Celiac Disease

The one diagnosis where the ORDER of events decides whether you can make it at all

Test first
then change the diet

⚠ THE SEQUENCING RULE *the single most consequential point on this page*

TEST BEFORE THE DIET STARTS

A gluten-free diet normalizes serology and heals the mucosa within weeks to months, so a patient who has already stopped gluten can be neither confirmed nor excluded. They are left with either **a lifelong restrictive diet on no evidence**, or **a missed diagnosis with real complications**. Never suggest a gluten-free trial before the serology is sent.

IF THEY HAVE ALREADY STOPPED

Two options. **Formal gluten challenge**: several weeks of adequate daily gluten before repeat serology and biopsy - many patients decline because symptoms return. Or **HLA-DQ2/DQ8 typing, which is useful ONLY to EXCLUDE**: a negative result makes celiac disease essentially impossible, while **a positive result is common in the general population and proves nothing**.

WHO TO TEST

Unexplained iron deficiency anemia (often the only clue), chronic diarrhea, malabsorption, IBS-type symptoms not responding to standard care, unexplained transaminitis, premature osteoporosis, infertility or recurrent miscarriage. **Associated disease:** type 1 diabetes, autoimmune thyroid disease, Down and Turner syndromes, IgA deficiency, autoimmune hepatitis. **First-degree relatives** (roughly ten-fold risk, often asymptomatic). Do not screen the general population.

THE MECHANISM, BRIEFLY

Gluten peptides deamidated by tissue transglutaminase drive a T-cell response in people carrying HLA-DQ2 or DQ8 (essentially all patients do), producing villous atrophy, crypt hyperplasia and intraepithelial lymphocytosis. That is why the antibody target is tTG, why HLA typing excludes rather than confirms, and why **the disease is one of malabsorption even when the presentation is not obviously intestinal**. Prevalence is roughly 1%, and it remains substantially underdiagnosed.

SEROLOGY AND BIOPSY *two traps, both of which cause false negatives*

Step	Detail
tTG-IgA *first-line*	High sensitivity and specificity, inexpensive -the test to order when ordering only one. **Must be on a gluten-containing diet.** Titer correlates loosely with mucosal damage, and very high levels (≥ 10x upper limit) support the diagnosis strongly
⚠ ALWAYS add total IgA	**Selective IgA deficiency is far more common in celiac disease than in the general population**, and an IgA-deficient patient **cannot make the antibody the test measures** -a falsely negative result in exactly the population you are trying to diagnose. **Low IgA means switching to IgG-based testing** (deamidated gliadin peptide IgG or tTG-IgG). Ordering tTG-IgA alone is a leading reason the diagnosis is missed
EMA-IgA	Highly specific; used to confirm an equivocal tTG
⚠ Duodenal biopsy *confirms in adults*	**At least FOUR biopsies from the distal duodenum plus one or two from the bulb**, because **the disease is patchy** and undersampling is a well-recognized cause of a false negative. Histology: intraepithelial lymphocytosis, crypt hyperplasia, villous atrophy (Marsh graded). Children have a no-biopsy pathway at very high titers; **adults are generally still biopsied**
Villous atrophy is NOT specific	With negative serology and an abnormal biopsy, consider **giardiasis, small intestinal bacterial overgrowth, common variable immunodeficiency, tropical sprue, Crohn disease, autoimmune enteropathy, and olmesartan-associated enteropathy**

PRESENTATION: THE TEXTBOOK PICTURE IS THE MINORITY *which is exactly why it is missed*

MOST ADULTS DO NOT HAVE DIARRHEA

The commonest adult presentations are **extraintestinal**: **iron deficiency anemia unresponsive to oral iron**, fatigue, **osteoporosis or unexplained fracture**, transaminase elevation, **infertility or recurrent miscarriage**, neuropathy, headache. GI symptoms when present are often bloating and pain **labeled IBS for years**. **Dermatitis herpetiformis** -intensely pruritic vesicles on elbows, knees and buttocks- is celiac disease of the skin and diagnostic in its own right (dapsone controls the rash while the diet takes effect; check G6PD first).

AT DIAGNOSIS, LOOK FOR THE CONSEQUENCES

CBC, iron studies and ferritin, B12, folate, vitamin D, calcium -deficiencies are common and often the reason the patient presented. **Liver enzymes** (transaminitis usually resolves on the diet) and **TSH** for the thyroid association. **DEXA**, because celiac disease is a recognized secondary cause of osteoporosis. **Pneumococcal vaccination** for functional hyposplenism. **Screen first-degree relatives** -the diagnosis is a family event.

TREATMENT AND NON-RESPONSE *the diet needs a dietitian, and non-response is usually gluten*

Item	Detail
The diet	**Strict lifelong avoidance of wheat, barley and rye.** Refer to a **celiac-experienced dietitian as part of treatment, not as optional advice**: hidden gluten in sauces, processed foods and medications, plus cross-contamination, is the main cause of failure, and label-reading is a taught skill. **Oats are tolerated by most if certified gluten-free.** Replace iron, B12, folate, vitamin D and calcium; gluten-free products are often unfortified
Set expectations	**Symptoms improve within weeks, but mucosal healing takes months to years in adults and is frequently incomplete** -say this up front so slow recovery is not read as failure
Follow-up	**Recheck tTG-IgA at 6 and 12 months, then annually**: falling titers indicate adherence, a plateau or rise indicates ongoing exposure. **Serology tracks adherence, not healing** -normal antibodies do not guarantee a healed mucosa
⚠ Non-response	**Continued, usually inadvertent, gluten exposure explains the large majority**: re-refer to the dietitian and review medications before anything exotic, and **verify the original diagnosis was actually confirmed**. Then consider **lactose or fructose intolerance, bacterial overgrowth, microscopic colitis, pancreatic exocrine insufficiency, IBS overlap**
Refractory disease	Rare: persistent symptoms and villous atrophy despite 6-12 months of strict adherence. Belongs at a specialist center, and carries a risk of **enteropathy-associated T-cell lymphoma** -so **new weight loss, pain, fever or obstruction in an established patient needs prompt evaluation, not more dietary education**
Why untreated disease matters	Persistent villous atrophy drives **iron, B12, folate and fat-soluble vitamin deficiency; osteoporosis and fracture; infertility and adverse pregnancy outcomes; functional hyposplenism; and a small increased risk of small bowel adenocarcinoma and lymphoma**. **The diet is not a lifestyle preference**, which is the framing patients most often arrive with

PEARLS & PITFALLS

- **Iron deficiency anemia that does not respond to oral iron is a celiac presentation** until proven otherwise -the malabsorption is why the iron is not working.
- **Non-celiac gluten sensitivity is not celiac disease:** symptoms with gluten but negative serology and normal biopsy *on gluten*. No autoimmune enteropathy, no malignancy risk, no need to screen relatives.
- **Wheat allergy is a separate, IgE-mediated entity** with urticaria, angioedema or anaphylaxis and a different testing pathway entirely.
- **A patient labeled celiac without confirmatory testing is common**, and the wrong label costs a lifetime of unnecessary restriction -worth re-verifying before managing "refractory" disease.

References: ACG clinical guideline on the diagnosis and management of celiac disease · AGA clinical practice update on the diagnosis and monitoring of celiac disease · ESPGHAN guidelines for diagnosing coeliac disease (no-biopsy pathway in children) · NASPGHAN and BSG guidance on serologic testing and IgA deficiency.

Educational aid; verify against current guidance, local formulary and patient factors.

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