Coeliac disease in the elderly

A quarter of all new patients diagnosed with coeliac disease are in their seventh decade or older. Coeliac disease presents with a wide range of symptoms. It is under diagnosed, especially in the elderly who may present with only iron deficiency anaemia. The mean delay in diagnosis in elderly patients is around 17 years. Early treatment is necessary to avoid potential associated complications.

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Coeliac disease is a relatively common condition thought to affect 0.3–1% of the population. It is most common in the northern hemisphere with a prominence in Western Ireland and Sweden. The true prevalence is difficult to estimate because many patients have few or no symptoms.

Although coeliac disease was previously believed to develop predominantly in children, it is now understood that the condition usually affects adults, with about 25% patients receiving their diagnosis after 60 years of age.

Coeliac disease presents with a range of symptoms and signs (see box 1). Those once described as typical, including features of malabsorption such as diarrhoea and weight loss, are now considered uncommon. As many as 80% of patients have no gastrointestinal symptoms, and coeliac disease has also been reported in obese patients.

Atypical symptoms and signs include iron deficiency anaemia; osteoporosis; idiopathic elevation of liver transaminases; and neurological symptoms, such as ataxia, peripheral neuropathy, mononeuritis multiplex, and myopathy. These symptoms present a diagnostic challenge to clinicians, and can easily lead to delayed or missed diagnosis.

Pathophysiology

Also known as coeliac sprue or gluten-sensitive enteropathy, coeliac disease is a malabsorption disorder of the small intestine that occurs in genetically susceptible individuals after ingestion of wheat gluten.

It predominantly affects the small intestine; abnormalities are most marked proximally and decrease in severity with distal progression. In severe cases, the lesion may affect the ileum and
even the stomach and rectum.10

Flattening of the mucosa is variable, from mild and partial villous atrophy to total absence of villi. Classically, in untreated coeliac disease, there is a flat mucosa with no villi (total villous atrophy), but more usually there is a reduction in the normal villous height, resulting in a reduced villous height: crypt depth ratio. The thickness of the mucosa is usually increased because of crypt hyperplasia.11

An increased number of intra-epithelial lymphocytes is the earliest pathological change following gluten challenge, and a high count may be the only sign of gluten sensitivity.12

**Genetics and environment**

Coeliac disease is caused by both genetic and environmental factors (ie. gluten). Genetic susceptibility is suggested by an approximately 70% concordance between monozygotic twins13 and an association with certain type II human leukocyte antigens (HLA). The disease is associated with HLA DQ2 (HLA-DQA1*05-DQB1*02) in up to 95% of patients, while most other patients have HLA DQ8 (HLA-DQA1*03-DQB1*0302).14–16

Coeliac disease is now thought to be mediated by an inappropriate T-cell driven immune response to ingested gluten17 with a significant increase in the number of T-cell receptor +ve lymphocytes in the surface epithelium of the small intestine. The interplay between genetic (both HLA and other types) and environmental factors leads to the intestinal damage typical of the disease.17

**Diagnosis**

The gold standard in the diagnosis of coeliac disease is histology of a duodenal biopsy, which usually shows characteristic changes.4 Findings include intraepithelial lymphocytosis, crypt hyperplasia and villous atrophy. Symptomatic and histological improvement on gluten withdrawal confirms the diagnosis.18

A positive anti-endomysial antibody (EMA) test identifies coeliac disease with a sensitivity of almost 90% and specificity of 100%.19 Tissue anti-transglutaminase antibodies (tTGA) are less sensitive than anti-endomysial antibodies; however, the two tests combined identify coeliac disease with a sensitivity of over 95%.20 As EMA and tTGA are IgA antibodies, these will be falsely negative in IgA deficiency. This is 10–15 times more common in coeliac disease patients than in healthy individuals. Overall, 2–3% of patients with gluten-sensitive enteropathy have selective IgA deficiency. Because these patients may not produce the IgA antibodies required to

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**Box 1: Symptoms, signs, and conditions that require serological testing**

**Gastrointestinal**
- Chronic or intermittent diarrhoea
- Unexplained nausea and vomiting
- Recurrent abdominal pain
- Weight loss

**Neurological**
- Ataxia
- Peripheral neuropathy
- Mononeuritis multiplex
- Myopathy

**Other**
- Iron deficiency anaemia
- Osteoporosis
- Cryptogenic hypertransaminasemia

**Conditions**
- Thyroid disease
- Irritable bowel syndrome
- Type 1 diabetes
- First-degree relatives of patients with coeliac disease
make a diagnosis, IgG EMA and tTGA must be checked when IgA deficiency is suspected.21

Negative serology does not rule out coeliac disease; duodenal biopsies should always be performed if clinical suspicion is high.22

NICE outlined the order for serology testing in guidance published in 2009 (see box 2).23

HLA analysis helps recognise high-risk groups and exclude coeliac disease in equivocal cases.24

Coeliac disease is very unlikely when both HLA DQ2 and HLA DQ8 are absent. The diagnosis of coeliac disease has been based on criteria of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition, revised in 1990. However, presentation can be muted or atypical in elderly patients. It can be hard to judge symptomatic relief after gluten withdrawal. The five forms distinguished are: classic, subclinical, latent, potential and silent.25

Elderly patients
A study reports that 34.1% of all patients new diagnosed with coeliac disease are in the seventh decade or above.26 Swinson et al27 demonstrated a bimodal distribution for age at adult diagnosis, with an initial peak in the fourth decade (predominantly women) and a later peak in the sixth and seventh decades (mostly men).

Hankey and Holmes28 drew attention to coeliac disease being as much a disease of the elderly as of children, finding that 16% of their patients (19% of those aged 15 years and over) were diagnosed in their seventh decade and beyond. Cook et al2 found that 12% (15% of those aged 15 years and over) were aged 60 or over at diagnosis.

Micronutrient deficiency is a common presenting clinical picture of intestinal malabsorption in the elderly; because symptoms of malabsorption are covert, diagnosis is often delayed, and nutritional deficiencies are more common and severe than in the young. As the elderly have less nutritional reserve than the young, these deficiencies are clinically more damaging.29

The mean delay in diagnosis of elderly patients is around 17 years.30 Morbidity rates increase with delay, suggesting that clinicians should be more alert to the possibility of coeliac disease in this population.31

Symptoms
Iron deficiency anaemia
This haematological deficiency is the most frequent extra-intestinal manifestation of coeliac disease, occurring in approximately 39% of patients.32

Mandal et al33 found that 1.7% of patients over 65 years of age presenting with iron deficiency anaemia have characteristic changes
of coeliac disease on duodenal biopsy. Up to 47% of adults with coeliac disease may have positive faecal occult blood tests.\textsuperscript{34,35} When the faecal occult blood test is used to screen for cancer, coeliac disease should be considered as a differential diagnosis.

As iron deficiency anaemia is common in elderly people (13.5% of patients over 70 years)\textsuperscript{34} and coeliac disease is often silent, all cases of unexplained iron deficiency should be considered for the diagnosis.

**Malabsorption**

Malabsorption may present with very few symptoms or the signs and symptoms of specific vitamin and nutritional deficiencies may be identified.

Most patients present with signs and symptoms of nutritional deficiency whereas gastrointestinal disturbance is the presenting complaint in around 20%\textsuperscript{36}.

The most likely presentation is a combination of microcytic anaemia, past or present, a family history of the disease, and feeling tired all the time.\textsuperscript{36}

Mandal et al found 21.4% of patients over 65 years presenting with chronic diarrhoea and iron deficiency anaemia will have coeliac disease.\textsuperscript{34}

**Osteoporosis**

Because the diagnosis of coeliac disease is often delayed into adult life, many patients experience malabsorption for prolonged periods and consequently develop osteopenia or osteoporosis. One study\textsuperscript{37} showed that 47% of women and 50% of men on a gluten-free diet had osteoporosis.

The cause of osteoporosis is likely to be calcium malabsorption leading to increased parathyroid hormone secretion, increased bone turnover, and cortical bone loss.\textsuperscript{38} Stenson et al\textsuperscript{39} found the prevalence of biopsy-confirmed coeliac disease to be much higher in patients with osteoporosis than those without it (3.4% versus 0.2%). Anti-tissue transglutaminase antibody levels correlated with the severity of osteoporosis as measured by T-score.

The authors recommend screening all patients with osteoporosis for coeliac disease.\textsuperscript{40}

**Neurological symptoms**

Seizures related to calcification of the cerebral occipital lobe have been described in patients with coeliac disease.\textsuperscript{40,41} In these cases, seizure control improved with anticonvulsants and introduction of a gluten-free diet.\textsuperscript{42}

Seizure cases are rare in the UK and tend to present in childhood. Gluten sensitivity has also been found to be a cause of apparently idiopathic ataxia. Necropsy showed that the ataxia was a result of immunological damage to the cerebellum, to the posterior columns of the spinal cord, and to peripheral nerves.\textsuperscript{43} A review by Hadjivassiliou et al\textsuperscript{44} found ataxia and peripheral neuropathy to be the most common neurological manifestations of coeliac disease. Myopathy and hyporeflexia have also been described.\textsuperscript{45}

**Complications**

Perhaps the most acknowledged complication of coeliac disease is the development of small bowel lymphoma. Lymphomas, mostly of T-cell type, and other malignant tumours of the small bowel, stomach and oesophagus, are associated with coeliac disease.\textsuperscript{46}

West et al\textsuperscript{47} found that people with coeliac disease have a 30% higher risk of gastrointestinal cancer and lymphoproliferative disease than the general population. However, the incidence of breast and lung cancer is decreased in patients with coeliac disease, for reasons so far unexplained. Prompt and strict dietary treatment has been...
found to decrease mortality in coeliac disease, emphasizing the importance of early diagnosis and institution of a gluten free diet.

I have no conflict of interest.

References

20. Hill ID. What are the sensitivity and specificity of serologic tests for coeliac disease? Do sensitivity and specificity vary in different

Key points

- One quarter of all new patients diagnosed with coeliac disease are in their seventh decade or older
- Coeliac disease may present with a wide variety or relative lack of symptoms in older people.
- Iron deficiency anaemia, malabsorption and osteoporosis are common presentations in the elderly
- The condition is often under diagnosed. The mean time of delayed diagnosis in the elderly is around 17 years
- The gold standard in diagnosis is the finding of characteristic histological changes on duodenal biopsy
- Patients with coeliac disease have a 30% higher risk of gastrointestinal cancer and lymphoproliferative disease than the general population.


