REVIEW

Coeliac disease and oats: a systematic review

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A systematic review of the literature related to the inclusion of oats in the gluten-free diet for patients with coeliac disease to assess whether oats can be recommended. A computerised literature review of multiple databases was carried out, identifying 17 primary studies, 6 of which met the criteria for inclusion in this review. None of the six studies found any significant difference in the serology between the oats and control groups. Two studies, however, identified a significant difference ($p<0.001$; $p=0.039$) in intraepithelial lymphocyte counts between the oats and control groups. Oats can be symptomatically tolerated by most patients with coeliac disease; however, the long-term effects of a diet containing oats remain unknown. Patients with coeliac disease wishing to consume a diet containing oats should therefore receive regular follow-up, including small bowel biopsy at a specialist clinic for life.

Coeliac disease is an immunologically mediated enteropathy resulting from the ingestion of gluten in genetically predisposed people. Patients classically present with chronic diarrhoea, fatigue, weight loss, failure to thrive, etc. However, many present atypically. The spectrum of coeliac disease has been shown to be broader than first believed. Multiple types of coeliac disease have been described, including silent coeliac disease, potential coeliac disease and latent coeliac disease, in addition to typical and atypical coeliac disease. Dermatitis herpetiformis also forms part of this spectrum. It has been shown that 80% of patients with dermatitis herpetiformis have frank villous atrophy, with all patients showing inflammatory changes in the small intestine.[1] All patients with dermatitis herpetiformis are therefore regarded as having a gluten-sensitive enteropathy.[2] The cornerstone of treatment for all types of coeliac disease and dermatitis herpetiformis is a gluten-free diet (GFD), which traditionally excludes gluten, barley, rye and oats. For the purpose of this review, this is referred to as the standard GFD. Strict adherence to a GFD should result in complete clinical and histological remission.

Cereal grains are taxonomically classified in the Poaceae family, within which there are several subfamilies. The Festucoidae subfamily contains the cereals wheat, barley, oats and rye. Rice and corn, both tolerated in coeliac disease, belong to the Oryzoideae and Panicoideae families, respectively.[3] Gluten compromises the water-insoluble proteins of wheat, barley, oats and rye. Proline is the alcohol-soluble fragment of gluten and its related proteins. These are known as prolamines, which are responsible for the toxicity. The prolamine in wheat is gliadin; in barley, hordeins; in rye, secalins; and in oats, avenins.

Studies have shown that tissue transglutaminase (tTG), a ubiquitous enzyme responsible for the cross-linking of proteins, is responsible for the deamination of glutamine and proline residues in prolamines. Coeliac disease is caused by a selective T lymphocyte intolerance of gluten. This produces T cell-stimulatory peptides known as neo-epitopes, which bind HLA-DQ2 molecules on antigen-presenting cells. This interaction activates intestinal T lymphocytes via the T cell receptor. In response, T cells release pro-inflammatory cytokines, including interferon γ, tumour necrosis factor α and interleukin 2, which damage enterocytes, producing the intestinal lesions typical of coeliac disease.[4] Recent research has shown coeliac disease to be strongly associated with HLA-DQ2 and HLA-DQ8 loci, which provide a genetic predisposition to coeliac disease. Both HLA-DQ2 and HLA-DQ4-restricted gluten-specific CD4 T lymphocytes have been isolated from small bowel biopsy specimens of patients with coeliac disease.[5] These T lymphocytes initiate an inflammatory cascade, the precise events of which are unknown, leading to the typical tissue damage seen in coeliac disease.

Recently, it has been hypothesised that patients with coeliac disease may be able to tolerate oats because of their lower prolamine content compared with wheat, rye and barley. The prolamine gliadin in wheat constitutes 40% of the cereal; the percentages are similar for rye and barley. However, in oats, avenins constitute only 15% of the cereal.[6] Avenins, the toxic fragment of oats, also contain fewer proline residues than the other cereals.[4] The inclusion of oats in the GFD diet remains highly controversial; recent studies have reported that some patients with coeliac disease and dermatitis herpetiformis can tolerate moderate amounts of oats in their diet.[6–16] If oats can indeed be tolerated, their inclusion in the GFD would be beneficial, as they provide a good source of fibre, have a higher satiety value than other gluten-free cereals and increase patient choice. However, several studies have reported isolated cases of oats intolerance, and increased numbers of

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Abbreviations: AGA, antigliadin antibody; ARA, antireticulin antibody; EmA, endomysial antibodies; GFD, gluten-free diet; GSRS, Gastrointestinal Symptom Rating Scale; IEL, intraepithelial lymphocyte; tTG, tissue transglutaminase

intraepithelial lymphocytes (IELs) in the small bowel mucosa of patients on an oat-containing GFD.[4 15] Some studies carried out at a molecular level have suggested that oats can be tolerated.[12] However, others have shown that children with coeliac disease had markedly higher levels of antibodies to avenin than the control group, and that antibody levels correlated with levels of gliadin antibodies.[17] The mixed conclusions drawn from the many published works both at molecular level and on feeding challenges make the topic ideal for a systematic review.

It is of real clinical importance to determine whether oats should be included in the GFD. In patients with changes in small bowel histology on a GFD containing oats, it would be difficult to ascertain whether these changes are attributable to oats intolerance, poor adherence to GFD or accidental contamination of the GFD. Patients with poorly controlled coeliac disease have been shown to experience higher rates of gastrointestinal malignancies, particularly lymphomas and carcinoma of the jejunum and oesophagus.[18] Poor dietary control can lead to multiple complications of coeliac disease, the most common being disorders of bone and calcium metabolism resulting in rickets, osteoporosis and osteomalacia. In addition, splenic atrophy, reproductive disorders, ulcerative jejunoileitis and mesenteric lymph-node cavitation are all recognised complications of coeliac disease.

The increased risk of many complications, particularly malignancies such as small bowel lymphomas, can be reduced to that comparable with the general population by strict adherence to the GFD.[19] It is therefore essential to ascertain whether patients can tolerate oats without changes in their small bowel histology, regardless of whether they can tolerate oats clinically.

OBJECTIVES

We aimed to systematically identify and review literature related to the inclusion of oats in the GFD for patients with coeliac disease, to determine the extent of previous research efforts and current knowledge about the safety of oats in the GFD.

METHODS

This review used standard methods based on guidance from *Systematic reviews to support evidence based medicine*[20] and the guidelines published in the *Cochrane handbook of systematic reviews of interventions*.

We carried out a computerised literature search up to 2005 of Medline, Embase, SIGLE, National Research Register, The Research Findings Register, The Cochrane Central Register of Controlled Trials, MetaRegister of Current Controlled Trials and The Science Citation index. We hand-searched articles for additional citations.

Studies were included if they were experimental in design and studied patients with coeliac disease confirmed by gastroduodenal biopsy. The intervention was a GFD containing oats compared with a strict GFD. The primary outcome for inclusion was gastroduodenal biopsy carried out before and after the diet.

We excluded studies in which the diagnosis of coeliac disease was unclear, patients were either non-compliant on their GFD or already consuming a GFD containing oats. Studies that did not compare a group of patients receiving a GFD containing oats with those on a strict GFD were excluded, as were those in which gastroduodenal biopsy was not carried out. Studies that took the form of case series or case reports were also excluded.

All studies identified by the literature search were reviewed by three independent researchers, each of whom separately coded them as appropriate or not for inclusion in conjunction with the study inclusion and exclusion criteria. Any disagreements were resolved by consensus. Each study was allocated a study identifier number, which was used to randomly select a quarter of all studies for review by a fourth researcher.

Data extraction and quality assessment

We assessed the quality of the included studies by using the Sindhu Quality Assessment tool to rate the methodological quality of primary studies to be included in a meta-analysis.[21] A Delphi technique including several rounds of questions to seek consensus on criteria important in a randomised controlled trial is used, focusing on randomisation, blinding, withdrawals and dropout rates, appropriate statistical analysis, adherence and outcome measures.

RESULTS

Trial flow

Our literature search identified a total of 17 primary papers. Eleven primary studies were excluded from the review, applying the exclusion criteria described earlier. The most common reason for exclusion was lack of comparison of patients on a GFD containing oats with those on a strict GFD.[9 15 22 23] Tables 1 and 2 summarise the six studies included in this review. J1, J2 and J3 share authors, with J3 being a 5-year continuation of J1. J1 and J2 focus on different aspects of oats intolerance in coeliac disease. We aimed to complete a meta-analysis through this review. However, on closer examination of the papers, it became obvious that any form of pooled statistical analysis would not be possible owing to the lack of raw data presented in several of the primary papers. This is compounded by the fact that the studies use several different methods for assessing each outcome. For example, the primary outcome of concern, small bowel histology, has been reported as Marsh Score in J1, J3 and H, villous height:crypt depth ratio in R, and was not reported by J2 and P. Table 3 summarises the aspects of study quality, which also shows the comparative rank for each table in relation to the other studies.

Changes in small bowel histology

Six of the studies included in this review assessed changes in small bowel histology obtained on endoscopy. J1 reported no statistical difference in the grade of villous atrophy between the GFD-oats and the standard GFD group in the patients with coeliac disease in remission. J3 continued J1's study for 5 years in an attempt to examine the long-term effects of a GFD containing oats in patients with coeliac disease. The authors contacted their original study population and discovered that after 5 years, 65.7% of patients in the original oats group still consumed oats. The 12 patients who had reverted to a traditional GFD had done so because of concerns about the safety of oats at that time. The study showed an improvement in the villous architecture of both groups after 5 years: the oats group had a mean villous atrophy of 0.19 compared with 0.66 at 6–12 months after starting on GFD-oats. This represents a change of −0.55. The control group showed a similar change of −0.52, with the mean villous atrophy grade decreasing from 0.65 to 0.21. The difference in change between the two groups was 0.2, showing improvement in both groups, but neither of them returned to normal, and no quantitative count of IELs was carried out in both studies.

H also used the Marsh Classification to assess changes in small bowel biopsy specimens before and after the study diet. The authors reported that at the start of their study, all patients showed an enteropathy consistent with that of newly diagnosed coeliac disease. At the end of the 1-year study period, all but two patients had normal small bowel histology. Both children with abnormal histology were in the

Table 1 Primary studies included

Author	Year	Study identifier	Sample size	Study population	Study period	Outcomes assessed
Janatuinen *et al*[6]	1995	J1	92	40 adults with newly diagnosed CD, 52 adults with CD in remission	6–12 months	Marsh Score, GSRS, physical examinations, IEL count, laboratory values
Janatuinen *et al*[7]	2000	J2	92	40 adults with new diagnosed CD, 52 adults with CD in remission	6–12 months	Serology, IEL count
Janatuinen *et al*[8]	2002	J3	63	63 adults with CD	5 years	Marsh Score, IEL count, serology
Reunala *et al*[10]	1998	R	23	23 adults with DH on a standard GFD	6 months	Villous height:depth ratio, IEL count, rash presence, skin biopsy, serum samples
Peräaho *et al*[13]	2004	P	39	39 adults with CD on a standard GFD	12 months	GSRS, quality of life, IEL count, serology
Högberg *et al*[14]	2004	H	116	116 children with newly diagnosed CD	12 months	Villous height:depth ratio, IEL count, serology

CD, coeliac disease; DH, dermatitis herpetiformis; GFD, gluten-free diet; GSRS, Gastrointestinal Symptom Rating Scale; IEL, intraepithelial lymphocyte.

control group. The authors did not report any further details or raw data, making the inclusion of these data in any form of statistical analysis in combination with the results from J1 and J3 impossible.

P assessed changes in small bowel biopsy specimens between the GFD-oats and GFD-standard groups by calculating the mean villous height:crypt depth ratio (V:CrD). After 1 year, they found no significant difference between the mean V:CrD in the oats group (2.5) and that of the control group (2.1). No other raw data were given. Reunala *et al*[10] also measured V:CrD in their patients with dermatitis herpetiformis being challenged with oats, the mean V:CrD decreased slightly over the 6-month study period from a mean of 3.0 to 2.8. This was lower than the mean V:CrD of the controls (3.8); however, the control group comprised 28 patients with dyspepsia without gluten intolerance. This difference was not significant ($p = 0.082$).

J2 conducted a randomised controlled intervention study attempting to compare the immunological response of the small intestine between a standard GFD and a GFD-oats. They studied two groups of patients: 40 patients with newly diagnosed coeliac disease and 52 patients with coeliac disease in remission. Patients were randomly allocated to either GFD-oats or standard GFD. They counted the numbers of IEL per 100 epithelial cells in sections of small bowel biopsy specimens. No significant difference in IEL counts was found at any point in the study in either newly diagnosed patients or patients in remission between the patients on standard GFD and those on GFD-oats.

The findings of J2 are not supported by those of P, which measured the number of IELs per millimetre of epithelium after 1 year. The authors of P found a significantly higher IEL count in the oats group (44.6) than in the controls (26.7), with a p value of 0.039 indicating a significant difference between the two groups. R also reported a significant difference ($p<0.001$) in numbers of T cell antigen receptor-positive IELs between the patients challenged with oats and the controls. The patients receiving oats had a mean IEL count of 9.3 cells/mm of epithelium at baseline and 6.0 cells/mm after 6 months on the oats-containing diet. The controls had a mean IEL count of 1.5 cells/mm of epithelium.

In contrast with the findings of P, those of H showed no difference in the IEL count/100 enterocytes between patients consuming a standard GFD and those on GFD-oats. Both groups had a mean count of 16 IELs 100 enterocytes.

The first paper published by J1 assessed the grade of mononuclear cell infiltration between patients on a standard GFD and those consuming oats in both newly diagnosed patients and patients in remission. They found no significant differences between the two groups. J3, a continuation of J1, which assessed the effects of a GFD containing oats over 5 years, also showed no significant difference between the two groups.

Serology

J2 studied levels of antigliadin antibodies (AGA) and antireticulin antibodies (ARA). The median levels of AGA (immunoglobulin (Ig) A and IgG) and ARA (IgA) did not, at any point in the study, differ significantly between the standard GFD and the oats group. In the newly diagnosed group, the time taken for antibody levels to normalise was similar between the oats and standard GFD groups. J3 found no significant differences in ARA, AGA IgA, AGA IgG or endomysial antibodies (EmA) IgA between the oats and control groups after 5 years. Abnormally high antibody titres were attributed to poor adherence to the GFD in both groups. Of the 39 patients included in P, only four were positive for EmA or tTG antibodies at the time of enrolment; the antibody titres decreased in three of these patients, and increased marginally in one patient. At presentation, H reported that

Table 2 Study quality and rank

	Aspect of study quality assessment				
Study	Randomisation score (Max 10)	Blinding score (Max 6)	Withdrawals and dropouts (Max 24)	Compliance (Max 4)	Outcome measures (Max 14)
J1	2.5	4	14	0	14
J2	2.5	2	14	0	14
J3	2.5	4	12	4	14
R	0	0	4	0	12
P	7.5	0	4	4	14
H	1	6	14	4	14

Table 3 Study results

Study	Outcomes measured	Vil.H:Cr.D	IEL	Serology	GSRS
J1	Marsh Score, GSRS, physical examinations, IEL count, laboratory values	Not significant	Not significant	Not conducted	Not significant
J2	Serology, IEL count	Not conducted	Not significant	Not significant	Not conducted
J3	Marsh Score, IEL count, serology	Not significant	Not significant	Not significant	Not conducted
R	Villous height:depth ratio, IEL count, rash, skin biopsy, serum samples	Not significant	Significantly higher IEL counts observed in the oats group than in the control group ($p<0.001$)	Not significant	Not significant
P	GSRS, quality of life, IEL count, serology	Not conducted	IEL count was significantly higher in the oats group than in the control group; $p=0.039$	Not significant	Patients in the oats group had significantly more diarrhoea; $p=0.01$
H	Marsh Score, IEL count, serology	Not significant	Not significant	Not significant	Not conducted

IEL, intraepithelial lymphocyte; GSRS, Gastrointestinal Symptom Rating Scale; Vil.H:Cr.D, villous height:crypt depth ratio.

46% of the children with newly diagnosed coeliac disease in their study had positive IgA AGA titres; after 3 months, these had normalised in most children, with no difference between the oats and control groups. At diagnosis, 94% of children had positive IgA EmA titres; during the study period, these became negative in 72% of children, again showing no differences between the oats and control groups. tTG antibodies were positive in 90% of children at diagnosis, falling to 13% at 1 year; there were no significant differences in tTG positivity between the two groups. However, interestingly, we found a significant difference between median tTG antibody titres, with significantly higher titres observed in the control group (GFD-oats median 7.0 (range 5.1–11.0), standard GFD 12.0 (range 5.7–15.0); $p = 0.04$).

Quality of life

One study, P, assessed the quality of life using the Psychological General Well-Being Questionnaire, a tool developed to assess subjective well-being by measuring emotional state. As no other study examined this topic, we thought that it was largely beyond the scope of this review.

Quantity of oats consumed

Daily oats consumption was almost identical in all the six studies. In the oats group, daily oats consumption in J1, J2 and J3 was 50–70 g. Daily oats consumption in P and R was 50 g, whereas that in H was 25–50 g. No specific conclusion can therefore be inferred from the quantity of oats ingested in the six trials.

Cutaneous findings in dermatitis herpetiformis

One of the six studies included in this review assessed whether oats could be tolerated in patients with dermatitis herpetiformis (P). In these patients, the presence or absence of a rash was recorded throughout the study period. Skin biopsy specimens were also taken at baseline and at the end of the study, and IgA fluorescence was assessed. These outcomes are largely beyond the scope of this review, as they are relevant only to this paper. R reported that IgA was only observed in the skin of only one patient who had had a negative biopsy result at baseline. The other 11 patients showed no change or showed an improvement in their skin biopsy results. Three of the 12 patients who consumed oats had mild flare-ups of their rash; however, 4 of the 11 patients in the control group also had flare-ups of their rash.

Withdrawals

Table 4 gives the details of the withdrawals from all six studies. No study reported a significant difference in withdrawal frequency between the oats and control groups. The most common reason for withdrawal from the oats group was abdominal symptoms. Only J2 stated that the patients who dropped out due to abdominal symptoms showed no signs of clinical or histological deterioration.

DISCUSSION

As coeliac disease is a small bowel enteropathy that affects genetically predisposed people regardless of their age, studies of both children and adults were included in our review.

Several studies used the Gastrointestinal Symptoms Rating Scale (GSRS) to assess differences in the numbers of symptoms reported between patients on a standard GFD and those on GFD-oats. Although the use of GSRS has been well validated in coeliac disease,[24] its use in this setting is reasonably limited. Many patients with coeliac disease present atypically, and some may seem to be symptom free—a subset known as ''silent coeliac disease''. The presence of symptoms is therefore not indicative of the changes occurring in the small intestinal mucosa. There is increasing evidence that coeliac disease is strongly associated with other gastrointestinal disorders, including inflammatory bowel disease.[25] A relevant association has also been shown between irritable bowel syndrome and coeliac disease[26]; therefore, it would be impossible to attribute any gastrointestinal symptoms to the effects of oats alone. For these reasons, there is relatively little use in assessing changes in GSRS between the oats and control groups and so we have not included them in this review.

The use of serum markers including AGA and ARA is increasing, but AGA can be found in some people without coeliac disease, both in healthy people and in those with gastrointestinal diseases such as Crohn's disease.[27] Some clinics have advocated the use of serum AGA to assess adherence to the GFD, as AGA in most patients disappear after the adoption of a GFD, reappearing after exposure to gluten. However, it has been shown that after prolonged exposure to gluten, AGA levels in many patients with coeliac disease fall and may normalise despite pathological changes in small bowel histology.[28] The use of EmA and ARA has recently been widely accepted as a sensitive and specific test

Table 4 Details of withdrawals

Study	Study population	Total withdrawals	Withdrawals on GFD-oats	Reasons for withdrawals in the oats group	Clinical status of withdrawals from the oats group	Withdrawals from standard GFD	Reasons for withdrawals in the control group
J1	92	11	6	Abdominal symptoms (2), itching (3), no reason given (1)	Unknown	5	Itching (2), no reason given (3)
J2	92	11	6	Itching (2), symptoms (2), no reason given (2)	No clinical or histopathological evidence of deterioration on serology or small bowel biopsy	5	Itching (2), no reason given (3)
J3	63	15	16	No reason given (4), concerns regarding long-term safety of oats (12)	Unknown	14	Pregnancy (1), malignancy (2), no reason given (11)
R	23	3	3	No reason given (1), mild rash (2)	No immune deposits in the skin of patient with rash	0	N/A
P	39	3	3	Gastrointestinal pain and abdominal distension (3)	2 cases of biopsies in controls showed incomplete healing, serology normal in all 3	0	N/A
H	116	22	15	Symptoms (6), unable to follow diet (6)	Unknown	7	Symptoms (2), no reason given (5)

GFD, gluten-free diet; GFD-oats, GFD containing oats.

for all forms of coeliac disease. However, these are IgA, and an association has been shown between selective IgA deficiency and coeliac disease. Patients who test negatively for EMA and ARA should therefore also be tested for IgG ARA or AGA, the specificity of both of which for coeliac disease is controversial. It is for these reasons that small bowel histology remains the gold standard for diagnosis of coeliac disease. No serological tests were carried out in J1. The serological tests measured in J2 and J3 were restricted to AGA and ARA. Anti-EmA were used in H, R and P studies, whereas tTG was only measured in the P study. The level of serum immunoglobulins and, particularly, IgA level were not assayed in any of the six trials. The significance of the serology used therefore remained questionable.

Two of the six studies included in this review found evidence of minimal difference in small bowel changes (villous height and crypt depth) in patients with coeliac disease consuming GFD-oats, although not significant (J1 and J3). Two studies did report significant changes in IEL counts between those taking oats and those on a standard GFD (R and P); although this finding raises concern, it must be contemplated alongside the small sample sizes (23 and 39) of these two studies. The two studies of largest sample size (116 and 92) did not report a significant difference in IEL count (H and J2.) However, these patients were followed up only for 6–12 months. It would have been more useful to have followed up patients with increased IEL count for a prolonged period of time. It has been suggested that IEL changes are the last to disappear before normalisation of the mucosa; additionally, raised IEL counts are the earliest indicator of villous atrophy and clinical relapse.[29] Recently, it has been shown that 10–40% of patients with raised IEL count and normal villous architecture have latent coeliac disease and may, with time, develop frank villous atrophy.[29] It would therefore be prudent to suggest that patients with raised IEL counts on GFD-oats return to consuming a standard GFD.

Although Marsh[30] states that as many as 40 IELs/100 enterocytes can be normal, other studies have shown that the range of the number of IELs in duodenal biopsy specimens from patients with confirmed coeliac disease is much broader,[31–34] and it can be as low as 13 IELs 100 enterocytes. Thus, coeliac disease may be underdiagnosed by pathologists who adhere strictly to the higher threshold, especially in evaluating biopsy specimens with only minor or focal villous injury.

The precise role of IEL in the pathogenesis of coeliac disease remains largely unknown. IELs have been shown to infiltrate into the epithelium and lamina propria before gross morphological changes become evident.[30] The IEL count is therefore regarded as a sensitive indicator of the local immune response and of early mucosal damage occurring before small bowel biopsies show villous atrophy.

Most patients with coeliac disease are able to tolerate oats. However, caution must be exercised, as the longest length of follow-up of a study included in this review was 5 years (J3). It has been suggested that oats might exert a latent effect, with small bowel biopsy specimens becoming deranged after several years.[4] It would therefore be prudent to suggest that patients wanting to include oats in their diet undergo annual screening biopsies to ensure that subclinical changes are not occurring in the small bowel mucosa. Patients with coeliac disease or dermatitis herpetiformis wishing to include oats in their diet must also ensure that the oats they consume is not contaminated during growth or during the milling process with gluten.

The high withdrawal frequency in the primary studies included in this review raises concerns, as not all patients who withdrew were sufficiently followed up to determine whether they had relapsed. Ideally, all patients who dropped out should have undergone small bowel biopsy; however, in reality, many patients would probably not consent to this. In practice, patients who dropped out should have had full serology, including AGA, ARA and anti-tTG. R reported that all three patients who dropped out of their study due to abdominal symptoms had normal serology. It is of concern that several of the studies made no attempt to follow-up patients who dropped out and ensure that they were not relapsing. If oats intolerance was to affect a small minority of patients with coeliac disease and dermatitis herpetiformis, these dropouts might be indeed oats intolerant; therefore, some attempt to follow them up should have been made. If

any of these patients was oats intolerant and had developed gastrointestinal symptoms, they would be likely therefore to withdraw from the study on account of the unpleasant symptoms. It is vital that these patients are then followed up with small bowel biopsy if possible and at least serological testing to exclude oats intolerance as a cause of these symptoms.

A recently published study raises the possibility of oats intolerance in some patients with coeliac disease.[4] Arentz-Hansen *et al*[4] studied nine patients with coeliac disease and a history of exposure to oats. Four of the patients ate and tolerated oats, one patient had slight mucosal inflammation and symptoms on oats ingestion, another had slight mucosal inflammation but remained well, one patient experienced anaphylactoid symptoms after ingestion of oats but no mucosal inflammation, and two patients were referred by general practitioners for complicated coeliac disease. Small bowel biopsy specimens from all patients were compared. Three patients developed villous atrophy. Arentz-Hansen *et al* also produced T lymphocyte lines reactive to avenin from intestinal biopsy specimens of patients consuming oats and therefore exposed to avenin. Responses to avenin were detected in T cell lines from all three patients described earlier who developed villous atrophy on ingestion of oats. More interestingly, intestinal T cell responses were also noted in two of the other six patients who did not develop villous atrophy. Intestinal T cells specific for wheat gluten and gliadin were identified in all nine patients. It is impossible to show directly that T cells reactive for avenin or indeed gluten cause disease. However, the fact that these T cells are uniquely restricted by HLA-DRQ 2, which confers a genetic predisposition to coeliac disease, and that they are activated by prolamines, including avenin, indicates that they are possibly involved in the disease process. The finding of avenin-reactive T cell lines in patients apparently able to tolerate oats is of concern. As avenin is less immunogenic than gluten for reasons described earlier, it might take a considerably longer time period to trigger a relapse. During this latent period, subtle changes at the level of the small bowel mucosa could potentially confer an increased risk of developing complications associated with coeliac disease. This study is the first to show the association of changes in small bowel biopsy specimens with T cell lines reactive to avenin. The authors suggested that it might be possible in the future to test patients with coeliac disease for oats intolerance by the monitoring of T cell responses to avenin epitopes in vitro.

As the prevalence of oats intolerance is unknown, it seems prudent that if patients wish to include oats in their GFD, they undergo regular review, including small bowel biopsy under the care of a specialist.

We were astonished at the comments made by the World Gastroenterology Organisation in their recently published guidelines on coeliac disease.[35] The document estimated that >95% of patients with coeliac disease can safely tolerate oats in their diet. This figure is obviously arbitrary and was not substantiated or evidence based. The same guidelines have neither defined nor predicted the group of patients who are oats intolerant. This issue is alarming, particularly when considering that most patients with coeliac disease have no gastrointestinal symptoms.

In light of recent case reports, although most patients with coeliac disease seem to be able to tolerate oats, a sizeable number of cases of intolerance to pure oats have been identified.[4 15] We suggest therefore that oats should be excluded when prescribing GFD, and can be included only if the patient is undergoing a lifelong regular review under specialist care. It must be emphasised that the long-term risks of the inclusion of oats in the GFD remain unknown and that the possibility of a link to increased risk of malignancy cannot be ruled out. For these reasons, we believe it is important that patients are informed of the controversy surrounding oats and helped to make an informed choice whether or not to include oats in their diet.

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