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GENERAL PRACTICE SUPERVISION AUSTRALIA

FAQ
FREQUENTLY ASKED QUESTIONS

PODCAST WEBINAR

How to teach a registrar about coeliac disease

The complexity of recognising and treating coeliac disease presents many clinical challenges for a GP registrar. Among these are the wide range of clinical manifestations and the potential for an existing gluten-free diet to impact on the accuracy of standard antibody tests. With these factors complicating disease recognition, imagine how daunting it must be for your registrar to diagnose and manage a patient's treatment.

This resource aims to help GP supervisors confidently teach their registrar about when and how to test for the disease and treatment plans for those who receive a positive diagnosis.

What is coeliac disease?

Coeliac disease is an autoimmune condition characterised by chronic inflammation of the small-intestinal mucosa and triggered by eating gluten. It is challenging to diagnose because of the myriad of ways in which it can present in all ages and genders.

SUMMARY OF THE 2013 OSLO DEFINITIONS FOR COELIAC DISEASE	
Classical coeliac disease	Dominated by symptoms, signs and sequelae of gastrointestinal malabsorption. Patients have positive coeliac antibodies and villous atrophy on duodenal biopsy.
Non-classical coeliac disease	The most commonly presenting variant of coeliac disease in which extraintestinal symptoms (such as fatigue) are predominant. There are no overt symptoms of malabsorption. Patients have positive coeliac antibodies and villous atrophy on duodenal biopsy.
Sub-clinical coeliac disease	Patients have no overt symptoms or signs so are below the threshold of clinical detection. They do test positive for coeliac antibodies (usually found on screening at-risk individuals) and evidence of intestinal damage on biopsy.
Potential coeliac disease	Previously known as latent coeliac disease. The diagnosis in patients with positive coeliac antibodies but no histological evidence of intestinal damage.

What key messages should I teach my registrar about coeliac disease?

- Coeliac disease is common and increasing
- Consider testing patients with:
  - – High-risk symptoms/signs or diseases
  - – Family members with coeliac disease
- Test first and test right
- HLA DQ2/8 gene test is useful in select cases
- Biopsy remains essential to diagnosis
- Do not accept "gluten sensitivity" as a diagnosis until other causes have been excluded
- A good dietician is invaluable
- Long-term follow-up is important and simple

What factors contribute to the disease?

Coeliac disease is an immune-mediated systemic disorder elicited by gluten in genetically susceptible people. Your registrar should understand that people who are genetically susceptible will not always develop the disease unless environmental factors trigger the condition. The three key factors for developing the disease are:

1. Dietary gluten – wheat, rye, barley and oats
2. HLA-DQ2/8 and other genes
3. Environmental – Microbiome plus others

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What clinical manifestations occur with this condition?

The chronic inflammation of the intestinal mucosa leads to a wide range of clinical manifestations, including malabsorption and abdominal symptoms and extraintestinal symptoms such as fatigue and skin rashes. In short, coeliac disease causes: autoantibodies; intestinal damage; impaired quality of life; and elevated morbidity and mortality.

Immune

- Autoimmune thyroid disease*
- Type 1 diabetes*
- Addison's disease
- Pernicious anaemia
- Sjogren's syndrome
- Alopecia

Haematologic

- Iron deficiency anaemia*
- Neutropaenia
- Thromobocytopaenia/ thromobocytosis
- Hyposplenism*
- Selective IgA deficiency
- Lymphoproliferative disease (esp T cell lymphomas)

Bone, joints, skin, teeth

- Low-trauma fracture and early-onset osteoporosis*
- Growth failure*
- Polyarthralgias and polyarthritis
- Dermatitis herpetiformis (itchy, blistering rash)
- Dental enamel defects*

Neurologic/psychiatric

- Peripheral neuropathy
- Autonomic instability syndromes
- Migraines
- Depression
- Epilepsy
- Ataxia

Gastrointestinal

- Recurrent oral apthous ulceration*
- Lymphocytic gastritis
- Reflux oesophagitis
- Microscopic colitis
- Pancreatic insufficiency
- Adenocarcinoma of the SI
- Abnormal LFTs, especially mild-modest elevation in transaminases*
- Autoimmune hepatitis
- Primary biliary cirrhosis
- Primary sclerosing cholangitis
- Non-alcoholic fatty liver disease

Obstetric/Gynaecologic

- Infertility (male or female)
- Miscarriage
- Premature delivery
- Intra-uterine growth retardation/low birth weight

Other

- Down's syndrome
- Turner's syndrome
- IgA nephropathy
- Sepsis, especially pneumococcal sepsis

*Common manifestations of coeliac disease

How common is coeliac disease?

It is believed coeliac disease affects 1.5 per cent (about 1 in 70) of the Australian population, however 80 per cent of sufferers remain undiagnosed. It is the most common of the autoimmune diseases: twice as prevalent as type 1 diabetes and more common than rheumatoid arthritis.

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Is it more common in males or females?

A population study in Victoria showed of the one in 70 Australians affected with coeliac disease, one in 60 are females and one in 80 are males. While this may be largely due to sex hormones, there may also be an ascertainment bias affect because men are more likely to seek help for a range of symptoms.

The same study showed GPs are less likely to test males for coeliac disease than a female with the same symptoms. While there is a 'sense' that the disease is less common in males, it is important you encourage your registrar not to underestimate the fact men also develop this disease.

Why do so many people go undiagnosed?

The Victorian-based study showed a frightening statistic: four out of five people (80 per cent) with coeliac disease remain undiagnosed. The disease is challenging to recognise because of the wide range of symptoms and risks. Patients may present with atypical symptoms such as feeling 'out of sorts', poor energy levels, bloating, infertility, headaches etc. There is also a sizeable asymptomatic population which makes the disease a challenge to detect in clinical practice.

Is there a different prevalence in Australia's indigenous and Caucasian populations?

While there have been limited studies on coeliac disease in Australia's indigenous population, the prevalence of HLA-DQ2/8 gene is lower than in the Caucasian population. Therefore, it is believed coeliac disease is less common in our indigenous population.

Is it more difficult to detect and treat the disease in rural locations?

Yes. There are unique issues in rural areas due to lower awareness of the disease and provision of gluten-free foods.

How common is coeliac disease globally?

It is believed 1-2 per cent of the international population has coeliac disease. There has been a four-fold rise in prevalence in the past 60 years in all continents, including increasing reports in Asia due to the adoption of western diets.

What age group is most commonly diagnosed with coeliac disease?

Once regarded as a rare condition affecting children, it is now known that coeliac disease is highly prevalent (but largely undiagnosed) in adults and children. The disease is most commonly diagnosed in adults (median age 40).

Is malabsorption a common presenting feature?

No. See summary of 2013 Oslo definitions for coeliac disease on page 1 of this resource sheet.

Are symptoms triggered by gluten highly specific?

No. GP supervisors should help your registrar understand that gluten-induced symptoms are not a good sign that coeliac disease is present.

Should we be concerned about the people who present in our practice who have not been diagnosed with coeliac disease, but have adopted a gluten-free diet anyway?

It is a clinical challenge for Australia that 10 to 30 per cent of people have adapted their diets because they believe they are wheat or gluten 'sensitive' or have tapped in to a fad mentality that gluten-free is a healthy lifestyle choice.

The challenge in clinical practice is to diagnose those who will medically benefit from a gluten-free diet. Equally, we need to help other patients correctly manage their symptoms if they have needlessly put themselves on a gluten-free diet.

A CSIRO Food and Health Survey, Australia (December 2010 to February 2011) showed 10.6 per cent of respondents avoided products containing wheat, however only 5.7 per cent claimed a formal medical diagnosis for doing so.

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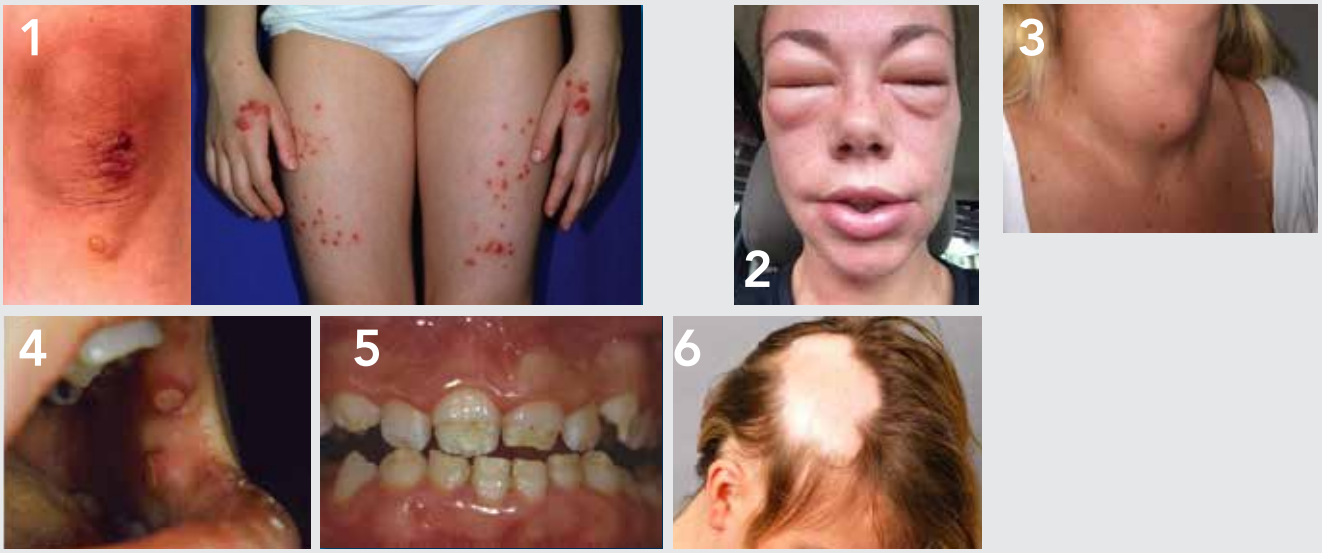
How can I demonstrate to my registrar that a wheat allergy does not imply coeliac disease is present?

The images below are a good example. Ask your registrar to choose which image is the odd one out – that is, which single clinical malifestation is less commonly associated with coeliac disease?

Poll - Which is the odd one out? (single response)



Discuss the clinical manifestations with your registrar. That is, the symptoms are:

Image 1 – Itchy, blistering rash

Image 2 – Substantial facial angioedema

Image 3 – Goita

Image 4 – Mouth ulcer

Image 5 – Dental enamel defects

Image 6 – Alopecia

The clinical malifestation which does not associate with coeliac disease is the facial angioedema in image two. The features in the remaining five images are commonly associated with coeliac disease.

Explain to your registrar that the facial angioedema in image two is seen as an allergy: coeliac disease is an autoimmune disease which does not have an allergic component. The woman photographed in image 2 has a wheat allergy which typically affects young children who grow out of it by their teens. This effect is less prevalent in adults than coeliac disease but there is a condition related to wheat allergy called wheat dependent exercise induced anaphylaxis. Its characteristic history is someone eats wheat, then exercises and develops an allergic response. This response is unrelated to coeliac disease.

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What is required to diagnose coeliac disease?

Diagnosis requires demonstration of villous atrophy

MUST HAVE

1. Gastroscopy and biopsies of small intestine = 

Villous atrophy

AND

Coeliac blood test result *supportive but not essential*

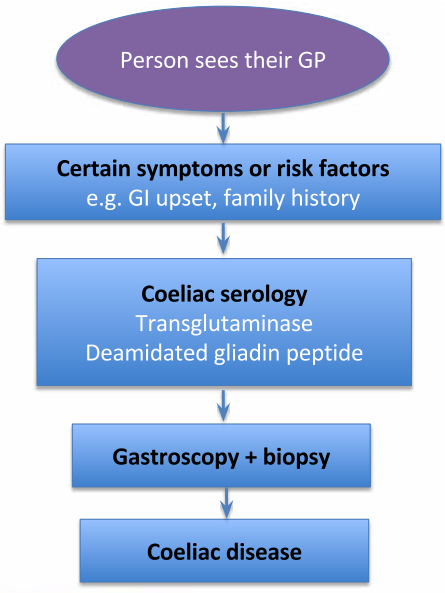
ALSO

2. **Improvement on gluten free diet (BIOPSY,** blood tests, symptoms)

Occasionally, deliberate gluten challenge with re-testing required to establish the diagnosis

ESPGHAN criteria 1990

What diagnostic approach to coeliac disease should I teach my registrar?



Current diagnostic approach

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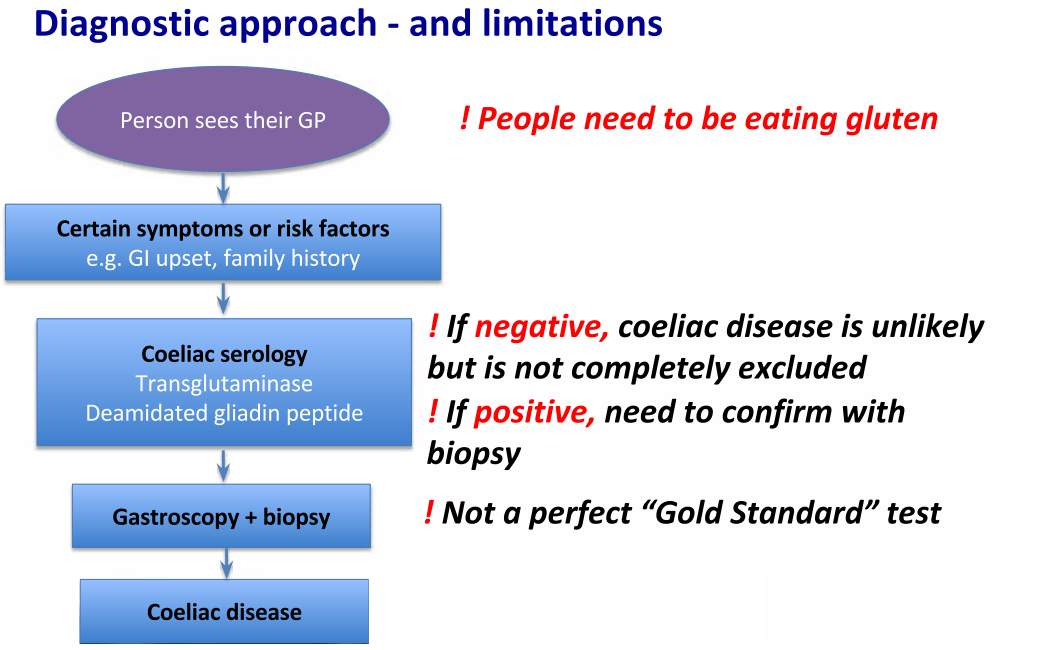
What are the limitations to this diagnostic approach?



When should serological testing be offered for coeliac disease?

NICE guideline NG20, Sept 2015 state **serological testing for coeliac disease should be offered** if:

- Persistent unexplained abdominal or GI symptoms
- Faltering growth
- Prolonged fatigue
- Unexpected weight loss
- Severe or persistent mouth ulcers
- Unexplained iron, vitamin B12 or folate deficiency
- Type 1 diabetes, at diagnosis
- Automimmune thyroid disease, at diagnosis
- Irritable bowel syndrome (in adults)
- First-degree relatives of people with coeliac disease

The NICE guidelines state testing should be considered if:

- Metabolic bone disorder (reduced bone mineral density or osteomalacia)
- Unexplained neurological symptoms (particularly peripheral neuropathy or ataxia)
- Unexplained subfertility or recurrent miscarriage
- Persistently raised liver enzymes with unknown cause
- Dental enamel defects
- Down's syndrome
- Turner syndrome

For more information, visit http://www.nice.org.uk/guidance/ng20

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What should I teach my registrar to request when ordering serological testing?

There are numerous tests, however the combination in Option A (below) is more expeditious than Option B.

Coeliac antibody testing (serology)

1. **Tissue transglutaminase antibody (tTG-IgA)** } **Sensitivity ~ 85-90%**
2. **Deamidated gliadin peptide (DGP-IgG)** } **Sensitivity ~ 85-90%**
3. Endomysial antibody (EMA-IgA) — **No longer widely available**
4. Anti-gliadin antibody (AGA-IgA and IgG) — **Old and inaccurate**

What to request:

Option A. tTG-IgA + DGP-IgG (MBS #71164; $39.90)

Option B. tTG-IgA + Total IgA level (MBS #71163; $24.75)

- Serology is not perfect: false positive and false negatives occur
- Serology cannot diagnose coeliac disease in isolation

Does accurate testing require active gluten consumption?

Yes. Your registrar must understand the importance of ensuring their patient is consuming gluten before ordering tests. Teach your registrar:

- When possible, test BEFORE patients remove dietary gluten
- Testing is still likely to be accurate within a month of commencing a gluten-free diet

  (Note: an "empiric" trial of a gluten-free diet is a bad diagnostic manoeuvre)
- If on a gluten-free diet for more than one month:

  Option 1: Coeliac HLA gene test

  – If gene test negative then coeliac disease can be excluded

  – If gene test positive, then proceed to Option 2

  Option 2: Undertake gluten challenge followed by investigation

  – Optimal challenge amount/duration not determined

  – Encourage regular gluten intake (approaching a "normal diet". That is, 15g gluten/d) for as long as possible (two weeks is sufficient in 70 per cent of cases) (Lefler et al, gut2013)

  – Therefore, suggest 3-6g gluten daily (~2-4 slices bread/day) for 4+ weeks

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Which test will exclude coeliac disease?

The coeliac HLA gene test can help *exclude* coeliac disease

The genes HLA-DQ2 (2.5 or 2.2) and/or HLA-DQ8 are found in:

Coeliac disease: 99.6% | **Community: 40-50%**

Karell et al, Hum Immunol 2003
Tye-Din et al, Int Med J 2015

- Performed on a simple blood test (some labs can do buccal scrape)
- Medicare reimbursed (MBS #71151; $118.85)
- Result does not depend on gluten intake
- **Absence of HLA-DQ2 and DQ8 can exclude the diagnosis**
- **Presence of HLA-DQ2 and/or DQ8 indicates susceptibility to coeliac disease only i.e. *most people with these genes will never develop coeliac disease***

When can HLA typing be helpful?

This gene test can be useful when:

- Patient is gluten free at the time of testing
- Unclear serology or biopsy result
- Patient is not improving on a gluten-free diet
- Determining need to further investigate people at-risk of coeliac disease (for example, if the test shows a gene negative family member, there is no point escalating investigations).

What treatment is necessary for a patient diagnosed with coeliac disease?

- **Strict gluten-free diet** – A challenge for many patients will be food availability, cost and palatability. Education by a dietician (ideally one with expertise teaching the gluten-free diet) will help maximise understanding and food options
- **Nutrient screen and supplementation**
  – Iron, B12, folate, vitamin D, zinc
- **Complication screening**
  – TSH, LFTs, BSL, DEXA
- **Family screening**
  – First-degree relatives have 10 per cent risk
  – Family screening guide at https://www.coeliac.org.au/s/coeliac-disease/family-screening
- **Join state coeliac organisation**
  – Need doctor's letter attesting to need for gluten-free diet
  – Joining template at https://www.coeliac.org.au/s/join-now

MEDICAL REVIEW

- GP review 3-4 monthly in the first year (annually once normalised)
- Antibodies usually normalise by 12 months (increased levels can be a sign of gluten exposure)
- Repeat biopsy at 2 years is important in adults to confirm mucosal disease remission (long-term risks relate to persistent villous atrophy)
- Long-term annual follow-up recommended

Note: CDM (Chronic Disease Management) template available at https://www.coeliac.org.au/s/article/Chronic-disease-management-including-for-children

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Who else can support a registrar in their patient's treatment of coeliac disease?

Encourage your registrar to establish a good relationship with a dietician. A dietician is invaluable in teaching their patient how to maintain a gluten-free diet which is high in fibre and palatable. A dietician will educate a patient diagnosed with coeliac disease how to read labels and about food options when dining at restaurants.

Given that a dietician can educate a person with coeliac disease about the intricacies of managing a gluten-free diet, what key messages should a GP registrar know about reading food labels?

There are four simple rules to remember:

1. If a label says "gluten free", it is gluten free
2. If you cannot see BROW (barley, rye, oats, wheat) on ingredients list, it is gluten free
3. If you see BROW on ingredients list, it is gluten-containing, unless it is an 'ose' (for example, wheat glucose is gluten free). The 'ose' indicates the product has been so highly processed that the basic sugars have been extracted and there is no residual gluten.
4. Check for 'contains' and 'may contain' statements

Shouldn't the four rules (above) be enough for a registrar to educate their patient with coeliac disease?

No. Food labelling is complex and may still 'mask' hidden ingredients.

A dietician should be consulted to help a patient understand the challenges of understanding these labels. Dieticians specialise in such complexities as a product which contains an 'ose' (gluten free) ingredient may still have other hidden sources of gluten. For example, soy sauce may contain wheat glucose syrup (gluten free) and malt vinegar from barley (gluten containing).

In addition, a dietician who can help the patient better understand food labels, may even reveal a range of foods the patient had unnecessarily been excluding.

If there is a small amount of gluten, does the patient need to be so obsessive about not eating that food?

Yes. Ensure your registrar understands that while there is a broad range of sensitivity among patients, even a small amount of gluten (10-50mg, or several crumbs of bread a day) can result in gut damage and other symptoms.

How should registrars manage patients who mention they are on a gluten-free diet because they believe they are wheat sensitive?

Gluten sensitivity can be frustrating for doctors and patients. Many people may wrongly conclude from Dr Google that they have wheat sensitivity. While the patient may be troubled by legitimate symptoms, they may also be frustrated by what they perceive to be dismissive medical care when their doctor has no evidence of gluten sensitivity.

Your registrar needs to understand that FODMAPs are also a major driver of bowel symptoms and investigate for evidence to define and manage gluten sensitivity. Tests may even reveal there is no gluten sensitivity or coeliac disease and reason to cease a patient's self-imposed gluten-free diet.

As a GP supervisor, your registrar needs to be encouraged to seek your support and guidance on this journey with patients who may, or may not, be resistant to treatment.

Does this resource need to be updated? Contact GPSA: P: **03 9607 8590**, E: admin@gpsa.org.au, W: gpsa.org.au
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