Gluten for Punishment:
Diagnosing Celiac Disease

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Celiac disease (CD) is a disease of the small intestine, characterized by abnormal small bowel mucosa and is associated with gluten intolerance. Once thought to be a rare GI disorder, studies using serological testing have revealed that CD can be detected in 0.5% to 1% of the general population in certain countries.[1] Although CD is still more frequently diagnosed in persons of Northern European descent, it crosses all racial and ethnic backgrounds.

Gluten and genetics

CD is a human leukocyte antigen- (HLA-) associated disease. Almost all affected patients express HLA DQ2 or DQ8 haplotypes. Ingestion of gluten-containing foods, such as wheat, rye or barley in genetically predisposed patients leads to activation of T lymphocytes, which damage the small intestinal villi. The loss of intestinal villi results in a malabsorption of nutrients and the classic presentation of watery, nonbloody diarrhea and weight loss.

Many patients do not present with classic symptoms of malabsorption, but rather, symptoms suggestive more of irritable bowel syndrome, such as:

- bloating,
- gas,
- cramps,
- fatigue and
- constipation.

Some patients present without any GI symptoms, but are seen for extraintestinal manifestations of the disease (Table 1).

Carmela's case:

- Carmela, a 35-year-old female of Italian origin, is referred for combined iron- and vitamin B12-deficiency anemia
- She admits that she has suffered from watery diarrhea for the past six months, associated with bloating and gassiness
- She has lost 13.6 kg (30 lbs.), despite continuing to eat well
- Her medical history is remarkable only for Grave's disease as a teenager

Table 1
Extraintestinal manifestations of celiac disease (CD)

Hematological	• Iron deficiency anemia • Folate deficiency anemia • Vitamin B12 deficiency
Endocrine	• Short stature • Hypogonadism • Amenorrhea • Infertility • Recurrent miscarriages • Type 1 diabetes
Neurological	• Seizures • Peripheral neuropathy • Cerebellar atrophy • Myelopathy
Miscellaneous	• Dermatitis herpetiformis • Arthritis • Cryptogenic hepatitis • Aphthous stomatitis • Alopecia • Exocrine pancreatic insufficiency • Osteopenia

Table 2
Serological tests for CD

Antibody test	Sensitivity	Specificity
IgA antiendomysial antibody	97% to 100%	98% to 99%
IgA antitransglutaminase antibody	95%	90%
IgA antigliadin antibody (AGA)	52% to 91%	85% to 94%
IgG AGA*	6% to 88%	88% to 92%

**IgA-deficient patients will have false negative serology, except for IgG AGA tests.*

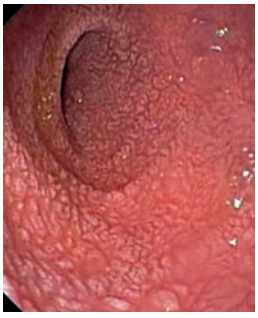

Figure 1. Mucosal fissuring.

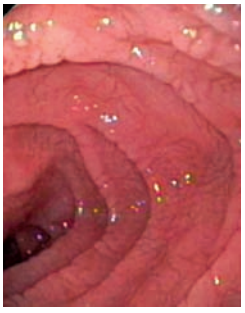

Figure 2. Scalloping of folds.

Because of its greater availability, relatively low cost and very high sensitivity and specificity, antitransglutaminase antibody is the serological test of choice.

Beyond the gut

The hematological manifestations of CD are due to malabsorption of either iron, folate or vitamin B12. Iron is primarily absorbed in the proximal small bowel, the area most affected by CD. Iron-deficiency anemia is common in CD patients, with 25% of untreated patients testing positive on fecal occult blood testing.[1] This can cause some confusion, but it usually resolves on a gluten-free diet.

Osteoporosis, though generally a result of calcium malabsorption, can also be due to vitamin D deficiency—a common effect of CD. Osteoporotic CD patients usually respond to a gluten-free diet, but there can be a considerable lag between improvement in villous atrophy and bone mass. In this case, biphosphonate treatment should be initiated. All newly diagnosed patients should have a bone densitometry.

Dermatitis herpetiformis is a pruritic, papulovesicular rash seen on the knees, elbows, buttocks and back. Ten per cent of patients with CD will develop dermatitis herpetiformis, which also responds to a gluten-free diet, albeit delayed and often necessitating alternate therapy.

Liver test abnormalities are seen in almost half of CD patients and will commonly normalize on a gluten-free diet.

Autoimmune diseases associated with CD include:

- liver diseases,
  - primary biliary cirrhosis
  - autoimmune hepatitis
- Type 1 diabetes,
- thyroid disease and
- joint disease.

Diagnosis of CD

The serological tests (Table 2) for celiac disease have improved dramatically and are the first line in investigation. Because of its greater availability, relatively low cost and very high sensitivity and specificity, antitransglutaminase antibody is the serological test of choice.

A positive blood test should be confirmed by a duodenal biopsy performed simply via a gastroscopy. Endoscopically, there are classic mucosal changes (Figure 1 and Figure 2) that can be identified, but a diagnosis is confirmed by seeing both villous atrophy and increased lymphocyte infiltration on histology. The biopsy must be done prior to initiating treatment as the mucosa may improve leading to an inconclusive analysis. This is especially important if the serology was negative or borderline positive.

Gluten-free diet

The treatment of gluten is simple in theory, but not always in practice. Patients need to avoid all gluten. Gluten is found in all forms of wheat (including durum, semolina, spelt, kamut, einkorn and faro) and related grains, rye and barley. Oats in pure form contain no harmful gluten; however, many oat products are contaminated in the milling process by machines that also process other grains. Therefore, oats in the pure form are acceptable. Patients should be referred to a dietitian and their local celiac support group for assistance.

Take-home message

- Consultation with a skilled dietitian
- Education about the disease
- Lifelong adherence to a gluten-free diet
- Identification of nutritional deficiencies
- Access to an advocacy group
- Continuous long-term follow up by a multidisciplinary team

Family screening

The CD prevalence rate among first-degree relatives is 1:22 and 1:39 among second degree relatives.[2] It is important to do serological screening in higher-risk patients in order to start treatment at an early age. Although there is little data at this time to support this claim, early treatment of CD may prevent the increased risk for cancer[3] (mainly small bowel lymphoma and adenocarcinoma) and autoimmune diseases. Dx

References
1. Shamir R: Advances in celiac disease. Gastroenterol Clin N Am 2003; 32(3):931-47.
2. Fasano A, Berti I, Gerarduzzi T, et al: Prevalence of celiac disease in at-risk and not-at-risk groups in the United States. Arch Intern Med 2003; 163(3):286-92.
3. Green PH, Fleischauer AT, Bhagat G, et al: Risk of malignancy in patients with celiac disease. Am J Med 115(3):191-5.

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