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FOR DEBATE . . .

Breakfast and Crohn's disease

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Summary

The breakfast habits in adult life of 34 patients with Crohn's disease were compared with those of 68 matched controls. Cornflakes were being eaten at least weekly by 23 of the patients (67·6%) at the time that their symptoms began, compared with 17 (25%) of the controls at the corresponding time. Only one of the 34 patients had not eaten cornflakes at all, compared with half of the controls. A significant but weaker association was found between Crohn's disease and the eating of wheat cereals. However, in both patients and controls the taking of cornflakes and of wheat cereals were correlated, and the observed preponderance of wheat eating among the patients was almost entirely ascribable to this association of habits.

Eating of rice cereals and of porridge was not associated with Crohn's disease, though it was correlated with eating cornflakes. There was an excess of bran eaters among the propositi, but this, too, was attributable to their being also cornflake eaters. Other breakfast foods were taken with equal frequency, and omission of breakfast was equally common. Six of the 68 controls, but none of the patients, ate cornflakes later in the day but not at breakfast.

The results need confirmation. There was no evidence that bias could have caused the correlation found. The association of Crohn's disease with the eating of cornflakes is strong and unlikely to be indirect. Variable digestive secretory behaviour after waking may play a part in determining susceptibility to Crohn's disease.

Introduction

While the incidence[1] of Crohn's disease increases rapidly its cause remains unknown. Although foodstuffs seem possible causal agents none has been identified as such.[2] I describe an investigation of breakfast habits, which was begun on the assumption that food taken on a completely empty stomach is more likely to reach the areas usually affected by the disease. The habits of patients with Crohn's disease were compared with those of matched controls.

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Patients and controls

The patients were 16 men and 18 women, and all were patients of Hillingdon Hospital or of Hayes Cottage Hospital. Their ages ranged from 19 to 64 years (mean 37·17 years; SD 12·82). The diagnosis was confirmed by radiography in all, and acceptance for the series preceded dietary inquiry. The small intestine alone was involved in 16, the large alone in 7, and both in 11. Nineteen had had resections, three more than once.

There were 68 controls, two for each propositus. They, too, were patients of the hospitals. Each was of the same sex as the corresponding propositus, and within 11% of his age; the mean age of the controls was 37·29 years (SD 12·93). They were being treated for a wide variety of conditions and had had no major gastrointestinal symptoms. All but six resided in the same area as the propositi.

THE INQUIRY

The questioning was done by me and the study was not, therefore, a blind one. I asked each subject whether he ate breakfast and then specifically about each of a list of foodstuffs. The patients were asked about their habits up to the time of onset of their symptoms, and the controls up to the corresponding time. A form was used that tabulated the foodstuffs on one axis and the frequencies with which they were eaten on the other; a reply was recorded in respect of each food.

The foodstuffs listed were: breakfast foods in general; cornflakes; wheat cereals (shredded wheat and wheat biscuits were not distinguished); rice cereal (rice enriched with wheat gluten was classified as rice; no patient professed to eat other mixtures); bran; oats or porridge (all types of porridge preparations were classified together); muesli; toast; egg; fried foods; milk taken alone. The frequencies recorded were: daily; at least once a week; monthly; rarely; at weekends; on holiday; never. When a habit had been adopted or abandoned the fact and the date were noted. The subjects were also asked whether they ate cereals at meals other than breakfast.

The results were subsequently classified as follows: regularly (daily, at least once a week, and at weekends), or otherwise (monthly, rarely, and never). In some tables the categories of daily or never were shown. The replies tabulated referred to the period until symptoms began. Few subjects could recall their habits before they left school. Three patients had developed their symptoms before school leaving age (at ages 11½, 14, and 15½ respectively) and were able to remember their previous eating habits; otherwise the inquiry related to adult life only.

TABLE I—*Numbers of patients and controls who ate various cereals regularly or otherwise*

	Cornflakes		Wheat		Porridge		Rice		Bran		Muesli	
	Patients	Controls	Patients	Controls	Patients	Controls	Patients	Controls	Patients	Controls	Patients	Controls
Regularly	23	17	16	12	11	15	8	10	6	2	4	3
Rarely or never	11	51	18	56	23	53	26	58	28	66	30	65
χ^2c	15·55		8·42		0·78		0·68					
P value	<0·001		<0·01		0·5>P>0·1		0·5>P>0·1		0·0157*		0·165*	

*Calculated[a] probability of the observed or a greater preponderance occurring by chance.

Results

The positive findings relate to breakfast cereals. Table I shows the number of patients and controls who regularly—that is, at least weekly—ate the various cereals shown. A large preponderance of the patients with Crohn's disease were regular eaters of cornflakes. A less strong association was found for wheat cereals, but for porridge and rice the preponderance was insignificant. For bran and muesli the numbers are small, but the excess of bran eaters among the patients with Crohn's disease would have occurred by chance only once in 64 trials; that for muesli, on the other hand, would have occurred once in six trials.

Table II shows the percentage of subjects in each category who had never, as adults, eaten the four most popular cereals. Only one patient with Crohn's disease had never eaten cornflakes, whereas half of the controls had never done so. On the other hand 10 of the patients with Crohn's disease (29%) had never eaten wheat breakfast foods, even though a significantly larger proportion of the controls had never done so.

Table III shows the number of subjects in the whole series, both patients and controls, classified according to whether they ate cornflakes regularly or not, and according to whether they also ate the other cereals, or not. The data show that eaters of cornflakes tended to eat several other cereals more often than did those who did not eat cornflakes. The association was strong for wheat cereals, less so but significant for porridge, rice and bran, and insignificant for muesli.

TABLE II—*Number (%) of patients and controls who had never eaten certain cereals during adult life*

	Patients (n = 34)	Controls (n = 68)
Cornflakes	1 (2·9)	34 (50·0)
Wheat	10 (29·4)	37 (54·4)
Porridge	13 (38·2)	34 (50·0)
Rice	20 (58·8)	51 (75·0)

TABLE III—*Number of patients and controls who regularly ate cornflakes or not, and those who also regularly ate other cereals, or not*

	Regularly	Rarely or never
Wheat:		
Regularly	23	5
Rarely or never	17	57
	χ^2c = 27·4; P<0·001	
Porridge:		
Regularly	17	10
Rarely or never	23	52
	χ^2c = 7·39; P<0·01	
Rice:		
Regularly	12	5
Rarely or never	28	57
	χ^2c = 6·92; P<0·01	
Bran:		
Regularly	8	
Rarely or never	32	62
	P = 0·00035*	
Muesli:		
Regularly	4	3
Rarely or never	36	59
	P = 0·268*	

*See footnote to table I.

Table IV shows the percentages of patients and controls who ate foods other than cereals, and also of those who did not take a daily breakfast; none of the differences were significant. In tables I to IV the data relate to breakfast habits only. Table V gives the number of subjects who regularly or rarely ate cornflakes at some time other than breakfast; usually it was in the evening. Although several patients with Crohn's disease ate cornflakes in the evening (numbers not shown in table V) none ate them solely in the evening.

The relationships of cereal eating habits to the site of the disease were examined, but no correlations were found and the results are not tabulated.

TABLE IV—*Number (%) of patients and controls who regularly ate foods other than cereals or who did not take a daily breakfast*

	Patients (n = 34)	Controls (n = 68)
Toast	24 (70·6)	52 (76·5)
Egg	17 (50·0)	29 (42·6)
Fried foods	17 (50·0)	25 (36·8)
Milk	5 (14·7)	5 (7·4)
No daily breakfast	11 (32·4)	23 (33·8)

TABLE V—*Number of patients and controls who ate cornflakes at meals other than breakfast, or not at all, or at breakfast*

	Cornflakes	
	Other meals only	Not at all or at breakfast
Patients	6	34
Controls		62
	P = 0·081*	

*See footnote to table I.

Discussion

Any conclusion based on a small series can only be tentative. Though small, the series suffices virtually to eliminate chance as a cause of the association found. Bias, however, in sampling or observer, is possible. Bias in sampling is unlikely to apply to the patient series which must have comprised most of the affected members of the local community. In the selection of the controls every effort was made to secure comparability; the population was compact and fairly homogeneous, and was the source of nearly all patients and controls.

Observer bias is unlikely to have produced the correlation found—not only because the correlation is strong, but because there is no trend towards bias during the investigation. Among the second controls of each pair, interviewed during the later part of the study, the proportion who did not eat cornflakes (41%) was lower than among the first set of controls (59%). The association could have arisen indirectly through some third factor. For example, cereal eaters might be hasty and irregular in their eating habits, and thus more subject, for some reason, to Crohn's disease. Such a suggestion is not borne out by the data shown in the last line of table IV, which show that neglect of breakfast was equally common among both groups. Nor can milk be such a factor since the association would then extend to

all cereals, milk having been taken with all. Milk drinking at breakfast was a little less rare among patients with Crohn's disease, but it was still unusual.

Apart from the absence of an obvious common factor, the observed association of Crohn's disease with cornflake eating is so strong as to make it unlikely to be indirect. The weaker association of the other cereals with Crohn's disease may adequately be explained by the correlation of habits shown in table III. Wheat and bran eating would thus be linked with Crohn's disease secondarily through their association with cornflake eating. The association of porridge and of rice eating with cornflake eating, though significant, are not strong enough to bring these habits, too, into association with Crohn's disease.

If these findings should be confirmed on a wider scale and in other communities and populations, they would require a re-examination of the question of a dietary factor in Crohn's disease. Lewkonia and McConnell[3] cite the paucity of reports of affected spouses as evidence against the existence of such a factor. There is also evidence for a transmissible agent of viral size,[4] for which the cornflake would seem an improbable vehicle. Further, cornflakes are made from maize, which has long been a traditional foodstuff of several major populations. They have, however, the new property of being ready to eat, which makes it possible to eat them soon after waking when, as will be mentioned below, special digestive conditions obtain. This concept, which was the point of departure for this investigation, finds some support in the data of table V, though they fall short of significance. The absence among the patients of people who eat cornflakes not at breakfast but later, and their presence among the controls, show that the significant association is not simply with eating cornflakes but with doing so at breakfast.

From the data presented, and taking the prevalence of Crohn's disease as 30 per 100 000, one may estimate that the disease will be found in one of 1200 who have regularly eaten cornflakes since leaving school, and in one in 3000 of those who have occasionally done so. Susceptibility to Crohn's disease may thus be rare; some of it may be inherited and possibly racial,[3] and it may perhaps depend on abnormal immune responses.[5] A further factor, in the light of the present findings, may be the individually different readiness with which digestive secretion begins after waking. The "waking secretion"[6] of the stomach is sometimes immediate and rapid,[7] but in unpublished observations among other individuals I have found it to be sluggish or even undetectable. In subjects of the latter kind breakfast foods will not be exposed to gastric acid nor to pepsin, nor possibly to pancreatic enzymes; some part of such foods could thus reach the lower intestine unaltered. Further work would be necessary to show whether such a pattern of secretory behaviour is indeed associated with Crohn's disease.

I am grateful to colleagues for help with case finding and for allowing me to see their patients, to Dr H V L Finlay for advice, and to the patients for their willing co-operation.

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SIDE EFFECTS OF DRUGS

Chloroquine induced involuntary movements

Four cases of involuntary movements induced by amodiaquine were recently reported.[1] Chloroquine is similar to amodiaquine and both are used effectively in the treatment of malaria. Chloroquine has many well-recognised, minor side effects including transient headache, visual disturbances, gastrointestinal upset, and pruritus.[2] T wave changes in the electrocardiogram (without evidence of cardiovascular damage), visual symptoms, and mild skin eruptions[3] have been noted in patients given large doses of chloroquine over a period. Long-term chloroquine treatment also frequently causes retinopathy; while ototoxicity has been reported in a few cases.[4] No accounts exist, however, of involuntary movements after chloroquine. We report here five cases of chloroquine-induced involuntary movements.

Case reports

Case 1—A boy aged 12 presented with persistent protrusion of the tongue with fasciculation, excessive salivation, and difficulty in swallowing. The previous day he had been given an injection of chloroquine phosphate together with two tablets by mouth and had repeated the dose of tablets the next morning. There was no previous history of adverse reaction to chloroquine tablets, though he remembered having taken them before. He seemed well-adjusted, and it was assumed that the symptoms were induced by chloroquine. No other drug had been taken. Over the next 48 hours the symptoms receded under treatment with chlorpromazine. His parents were advised not to give him chloroquine again, but eight months later the boy was readmitted with the same symptoms having been given chloroquine sulphate tablets for an attack of malaria.

Case 2—A girl aged 16 was admitted to hospital one evening by the nurses. She had abdominal pain, nausea, fever, and poor appetite, and was given two tablets of chloroquine and two tablets of paracetamol. The next morning she was seen by the doctor, who diagnosed urinary tract infection. She was then given a triple dose of sulphonamide tablets and an injection of dipyrone. Later that afternoon she developed protrusion of the tongue, the neck was involuntarily pulled to one side, and her speech was slurred. These symptoms abated during the next 48 hours, though all treatment apart from chloroquine was continued.

Case 3—A civil servant aged 26 presented with paraesthesia of the right side of the face and neck. There was no previous history of fits. The previous day he had had a fever and had taken two tablets of chloroquine and two tablets of aspirin. On examination the neck was drawn to the right and there was fasciculation of the facial muscles. His blood pressure was 140/100 mm Hg and a diagnosis of stroke was considered. He was admitted to hospital and developed protrusion of the tongue that evening. No more chloroquine was given, and the symptoms abated during the next 36 hours on treatment with diphenhydramine and methocarbamol.

Case 4—A housewife aged 19 presented with typical symptoms of malaria —fever, headache, aches and pains, and palpitation. Chloroquine phosphate 4 ml intramuscularly, chloroquine tablets, two daily for four days, and aspirin two tablets three times daily were prescribed. Two days later she presented with twitching of the left side of the face and difficulty in keeping her eyes open. She could not open her mouth fully. She was made to lie down quietly and given chlorpromazine 25 mg intramuscularly. Two hours later she had recovered and was allowed home.

Case 5—A young nurse aged 23 had malaria and was given chloroquine phosphate 4 ml intramuscularly and two tablets of chloroquine. After three hours she complained of involuntary turning of the neck to one side. Later protrusion of the tongue and excessive salivation developed. She had used chloroquine in the past without any such reaction. She was known to be a timid person and the possibility of hysteria was raised. No further chloroquine was given, however, and during the next 48 hours the symptoms abated after treatment with diazepam and diphenhydramine. She was encouraged to take chloroquine again the next time she had malaria. Three months later an attack of malaria occurred and the side effects were repeated on taking two chloroquine tablets.