Amended coeliac disease guidelines mean some symptomatic children can now be diagnosed without having to have a biopsy of their small bowel

**Childhood coeliac disease: diagnostic pathways update**

In this article...
- What to look out for to identify coeliac disease in children
- How the diagnostic pathways have been amended
- Benefits of the amended guidelines

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The modification of European guidelines now enables coeliac disease to be diagnosed without a small-bowel biopsy in a selective group of symptomatic children. The recommendations have been adopted by the Coeliac UK and the British Society of Paediatric Gastroenterology, Hepatology and Nutrition. As well as highlighting how health professionals can help identify coeliac disease at an earlier stage, this article details the amendments to the guidance and the diagnostic pathways that should be followed.

**Keywords** Coeliac disease, Children, Paediatrics, Nutrition, Gluten

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**Blood testing**

- Box 1: Blood testing with anti-tissue transglutaminase (anti-tTG) titres is necessary for children who are symptomatic and those at high risk of developing coeliac disease.

**Children who are symptomatic and have an anti-tTG titre that is >10 times the upper limit of normal (>10xULN) can be diagnosed serologically without small-bowel biopsies, provided they test positive for HLA-DQ2 and/or HLA-DQ8 haplotype.

**Children with no symptoms, regardless of their anti-tTG titre, and those with symptoms with an anti-tTG titre that is <10xULN still require histological confirmation on small-bowel biopsy.

**Testing for coeliac disease should be carried out only when patients are on a normal diet that contains gluten.

**Management of coeliac disease requires a lifelong gluten-free diet.**

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**Coeliac disease (CD) is an immune-mediated systemic disorder that occurs in people who are genetically susceptible to ingested gluten and related prolamin (the group of plant storage proteins that have a high proline content, such as gliadin, hordein). It is characterised by the presence of a variable combination of:**

- Gluten-dependent clinical manifestations;
- CD-specific antibodies;
- Human leucocyte antigen (HLA)-DQ2 or HLA-DQ8 haplotypes;
- Small bowel enteropathy (disease of the intestine) (Murch et al, 2013).

- The immune-mediated enteropathy is triggered in susceptible individuals by the ingestion of gluten found in wheat, rye and barley (Paul and Spray, 2014).

- CD is common, with a prevalence of 1:100 in the UK (National Institute for Health and Care Excellence, 2009). However, research suggests 90% of cases remain unidentified and so greater awareness is necessary to recognise and diagnose the condition early (Ravikumara et al, 2007).

**Symptoms and screening**

CD is a multi-organ condition that generally presents with:

- Persistent diarrhoea;
- Abdominal pain;
- Weight loss.

Other symptoms that are increasingly being reported include unexplained iron deficiency anaemia, idiopathic short stature, faltering growth, constipation, liver disease, arthropathy, mouth ulcers, muscle weakness, delayed onset of puberty, and, in adults, infertility and osteoporosis (Murch et al, 2013; Husby et al, 2012; NICE, 2009). Many of these symptoms can be non-specific, so health professionals should consider CD in children who present with any of them. It should also be suspected in children belonging to a group at high risk of developing CD, including those with Down’s syndrome, diabetes, autoimmune hypothyroidism or a family history of CD in first-degree relatives (Murch et al, 2013).

It is currently recommended that serological screening (blood test) for CD is undertaken in children who are symptomatic or those who are asymptomatic but belong to a high-risk group (Box 1) (Husby et al, 2012; Jenkins et al, 2012; NICE, 2009).
Diagnosing CD

Children presenting with symptoms suggestive of CD need to undergo serological screening with immunoglobulin A (IgA)-based anti-tissue transglutaminase (anti-tTG) antibodies (Paul and Spray, 2014; Husby et al, 2012; Kurppa et al, 2012; NICE, 2009). It is important to check the IgA level at the same time, as 1% of children with CD are known to be IgA deficient (Jenkins et al, 2012; NICE, 2009). NICE (2009) recommends that all children with high anti-tTG titres undergo upper gastrointestinal endoscopy and small-bowel biopsies to confirm the diagnosis.

It is important that health professionals explain to parents that their child should remain on a normal diet that contains gluten until the endoscopy and biopsy have been done to ensure false-negative results are avoided. Mucosal healing of the atrophied intestinal villi (finger-like projections found in the small bowel wall) will begin when a child starts on a gluten-free diet (NICE, 2009).

Auto-antibodies react with the gluten and raise an inflammatory reaction in the small bowel wall, which results in the stunting of the villi (Figs 1 and 2). The atrophied villi hamper absorption of important nutrients, as well as fat-soluble vitamins and minerals; this is what can cause faltering growth, iron deficiency anaemia, vitamin D deficiency and osteoporosis, among other conditions.

Guidelines update

European guidance for diagnosing CD in children was modified by the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) in 2012; it now recommends that a diagnosis of CD in a select group of symptomatic children – those with anti-tTG titres of >10 times the upper limit of normal (10xULN) – can be made without a small-bowel biopsy (Husby et al, 2012). This will not only be a less-invasive approach for the child, but the pathway is likely to be financially beneficial to health services.

For a serological diagnosis of CD, however, these children will need positive blood results for IgA-based anti-endomysial antibodies (EMA) and the HLA DQ2/DQ8 haplotype (Husby et al, 2012). However, if the HLA DQ2/DQ8 haplotype or EMA is negative, children who are symptomatic (with anti-tTG titres of >10xULN) will still need to undergo small-bowel biopsies and remain on a normal gluten-containing diet for the diagnosis to be confirmed histologically (Paul and Spray, 2014; Husby et al, 2012).

The modified guidelines from the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) have been endorsed, and adapted with minor amendments, by the British Society of Paediatric Gastroenterology, Hepatology and Nutrition.

![Fig 1. Normal small intestinal mucosa](image1)

![Fig 2. Villous atrophy in coeliac disease](image2)

![Fig 3. Diagnostic pathway](image3)
(BSPGHAN) and Coeliac UK (Murch et al, 2013). Paediatricians and paediatric gastroenterologists in the UK appear to be adhering to this guidance (Paul and Spray, 2014). The amendment to the ESPGHAN guidelines suggests that, for a serological diagnosis of CD in laboratories where EMA testing is unavailable, a sample for a second anti-tTG titre should be sent; this must also be >10xULN (Murch et al, 2013).

The need for a positive HLA DQ2/Q8 haplotype remains unchanged in the BSPGHAN guidelines.

Fig 3 shows an algorithm based on the joint BSPGHAN and Coeliac UK guidelines (Murch et al, 2013) for serological diagnosis of CD in children who are asymptomatic and have an anti-tTG titre of >10xULN.

The modified ESPGHAN guidelines also recommend that children who are symptomatic and whose anti-tTG titre is >10xULN, along with all those who are asymptomatic and have a raised anti-tTG titre (irrespective of the level), will still need an endoscopy and small-bowel biopsy for CD to be diagnosed (Murch et al, 2013; Husby et al, 2012). UK guidelines have accepted the ESPGHAN guidelines for this group of children and small bowel biopsies are necessary for the diagnosis.

Managing CD
The overall management of CD in children remains the same, no matter whether the pathway was used for the initial diagnosis – serological or histological. This includes:

- Adhering to a strict gluten-free diet;
- Ongoing involvement of a specialist paediatric dietitian;
- Follow-up with a paediatrician or paediatric gastroenterologist to ascertain whether symptoms have resolved, anti-tTG titres have normalised, the gluten-free diet is being adhered to and autoimmune associations such as diabetes or hypothyroidism can be identified early (Paul and Spray, 2014).

Considerations for health professionals
Symptomatic children can now be diagnosed with CD without the need for an invasive endoscopy and small-bowel biopsy if their anti-tTG titre is >10xULN.

It is vital that health professionals working with children – for example, school nurses, practice nurses, health visitors and nurse specialists – can:

- Identify symptoms of CD;
- Identify individuals who belong to high-risk groups;
- Ensure serological anti-tTG testing is arranged without delay;
- Explain why it is necessary to continue on a normal diet that contains gluten until a diagnosis of CD is made.

Health professionals play an extremely important role in ensuring that a gluten-free diet is strictly adhered to and that provisions for the regular supply of gluten-free products are easily made available on prescription. Supporting such a diet for school meals and school trips is vital, as accidental exposures can lead to recurrence of symptoms and abdominal pain, along with further mucosal damage and the malabsorption of nutrients.

Children diagnosed at a young age or in their teenage years are at increased risk of non-adherence to the gluten-free diet; this was evident from a nationwide study in Finland (Kurppa et al, 2012) and the same could be true in the UK. It is therefore important to provide these groups with extra support. Specialist nurse-led and dietitian-led CD clinics have been found to be equally effective as those provided by paediatricians or paediatric gastroenterologists in managing children with CD; this may provide better continuity of care and is also appreciated by families (Rajani et al, 2013).

Other autoimmune associations, such as diabetes and hypothyroidism, should also be considered at follow-up. Some symptoms are indicative of these associations (Table 1) so health professionals may consider asking a few questions during a follow-up in outpatient clinics to ascertain whether or not the patient is experiencing any of these.

Conclusion
Improved awareness of CD in children, along with easier availability of specific serological screening tests, enables both the high-risk groups for developing CD to be identified and the condition to be diagnosed earlier. If health professionals work in accordance with the modified ESPGHAN guidelines the diagnostic process is expected to be streamlined by allowing for faster diagnosis in a selective group of symptomatic children, while more will be done to ensure children adhere to a gluten-free diet throughout their lives, thereby managing their CD more successfully.

For more on this topic go online...

- Nutrition in children – growth faltering, food allergy and other common problems
- Bit.ly/NTChildrensNutrition

TABLE 1: OTHER AUTOIMMUNE ASSOCIATIONS WITH CD

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Autoimmune association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increasing tiredness</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Increased toileting, recurrence of bedwetting in older children</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Increased thirst</td>
<td>Diabetes</td>
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<tr>
<td>Excessive weight loss</td>
<td>Diabetes</td>
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<tr>
<td>Excessive weight gain</td>
<td>Hypothyroidism</td>
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<tr>
<td>Deterioration in school performance</td>
<td>Diabetes, hypothyroidism</td>
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<tr>
<td>Constipation</td>
<td>Hypothyroidism</td>
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<tr>
<td>Faltering height gain</td>
<td>Hypothyroidism</td>
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<tr>
<td>Decreasing physical activity, new-onset sedentary lifestyle</td>
<td>Hypothyroidism</td>
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References

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