Occasional Review

Is coeliac disease underdiagnosed?

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At Northwick Park Hospital about 13 new cases of coeliac disease in adults are diagnosed each year. Discussions with other doctors indicated that this number was much higher than in other local hospitals and led us to investigate the factors responsible for the relatively high diagnosis rate at Northwick Park.

Patients and methods

The notes of the 88 patients with adult coeliac disease diagnosed at Northwick Park from September 1970 to the end of 1979 were reviewed to assess symptoms at presentation and laboratory evidence of ill health at diagnosis. All patients had had the diagnosis confirmed histologically on small bowel biopsy.

Members of the Coeliac Society in regions of England and Wales per 100 000 population. Overall there were 27 members per 100 000 (1 in 3700).

With the co-operation of local pathologists, all the small bowel biopsies carried out in two hospitals in adjacent area health authorities, one (hospital A) with a specialist gastroenterological unit and one (hospital B) with no special interest in gastroenterology, were identified for 1976-8. The request and report forms were reviewed to determine the number of new patients with adult coeliac disease diagnosed in

each hospital. These numbers were compared with the numbers diagnosed at Northwick Park and related to the number of people attending as new general medical outpatients at each hospital. The principal reason for biopsy recorded on the pathology form for each small bowel biopsy carried out in 1978 was then classified and compared with equivalent data from Northwick Park.

Through the co-operation of the Coeliac Society a count was made of the total number of members in each postal county in England and Wales in February 1980. The manufacturers of the two single-specimen biopsy capsules most commonly used in this country kindly supplied sales figures to individual hospitals in England and Wales for 1977-9 (capsule A) and 1977 to June 1979 (capsule B). Figures for Coeliac Society membership and sales of small bowel biopsy capsules were then grouped geographically according to the Post Office grouping for parcel post deliveries, which reflects major communication networks and thus is likely to reflect referral patterns in different parts of the country.

The population estimates used were those for mid-1978.¹ Conventional statistical techniques—namely, the unpaired *t*-test, Mann Whitney U test, χ^2 test, and multiple regression analysis were used as appropriate with the help of members of the division of computing and statistics, Clinical Research Centre.

Results

NORTHWICK PARK HOSPITAL

Table I shows the age at diagnosis for all 88 patients and for the men and women separately. The distribution appeared to be bimodal, the early peak being accounted for mainly by women and the later peak by men, though this failed to reach statistical significance.

TABLE I—Age at diagnosis in both sexes. Results are numbers (percentages) of patients

Age (years)	All (n = 88)	Women (64)	Men (24)
<20	2 (2)	1 (2)	1 (4)
20-29	16 (18)	14 (22)	2 (8)
30-39	19 (22)	16 (25)	3 (13)
40-49	13 (15)	10 (16)	3 (13)
50-59	14 (16)	7 (11)	7 (29)
60-69	14 (16)	8 (13)	6 (25)
70-79	9 (10)	8 (13)	1 (4)
80-89	1 (1)	0	1 (4)
Median (years)	42.5	40.5	54.5
Mean $\pm$ SD (years)	45.8 $\pm$ 17.2	44.1 $\pm$ 17.3	50.3 $\pm$ 16.6

Fifty-six of the patients (64%), including four identified through family screening studies, had trivial, transient, or unrelated symptoms at presentation. These included minor degrees of tiredness and depression, indigestion, offensive wind, and transient acute gastrointestinal upsets. In 39 of these the diagnosis was first suspected because of an unexplained abnormality on a routine blood count. This abnormality was macrocytosis (mean cell volume > 92 fl) without evidence of anaemia in 19, mild anaemia (haemoglobin 11.0-12.9 g/dl in men, 10.0-11.9 g/dl in women) in 11, and moderate anaemia (9.0-10.9 g/dl in men, 8.0-9.9 g/dl in women) in the remaining nine.

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Three patients had been diagnosed in childhood but at presentation thought they had been cured. Ten had a variety of minor abnormalities on investigation, which combined with clinical suspicion enabled the diagnosis to be made, and one was diagnosed coincidentally during investigation of hypogammaglobulinaemia.

Only 23 (26%) of the patients presented with classical symptoms of coeliac disease: steatorrhoea, osteomalacia or severe anaemia. The remaining nine had either dermatitis herpetiformis or severe mouth ulcers, conditions known to be associated with coeliac disease.

TABLE II—Haematological values and faecal fat estimations in 88 patients with coeliac disease diagnosed at Northwick Park Hospital according to presenting symptoms. Values are means $\pm$ SD and numbers of patients tested are given in parentheses

	Normal range	Patients with trivial symptoms	Patients with classical symptoms	p value
Age		44.6 $\pm$ 15.7 (56)	48.3 $\pm$ 19.3 (23)	NS
Male:female ..		12:44 (56)	8:15 (23)	NS
Hb (g/dl) ..	12.3-17.0	11.9 $\pm$ 1.8 (56)	11.1 $\pm$ 2.8 (23)	NS
MCV (fl) ..	80-92	89.6 $\pm$ 13.9 (55)	80.7 $\pm$ 12.7 (22)	0.01
Faecal fat (g/24 h) ..	1.0-5.0	10.5 $\pm$ 6.6 (46)	24.9 $\pm$ 18.6 (18)	0.005

Probability values were calculated using the χ^2 test for male:female ratios and the unpaired *t* test for other parameters.

TABLE III—Number of cases of coeliac disease diagnosed at each of the three hospitals in relation to number of new general medical outpatients seen

Hospital	Newly diagnosed patients with adult coeliac disease			New general medical outpatients			Diagnosis rate of coeliac disease in new general medical outpatients
	1976	1977	1978	1976	1977	1978	
Northwick Park	11	16	11	4629	4876	4835	1 in 377
Hospital A	3	1	3	2771	2575	2317	} 1 in 1194
Hospital B	1	1	1	1470	1415	1406	

TABLE IV—Positive biopsies in each hospital according to the indication for biopsy

Indication for first biopsy 1978	Northwick Park		Hospital A		Hospital B	
	All biopsies	Newly diagnosed coeliac patients	All biopsies	Newly diagnosed coeliac patients	All biopsies	Newly diagnosed coeliac patients
Gastrointestinal ..	41	4	101	2	1	1
Haematological ..	16	4	4	1	0	0
Family studies ..	4	1	0	0	0	0
Other ..	19	1	0	0	0	0
Not stated on form ..	2	1	0	0	0	0
Totals	82	11 (13%)	105	3 (3%)	1	1 (100%)

Patients presenting with trivial symptoms had significantly higher mean cell volumes and significantly lower faecal fat estimations than those presenting with classical severe symptoms, although there were no significant differences between the haemoglobin estimations in the two groups. The mode of presentation, trivial or classical, was not related to either age or sex (table II).

COMPARISONS WITH LOCAL HOSPITALS

Table III shows the number of patients with newly diagnosed adult coeliac disease at each of the three hospitals in 1976, 1977, and 1978 in relation to the numbers of new general medical outpatients. The diagnosis rate at Northwick Park was about three times that in the other two hospitals combined (χ^2 , 0.01 $>$ $p >$ 0.001).

In 1978, 82 small bowel biopsies were carried out at Northwick Park on adults who had not previously undergone biopsy compared with 105 at hospital A and 1 at hospital B, resulting in the diagnosis of 11, 3, and 1 new patients with coeliac disease respectively. These differences were statistically highly significant (χ^2 ; $p <$ 0.001). The differing indications for biopsy are set out in table IV.

NATIONAL DATA

The number of patients nationally with coeliac disease is not known accurately, but those diagnosed can be estimated from the numbers known to the Coeliac Society. In February 1980 there were 13 300 members of the Coeliac Society living in England and Wales. Overall this gave a prevalence estimate of 27 per 100 000 of the population, but as the figure shows there was a two- to three-fold variation in estimates of prevalence in different geographical areas. This variation is unlikely to have arisen by chance (χ^2 ; $p <$ 0.001). The number of members in each area was significantly related to population (multiple regression analysis, $p <$ 0.001).

During the periods for which figures are available 190 new A capsules and 46 new B capsules were supplied to hospitals in England and Wales. The number of members of the Coeliac Society in each geographical area was significantly related to the number of biopsy capsules sold to that area even when the population was taken into account (multiple regression analysis, $p <$ 0.02).

Discussion

Classical accounts of coeliac disease emphasised severe disease with major constitutional symptoms and signs. A comprehensive review² written in 1953, before coeliac disease could be defined other than clinically, listed severe symptoms with weight loss, glossitis, anaemia, osteomalacia, and tetany. When peroral biopsy was introduced^{3,4} in the late 1950s it became possible to define coeliac disease pathologically in terms of the abnormal jejunal morphology originally recognised in operative surgical specimens⁵ and further refine the definition in terms of recovery of the abnormal jejunal morphology on gluten withdrawal. This more precise definition enabled the spectrum of disease recognised to be broadened as patients with more minor symptoms were found to have the same pathological lesion in their small bowel mucosa.

In our study 64% of the patients presented with trivial,

transient, or unrelated symptoms and did not have severely abnormal haematological values or faecal fat estimations. Despite their minimal symptoms, however, these patients all felt vastly improved on gluten withdrawal. The diagnosis should be suspected in any patient with an unexplained minor abnormality on a Coulter Counter blood count, particularly a macrocytosis; those with a childhood or family history of coeliac disease or conditions known to be associated with it, such as dermatitis herpetiformis; and those with classical symptoms of steatorrhoea, osteomalacia, or severe anaemia.

The diagnosis rate among new general medical outpatients at Northwick Park over three years was significantly higher than that at two other local hospitals serving an essentially similar population. There were also highly significant differences between the numbers of new patients diagnosed compared with the numbers of small bowel biopsies carried out for the first time at the three different hospitals. The diagnosis of coeliac disease depends on showing the typical morphological abnormality in the jejunal mucosa and, ideally, showing its return towards normal after gluten withdrawal. Thus if few small bowel

biopsies are carried out (hospital B) coeliac disease is probably underdiagnosed. The corollary of this is that once more biopsies are carried out some will inevitably be negative. In 1978 to diagnose 11 new patients with coeliac disease the positive biopsy rate at Northwick Park was 1 in 7.5 biopsies. Nevertheless, coeliac disease is still likely to be underdiagnosed even if many biopsies are carried out (hospital A) if the indications for biopsy do not take account of the full range of presenting symptoms. Figures for the number of biopsies carried out for gastro-intestinal indications are not strictly comparable because a one-tube test for the investigation of suspected steatorrhoea is used at hospital A which is not used at hospital B or Northwick Park. There are, however, still striking differences in the numbers of biopsies carried out for haematological and other reasons. Table III shows that at Northwick Park in 1978 half the biopsies were done for non-gastrointestinal reasons and that these resulted in the diagnosis of 64% of the adults with coeliac disease.

It has been well recognised since the introduction of peroral biopsy techniques that coeliac disease may present at any age. In one large series⁶ the age at presentation was distributed in an approximately normal manner around a median in the fourth decade. Only just over 7% of cases presented in the seventh decade of life. Our data contrasted with this: the age at diagnosis tended to be bimodally distributed, with an early peak in the fourth decade principally accounted for by women and a later peak in the sixth and seventh decade principally accounted for by men. The age at which patients join the Coeliac Society tends to be closely related to the age at diagnosis (unpublished observations); and the 1073 adults who joined the society from June 1978 to May 1979⁷ showed a similar bimodal distribution to our patients, with relatively more men in the older age groups. Overall 24 (27%) of our patients presented in the seventh decade or above.

Coeliac Society membership figures show significant regional variations. The use made of small bowel biopsy capsules is likely to be reflected in the frequency with which they have to be replaced. Thus the significant relation between the numbers of members of the Coeliac Society in a region and the number of small bowel biopsy capsules bought over a three-year period, which was independent of population, suggests that an important reason for the regional variation is that in some areas of the country not enough small bowel biopsies are being done to diagnose the coeliac patients who are there. Genuine regional variations in the incidence of coeliac disease are unlikely to contribute significantly to the variation in estimates of prevalence. There are recognised variations in the incidence of coeliac disease in different populations. For example, Mylotte *et al*⁸ reported a very high incidence of 1 in 303 in the west of Ireland, which contrasts with the 1 in 1850⁹ that is commonly accepted for the incidence in Britain. Whether there are regional variations in the incidence of coeliac disease within Britain is not known. Susceptibility to coeliac disease is thought to have a genetic basis related to HLA type, and whether a particular individual develops the disease is then thought to depend on a wide variety of environmental factors, including the gluten content of the diet. In England and Wales there are regional variations in HLA type, but these are relatively minor and unlikely to result in differing susceptibilities sufficient to account for the two- to three-fold variation in prevalence estimates derived from the Coeliac Society membership figures. Although variation in the proportions of patients with diagnosed coeliac disease joining the Coeliac Society in different parts of the country would obviously also affect these prevalence estimates this is again unlikely to be a major effect. Most doctors who diagnose coeliac disease recognise the valuable work the Coeliac Society does and encourage their patients to join. There is no reason to suppose that patients heed their doctors more or less in different parts of the country. In a series of patients from Bristol¹⁰ 85% joined the Coeliac Society.

It is possible to speculate on the extent of this underdiagnosis of coeliac disease. McCrae's⁹ commonly accepted figure for

coeliac disease of 1 in 1850 suggests that there should be 26 000 patients in England and Wales, which contrasts with the 13 300 known to the Coeliac Society. Even taking into account the fact that not all patients will join the Society, there would still be about 8000 "missing" patients with coeliac disease if 75% of patients joined. This figure leaves no room for complacency.

We are grateful to the Coeliac Society; the manufacturers of the small bowel biopsy capsules commonly used in this country; consultant histopathologists at neighbouring hospitals; the departments of haematology, clinical chemistry, and histopathology at Northwick Park Hospital; and members of the division of computing and statistics, Clinical Research Centre, for their help and co-operation in carrying out this study.

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Is otitis externa a common sequela of syringing wax from the ear?

If carried out correctly with sterile physiological saline and sterile aural syringe syringing of the ears to remove wax will not lead to otitis externa. If there is a history of otitis externa or if the tympanic membrane is perforated it is safer to remove wax under direct vision using a ring-ended probe, such as the Jobson Horne probe. If the wax is hard it should be softened by oil before syringing is attempted. Care must always be taken to avoid damage to the delicate skin lining of the external auditory canal, and the ear canal should be dried by a soft wool mop when the procedure is completed.

What are the risks of a surgeon catching hepatitis from doing minor operations without wearing surgical gloves?

The risk of medical workers acquiring hepatitis B seems to correlate with their degree of exposure to patients' blood. Inoculation of tiny quantities of infective blood may produce hepatitis, but most of the medical staff who contract hepatitis B cannot remember any "needle-stick" accidents or other minor injuries. Possibly, therefore, even simple contamination of the skin with blood that is positive for hepatitis B surface antigen (HBsAg) may produce hepatitis. A study of renal dialysis workers showed that hepatitis was less common in those who always wore gloves when dialysing,¹ and wearing gloves probably reduces the risk to surgeons. Special precautions will be taken in the operating theatres when the surgeon knows that the patient has liver disease or is a possible HBsAg carrier, but this will have a limited effect on the risk of hepatitis since most HBsAg carriers are healthy and cannot be identified from the history.² The chances of a person in Britain being an HBsAg carrier, however, are small (1:500), and only a small proportion of these will be infective—that is, as shown by presence of e antigen—so the risks overall of a surgeon catching hepatitis B are small.

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