transmural inflammation (29%) or granulomas (39%).

MICHAEL J S LANGMAN, MD, FRCP, professor of therapeutics

Correspondence to: Dr R F A Logan.

Each patient was matched with two controls, who were chosen by visiting the patient's general practice and using the practice records or age and sex register to select the next two people alphabetically of the same sex and age within two years. Whenever possible two reserve controls were taken in case selected controls had moved or died, but they were not otherwise used. Before we approached the controls the general practitioners were asked if there were medical or other reasons for not approaching them; the controls were not necessarily current attenders at the practice but were simply registered there.

The patients and matched controls were posted similar material consisting of a two page questionnaire with general questions about family size, occupation, marital state, and intake of beverages on the first page and an inquiry about past and present smoking habits on the second. If no reply was returned after six to eight weeks a second questionnaire was sent, with a third reminder eight weeks later.

Smoking was arbitrarily defined as smoking more than five cigarettes, three cigars, or 14 g  $(\frac{1}{2} \text{ oz})$  pipe tobacco weekly for at least one year. For patients, smoking habit at onset of disease was taken to be the habit reported three months before the onset of clinical disease; the smoking habit at the equivalent age was examined in the controls. To preserve the matched design of the study we used Miettinen's method for matched triplets, which permits analysis of complete and incomplete matched sets.<sup>7 8</sup> For other analyses we used the  $\chi^2$  test with Yates's correction and unpaired Student's t test.

TABLE I—Details of cases approached

	Men	Women	Total
No of cases	29	53	82
Current mean age (years)	36	40	38.5
Mean age (years) at diagnosis (range)	29 (11-73)	32 (10-68)	31
Extent of disease:			
Small bowel only	7	7	14
Large bowel only	7	18	25
Large and small bowels	15	28	43
Multiple attacks	23	48	71

# Results

Eighty one of the 82 patients replied; the remaining patient was found to have left the United Kingdom. One hundred and thirty six of the 164 controls approached (83%) replied. In 57 case-control sets the patient and both controls replied and in 21 only one control replied, giving 78 sets for matched analysis. In four sets either the patient or both controls did not reply.

Table II gives the smoking habits of patients in relation to onset of disease and lifetime habit together with the relative risks when patients were compared with controls.

Current smoking—In 37 case-control sets the patient reported being a current smoker and one or both controls were non-smokers, and in 14 sets the converse was true. Patients with Crohn's disease were more likely than controls to be smokers, and the relative risks, which were similar for men and women, were highly significant (women 3.9, 95% confidence limits 1.7-9.0, p<0.009; and men 3.0, 95% confidence limits 1.1-8.0, p<0.05). Lifelong non-smokers were also less common among patients than controls (relative risk of Crohn's disease in people who had ever smoked 4.0, 95% confidence limits 1.9-8.1, p<0.001 for both sexes combined).

Smoking at onset of disease—In 43 case-control sets the patient reported having been a smoker three months before the onset of clinical disease and one or both controls were estimated to have been non-smokers at that time, and in 10 sets the converse was true. In three patients it was difficult to determine the smoking habit at the onset of disease, and they were excluded from the estimation of relative risk. Patients, particularly women, were more likely to have been smokers than non-smokers three months before the onset of disease compared with the controls at that age, the relative risks

Departments of Therapeutics and Community Health, University Hospital, Queen's Medical Centre, University of Nottingham, Nottingham NG7 2UH

KEVIN W SOMERVILLE, MB, FRACP, lecturer in therapeutics

RICHARD F A LOGAN, MSC, MRCP, senior lecturer in clinical epidemiology

MARGARET EDMOND, BSC, research assistant

being 8.2 for women smokers (95% confidence limits 2.8-24.0, p < 0.001) and 2.7 for men (95% confidence limits 0.96-7.1, p < 0.06). Table III shows that the relative risks for smoking and Crohn's disease did not differ materially according to the site of the disease in the bowel.

Social class and other aspects of smoking and disease (tables IV and V)-The social class distribution (Registrar General's classification) of patient's and controls is shown in table IV.9 The excess of smokers among patients with Crohn's disease occurred in all social classes. Although patients and controls were not matched by social class, the distributions in patients and controls were similar. Almost all patients smoked cigarettes (97%) rather than pipes (1%) or cigars (2%), and the estimated relative risk was not significantly different when cigarette smoking alone was considered. Of the 18 patients who had stopped smoking seven had done so at the time of the onset of their disease and five afterwards; the remaining six had stopped before the onset of their disease. When the sexes were combined the mean age at stopping smoking was 10 years later in the patients than the controls (39.5 (SEM 2.8) v 29.5 (2.1) years, p <0.025).

TABLE I

11—Distribution of s	tribution of smoking habit							
-	No (%)           Cases           (n = 29)	$\frac{\text{Oontrols}}{(n=41)}$	$\frac{\text{No}(\%)}{\text{Cases}}$ (n = 52)	Controls (n = 95)	- Combined relative risk	95 % confidence limits	χ²	
noked it smokers d at onset of disease	22 (75) 18 (62) 19 (65)	27 (65) 15 (37) 18 (45)	37 (72) 27 (51) 33 (63)	37 (38) 20 (21) 23 (24)	4·0* 3·5* 4·8*	1·9-8·1 1·8-6·6 2·4-9·7	14·2* 14·9* 21·0*	

\*p<0.001.

Smoked at onset of disease

Ever sm

TABLE III-Relative risk of smoking and Crohn's disease: distribution of disease and histopathological findings

	No of cases	Relative risk	95 % confidence limits	χ²
Distribution of disease:				
Small bowel only	14	3.5	0.8-14.6	1.78
Large bowel only	25	4.7	1.4-16.1	6.29
Large and small bowels	43	4.5	1.8-11.5	10.1
Histological findings:				
Granulomas	32	5.2	1.7-15.4	9.43
Transmural inflammation				
(no granulomas)	24	4.2	1.2-15.5	4.6

TABLE IV—Smoking at onset of disease by social class

	Cases		Controls	
Social class	No (%)	No (° <sub>0</sub> ) smoking at onset	No ( 👷	No (%) smoking at onset
I and II III IV and V Not known	19 (22) 47 (58) 13 (16) 2 (4)	14 (74) 29 (62) 9 (67)	29 (21) 73 (54) 25 (18) 9 (7)	7 (24) 27 (37) 7 (28)

# Discussion

We have shown that, unlike in patients with ulcerative colitis, a higher proportion of our patients with Crohn's disease were smokers than their matched controls, and that this difference antedated the onset of disease and was not explained by variations in social class.

No single study can exclude the possibility of a chance association. Although we approached only 82 patients, however, the estimated relative risks are substantial, with accordingly small p values. We do not think that our results are explained by any unidentified systematic bias in our method of inquiry as in our earlier study of ulcerative colitis, in which we used an identical technique, we found the opposite results-namely,

TABLE V—Aspects of smoking in cases and controls

	Cases	Controls
Current smoking habit in men:		
No of men	18	15
No (%) smoking:		
Cigarettes only	15 (83)	13 (86)
Cigars	2 (11)	1 (7)
Pipe	1 (6)	1 (7)
Reported age of starting smoking (years):		
Men	16.4	16.7
Women	17.7	18·2
Reported age of stopping smoking (years):	45.0	05 51
Men	45.0	25.5*
Women	36.8	32.0*
Reported maximum No of cigarettes smoked daily for		
a year: Men	27	20
Women	27 15	20 16
	15	10
Reported quantity of cigarettes currently smoked daily: Men	18	13
Women	12	13
women	12	13

\*p<0.05.

that patients with colitis tend to have been non-smokers at the onset of the disease.<sup>6</sup> To ensure comparability we took care to construct our case series only from patients registered with the practices we had approached previously. After the end of the study two further patients with Crohn's disease were referred to our clinic from these practices and both were smokers. We took care also to include only patients in whom the diagnosis of Crohn's disease was beyond reasonable doubt; in practice this resulted in the inclusion of patients with histological confirmation of Crohn's disease or with typical Crohn's disease of the small bowel on radiography. Some patients in whom the diagnosis rested only on the findings on barium enema or colonoscopy were therefore excluded.

Our findings differ from those of Harries et al in Cardiff, who found that the proportion of smokers among patients with Crohn's disease was similar to that among the control population used.<sup>1</sup> The proportion of patients with Crohn's disease reporting smoking in their study, however, was not significantly different from the proportion in our study; possibly their study was biased against detecting a true difference because the proportion of responders was low and they used patients attending a fracture clinic as controls, who were not matched for age and sex and of whom 44% were smokers. The reported smoking habits of our controls were similar to those found in recent national data showing 38% of men and 32% of women to be current smokers.

We can offer no explanation for why Crohn's disease might tend to occur more commonly in smokers and ulcerative colitis in non-smokers. These two contrasting associations are, however, consistent with the hypothesis of a genetic predisposition to inflammatory bowel disease with smoking habit determining which of the two diseases develops.<sup>10</sup> Assuming the existence of a population of such predisposed people, it is interesting that when the data from our study of ulcerative colitis, in which 18% of the patients smoked at the onset of their disease, are combined with the data in this study the prevalence of smoking at the onset of disease for both diseases (37%) is similar to that in the combined control groups (41%). It is also noteworthy that cigarette smoking is associated with increased consumption of refined sugar, which is the only environmental factor that has been consistently associated with Crohn's disease.<sup>11 12</sup>

Several studies have shown that patients with Crohn's disease consume roughly twice as much refined sugar as matched controls, and, ignoring the difficulties of retrospective dietary assessments, this association appears to antedate the onset of the disease.<sup>13-17</sup> The possibility arises, therefore, that the association of cigarette smoking and Crohn's disease may reflect differences in sugar consumption or vice versa. As the diet studies found no association between consumption of sugar and ulcerative colitis, however, it is equally, if not more, likely that it is the associations with smoking habit that are primary.

So little is known of the aetiology and pathogenesis of Crohn's disease and ulcerative colitis, or of the effect of smoking on the colon, that it is difficult to suggest a mechanism to account for the observed associations with smoking habit. Possible mechanisms include changes in bowel motility or in susceptibility to some as yet unidentified pathogen. In this respect, smoking has been reported to produce complex changes in immune function including reduced natural killer cell activity in peripheral blood leucocytes and decreased immunoglobulin concentrations in serum and saliva.18 19

Other factors besides smoking must play a part in the development of Crohn's disease; smoking does not account for the occurrence of the disease in children. Nevertheless, an association of Crohn's disease with smoking, if confirmed, could account at least in part for the emergence of the disease during this century.

We gratefully acknowledge the generous support given to RFAL by the Wellcome Trust.

#### References

- Harries AD, Baird A, Rhodes J. Non-smoking: a feature of ulcerative colitis. Br Med J 1982;284:706.
   Jick H, Walker AM. Cigarette smoking and ulcerative colitis. N Engl J Med 1983;308:261-3.

- Jick H, Walter AM. Cigarette smoking and ulcerative colitis. N Engl J Med 1983;308:261-3.
   Bures J, Fixa B, Komarkova O, Fingerland A. Non-smoking: a feature of ulcerative colitis. Br Med J 1982;285:440.
   Gyde SN, Prior P, Taylor K, Allan RN. Cigarette smoking, blood pressure and ulcerative colitis. Cut 1983;24:A998.
   Holdstock G, Savage D, Harman M, Wright R. Should patients with inflammatory bowel disease smoke? Br Med J 1984;288:362.
   Logan RFA, Edmond M, Somerville KW, Langman MJS. Smoking and ulcerative colitis. Br Med J 1984;288:751-3.
   Miettinen OS. Estimation of relative risk from individually fnatched series. Biometrics 1970;26:75-86.
   Breslow NE, Day NE. Statistical methods in cancer research. Vol I. The analysis of case-control studies. IARC. Lyons: International Agency for Research on Cancer, 1980.
   Office of Population Censuses and Surveys. Classification of occupations. London: HMSO, 1980.
   Kirsner JB, Shorter RG. Recent developments in "nonspecific" inflammatory bowel disease. N Engl J Med 1982;306:775-85, 837-48.
   Bennett AE, Doll R, Howell RW. Sugar consumption and cigarette smoking. Lancet 1970;i:1011-4.
   Elwood PC, Waters WE, Moore S, Sweetnam P. Sucrose consumption and ischaemic heart disease in the community. Lancet 1970;i:1014-6.
   Martini GA, Brandes JN. Increased consumption of refined carbohydrates in patients with Crohn's disease. Klin Wochenschr 1976;54:367-71.
   Thornton JR, Emmett PM, Heaton KW. Diet and Crohn's disease: characteristics of the pre-illness diet. Br Med 7 1971;:102-4.

- patients with Crohn's disease. Klin Wochenschr 1976;54:367-71.
  14 Thornton JR, Emmett PM, Heaton KW. Diet and Crohn's disease: characteristics of the pre-illness diet. Br Med J 1979;ii:762-4.
  15 Kasper H, Sommer H. Dietary fibre and nutrient intake in Crohn's disease. Am J Clin Nutr 1979;32:1898-901.
  16 Mayberry JF, Rhodes J, Newcombe RG. Increased sugar consumption in Crohn's disease. Digestion 1980;20:323-6.
  17 Jänerot G, Jarnmark I, Nilsson K. Consumption of refined sugar by patients with Crohn's disease, ulcerative colitis or irritable bowel syndrome. Scand J Gastroenterol 1983;18:999-1002.
  18 Ferson M, Edwards A, Lind A, Milton GN, Hersey P. Lower natural killer cell activity and immunoglobulin levels associated with smoking in human subjects. Int J Gancer 1979;23:603-9.
  19 Hersey P, Prendergast D, Edwards A. Effects of smoking on the immune system: follow-up studies in normal subjects after cessation of smoking. Med J Aust 1983;2:425-9.

(Accepted 20 July 1984)

# Injuries to children riding BMX bikes

CYNTHIA M ILLINGWORTH

#### Abstract

One hundred children presented over 40 days with BMX bike injuries, 40 of which had been sustained while trying to perform stunts. Injuries in this series were compared with previously reported injuries from accidents on ordinary bicycles.

BMX bike injuries differed little from ordinary bike injuries except in the greater proportion of injuries due to stunts and the smaller incidence of head injuries.

#### Introduction

By means of a proforma, I recorded 100 consecutive children attending the accident and emergency department at this hospital for injuries sustained after falling off their BMX bikes.

Accident and Emergency Department, Children's Hospital, Sheffield S10 2TH

CYNTHIA M ILLINGWORTH, FRCP, consultant

#### Patients, methods, and results

Over 40 days from 25 May 1984, 100 children with BMX bike injuries attended the department. Eighty one presented in June, when the total new attendances were 2673. The mean age was 10 (range 2-15). Ninety three were boys, and 28 had had previous bike injuries. Three had cycling experience of seven days or less. Of 81 who owned a BMX bike, eight had done so for seven days or less.

Forty accidents were due to "stunts." These have their own descriptive jargon—for instance, "bunny hops" (jumping the cycle over an obstacle), "ramp hops," "kerb endo" (getting over a vertical kerb, one wheel at a time), "swerving into the sweeper berm" (on a cambered corner), "hitting the monster camel" (jumping over two obstacles), and "wheelies" (riding on one wheel). Twenty one accidents resulted from ramp hops, five from wheelies, and one from a kerb endo. Other causes included standing on the cycle, riding side saddle, and cycling down steps.

Eighteen accidents were due to hitting an obstacle: three boys rode into cars, eight collided with other cycles, and others hit bumps, a brick, or a road grate; one rode into a wire fastened between two posts. Six accidents were due to brake failure: one of these resulted from trying to control speed by a foot on the tyre and another by a foot between spokes. Six children fell over handlebars after braking too suddenly. Two accidents were due to two children riding on one cycle: in one case a child caught a foot in the spokes; in the other the front wheel broke under the weight. Seven children skidded, and others fell because of speeding, a foot slipping off the pedal, or because of slipping off the saddle.

The severity of the injuries was roughly graded from one to five, as follows: grade 1, injuries that were so trivial that no treatment or follow up was necessary; grade 2, minor lacerations and soft tissue injuries, bruises, and undisplaced fractures of fingers or toes; grade 3,