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Coeliac disease and Type 1 diabetes mellitus – the case for screening

G. K. T. Holmes

Derbyshire Royal Infirmary, Derby, UK

Accepted 24 December 2000

Abstract

Aim To review the relationship between coeliac disease and Type 1 diabetes mellitus with emphasis on prevalence of coeliac disease, presentation and implications for screening.

Methods Papers collected over many years by the author have been included in the review and a literature search employing Medline was undertaken to August 2000. Search words used were coeliac disease and diabetes mellitus.

Results Twenty papers exploring the prevalence of coeliac disease by serological screening of Type 1 diabetes in children, eight in adults and two including both groups were found. An additional 48 papers are included and relate to serological screening tests for coeliac disease, expressions and complications of coeliac disease, the value of GFD and the genetics of the two conditions. Unless formal screening studies are undertaken coeliac disease will not be diagnosed because patients are asymptomatic, have atypical symptoms or even in those with symptoms the diagnosis is overlooked. Based on small bowel biopsy, diagnosis the prevalence of coeliac disease in Type 1 diabetes in children is 1:6 to 1:103 and in adults 1:16 to 1:76. Patients may improve following the start of a gluten-free diet (GFD) in terms of symptoms, growth in children, serum antibody levels, haematological and biochemical indices, morphology of the small intestinal mucosa and control of diabetes.

Conclusion Coeliac disease commonly occurs in Type 1 diabetes. It is recommended that screening for coeliac disease should be part of the routine investigation and offered to all patients because of the high prevalence and the potential benefits of treatment with a GFD. This includes control of symptoms, stabilization of diabetes and prevention of complications associated with coeliac disease. The cost per patient diagnosed with coeliac disease from the existing population with Type 1 diabetes would be £860 and for those newly arising £950.

Diabet. Med. 18, 169–177 (2001)

Keywords coeliac disease, diabetes mellitus, Type 1 diabetes mellitus

Abbreviations AEA, anti-endomysial antibodies; AGA, anti-gliadin antibodies; ARA, anti-reticulin antibodies; AtTG, anti-tissue transglutaminase antibodies; ELISA, enzyme-linked immunosorbent assay, GFD, gluten-free diet; IEL, intraepithelial lymphocytes; tTG, tissue transglutaminase

Correspondence to: Dr G. K. T. Holmes, Derbyshire Royal Infirmary, London Road, Derby DE1 2QY, UK.

Background

Coeliac disease is one of the commonest lifelong disorders encountered in western countries with a prevalence of 0.3–1% and current concepts have been recently reviewed [1–3]. The condition is characterized by immune mediated damage to the jejunal mucosa that is triggered by gluten, a protein complex in wheat, rye and barley. The toxicity of oats has recently been questioned, as moderate amounts ingested over relatively short periods have not caused deterioration in the small bowel mucosa or clinical deterioration in patients with coeliac disease or dermatitis herpetiformis. However, the long-term consequences of taking larger amounts are still unclear. It remains current practice to exclude oats from the diet but this policy may change in the near future as more information becomes available [4].

The diagnosis of coeliac disease is based on characteristic small bowel biopsy appearances referred to as villous atrophy and crypt hyperplasia. In those patients who present in ever increasing numbers with non-specific, mild or atypical symptoms, coeliac disease is easily overlooked. In those who deny any symptoms, the diagnosis may only be suspected from abnormalities found in blood tests such as anaemia or iron or folic acid deficiency. The advent of serological tests has greatly aided diagnosis. Anti-gliadin antibodies (AGA), introduced in the early 1980s, were the first serological markers to be used widely in clinical practice. IgA class AGA measured by ELISA have a sensitivity of 75–93% with a high specificity of 90–95%. Anti-endomysial antibodies (AEA) are autoantibodies directed against antigens in the collagenous matrix. The sensitivity is about 90% so that the diagnosis could be missed if this were the only test to be used. The specificity approaches 100%. So-called false positive tests may indicate potential coeliac disease. This term refers to patients with normal looking villi and immunological abnormalities associated with coeliac disease including AEA, who may go on to develop overt coeliac disease [5,6]. Recently, tissue transglutaminase (tTG) has been identified as the putative autoantigen responsible for AEA positivity in coeliac disease. ELISA methods are available for the determination of anti-tTG autoantibodies, which could replace the AEA assay [7,8]. IgA antibodies will not appear or be present in very low titre in IgA-deficient individuals which may cause diagnostic confusion but this difficulty may be overcome by the tTG assay [9]. While positive serological tests are strong indicators of coeliac disease, uncertainties still remain about their interpretation so that histological confirmation of the diagnosis is mandatory. It is important to establish the diagnosis of coeliac disease because a gluten-free diet (GFD) will restore most patients to full health and also prevent or reduce risks of conditions such as osteoporosis and malignancy, particularly lymphoma [10,11].

Many disorders occur in association with coeliac disease [12]. The great majority of these are merely chance associations. However, Type 1 diabetes mellitus, thyroid disease, pulmonary and liver disorders, inflammatory bowel disease, rheumatic complaints as well as other conditions with a possible immunological aetiology, may occur among coeliac patients more commonly than by chance alone. In those with an established diagnosis which is considered to account for the clinical picture, coeliac disease is likely to remain undetected. Conversely, a second diagnosis in a coeliac patient may also not be diagnosed. Clinicians need to be aware of these associations to ensure appropriate management. This review is concerned with diabetes mellitus, particularly Type 1, which is the commonest and best researched associated condition and asks whether screening for coeliac disease in Type 1 diabetes should be routine.

Prevalence of coeliac disease in diabetes

Children

Attention was drawn to the association of childhood diabetes mellitus and coeliac disease over 40 years ago [13,14]. In an early clinical study, from among approximately 400 children with diabetes mellitus, six were found to have coeliac disease diagnosed by small bowel biopsy and all presented with typical symptoms such as foul, bulky stools, abdominal distension, anorexia and poor growth [15]. All of the children responded to a GFD and control of the diabetes also improved with fewer and less severe hypoglycaemic episodes. The authors commented that the diagnosis of coeliac disease was sometimes delayed because of the preoccupation with diabetes. A clinical study of 300 children with diabetes revealed that eight had symptoms indicative of coeliac disease with stunted growth [16]. All had steatorrhoea and jejunal biopsies carried out in six showed villous atrophy In these six, control of diabetes was poor in five and hypoglycaemic convulsions frequently occurred. Adherence to the GFD was poor. By using population-based registers covering children and adults in an area of central England, eight patients were found to have both coeliac disease and insulin-treated diabetes [17].

Maki *et al*. [18] screened 215 children with diabetes by detecting anti-reticulin antibodies (ARA) in the serum and found nine positive subjects all of whom had biopsies of the small intestinal mucosa. Four new cases of coeliac disease were found and as one was already known, the prevalence in this group was 1:43. The children had symptoms that could be attributed to coeliac disease but none had diarrhoea or symptoms of malabsorption. The authors concluded that all children with diabetes should be screened for coeliac disease with subsequent confirmation of the diagnosis by small bowel biopsy and treatment with

Table 1 Prevalence of coeliac disease in diabetes mellitus found in screening studies in children

Ref	Year	Country	*n*	Screen	Positive screen	Not biopsied	Coeliac by biopsy	Prevalence	
[18]	1984	Finland	215	ARA	9	9	4 (+ 1)	1: 43	2.3%
[19]	1986	Finland	201	AGA ARA	–	–	7	1:29	3.5%
[20]	1987	Italy	146	AGA	9	9	5	1:29	3.4%
[21]	1988	Germany	1032	AGA	17	9	2 (+ 8)	1:103	0.97%
[22]	1991	Italy	498	AGA	30	22	16	1:31	3.2%
[23]	1992	Australia	180	AGA	19	18	4	1:45	2.2%
[24]	1993	Sweden	436	AGA ARA	28	26	15 (+ 6)	1:21	4.8%
[25]	1993	USA	211	AEA	10	3	3	1:70	1.4%
[26]	1994	Australia	273	AEA AGA	5	5	5	1:55	1.8%
[27]	1996	Finland	776	AGA ARA	36	19	19	1:41	2.4%
[28]	1996	Italy	133	AGA ARA AEA	6	6	5	1:27	3.7%
[29]	1996	Italy	172	AGA	7	7	6	1:29	3.5%
[30]	1996	Algeria	116	AGA AEA	13	13	16*(+ 3)	1:6	16.4%
[31]	1996	Spain	141	AGA	12	12	4 (+ 2)	1:24	4.2%
[32]	1997	Italy	200	AGA AEA	14	11	8	1:25	4.0%
[33]	1998	Canada	236	AEA	19	17	12	1:20	5.0%
[34]	1998	UK	167	AEA AGA	11	9	8	1:21	4.8%
[35]	1999	Sweden	115	AEA AGA	9	6	5(+ 2)	1:16	6.2%
[36]	2000	Austria	403	AEA AGA	14	13	6	1:67	1.5%
[37]	2000	Germany	520	AtTG AEA AGA	23	13	9	1:58	1.7%

*Three patients with negative serology biopsied on clinical grounds and all had coeliac disease.
Numbers in brackets indicate patients with coeliac disease diagnosed before screening.

a GFD. Other workers from several countries have since reported the prevalence of coeliac disease among children with diabetes to fall between 0.97 and 6.2% with the exception of children from Algeria who have a prevalence of 16.4% (Table 1). It is of interest that coeliac disease is very common among children from the Sahara with 5–6% affected [38]. The prevalence figures shown in the tables are based on a small bowel biopsy diagnosis of coeliac disease and in some series would have been higher if all those with positive serological tests had been biopsied.

Adults

The association has also been confirmed in adults. An early clinical study identified 14 patients with coeliac disease among 24 000 diabetic patients [39]. Of these 14 cases, 10 had Type 1 diabetes. Another clinical study found 24 patients with coeliac disease and Type 1 diabetes from a group of approximately 5500 diabetic patients [40]. Among 195 consecutive patients with Type 1 diabetes screened for ARA, eight were found to be positive and all had villous atrophy [41]. In a large investigation, Page *et al.* [42] screened 1789 diabetics (43% Type 1, 57% Type 2) for coeliac disease using IgA AGA to identify those requiring intestinal biopsy for confirmation of the diagnosis. Fourteen new coeliac patients were diagnosed of whom 11 had Type 1 diabetes giving a prevalence of approximately 1:50 (four patients with Type 1 diabetes were already known in the series). Screening studies have shown the prevalence to be between 1.3 and 6.4% (Table 2). In two series, children and adults were included together [8,45]. In an Italian multicentre study, 122 coeliac patients (aged 15 months to 30 years) were found among 4514 patients with Type 1 diabetes but this investigation was carried out primarily to determine which diagnosis was made first [50]. Coeliac disease has also been found in

Table 2 Prevalence of coeliac disease in diabetes mellitus found in screening studies in adults

Ref	Year	Country	*n*	Screen	Positive screen	Not biopsied	Coeliac by biopsy	Prevalence	
[41]	1989	Finland	195	ARA	8	8	8	1 : 24	4.1%
[42]	1994	UK	767	AGA		22	11 (+ 4)	1 : 51	2.0%
[43]	1994	Italy	383	AEA	12	10	10	1 : 38	2.6%
[44]	1996	USA	47	EMA	3	3	3	1 : 16	6.4%
[45]*	1996	Italy	1114	AGA AEA	121	78	63	1 : 18	5.6%
[46]	1997	Ireland	101	AEA	8	8	5	1 : 20	5.0%
[47]	1997	USA	185	AEA	9	5	4 (+ 3)	1 : 26	3.8%
[48]	1998	Germany	848	AGA AEA	14	7	7(+ 8)	1 : 57	1.8%
[49]	1998	Scotland	607	AGA	17	10	8	1 : 76	1.3%
[8]*	1999	Germany	305	AtTG	12	5	5	1 : 61	1.6%

*Series include adults and children.
Numbers in brackets indicate patients with coeliac disease diagnosed before screening.

association with Type 2 diabetes at frequencies of 1:340 [42] and 1:372 [48]; much as would be expected to occur in the general population.

Genetic factors relating coeliac disease and diabetes

Coeliac disease and Type 1 diabetes are in part genetically determined and are associated with the HLA markers B8 and DR3 [40]. Six of seven patients with both disorders had the HLA-B8 and -DR3 combination compared with 41% of other diabetic patients [19]. HLA typing was performed in eight patients with Type 1 diabetes and coeliac disease and six showed HLA-DR3 while two not tested for -DR3 were HLA-8 positive [21]. In patients with both diseases the incidence of HLA-B8, -DR3 and -DQW2 was significantly higher than in the patients with Type 1 diabetes alone [22]. Of 19 patients with coeliac disease and Type 1 diabetes, 74% were positive for HLA-B8 and/or -DR3 and 17 of 18 had the HLA-DQB1*0201 allele [27]. It is known that approximately 90% of patients with coeliac disease have a particular DQ2/heterodimer encoded by DQA1*0501 and DQB1*0201 alleles inherited in *cis* with DR3 or in *trans* with DR5/DR7 [51]. Five of six patients with coeliac disease and Type 1 diabetes had this heterodimer [29].

Diabetes-related autoantibodies

Diabetes-related autoantibodies occur in patients with coeliac disease [52,53]. As for first degree relatives of those with Type 1 diabetes, approximately 7% of a population of coeliac patients in Israel had such antibodies [53]. It is not known whether these are predictive for the future development of diabetes in coeliac patients or are only indicative of a generalized immunological disturbance. It seems likely that they do have predictive value [54]. IgA AGA at low titre and IgG AGA may also be present as a transient phenomenon at the onset of diabetes in patients with normal small bowel biopsies [21,32,35,55–57]. The presence of these antibodies may simply reflect events at the onset of diabetes such as disturbed immunity or an increase in intestinal permeability.

Screening for coeliac disease in diabetes

Since patients with Type 1 diabetes have a high prevalence of coeliac disease, the question arises whether this population should be screened routinely using the sensitive and specific serological tests that are now available. It is noteworthy that a number of workers recommend routine screening in children [18,22,25,27,28,29,31,33,35,45] and adults [8,43,45,46,47,49]. There are however, a number of questions. Will those with Type 1 diabetes found to have coeliac disease experience health benefits in terms of improvement in symptoms, better control of diabetes, and a reduction in complications associated with coeliac disease if they are treated with a GFD? Will patients comply with a GFD or will this be seen as an unacceptable imposition on those already confined by a diabetic diet? Would a screening programme be cost-effective?

Presentation

The diagnosis of coeliac disease may precede that of Type 1 diabetes (Tables 1 and 2) but in most cases, about 90%, diabetes is diagnosed first [50]. In the various reports there is divergence in the number of patients with symptoms and signs which probably reflects how carefully these were sought. It is likely that in some instances patients were labelled as asymptomatic when they were not. Only about 5% of 352 adults patients in my coeliac clinic were asymptomatic at diagnosis if a careful history was taken, although in about one-third there were no abnormal signs

[3]. Many patients are only able to recognize the full extent of their ill-health retrospectively, following the benefits conferred by a GFD.

At the time of screening most children do not have gastrointestinal symptoms [18–21,23,25,26,28,31,32,37] but failure to thrive [34] and severe gastrointestinal symptoms [24,34] may occur. Mild gastrointestinal symptoms may only be recognized in retrospect [34]. In one series, bowel symptoms were found in 56% of cases [22]. Of 15 patients, seven had gastrointestinal symptoms of whom three only recognized these in retrospect [24]. Short stature is reported in about one-third of children [22,29,50] but in some series is not a feature [25,33,58]. Elevated serum aminotransferase activity in children with Type 1 diabetes may indicate the presence of coeliac disease [29,59] as may hypoglycaemia and a reduction of insulin requirements [60].

Adults may be asymptomatic [41,42,48] or have symptoms indicative of untreated coeliac disease (43,44,46,47) such as lethargy, bloating, vomiting and diarrhoea which can be severe and in some series affect half or more of patients [42,49]. In the series reported by De Vitis *et al*. [45], 24% with both disorders had diarrhoea but 22% were symptom-free. Recurrent hypoglycaemia may be a presenting symptom of coeliac disease [61–63]. Abnormal laboratory findings were not prominent in some series [34] but in others, anaemia and iron and folate deficiency were commonly encountered [29,42,43,46,48].

Control of diabetes

In early clinical studies, coeliac disease was diagnosed in diabetic patients because they developed features of malabsorption. When a GFD was commenced in these patients and absorption corrected, diabetic control usually improved with a reduction in hypoglycaemic episodes [15,39,40]. In patients with coeliac disease detected by screening, the influence of a GFD on diabetic control as judged by insulin requirements and glycosylated haemoglobin has been variable. Some report no effect [19,23,34,36,43,46,58,64] or improved control [23,31] with less hypoglycaemic episodes [24,29,52,53,60,63]. Adherence to a GFD was not strict in some cases making a proper assessment difficult.

Complications of coeliac disease

If patients with diabetes also have undiagnosed coeliac disease they would be expected to develop osteoporosis and lymphoma which are the most notable complications of coeliac disease. If this could be demonstrated it would strengthen the case for screening, because a GFD will prevent or reverse osteoporosis in coeliac disease and reduce the lymphoma risk [10,11]. Lymphoma has been found in association with Type 2 diabetes by some [65,66,67] but not others [68]. O'Connor [69] reported four patients with Type 1 diabetes and lymphoma, two of whom had enteropathy-associated T cell lymphoma, one a B cell lymphoma not affecting the bowel and one Hodgkin's disease. Investigations of this type are difficult to carry out and further studies of the causes of death are warranted. It may well be that more are dying of lymphoma than is currently thought, although there is little supportive evidence. A reduction in bone mineral density (BMD) is a feature particularly of Type 1 diabetes [70,71] and predisposes to low-energy fractures [71]. Treatment of coeliac disease may improve low BMD if this were a contributing factor in some patients. There is evidence that lymphoma and osteoporosis may affect asymptomatic coeliac patients [11].

Other health risks in coeliac disease include neurological disturbances and epilepsy and problems associated with reproduction, in particular late menarche, early menopause, infertility, miscarriages and low birthweight babies [11,72]. It was suggested in one study that pregnant women should be screened for coeliac disease to try and reduce unfavourable outcomes [72]. With improved diabetic control, fertility is probably only slightly lower than for non-diabetic women but an unfavourable outcome of pregnancy may occur. If a contribution to this poor outcome resulted from coeliac disease, improvement might be effected by a GFD.

Expressions of coeliac disease and implications for screening strategies

It is now clear that the spectrum of gluten sensitivity is wider than previously recognized and incorporates potential and latent coeliac disease [5,6]. In potential coeliac disease the mucosa has normal appearing villi but subtle changes are present such as an increased number of intraepithelial lymphocytes (IELs) bearing the γ/δ T cell receptor and aberrant HLA-DR expression in crypt epithelial cells. AEA may be present in the serum and in time the mucosa may become flat [6]. Latent coeliac disease is used to describe patients who have a normal biopsy on normal diet that at some other time, while still on normal diet, becomes flat and recovers on a GFD [5]. Patients with diabetes may have potential or latent coeliac disease. This was shown in an informative study by Maki *et al*. [73]. Of 238 children with diabetes, 16 were positive for IgA ARA but 11 of these were negative at the first screening. Nine cases, all with high titres of ARA, had small bowel biopsies characteristic of coeliac disease. In four children subsequently found to have coeliac disease and with positive ARA, earlier serological tests had been negative so that biopsies were not pursued. The histories of two of the children are particularly interesting. Both of these at the diagnosis of diabetes had normal small bowel biopsies and were negative for ARA. After 1 year, one of these had an

ARA titre of 1:100 but a biopsy was still normal. After a further year the ARA titre had risen to 1:200 and the mucosa was flat. Latent coeliac disease was thus confirmed in this case and documented by others [32,33,74]. The other child subsequently developed ARA but after 8 years' follow-up the mucosa still showed normal architecture. However, a 10-fold increase in the density of IEL-bearing the γ/δ T cell receptor was observed together with aberrant HLA-DR expression in crypt epithelial cells. This patient therefore, has potential coeliac disease. An intriguing question is whether other patients in the series with low ARA titres and normal biopsies will go on to develop coeliac disease. Others have encountered potential coeliac disease in patients with Type 1 diabetes [32,36,46]. Patients with Type 1 diabetes and normal jejunal morphology but with positive serology and the genetic markers associated with coeliac disease may go on to develop coeliac disease [27].

Coeliac disease was searched for at the diagnosis of Type 1 diabetes and at 6, 12, 18, 24 and 36 months thereafter, in 776 children by the detection of AGA and ARA [27]. At the diagnosis of Type 1 diabetes, nine were found to be serologically positive and coeliac disease was confirmed by small bowel biopsy. Nine children who were serologically negative at this time developed antibodies within 2 years and had coeliac disease confirmed by biopsy. Others have also drawn attention to the importance of serial testing [32,33] but it is uncertain what the intervals between tests should be and for how long testing should be continued. Maki *et al*. [73] screened asymptomatic patients at the diagnosis of diabetes and then annually (for 8 years at the time of their report) and others have supported annual screening [29,35]. Others have advised that screening should be carried out 1–2 years after the diagnosis of Type 1 diabetes to allow the tests to become positive [21,33] or at the diagnosis of Type 1 diabetes and at 1, 3, and 5 years [27]. Until more information becomes available, it seems prudent to test at the diagnosis of Type 1 diabetes and then yearly for 3 years, then at 5 years and 5 yearly thereafter or at any other time if there are clinical indications. It has been suggested that screening for coeliac disease should extend to the first degree relatives of those with Type 1 diabetes for they frequently have silent coeliac disease [75].

Value and acceptance of a GFD

A GFD dramatically benefits most patients with coeliac disease and this also prevails in those with associated diabetes. Improvement occurs in symptoms [24,34,42,46], growth in children [28,29], serum antibody levels [18,20,24,29,34,35,43,46], haematological and biochemical indices [42,43,46] and villous architecture [18,19,23,24,34,42,46]. Those who regard themselves as asymptomatic often experience a sense of improved wellbeing and vitality following commencement of the diet. Those who have symptoms are more likely to accept and adhere to a GFD than those without symptoms because they have more to gain [42]. A diabetic diet and a GFD can be combined quite readily and all patients should have access to a sympathetic dietitian skilled in this area.

Cost–benefit assessment

EMA and tTG tests cost about £10 each and a diagnostic upper gastrointestinal endoscopy approximately £280. These figures will vary depending on factors such as the number of tests being carried out in a particular hospital. Costs would initially include screening the established population with Type 1 diabetes. Assuming a prevalence in the population of Type 1 diabetes of 0.4%, then for a hospital serving 500 000 people there would be 2000 existing patients with the condition. The cost of screening these at 1, 5 and 10 years and performing small intestinal biopsies on the 5% who were positive would be about £86 000 or, if all the EMA-positives proved to have coeliac disease, £860 per patient diagnosed. While most cases would be picked up at the first screening, it is assumed 80% for the purposes of these calculations, some would not be detected until subsequent screenings were undertaken.

The incidence of Type 1 diabetes in the UK is probably 15–20/100 000 new cases per year [76]. If the lower figure is used, 75 new cases would occur each year from a population of 500 000 and the cost of screening and performing small intestinal biopsies at 1, 2, 3, 5 and 10 years over a decade would be £36 000 or £950 per case found. For an incidence of 20/100 000 the corresponding cost would be £48 000 and the cost per case found would be the same at £950. Screening new cases of Type 1 diabetes over subsequent decades would incur similar costs. Not all patients would be willing to accept these investigations, some would be unsuitable, a proportion would die and these circumstances would modify the costs. The expense should be viewed in the context of expenditure on unavailing investigations, treatments, clinic visits and hospital admissions for patients with Type 1 diabetes who are ill with unrecognized coeliac disease as well as the financial and social consequences of interrupted employment. While direct comparisons are difficult to make, it is interesting to look at some screening programmes that are well established and have been costed, e.g. for congenital hypothyroidism the median cost per true case has been estimated at £14 860, for cystic fibrosis approximately £4500 and for phenylketonuria about £25 000 [77]. The NHS breast screening programme costs £25 142 per death prevented and £2522 per life year saved [78].

Conclusions

Coeliac disease and Type 1 diabetes commonly occur together. Patients may have symptoms indicative of coeliac

disease while others regard themselves as asymptomatic. In this latter group however, a carefully taken history will often reveal subtle complaints that have been disregarded. Many patients may only recognize symptoms in retrospect after commencing a GFD. Malabsorption commonly occurs. Unstable diabetes and growth failure in children may indicate the presence of coeliac disease. Coeliac disease is associated with health risks such as the development of lymphoma and osteoporosis that are reversed by a GFD and it is likely that this applies to coeliac disease associated with diabetes. Patients already on one diet will have to contend with another, although difficulties can be minimized by an expert, sympathetic dietitian.

Coeliac disease could be diagnosed either by employing a programme of case-finding whereby only those with features indicative of coeliac disease are tested or by screening all patients with Type 1 diabetes. What are the merits of these two approaches? A case-finding strategy would miss those with atypical or no symptoms although such may still have unrecognized ill-health and and malabsorption and be prone to the health risks associated with untreated coeliac disease. A screening programme is preferable because of the high prevalence and potentially correctable health risks of coeliac disease and all cases would be identified. Patients who gave informed consent to be tested would then, if found to have coeliac disease, be equipped to make informed choices about how they would like to proceed. Some who are serologically positive may refuse the confirmatory small bowel biopsy and some diagnosed by biopsy may not wish to accept a GFD. Such patients however, could then be monitored carefully for the appearance of symptoms or the emergence of anaemia or deficiencies in iron, folate and calcium or growth failure in children. If these ensue rapid action could be taken.

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