Key messages

- Incidence of acute lymphoblastic leukaemia in young children increased with the "entropy" attributable to migration into their districts of residence
- Population mixing even at relatively low levels may be important in the aetiology of childhood leukaemia
- The results provide further epidemiological evidence that childhood leukaemia might be a rare response to infection
- Previous studies finding increased incidence in more affluent areas may have been indirectly observing a population mixing effect

SOCIOECONOMIC STATUS

Our results on the relation between socioeconomic status and incidence of acute lymphoblastic leukaemia are similar to those of Draper and colleagues.[6] This is not surprising as the two analyses have a large number of cases in common. In multivariate analysis, no two indicators of population mixing and socioeconomic status were of independent significance. The two types of variable are correlated; in particular, areas of low unemployment naturally attract more incoming families and families of higher social class tend to be more mobile. Thus it is impossible to tell the extent to which each of these factors is independently of importance in affecting the incidence of childhood acute lymphoblastic leukaemia. As population mixing is more likely than socioeconomic status to increase rapidly and some of the highest incidence rates for leukaemia have been found in situations of very high increases in levels of mixing, it seems reasonable to conclude that population mixing is of more fundamental importance. Previous studies which have revealed a social class effect on the incidence of childhood leukaemia may in fact have been observing indirectly a population mixing effect.

The present study has provided evidence of an effect of population mixing on the incidence of childhood leukaemia which is not confined to areas experiencing the most extreme levels of mixing. The analysis at district level is nevertheless arguably not sufficiently sensitive and we propose in future to analyse more recent, and hence independent, incidence data at ward level by using flow data from the 1991 census. That census is also the first to provide reliable migrant flow data disaggregated by age group, thus making it possible to investigate specifically the possible effect on incidence of leukaemia of the diversity of origins of incoming children. These further analyses may also enable the effects of population mixing and socioeconomic status to be disentangled more completely.

We are grateful to regional cancer registries, regional children's tumour registries, the UK Children's Cancer Study Group, the Clinical Trial Service Unit, and OPCS for providing notifications of cases of childhood leukaemia. We thank the many people who have worked on the National Registry of Childhood Tumours, particularly Mrs M B Allen, Mr T J Vincent, Dr E M Eatock, Mr M J Loach, Mrs P A Brownbill, Mrs J Williams, Miss A Berry, and Miss A Sabin. We thank Mrs E M Roberts for secretarial assistance. The 1981 census data are Crown Copyright.

Funding: The Childhood Cancer Research Group is supported by the Department of Health and the Scottish Home and Health Department.

Conflict of interest: None.

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(Accepted 24 September 1996)

Absence of oats toxicity in adult coeliac disease

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BMJ 1996;**313**:1300–1

Coeliac disease is a gluten-sensitive disorder characterised by malabsorption and a typical histological lesion. Treatment with a strict gluten-free diet results in complete clinical and histological recovery. The conventional gluten-free diet used to treat coeliac disease proscribes oats cereal as well as wheat, barley, and rye.[1] However, the issue of oats toxicity has not been conclusively resolved, and the prohibition of this important cereal deprives patients of a valuable source of fibre and nutrients. The aim of this study was to examine the clinical, histological, and immunological responses of adult patients with coeliac disease to challenge with oats.

Patients, methods, and results

Ten adult patients with coeliac disease in clinical and histological remission were recruited from the coeliac

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Table 1—*Serological and quantitative histological analysis of 10 patients with coeliac disease before and after oats challenge for 12 weeks*

Patient	Gliadin antibody titre*		Endomysial antibody titre		Histology		Intraepithelial lymphocyte count (%)		Enterocyte height (μm)	
	Before challenge	After challenge	Before challenge	After challenge	Before challenge	After challenge	Before challenge	After challenge	Before challenge	After challenge
1	<1.0	<1.0	Negative	Negative	Normal	Normal	16	14	36.3	35.3
2	<1.0	<1.0	Negative	Negative	Normal	Normal	26	15	36.0	38.3
3	<1.0	<1.0	Negative	Negative	Normal	Normal	19	13	40.8	37.9
4	<1.0	<1.0	Negative	Negative	Normal	Normal	6	13	44.9	37.6
5	<1.0	<1.0	Negative	Negative	Normal	Normal	22	32	32.8	28.8
6	<1.0	<1.0	Negative	Negative	Normal	Normal	17	18	28.8	27.1
7	7.0	8.0	Negative	Negative	Normal	Normal	36	20	38.4	42.6
8	<1.0	<1.0	Negative	Negative	Normal	Normal	15	13	31.1	34.7
9	<1.0	<1.0	Negative	Negative	Normal	Normal	23	13	29.8	30.6
10	<1.0	<1.0	Negative	Negative	Normal	Normal	13	13	30.2	36.8
Mean (SE)							19 (2.5)	16 (1.9)	35 (1.7)	35 (1.5)

*Reference range for adult gliadin antibody titres is 0-3.0.

outpatient clinic in St James's Hospital, Dublin. Each patient consumed 50 g of oats (as porridge) daily for 12 weeks while maintaining a strict gluten-free diet. Patient compliance was recorded daily using diaries, and all patients complied fully with the study protocol. The oats cereal (Peter Kölln, Germany) used in the study was tested for evidence of gluten contamination using reverse phase high performance liquid chromatography, enzyme linked immunoassay, and polymerase chain reaction techniques and was shown to be entirely gluten free.

The patients were assessed clinically at 0, 1, 4, and 12 weeks. Laboratory investigations were performed at each of these visits and included full haematological and biochemical profiles and serological tests for antibodies to gliadin and endomysium. Duodenal biopsies were obtained endoscopically before the start of oats challenge and after 12 weeks. The biopsy specimens underwent standard evaluation for evidence of morphological damage. Furthermore, two independent observers performed intraepithelial lymphocyte counts, and enterocyte height (in μm) was measured by computerised image analysis.

Throughout the oats challenge all patients remained asymptomatic with normal haematological and biochemical indices. Endomysial and gliadin antibody values were unaltered by the oats supplement. No morphological damage was evident on standard histological evaluation. Quantitative histological examination showed no significant change in intraepithelial lymphocyte count or enterocyte height (table 1). Two patients were subsequently given a gluten "microchallenge" consisting of 500 mg of gluten daily for six weeks: both developed histological evidence of relapse, and in one patient the antibody tests became positive.

Comment

This study shows the safety of adding oats to the gluten-free diet of 10 patients with coeliac disease. Seven of the patients have continued to take the same quantity of oats for more than 12 months without adverse effect. These findings are in agreement with a recently published study.[2] In that study, however, the authors stated that they excluded coeliac patients with "severe" disease. No such policy was adopted in our study, and two of our patients were subsequently shown to be exquisitely sensitive when given a gluten microchallenge. A third patient was also shown to be very sensitive to trace quantities of gluten taken inadvertently.

Activation of the immune system by cereal protein is likely to be centrally involved in the pathogenesis of coeliac disease,[3] and evidence of immunological stimulation is a sensitive marker of disease activation. Such evidence includes lymphocyte infiltration of the surface epithelium[4] and the production of antibodies to endomysium and gliadin. Oats challenge caused no change in these parameters whereas in the patients given a gluten microchallenge, abnormalities were observed.

Our results suggest that oats cereal is neither toxic nor immunogenic in coeliac disease. This has important implications for the coeliac population since the inclusion of oats would substantially improve the fibre and nutrient content of their gluten-free diet.[5] The knowledge that oats are not toxic may help to define the toxic moiety in other cereals.

Funding: None.
Conflict of interest: None.

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(Accepted 18 July 1996)