

# Clinical presentation of coeliac disease in adult gastroenterological practice

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## SUMMARY

*Clinical features, complications and results of investigations are analysed in 50 patients diagnosed by jejunal biopsy as having coeliac disease at the Adult Gastroenterology Unit, Royal Victoria Hospital, Belfast, between 1969 and 1983. Only one patient was entirely asymptomatic, but 22% had no disturbance of bowel habit, and 50% had not lost weight. There were relatively few physical abnormalities on clinical examination. Screening tests using standard haematological and biochemical methods were positive only in between 8% and 52% of patients. More specific tests for malabsorption were positive in between 54% and 84% of patients. Jejunal biopsy remains the definitive procedure to identify patients with coeliac disease.*

## INTRODUCTION

Only in the past 30 years has 'idiopathic steatorrhoea' or 'non-tropical sprue' been accepted to be the adult variety of coeliac disease. The gluten-free diet was first used to treat adults with this condition in 1952,<sup>1</sup> and it is current practice that this dietary modification is recommended 'for life' to ensure continued clinical remission. It is clearly vital, therefore, that an accurate diagnosis of the disorder is made. Crosby capsule biopsy of the jejunum combined with an assessment of clinical and histological response to gluten withdrawal has become accepted as the essential approach to diagnosis. The clinical features which warrant this procedure and the role of screening blood tests and dynamic studies of absorptive function are not so well defined.

We have examined the case records of 50 consecutive patients diagnosed as having coeliac disease in the Adult Gastroenterology Unit, Royal Victoria Hospital, Belfast, between 1969 and 1983. We describe the presenting symptoms and signs of these patients and the results of their initial screening investigations.

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## METHODS

A retrospective survey in the Medical Records Department, Royal Victoria Hospital, Belfast, identified 50 patients who were investigated and diagnosed as having coeliac disease in the Gastroenterology Unit of that hospital between 1969 and 1983.

Patients were accepted into the study if they had histological evidence of severe partial villous atrophy or subtotal villous atrophy on jejunal biopsy and if a good clinical response to gluten withdrawal had been observed. For each patient, details of presenting symptoms and signs, screening blood tests and malabsorption studies were recorded. Body weight at presentation and at outpatient review after institution of the gluten-free diet was also noted. Complicating illness or associated disease in these patients were documented.

### *Interpretation of tests for malabsorption*

An abnormal faecal fat collection was recorded if a patient excreted more than 5g fat daily over a three-day period while on a 50g fat diet. In the fat breath test, breath radioactivity was measured at five, six and seven hours after administration of an oral dose of 5  $\mu\text{Ci}$   $\text{C}^{14}$ -labelled glyceryl tripalmitate, and fat malabsorption was diagnosed if the maximum concentration of  $^{14}\text{C}$  per millimole  $\text{CO}_2$  in expired air was less than  $20 \times 10^{-14}\%$ . The D-xylose test was performed with a 25g dose in eight patients, and impaired xylose absorption was recorded if less than 17% of the oral dose was collected in a five-hour urine collection; a 5g dose was used in 33 patients and absorption considered to be impaired if less than 23% of the oral dose was collected in a five-hour urine collection. A glucose tolerance test was reported as showing a flat response due to malabsorption if the maximum blood glucose rise after a 50g oral dose was less than 2.2 mmol/l.

## RESULTS

The age of patients at presentation to hospital for assessment was widely varied. There were 16 men whose ages ranged from 15 to 57 years (median, 30 years) and 34 women whose ages ranged from 13 to 71 years (median, 30 years). Initial body weight recordings for the men ranged between 48 and 85 kg, while the women at presentation weighed between 26 and 61 kg. A value for body weight was recorded at outpatient review between four and 12 months after commencement of the gluten-free diet in 45 of the patients. The men showed a mean weight gain of 7.2 kg and the women a gain of 6.6 kg. Symptoms and clinical signs in all 50 patients at initial presentation are summarised in Tables I and II. Results of haematological and biochemical screening blood tests are illustrated in Tables III and IV. The spectrum of initial blood haemoglobin values and red cell mean corpuscular volume values in men and women are illustrated in the Figure.

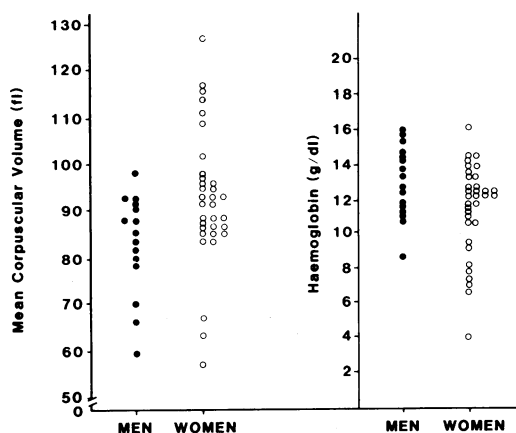


Figure. Haemoglobin and red cell mean corpuscular volume in men and women with coeliac disease.

TABLE I  
Presenting symptoms in 50 coeliac patients

<i>Symptom</i>	<i>% men (n = 16)</i>	<i>% women (n = 34)</i>	<i>% overall</i>
Weight loss	56	47	50
Diarrhoea	75	74	74
Steatorrhoea	38	50	46
Tiredness	38	47	44
Abdominal pain	50	38	42
Carpopedal spasm	6	18	14
Abdominal fullness	12	9	10
Vomiting	0	12	8
Constipation	0	6	4
Bone pain	0	6	4

TABLE II  
Presenting signs in 50 coeliac patients

<i>Signs</i>	<i>% men (n = 16)</i>	<i>% women (n = 34)</i>	<i>% overall</i>
Skin pallor	31	35	34
Glossitis	12	18	16
Muscle wasting	12	6	8
Mouth ulcers	12	18	16
Peripheral oedema	0	9	6
Dermatitis herpetiformis	6	3	4
None	63	32	42

TABLE III  
Haematology investigations at presentation

	<i>Abnormal value</i>	<i>% Abnormal men (n = 16)</i>	<i>% Abnormal women (n = 34)</i>	<i>% Abnormal overall (n = 50)</i>
Haemoglobin	<12 g/dl	38	44	42
Mean corpuscular volume	< 84 fl	38	9	18
	>100 fl	0	21	14
Folic acid	<2.0 µg/l	44	35	38
Vitamin B12	<200 ng/l	13	21	18
Iron — men	<16 µmol/l	44	—	40
	women	<11 µmol/l	—	
Total iron binding capacity	> 70 µmol/l	31	32	32
Prothrombin time	> 15 seconds	25	18	20
ESR	> 10 mm/1st hour	25	47	40

TABLE IV  
Blood biochemistry tests at presentation

	<i>Number measured</i>	<i>Abnormal value</i>	<i>Number abnormal</i>	<i>% abnormal</i>
Ca <sup>2+</sup>	50	< 2.20 mmol/l	26	52
Mg <sup>2+</sup>	18	< 0.70 mmol/l	3	17
Zn <sup>2+</sup>	12	< 8.4 µmol/l	1	8
Albumin	48	< 30 g/l	5	10
		< 35 g/l	13	27
ALT	9	> 45 i.u.	3	33

Results of malabsorption tests are summarised in Table V. Only eight patients received a 25g dose of D-xylose and, of these, six had an abnormal result. Of the 33 patients who were given a 5g dose of D-xylose, 16 had an abnormally low urinary excretion.

TABLE V  
Malabsorption tests at presentation

	<i>Number measured</i>	<i>Abnormal value</i>	<i>Number abnormal</i>	<i>% abnormal</i>
Serum carotene	30	< 1.1 µmol/l	21	70
Faecal fats	8	> 5g/day	6	75
C <sup>14</sup> fat breath test	29	*Max value < 20.0	24	83
D-xylose test	41	< 23% 5g < 17% 25g	22	54
Glucose tolerance test	31	blood sugar rise < 2.2 mmol/l	26	84
Urinary indican	29	> 220 µmol/24 hour	17	59
Small bowel series	37	'malabsorption picture'	29	78

At the time of diagnosis of coeliac disease, two patients, one man and one woman, were found to have dermatitis herpetiformis. This condition developed subsequently in two other women eight and nine years after the detection of coeliac disease. Only one patient, a woman, developed a lymphoma, and this affected the larynx rather than the gastro-intestinal tract. The lymphoma was detected five years after the diagnosis of coeliac disease. One woman, who had unequivocal subtotal villous atrophy on jejunal biopsy, and who responded well to gluten withdrawal, developed hyperparathyroidism and then jejunal Crohn's disease eight years after coeliac disease had been diagnosed. Three patients had evidence of pancreatic exocrine insufficiency suggested by an abnormal PABA test (para-amino benzoic acid absorption). All three had persisting or recurrent gastro-intestinal symptoms.

A repeat jejunal biopsy after gluten withdrawal in adult patients with coeliac disease was not routine clinical practice during most of the period covered by our survey. Seventeen of our patients were re-biopsied recently, between one and 15 years after gluten was excluded from the diet. Thirteen patients were entirely asymptomatic, three had occasional abdominal cramps and diarrhoea, and one patient had a severe clinical relapse with weight loss and marked diarrhoea. The repeat jejunal biopsies were entirely normal only in six patients, and mild villous atrophy was seen in 10 patients. The patient with severe clinical relapse had subtotal villous atrophy and responded well to treatment with oral prednisolone. A careful dietary history taken at the time of repeat biopsy revealed that 44% of these patients continued, often unknowingly, to consume small amounts of gluten. The patient with clinical relapse appeared to be adhering strictly to a gluten-free diet.

## DISCUSSION

The wide spectrum of clinical findings in adult patients with untreated coeliac disease has been illustrated in this study. However, it is likely that our data underestimate the number of asymptomatic or mildly symptomatic individuals, since these people may not present themselves for investigation. If screening of families of coeliac patients became accepted clinical practice, it is possible that an even higher number of asymptomatic individuals would be identified.

Increasing awareness of the malabsorption disorders and increasing use of screening biochemical and haematological tests by hospital physicians and general practitioners might be expected to increase the detection of mild cases of coeliac disease. Only one of our patients was completely asymptomatic, although 22% had no disturbance of bowel habit. A higher incidence of diarrhoea was observed in some of the earlier studies (97% of patients in one report<sup>2</sup>) although the classic paper of Cooke and colleagues in 1953 described diarrhoea in only 80% of 100 patients with idiopathic steatorrhoea.<sup>3</sup>

Weight loss is regarded by many as a cardinal feature of the malabsorption syndrome and yet this symptom was only recorded in 50% of our patients. Minor degrees of weight loss may not have been noted by some individuals. Many adult patients are likely to have been malabsorbing to some extent for long periods of time before the hospital assessment, and a failure to maintain adequate weight rather than weight loss may have been a feature of their illness. Earlier retrospective surveys of symptoms in coeliac patients recorded weight loss as a feature in 97-100% of patients.<sup>2, 3</sup>

An important symptom in many of our patients was abdominal pain or fullness. An erroneous diagnosis of irritable bowel syndrome may be suggested by these findings unless malabsorption is given due consideration. The more specific symptom of tetany was observed in only 14% of patients in contrast to 38.50% of patients in earlier studies.<sup>2, 3</sup>

Abnormal findings on physical examination were detected infrequently in our survey. It is surprising that no patient was recorded to have finger clubbing or abnormal pigmentation as these signs have been well documented in severe coeliac disease.<sup>3</sup> Earlier presentation to hospital for diagnosis in recent years may have influenced the development of signs normally associated with severe long-standing disease, but it is also possible that subtle alterations in skin pigmentation or mild clubbing were overlooked or not recorded by the admitting physicians.

Screening blood tests frequently raise the suspicion of malabsorption. A low blood haemoglobin level was found in only 42% of our patients, which illustrates the danger in relying on such tests to exclude the presence of malabsorption. Cooke and Holmes<sup>4</sup> also detected a haemoglobin level of <12 g/dl in 42% of 170 coeliac patients in England, although an Australian survey described anaemia in 70% of patients.<sup>5</sup> A macrocytic blood picture was detected in only 14% of our study group. Folate deficiency is the commonest cause and a serum folate level of <2.0 µg/l was found in 38% of patients. The absence of macrocytosis in some of these individuals was probably related to coexistent iron deficiency. Hallert and colleagues<sup>6</sup> noted low serum folate levels in 85% of coeliac patients and found a high yield of coeliac disease when patients with unexplained low folate levels were subjected to jejunal biopsy. Vitamin B<sub>12</sub> deficiency is a less frequent abnormality as this is normally absorbed in the terminal ileum which usually remains free of mucosal damage. Of our patients 18% had a low serum B<sub>12</sub> level, but in some of these individuals fast small bowel transit rather than terminal ileal damage may have produced impaired absorption of this vitamin. Only 18% of our patients had a microcytic blood picture but this finding was more common in males. The explanation for the difference between males and females is not clear. Iron deficiency was suggested by a low serum iron in over 40%, and by a high total iron binding capacity in 32% of the group. Associated folate or B<sub>12</sub> deficiency may have prevented the development of microcytosis in some of these individuals.

With regard to the blood biochemistry tests, hypoalbuminaemia reflects impaired protein synthesis and, in some cases, protein loss into the gastro-intestinal tract. Early reports described this finding in over 50% of patients with coeliac disease,<sup>2, 7</sup> although a recent survey had detected serum albumin levels of <40 g/l in 28% and <30 g/l in only 4% of patients.<sup>4</sup> Our findings are fairly similar, 27% of patients having a serum albumin <35 g/l and 10% a level <30 g/l. Hypocalcaemia might simply reflect the low serum albumin concentration, but 52% of our patients had low serum calcium levels — a higher percentage than had hypoalbuminaemia. When the serum calcium level was corrected for the serum albumin level only 3 of the abnormal results became normal, so it is likely that most hypocalcaemia was due to true calcium or vitamin D deficiency as part of the malabsorption syndrome.

Several investigations aid definition of the type of malabsorptive disorder and some of these have been regarded as valuable screening tests for coeliac disease. The D-xylose test assesses passive absorption of a non-digestible sugar across the small bowel mucosa. Abnormal results were recorded in over 90% of patients in two surveys,<sup>8, 9</sup> but other investigators have questioned its value.<sup>10, 11</sup> In our survey, only 54% of patients had an abnormal D-xylose excretion. Most received a 5g load of xylose, but of those eight patients who were given 25g xylose, 75% had abnormal results. Rinaldo and Gluckman (1964) also found that a 5g load of D-xylose was less efficient than the 25g dose at detecting coeliac disease.<sup>12</sup> Clearly, reliance on the D-xylose test as a screening test to exclude malabsorption syndrome is misplaced and normal results with this investigation should not deter a clinician from proceeding to jejunal biopsy. Although 84% of patients had a flat glucose tolerance test, the value of this investigation is hindered by the occurrence of a flat response in a significant proportion of the normal population.<sup>13</sup>

Steatorrhoea is a classical feature of coeliac disease and several investigations give useful information regarding fat absorption. The traditional three-day collection of faeces for fat content was carried out in only eight patients and 75% of these had abnormal results. Fat breath tests measure the radioactivity of expired air after ingestion of a triglyceride labelled with  $^{14}\text{C}$ . Tripalmitate has been used in the Royal Victoria Hospital with satisfactory results for some years,<sup>14</sup> although American investigators found that the  $^{14}\text{C}$  triolein breath test provided more reliable discrimination, mainly due to greater specificity.<sup>15</sup> Of 29 patients in our study who had a tripalmitate breath test 83% had an abnormal result, which is not sufficiently sensitive to allow accurate selection of patients for jejunal biopsy.

Our observations have highlighted the clinical features of coeliac patients in adult gastroenterological practice in Northern Ireland. It appears that milder forms of the disease are being recognised than was the case in the 1950s when the condition was first defined. The presence of severe villous atrophy is rarely seen in conditions other than coeliac disease in adult patients, although this is not the case with children. In clinical practice a more difficult group to classify are those adult patients whose jejunal biopsies show only mild or moderate villous atrophy, findings which can be caused by many disorders. Some of these individuals were encountered in our survey, and although they had been treated by gluten withdrawal, they were not included in this analysis. Similarly, there were two or three individuals who were treated by gluten withdrawal, but for whom no histological confirmation of the diagnosis of coeliac disease was made because of technical failure of the Crosby capsule biopsy instrument. A repeat jejunal biopsy after gluten withdrawal followed by a period of gluten challenge and further biopsy would be of particular value in the assessment of these groups of patients whose diagnosis is less well established, before lifelong gluten avoidance is imposed.

A wide spectrum of haematological and biochemical disturbances may occur in coeliac patients but no single test offers a reliable method of screening for the condition. Tests of absorptive function have failed to identify sufficient patients to serve as reliable screening tests for coeliac disease. Better screening tests are required so that milder forms of the condition may be identified. Serum anti-gliadin antibody determination<sup>16</sup> and release of N-terminal glucagon<sup>17</sup> have been proposed as possible screening tests but further assessment of their sensitivity in adult patients is required. The former reflects the immunological response to gliadin, which is thought to be the toxic component of gluten, and abnormal levels have been found in about 90% of coeliac patients.<sup>16</sup> Release of N-terminal glucagon probably reflects increased stimulation of the distal ileum by food which is malabsorbed in the jejunum.<sup>17</sup> Thus, elevated plasma levels of this hormone are not specific to coeliac disease and are encountered in a variety of conditions associated with small bowel malabsorption. Jejunal biopsy with a Crosby capsule remains the definitive investigation to identify patients with coeliac disease. This procedure can be performed rapidly and without significant discomfort during upper endoscopic examination,<sup>18</sup> and should be undertaken when the diagnosis of coeliac disease is considered.

We are indebted to our predecessors in the Gastroenterology Unit, Royal Victoria Hospital, whose careful documentation of their coeliac patients made our survey possible.

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