cerned there were six cases of thrombocythaemia. This was easy to control in four (the increased number of platelets was not followed) and was complicated by thrombosis in two (thrombosis was controlled by heparin). In conclusion, a beneficial effect of splenectomy is still equivocal after this phase I trial. The proportion of postoperative deaths (three out of 18 has to be reduced if the procedure is to be advocated. We hope to achieve this when patients can be operated on and nursed for one month in an aseptic environment, which will be possible in the "microbiological gradient service" being built in the Hospital Paul-Brousse at Villejuif. One of the objectives of splenectomy was to completely eradicate the disease; the persistence of the Ph_1 chromosome after surgery, however, shows that this aim was not attained. Another objective was to prevent the well known splenic complication arising during the blastic crisis. In fact, all patients who did not die after splenectomy or aplasia died from a blastic crisis, which is the inevitable end-phase of C.M.L. But we have to evaluate the effect of splenectomy on the overall results of the treatment of blastic crisis in C.M.L.; table V and fig. 7

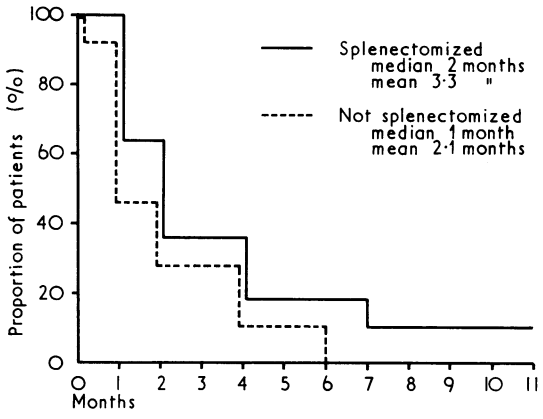

FIG. 7—Cumulative duration of survival from onset of blastic crisis in splenectomized and non-splenectomized patients.

TABLE V—*Effect of Splenectomy on Course of Blastic Crisis*

	Splenectomy	No Splenectomy
Blastic crisis	13/15	19/24
Complete remission obtained	2/13	3/19
Median survival time from onset of blastice crisis	2 Months	1 Month
Mean survival time from onset of blastic crisis	3·3 Months	2·1 Months

show that there were no differences in the development of blastic crises or in the frequency of remissions but that there was a slight difference in survival from the onset of blastic crisis.

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Incidence of Coeliac Disease in the West of Ireland

M. MYLOTTE, B. EGAN-MITCHELL, C. F. McCARTHY, B. McNICHOLL

British Medical Journal, 1973, 1, 703–705

Summary

During an 11-year period the incidence of coeliac disease presenting in children in the West of Ireland has been found to be 1 in 597. When allowance is made for presentation of the disease in adult life the incidence may be as high as 1 in 303. These figures are much higher than those reported for Britain.

Departments of Gastroenterology and Paediatrics, Regional Hospital and University College, Galway
M. MYLOTTE, M.B., B.A.O., Research Fellow
B. EGAN-MITCHELL, M.B., D.C.H., Research Fellow
C. F. McCARTHY, M.D., F.R.C.P.I., Associate Professor of Medicine
B. McNICHOLL, M.D., F.R.C.P., Professor of Paediatrics

Introduction

Estimates of the incidence of coeliac disease vary considerably. In 1950 Davidson and Fountain estimated the incidence to be about 1 in 8,000 in England and Wales and 1 in 4,000 in Scotland. Carter *et al.* (1959), in London, found an incidence of between 1 in 2,000 and 1 in 6,000, and McCrae (1969) calculated the incidence at 1 in 1,850 in Edinburgh. We report a much higher incidence in the West of Ireland.

Site of Study

The Regional Hospital, Galway, is the teaching hospital for University College, Galway. It is a 700-bed general hospital with a 50-bed paediatric unit. The paediatric unit has had a special interest in coeliac disease since its establishment in 1956. In 1969 a gastrointestinal unit was opened and, from this, knowledge of the occurrence of coeliac disease in adults was

TABLE I—*Evidence of Coeliac Disease*

	No. of Patients	Grade of Biopsy Specimen		Clinical Improvement	Effect of Gluten-free Diet		
					Mucosal Change		
		III	II		No. Rebiopsied	Normal	Slight or No Improvement
Children:							
Co. Galway	54	46	8	54	21*	13	8†
Co. Mayo and Co. Roscommon	43	39	4	43	17*	10	7†
Adults: Co. Galway	13	13	0	13	7	2	5‡

*After four years on gluten-free diet.
†These children were not keeping rigidly to their gluten-free diet.
‡Repeat biopsy performed two months after starting gluten-free diet.

obtained. The main drainage area of the hospital comprises Counties Galway, Roscommon, and Mayo, of which the populations are 148,000, 109,000, and 53,000 respectively. The population of these counties is relatively stable in that there is little turnover, in contrast to large urban areas. Virtually all children with coeliac disease in Co. Galway are seen in the paediatric unit of the Regional Hospital, as are most of the coeliac children from Co. Mayo and Co. Roscommon, since paediatric referral clinics staffed by the Regional Hospital are held in both these counties. Most of the adult patients with coeliac disease in Co. Galway are seen in the Regional Hospital but very few are seen from the other counties. It was therefore felt that a fairly exact incidence of coeliac disease could be estimated for Co. Galway. In Co. Mayo and Co. Roscommon a moderately accurate estimate of the frequency of childhood but not adult coeliac disease was possible.

Methods and Patients

Peroral duodenojejunal biopsy specimens were obtained with a Crosby capsule and examined with a dissecting microscope and by routine histological methods. They were classified as described previously (McNicholl and Egan, 1968).

Grade O (normal) specimens show a predominance of finger-shaped villi or narrow, leaf-shaped villi; histologically the structure and cells are normal. Specimens with mainly leaf-shaped villi, even if these are relatively broad, are adjudged normal if the villous heights are comparable to normal villi and the epithelium and lamina propria are found to be normal.

Grade I specimens have lower than normal villi, which are mainly broad leaves or ridges. Histologically there is some loss in height of the columnar epithelium, particularly on the tops of the villi, which have a stunted or bizarre shape. The lamina propria and submucosa show minimal round cell infiltration.

Grade II—In these specimens medium to low ridges or convolutions predominate and there are no normal villi. Histological examination shows squat villi with damaged epithelium and hypercellular lamina propria.

Grade III specimens generally have a flat mucosal surface with, in some instances, deep clefts, creating a mosaic appearance. Occasional low ridges or convolutions may be seen, these often forming oval lips around the mouths of the crypts of Lieberkühn. The flattest specimens are similar in appearance to gastric mucosa except that the mouths of the jejunal glands are bigger. Histological examination shows a flat surface with low cuboidal epithelium in which the nuclei appear crowded and the striated border is poorly defined. The gland layer is usually much thickened and the lamina propria heavily infiltrated with plasma cells and lymphocytes.

Patients who were found to have grade II or grade III changes in the duodenojejunal mucosa while on normal diets and who later showed satisfactory improvement on gluten-free diets were considered to have coeliac disease.

Children born between 1 January 1960 and 31 December 1970 who were diagnosed as having coeliac disease before September 1972 were included in the study, as were adults who were diagnosed between July 1969 and June 1972.

Results

The evidence for coeliac disease in the patients is set out in table I. The separation into the childhood or adult group was on the basis of presentation to the paediatric or gastrointestinal unit; under the age of 12 years children are seen in the paediatric unit. Six patients were excluded from the study—three who in all probability had coeliac disease but were excluded because they did not satisfy the criteria outlined above, two from Co. Galway who showed grade I changes on biopsy but had been on gluten-free diets for some time (one of them a coeliac dwarf), and a child from Co. Roscommon with grade I changes on biopsy.

Gluten was reintroduced into the diet of five children from Co. Galway and six from Cos. Mayo and Roscommon in whom the mucosa had reverted to normal on gluten-free diets; in all instances the mucosa reverted to grade III.

The number of live births for Co. Galway and the combined number of births from Co. Mayo and Co. Roscommon are compared in table II with the number of coeliac children born in each year. The incidence of childhood coeliac disease may be calculated for each year and for the 11-year period. For Co. Galway it varied from nil in 1964 to 1 in 355 in 1961 and was 1 in 597 for the 11-year period. For Co. Mayo and Co. Roscommon the incidence varied from 1 in 1,541 in 1962 to 1 in 385 in 1968, and it was 1 in 736 for the 11-year period. If the five asymptomatic children who were diagnosed during a family study carried out over the past two years are excluded the incidence falls to 1 in 833 for Co. Mayo and Co. Roscommon but is unchanged for Co. Galway, as no asymptomatic children were diagnosed in this county.

TABLE II—*Children who developed Coeliac Disease*

	Co. Galway		Co. Mayo and Co. Roscommon	
	No. of Births	Coeliac Children	No. of Births	Coeliac Children
1960	3,013	4	3,143	3
1961	2,840	8	3,054	3
1962	2,905	7	3,083	2
1963	2,996	4	2,951	5
1964	3,048	0	2,905	2
1965	2,958	5	2,782	7
1966	2,894	6	2,700	2
1967	2,833	3	2,746	3
1968	2,876	5	2,693	7
1969	2,977	6	2,831	5
1970	2,902	6	2,771	4
Total ..	32,242	54	31,659	43

Overall incidence: Co. Galway 1/597; Co. Mayo and Co. Roscommon 1/736.

These figures make no allowance for children who would develop coeliac disease later in life, and an attempt has been made to compensate this by calculating an incidence which includes the adults diagnosed during a three-year period. In all, 13 were diagnosed from Co. Galway but five had a history of symptoms dating back to childhood. These would probably have been diagnosed in childhood if a similar study had been in progress then and were therefore excluded. Of the remaining eight, two had been detected during the family study but were included as neither had had symptoms during childhood.

The mean number of adult coeliac cases diagnosed yearly was 2·66 after exclusion of patients with a history of symptoms in childhood. Combined with the average yearly number of childhood cases (4·91) this gave a yearly occurrence rate of 7·57 for Co. Galway. When this figure was related to the mean birth rate of 2,931 for Co. Galway it gave an incidence of 1 in 387.

The incidence was also estimated by considering the number of people from Co. Galway diagnosed in the paediatric and gastrointestinal units in the three years July 1969 to June 1972; 21 children and 13 adults were diagnosed during that period. Five of the adults were excluded as they had had symptoms in childhood. The mean number of coeliacs diagnosed each year was 9·66, and if these were related to the mean birth rate of 2,931 the incidence of coeliac disease was 1 in 303.

Discussion

It is clear that the incidence of coeliac disease is high in the West of Ireland, and although no figures are available for the remainder of the country discussion with colleagues suggests that the incidence in the country as a whole is also high. The varying incidences estimated for coeliac disease for England, Wales, and Scotland if correct mean that the disease is 6 to 20 times more frequent in the West of Ireland. It is also possible that the disease has a higher incidence elsewhere. None of the other studies (Davidson and Fountain, 1950; Carter *et al.*, 1959; McCrae, 1969) were able to draw on such a direct ascertainment from a small and relatively stable population. In one study (Davidson and Fountain, 1950) there was no biopsy confirmation of the diagnosis, and in another (McCrae, 1969) the estimate of incidence was based on a comparison with that of cystic fibrosis. This may mean that the incidence of coeliac disease elsewhere has been underestimated. It is also probable that there is a wide variation in incidence from one area to another depending on genetic and environmental factors.

Since genetic factors are involved in the aetiology of coeliac disease (Carter *et al.*, 1959; McDonald *et al.*, 1965; Mylotte *et al.*, 1973) the frequency of the condition in our community may reflect a high incidence of the genetic factor or factors in question. Environmental conditions may also be involved (Carter *et al.*, 1959), so the existence of notably different factors in areas with differing incidences of coeliac disease should be considered. A comparative study of environmental factors between the West of Ireland and parts of England where the disease is less common or between the West of Ireland and some parts of the eastern United States, where the disease seems to be rare, might be fruitful. A local factor which may be relevant is the very early and intensive feeding of wheat cereals to infants. Breast-feeding is rare, probably not more than 3% of infants being breast-fed. Cereals, predominantly wheat, are frequently given as early as 2 or 3 weeks of age. In contrast, rice is the first cereal fed to most infants in the eastern United States.

While earlier wheat-feeding should result in an earlier onset of the disease, whether it could also provide the stress necessary to provoke an otherwise latent disease is uncertain. Of interest in this context is a family recently studied (Mylotte *et al.*, 1973) in which five out of 13 siblings had coeliac disease. All the children in this family had been fed wheat cereals from between 4 and 6 weeks of age. If early wheat-feeding is responsible for the high expression rate of coeliac disease in genetically predisposed individuals it would be expected that the incidence of the condition in the relatives of coeliac patients in areas where early wheat-feeding is practised would be higher than the incidence in relatives where early wheat-feeding is not practised. The incidence of coeliac disease in first-degree relatives in the U.S.A. is 11% (McDonald *et al.*, 1965), in southern England 8% (Mortimer, 1970), and in the West of Ireland 10% (Mylotte *et al.*, 1973). There is a remarkable similarity between the figures from the U.S.A., where early wheat-feeding is rare, at least in the eastern States, and Ireland, where early wheat-feeding is common. The infant feeding pattern of the Birmingham area of England is similar to the pattern in Ireland, with infrequent breast-feeding and early wheat-feeding (Shukla *et al.*, 1972). Thus there is no evidence to relate early wheat-feeding to the high incidence of coeliac disease in the West of Ireland.

It is unlikely that the reliance of the rural Irish on the potato as the staple food for some centuries would result in undue tolerance to wheat gluten in subsequent generations, otherwise a similarly high incidence of coeliac disease would be expected in rice-eating races after a change to wheat-eating. We know of no evidence on these lines, nor do we have any evidence or impression concerning other environmental factors likely to account for the high incidence of coeliac disease in the West of Ireland.

The possibility of a high level of intermarriage in previous generations as a cause of the high incidence of coeliac disease is unlikely. No consanguinity was detected in the family histories of the patients studied. Marriage between relatives is not more frequent than elsewhere, except in the itinerant ("tinker") population, numbering about 1,500 in Co. Galway. Among this group there have been three children with coeliac disease in the 11-year period. The incidence of cystic fibrosis, a disease of autosomal recessive inheritance, is 1 in 2,303 births (calculated in the same manner as that for coeliac disease for the same 11-year period). This figure is similar to the unusually accepted incidence of 1 in 2,000 (Carter, 1967) and is not in keeping with a high rate of intermarriage. The incidence of congenital pyloric stenosis, calculated as for the other two diseases, was 1 in 948 births, a much lower incidence than that of 1 in 200 mentioned by Carter and Evans (1969). The low incidence probably indicates an interesting difference between the genetic background of our community and of those studied by Carter in relation to pyloric stenosis as well as in relation to coeliac disease. The incidence of pyloric stenosis was based on the numbers of Ramstedt's operations carried out in three smaller hospitals in the area in addition to those in this hospital and represents a virtually complete ascertainment, since medical treatment of this condition was not practised during the period in question. Ascertainment of the incidence of cystic fibrosis may not be as complete as for pyloric stenosis but is unlikely to be higher than 1 in 2,000.

We wish to acknowledge grants from the Medical Research Council of Ireland and the Wellcome Trust. We are grateful for the help of Drs. J. Humphreys, A. Sharkey, J. Jones, and M. McCormack. Sisters M. T. Farrell and M. Cabrini helped in collecting statistics.

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