GUIDELINES FOR THE MANAGEMENT OF PATIENTS WITH COELIAC DISEASE

SUMMARY
Coeliac disease is a life-long inflammatory condition of the gastrointestinal tract that affects the small intestine in genetically susceptible individuals. A typical district general hospital will care for one hundred and fifty subjects. A small intestinal biopsy is mandatory to confirm the diagnosis. Treatment involves a strict gluten-free diet that excludes wheat, rye, barley and oats which should be supervised by a dietician. Follow-up is important because of potential long-term complications.

INTRODUCTION
Definition: Coeliac disease (CD) may be defined as an inflammatory condition of the small intestinal mucosa, that is most marked proximally, and which improves morphologically when gluten is removed from the diet. The disorder may alternatively be termed gluten-sensitive enteropathy or non-tropical sprue. It has a UK prevalence of 1:1000 to 1:1500, the average District General Hospital usually caring for 150 patients. Dermatitis herpetiformis (DH) is a related disorder in which there is an itchy blistering skin eruption that frequently affects the knees, elbows, buttocks and back. Confirmation of a diagnosis of DH includes the finding of granular IgA at the dermo-epidermal junction of uninvolved skin on biopsy. The majority of patients with DH have a small intestinal enteropathy that improves with gluten withdrawal.

CD presents at all ages with protean manifestations. Patients may present with clinical or haematological features, or may be identified by serological screening of asymptomatic relatives.

SYMPTOMS
a: Child
Symptoms in children occur commonly following weaning with the peak incidence being between 9 months & 3 years. They include failure to thrive, diarrhoea, irritability and anorexia and occasionally generalised oedema.

MODES OF PRESENTATION
• Classical presentation aged 9-24 months
This is sometimes called the “usual” presentation. There is gradual failure to gain weight or loss of weight after introduction to cereals, the child having been previously well. This is accompanied by anorexia and alteration in stools which are softer, paler, larger and more frequent than unusual. There is abdominal distension, muscle wasting and hypotonia.

• Presentation in infants before 9 months - Vomiting is frequent and may be projectile in this age group. Diarrhoea may be severe, especially with intercurrent infections, not necessarily gastroenteritis. Abdominal distension may not be marked. It is difficult to distinguish from the post-enteritis/cow’s milk sensitive enteropathy syndrome.
• **Presentation with constipation** - These children can be hypotonic with marked abdominal distension. This is an uncommon presentation.

• **Presentation at older age** - Short stature, iron-resistant anaemia, rickets and personality problems all may occur. Diarrhoea is not a prominent feature. Such a mode of presentation is characteristic for children in Britain originating from the northern part of Indian sub-continent.

• **Presentation in asymptomatic siblings** - After a case of coeliac disease is positively diagnosed, siblings should have clinical history and growth checked. If a suspicion of coeliac disease arises, IgA gliadin antibody and IgA anti-endomysial antibody and serum immunoglobins should be done. A small intestinal biopsy should then be performed if there is presence of a circulating antibody.

**b: Adult**

The symptomatology in adults is often less acute. The peak incidence of diagnosis in adults is in the third decade with a further smaller one in the fifth and sixth decades.

- 80-90% have general lassitude.
- 75-80% have diarrhoea.
- 85% have asymptomatic iron/folate deficiency.
- 15-30% have vitamin D deficiency.
- 10% have vitamin K deficiency.

There are often rarer problems, such as reduced fertility and psychological disturbances. There is often a delay of several years before the diagnosis is made.

**INVESTIGATION**

**I. Diagnostic Tests**

**a: Intestinal Biopsy**

Diagnosis requires a small intestinal biopsy, the current usual practice being for endoscopic biopsies to be taken from the distal duodenum. Should there be any doubt, endoscopic biopsies should be repeated or, preferably, a jejunal biopsy should be undertaken using a suction peroral biopsy capsule, or a small bowel enteroscope.

The characteristic histological changes in a small intestinal biopsy are villous atrophy, crypt hyperplasia, a chronic inflammatory cell infiltrate of the lamina propria, lymphocytic infiltration of the epithelium, and a decrease in the epithelial surface-cell height. Confusion can occur when these changes are only mild, particularly when only one endoscopic duodenal biopsy is histologically assessed and when this has been cut tangentially. In such cases repeat biopsy is necessary, taking 4-6 samples which should be carefully orientated before sectioning. Definite cases do occur however where only mild histological changes are present.

It is now considered acceptable to take only a single biopsy in patients who have typical histological features, as long as they have positive antibodies to gliadin and endomysium and experience symptomatic remission on withdrawal of dietary gluten. The diagnosis is more certain, however, if a second biopsy is taken which shows histological improvement after gluten withdrawal.

Further biopsy is always required in two particular situations: (i) a child previously diagnosed as suffering from coeliac disease and having a gluten-free diet should be reinvestigated in order to fulfil these criteria if there is any doubt about the original diagnosis, particularly if the child was started on such a diet without a previous small intestinal biopsy; (ii) if the child was less than 2 years of age at the time of di-
agnosis. It must be appreciated that although a flat small intestinal mucosa is characteristic of coeliac disease, there are other causes of such a mucosa.

If the diagnosis is in doubt, it is mandatory to take an additional jejunal biopsy after a formal gluten challenge. This should comprise at least 10g of gluten that is contained in four slices of normal bread per day for a minimum of 2 weeks, although this may need to be much longer, and 6 weeks in the case of children. If the patient experiences severe symptoms on gluten challenge, the date of the biopsy should be brought forward. The development of symptoms on gluten challenge without evidence of an abnormal small intestinal biopsy is insufficient to make the diagnosis.

b: Antibody Studies

Serological screening tests can be performed for antibodies to gliadin, endomysium and reticulin. IgG and IgA anti-gliadin antibodies can be measured easily and cheaply, using ELISA techniques. They are highly sensitive markers, being present in 90% of patients with untreated disease but are not specific. They are most useful as a preliminary step in screening or to monitor the condition as levels tend to fall after treatment with a GFD.

II. Supportive Investigations

A number of routine blood tests should be carried out to identify nutritional deficiencies including haemoglobin, B12, folate, iron, serum albumin, and calcium. These should be measured at diagnosis, during symptomatic relapse, and during pregnancy. It is also reasonable to perform these routinely at annual follow-up. Tests of malabsorption can be used to assess severity of disease in conjunction with mucosal histology (see advice document on malabsorption). Small intestinal barium studies may be used to exclude other causes of malabsorption and diarrhoea, and for diagnosing complications of CD, such as strictures and small bowel lymphoma.

TREATMENT

I. Dietary Treatment

a: Gluten Exclusion

The cornerstone of therapy is adherence to a gluten free diet (GFD). This means the exclusion of foods containing wheat, rye, barley and oats, although the toxicity of oats is still debated. The avoidance of these cereals is a formidable task as they are found in bread, biscuits, cakes, pastries, breakfast cereals, pasta, beer, and most soups, sauces and puddings (Walker-Smith et al, 1990).

Recently evidence has been produced (Jantuinen et al, 1995) that oats may not be harmful in adults with coeliac disease. There is no comparable evidence in children. Hence the recommendation that a diet free of wheat, rye, barley and oats must remain for children with coeliac disease until a comparable study has been undertaken in this age group.

Patients may supplement their diet with commercial gluten-free products that are available on prescription by general practitioners and include gluten-free flour, bread, biscuits, and pasta. Prescriptions should be on FP10 forms clearly marked ACBS, an abbreviation for “according to the borderline substance act”. Many gluten-free flours and bread mixes are based on purified wheat starch from which most gluten proteins have been removed. Most patients with coeliac disease tolerate these products well, although a minority cannot. These individuals should be advised to take a strict GFD in which they ingest only commercial non-wheat starched based gluten-free products.

Seventy per cent of adults, and a greater proportion of children, respond promptly to a GFD, showing improvement of symp-
toms within weeks or days. Histological improvement usually takes many months to occur.

b: Total vs Partial Gluten Exclusion
It is probable that the risk of developing small intestinal lymphoma is increased in patients taking a gluten reduced diet, as opposed to a GFD. Nutritional deficiencies are also more likely to occur. It therefore seems reasonable to recommend a strict GFD, even if patients are asymptomatic on a low gluten intake. Good dietary compliance should reduce the risk of osteoporosis in later life.

c: Need For Life-Long Treatment
Adolescents may stop their diet in the mistaken belief that they have “grown out of” their CD. Should the diagnosis be in any doubt, a gluten challenge and repeat jejunal biopsy should be undertaken; if the diagnosis is established life-long treatment should be recommended.

d: Dietary Supplements
Many patients will be found to be suffering from dietary deficiencies at the time of diagnosis, the commonest being iron, folic acid, calcium and vitamin B12. Although these usually resolve spontaneously once on a GFD, it seems reasonable to ensure rapid correction with appropriate supplements.

e: Information and Support
As mentioned above, adherence to a GFD is not easy, even in ideal circumstances. For individual patients this task can be complicated by family and professional commitments, as well as peer pressure. Adolescence is often a particularly difficult time, when young patients may feel excluded from their peer groups by their dietary restriction. The value of careful explanation and encouragement cannot be overemphasised, and the need for supervision by a dietitian is mandatory. Written advice should be provided whenever possible, and all patients should be encouraged to join the UK Coeliac Society.

The Coeliac Society of the UK, PO Box 220, High Wycombe, Bucks, HP11 2HY
Tel: 01494 437273  Fax: 01494 474349

II. Follow-Up
In patients with a satisfactory response to diet, specialist outpatient follow-up should be at six to twelve month intervals to assess symptomatic improvement, nutritional state, and dietary compliance, and check routine blood tests. A check small intestinal biopsy four to six months after initiating treatment should be performed when improvement in the small intestinal villous architecture is expected.

It is important to review patients at times of stress, whether this be physical or emotional. Pregnancy is a particularly important time which may lead to a deterioration in symptoms, or asymptomatic nutritional deficiencies. Low levels of folic acid have been associated with miscarriage and foetal neural tube defects, and so should be carefully monitored.

Because of the possible long term complications of disease, such as lymphoma and bone disease, it is strongly recommended that life-long follow-up be maintained. The general practitioners should be aware of potential complications and request specialist review if required.

III. Management Of Poor Response And Relapse
The assessment of patients who fail to respond to diet involves three steps: (a) assess dietary compliance, (b) confirm the diagnosis, and (c) exclude other coincident disease. The management of patients who relapse after initial recovery is broadly similar, although more emphasis is given
to exclusion of coincident disease, including complications such as lymphoma.

\textbf{a: Dietary Compliance}
Careful questioning will identify most patients who are, knowingly or unknowingly, taking dietary gluten. Occasionally, very diligent patients continue to have symptoms due to very small amounts of ingested gluten, and the dietary history needs to be very detailed. In some cases identification of the source of dietary gluten may only be possible by admitting the patient to hospital, when the patient can be restricted to a supervised and carefully prepared GFD.

\textbf{b: Confirmation Of The Diagnosis}
This requires review of the original histology and associated clinical information. If there is any doubt, a repeat biopsy should be undertaken. Gluten challenge may be necessary, and if they have not already been performed, antibody studies can help to strengthen the diagnosis.

\textbf{c: Other Coincident Disease}
Isolated persistent symptoms should be investigated as in a patient without CD. Obviously, the most appropriate investigations will depend on the individual case. Particular attention should be paid to conditions which, though rare in the general population, occur more frequently in association with CD (see below).

\textbf{d: Immunosuppression}
Coeliac disease can be controlled with systemic corticosteroids, with rapid cessation of diarrhoea, weight gain, and improvement in fat absorption. However, within a few days of stopping treatment there is usually a deterioration. In general, they are best avoided, and with careful diagnosis and dietary assessment rarely need to be used.

\textbf{IV. Management Of Complications And Associated Conditions}

\textbf{a: Dermatitis Herpetiformis}
Dermatitis herpetiformis complicates 2-5% of cases of gluten-sensitive enteropathy, and the majority cases of DH exhibit a degree of gluten-sensitive enteropathy.

Dapsone is the drug of choice for the condition, although it does have significant side-effects. Patients should take a strict GFD, as this results in a significant improvement after six to twelve months and permits a reduction in the dose of, or elimination of the need for, dapsone. A few individuals are unable to tolerate dapsone because of side effects, which include a dose-dependent haemolytic anaemia, methaemoglobinemia, and headache. These patients can alternatively be treated with sulphapyridine.

\textbf{b: Malignancy}
(i) Lymphoma: The mechanism by which CD predisposes to lymphoma is unknown, though the association is not doubted. The commonest presentation involves the return of symptoms of diarrhoea, associated with both weight loss and lassitude in a patient with established coeliac disease. Standard investigations, including jejunal biopsy and small bowel barium studies, are likely to have a low yield, even when the lymphoma is suspected, because of the associated subtotal villous atrophy. The histological appearance of peripheral lymph nodes, the liver or bone marrow may be diagnostic, and ultrasound, computer aided tomography, or nuclear magnetic resonance scanning may be useful. Small bowel enteroscopy may be of help by allowing direct visualisation and biopsy of a greater proportion of the small intestine. Laparotomy or laparoscopy, with lymph node, liver, and full-thickness intestinal biopsies is a useful diagnostic tool, and often the only way to achieve a definitive diagnosis. Treatment is difficult and
usually involves surgery, radiotherapy and chemotherapy.

(ii) There is an increased risk of small bowel adenocarcinoma. It often presents with non-specific symptoms and there is often a significant delay in diagnosis. As a result, the patient often has metastatic disease with poor prognosis. Surgery with consideration of chemotherapy is the mainstay of treatment.

c: Ulcerative Jejuno-ileitis
This is an unusual complication in which unresponsive CD is associated with ulceration and stricturing. Patients may become very unwell and are often unresponsive to medical therapy. The discrimination between this and lymphoma can normally only be made at surgery, and in some instances lymphoma seems to have developed on a background of jejuno-ileitis. Patients should be advised to continue with a gluten-free diet, but early surgery is indicated if there is no resolution of symptoms.

d: Other Complications
A GFD is low in fibre and may exacerbate constipation or symptoms of irritable bowel. Carbohydrate intolerance, bacterial overgrowth, and colitis may also occur and there is an increased prevalence of diabetes mellitus. Infertility is common in untreated patients. Rarely neurological complications may occur. There is evidence that many coeliac patients suffer from osteoporosis in later life.

AUTHORSHIP
This guideline was prepared by members of the British Society of Gastroenterology and approved by Council.

We plan that this guideline will be revised from time to time. Comments or suggestions for use in subsequent editions should be sent to: The Clinical Services and Standards Committee, British Society of Gastroenterology, 3 St Andrews Place, Regent's Park, London NW1 4LB.

ADDITIONAL INFORMATION
The Coeliac Society of the UK, PO Box 220, High Wycombe, Bucks, HP11 2HY
Tel: 01494 437273 Fax: 01494 474349

Suggested Reading:


**Suppliers of Gluten-free Products**

Cantassium, 225-229 Putney Bridge Road, London, SW15 2PY (Tel: 0181 874 1130) (Trufree products)

Crookes Healthcare, PO Box 57, Central Park, Lenton Lane, Nottingham, NG7 2LJ (Tel: 0115 950 7431)

Food Watch, Butts Pond Industrial Estate, Sturminster Newton, Dorset, DT10 1AZ (Tel: 01823 332 5023)

General Designs Ltd, PO Box 38, Kingston upon Thames, Surrey, KT2 7YP (Tel: 0181 336 2323) (Ener-G and Pastariso Products)

Gluten Free Foods Ltd, 8 Queen Anne Street, London, W1M 9LD (Tel: 0181 954 7348) (Barkat products)

HJ Heinz, Hayes Park, Hayes End Road, Hayes, Middx, UB4 8HL (Tel: 0181 573 7757)

Jacob’s Bakery Ltd, Suttons Business Park, Earley, Reading, RG6 1AZ (Tel: 0173 449 2000) (Liga products)

Kallo Foods Limited, Sunbury on Thames, TW16 7JS (Tel: 01932 35 5303) (Kallo products)

Larkhall Green Farm Ltd, 225 Putney Bridge Road, London, SW15 2PY (Tel: 0181 874 1130)

The Mustard Shop, 3 Bridewell Alley, Norwich, NR2 1AQ (Genuine Mustard, coded GDSF) (Tel: 01603 62 7889)

Milupa, Milupa House, Uxbridge Road, Hillingdon, Uxbridge, Middx UB10 0NE (Tel: 0181 573 9966) (Prejomin products)

Nutricia Dietary Products Ltd, Newmarket Avenue, White Horse Business Park, Trowbridge, Wilts, BA14 0XQ (Tel: 01225 768 381) (Fax: 01225 768 847) (Glutenex Biscuits, GF Dietary, Glutafin, Loprofin, Rite Diet Products)

Scientific Hospital Supplies Ltd, 100 Wavertree Boulevard, Wavertree Technology Park, Liverpool, L7 9PT (Tel: 0151 228 1992) (Juvela, Lifestyle Products)

Ultrapharm Ltd, PO Box 18, Henley on Thames, Oxon, RG9 1AW (Tel: 01491 578016) (Aproten, Arnott’s Rice Cookies, Bi-aglut, Polial, Schar, Ultra products)