GLUTEN AND CELIAC DISEASE

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**NO DISCLOSURES**
GLUTEN

- From Latin gluten, "glue"
- Protein composite found in wheat and related grains, including barley and rye (oats can be tolerated by most but cross-contamination or hypersensitivity may limit tolerability)
- Gluten is the composite of the storage proteins, gliadin and a glutenin
- Conjoined with starch in the endosperm of various grass-related grains
- True gluten, with gliadin and glutenin, is limited to certain members of the grass family
GLUTEN

- Bread flours are high in gluten
- Pastry flours have a lower gluten content
- Gluten is often the basis for imitation meats
- Gluten is often present in beer and soy sauce
- Stabilizing agent in food products such as ice cream and ketchup
- Gluten is also used in cosmetics, hair products, and other dermatological preparations
WHAT IS GLUTEN?

It is a protein that is primarily found in grains:

- WHEAT
- RYE
- BARLEY
- OATS
THICKENER
- Sauces
- Soups
- Gravy
- Stock cubes
- Marinades
- Processed food

MEAT
- Sausages
- Vienna's
- Burger patties
- Processed meat

CEREAL
- All bran flakes
- Corn flakes
- Barley
- Semolina
- Spelt
- Rye

WHEAT
- Baked goods
- Pasta
- Bread
- Pastry
- Pizza
- Crumbed food
- Battered food
DEFINITIONS

- Non-celiac gluten sensitivity (gluten intolerance)
- Wheat allergy
- Celiac disease (gluten sensitivity)

* No evidence suggests negative side effects occur with gluten consumption outside of the small percentage of the population having gluten sensitivity.
NON-CELIAC GLUTEN SENSITIVITY (GLUTEN INTOLERANCE)

- Syndrome of gastrointestinal responses to gluten different from the immune response characteristic of celiac disease
- No scientific consensus exists to confirm gluten intolerance is a definable pathological condition
- Frequently, symptoms arise in individuals as a result of undiagnosed celiac disease
- Due to a reaction to other components of wheat, such as short-chain, fermentable carbohydrates called FODMAPs
Fermentable Oligo-, Di-, Mono-saccharides and Polyols

**COMMON FOODS CONTAINING FODMAPs**

<table>
<thead>
<tr>
<th>EXCESS FRUCTOSE</th>
<th>LACTOSE</th>
<th>FRUCTANS</th>
<th>GALACTANS</th>
<th>POLYOLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; Fruits</td>
<td>&gt; Milk</td>
<td>&gt; Vegetables</td>
<td>&gt; Legumes</td>
<td>&gt; Fruits</td>
</tr>
<tr>
<td>apples, pears,</td>
<td>cows', goats',</td>
<td>artichokes,</td>
<td>chickpeas,</td>
<td>apples,</td>
</tr>
<tr>
<td>nashi, mangoes,</td>
<td>sheep's milk,</td>
<td>asparagus,</td>
<td>lentils,</td>
<td>apricots,</td>
</tr>
<tr>
<td>tinned fruit</td>
<td>yoghurt, ice</td>
<td>Brussels</td>
<td>kidney beans,</td>
<td>peaches,</td>
</tr>
<tr>
<td>in natural</td>
<td>cream,</td>
<td>sprouts,</td>
<td>beans,</td>
<td>plums,</td>
</tr>
<tr>
<td>juice,</td>
<td>cabbage,</td>
<td>cauliflower</td>
<td>carrots,</td>
<td>prunes,</td>
</tr>
<tr>
<td>watermelon</td>
<td>fennel,</td>
<td>garlic,</td>
<td>leeks,</td>
<td>watermelon</td>
</tr>
<tr>
<td>&gt; Sweeteners</td>
<td>garlic,</td>
<td>eggs,</td>
<td>okra,</td>
<td>&gt; Vegetables</td>
</tr>
<tr>
<td>fructose, high</td>
<td>leeks,</td>
<td>onions,</td>
<td>onions,</td>
<td>avocados,</td>
</tr>
<tr>
<td>fructose corn</td>
<td>(e.g.,</td>
<td>spring</td>
<td>(white Mediterranean)</td>
<td></td>
</tr>
<tr>
<td>syrup</td>
<td>potatoes,</td>
<td>onions,</td>
<td></td>
<td>mushrooms</td>
</tr>
<tr>
<td>&gt; Large total</td>
<td>carrots,</td>
<td>(e.g.,</td>
<td>&gt; Sweeteners</td>
<td></td>
</tr>
<tr>
<td>fructose dose</td>
<td>brussels</td>
<td>Parsnips,</td>
<td>apricots,</td>
<td>apricots,</td>
</tr>
<tr>
<td>concentrated fruit</td>
<td>sprouts,</td>
<td>tomatoes,</td>
<td>peaches,</td>
<td>peaches,</td>
</tr>
<tr>
<td>sources, large</td>
<td>cauliflower</td>
<td></td>
<td>prunes,</td>
<td>prunes,</td>
</tr>
<tr>
<td>serves of fruit</td>
<td></td>
<td></td>
<td>(white</td>
<td></td>
</tr>
<tr>
<td>chews fruit,</td>
<td></td>
<td></td>
<td>kidney</td>
<td></td>
</tr>
<tr>
<td>fruit juice</td>
<td></td>
<td></td>
<td>beans,</td>
<td></td>
</tr>
<tr>
<td>&gt; Honey</td>
<td></td>
<td></td>
<td>beans,</td>
<td></td>
</tr>
</tbody>
</table>

**SUITABLE ON A LOW-FODMAP DIET**

<table>
<thead>
<tr>
<th>FRUIT</th>
<th>VEGETABLES</th>
<th>MILK PRODUCTS</th>
<th>GRAIN FOODS</th>
<th>OTHERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; Fruit</td>
<td>&gt; Vegetables</td>
<td>&gt; Milk</td>
<td>&gt; Cereals</td>
<td>&gt; Sweeteners</td>
</tr>
<tr>
<td>bananas, grapefruit, blueberries, grapes, honeydew melons, kiwi fruit, lemons, limes, mandarins, oranges, pawpaw, passionfruit, tangelo, raspberries, rock melons, strawberries, tangerines</td>
<td>bamboo shoots, broccoli, carrots, celery, capsicum, chokes, choy sum, corn, eggs, green beans, lettuce, chives, parsnips, pumpkins, silver beet, spring onions (green and pink), tomatoes</td>
<td>lactose-free, rice milk</td>
<td>gluten-free bread, cereal products</td>
<td>sugar (sucrose), artificial sweeteners not ending in “-ol”</td>
</tr>
<tr>
<td>&gt; Onion</td>
<td>&gt; Cheese</td>
<td>&gt; Bread</td>
<td>&gt; Rice</td>
<td>&gt; Honey</td>
</tr>
<tr>
<td>garlic</td>
<td>‘hard’ cheeses, and bell and camembert</td>
<td>100% spelt bread</td>
<td></td>
<td></td>
</tr>
<tr>
<td>substitutes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>garlic-infused oil</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

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A wheat allergy causes the immune system to abnormally respond to a component of wheat that it treats as a threatening foreign body. This immune response is often self-limiting and does not cause lasting harm to body tissue.

Wheat allergy and celiac disease are different disorders.
CELIAC DISEASE

- First described by Samuel Gee in 1888
- Recognized by Dutch pediatrician WWII food shortage
- Celiac lesion in proximal small bowel first described 1954
- Intestinal reaction to alpha-gliadin in gluten resulting in a loss of intestinal villi and a disruption of absorption
- Gluten sensitive enteropathy
CELIAC DISEASE

- Classic definition includes the following three features:
  - Villous atrophy
  - Symptoms of malabsorption such as steatorrhea, weight loss or other signs of nutrient or vitamin deficiency
  - Resolution of the mucosal lesions and symptoms upon withdrawal of gluten-containing foods (usually weeks to months)
CELIAC DISEASE: EPIDEMIOLOGY

- Multisystem disease
- 1% or 1/133 persons of US
- 1:70 to 1:300 in most countries
- Primarily in whites of Northern European ancestry
- Not specific to age or gender
- Familial (70% twins and 10% first degree family member)
Celiac Disease is one of the most common genetic autoimmune diseases on the planet!

313,000,000
Million Americans

1 in 133
People have Celiac Disease

97%
Don’t know they have it

9 Years
Average delay in adult diagnosis

www.GlutenFreePrairie.com
CELIAC DISEASE: GENETICS

- Intra familial occurrence and close association with HLA-DQ2 and/or DQ8 gene loci provide basis of current understanding
  - Immune disorder triggered by an environmental agent (gliadin) in genetically predisposed individuals
- HLA-DQ2 (95% of patients) and HLA-DQ8 (5% of patients); Absence of the DQ gene rules out celiac disease with 99% confidence
  - Presence of one of these markers is necessary but not sufficient for diagnosis
- DQ2 and 8 are present in 30-40% of the general Western population, suggesting other factors play a role
Investigators do not know every detail of how the immune system wreaks havoc with the intestinal lining of celiac patients, but they have identified a number of likely processes (below). Colorful arrows indicate events that might be blocked by interventions now being investigated [see table on opposite page].

1. Indigestible fragments of gluten
   Induce enterocytes to release the protein domain, which loosens tight junctions.

2. Indigestible gluten fragment
   Enterocytes

3. Zonulin
   Disrupted junction

4. Tissue transglutaminase (TG), an enzyme released by the damaged cells, modifies the gluten.

5. Antigen-presenting cell
   The gluten induces enterocytes to secrete interleukin-15 (IL-15), which arouses immune cells called intraepithelial lymphocytes against enterocytes.

6. Antigen-presenting cell
   The gluten presents antigens in the modified gluten to enterocytes.

7. Helper T cells
   Helper T cells that recognize the complexes secrete molecules that attract other immune cells and can directly damage enterocytes.

8. Antibodies against gluten
   Antibodies against TG
   B cells release antibody molecules targeted to gluten and TG. These antibodies might cause further damage when they hit their targets on or near enterocytes, but the role of antibodies in the disease is unclear.
CELIAC DISEASE

- Associated disorders (many autoimmune)
  - Endocrine (DM I, autoimmune thyroid, Addison’s, Osteopenia)
  - Mixed connective tissue disease (Sjogren's, RA)
  - Cardiopulmonary (Asthma, Sarcoid, Carditis, pulmonary hemosiderosis, fibrosing alveolitis)
  - Neurological (Seizures, Dementia, Peripheral neuropathy, Psychiatric disorders)
Associated disorders (many autoimmune)

- Skin (Dermatitis, Atopy, Psoriasis)
- Malignancy (Lymphoma, Esophageal, Oropharyngeal)
- Gastrointestinal (GERD, EoE, IBD-UC>CD, microscopic colitis)
- Reproductive (Amenorrhea, Infertility, recurrent spontaneous abortion)
- Immunologic (IgA deficiency)
- Down syndrome
WHAT ARE THE SYMPTOMS OF CELIAC DISEASE?

HAVE THESE SYMPTOMS? DON’T WAIT. GET TESTED.

**ORAL**
- Bad breath
- Gum disease
- Mouth sores
- Mouth ulcers
- Swollen gums
- Tongue sores
- Tooth enamel erosion

**BEHAVIORAL**
- ADD
- Anxiety
- Brain fog
- Depression
- Irritability
- Irrational anger
- Loneliness/isolation
- Loss of interest in activities
- Memory loss
- Mood swings
- Night terrors
- Panic attacks
- Short temper
- Suicidal

**FEMALE-SPECIFIC**
- Breast tenderness
- Early menopause
- Frequent miscarriages
- Hormonal level swings
- Heavy, painful periods
- Infertility
- Swollen bladder/cervix

**SKIN**
- Acne
- Brittle nails
- Bruising
- Burning scalp
- Dark rings under the eyes
- Eczema
- Flakier skin around the eyes
- Hives
- Itching
- Skin cancer
- Skin rashes

**INTESTINAL**
- Acid reflux
- Bloating
- Constipation
- Diarrhea
- Gas that would clean a room
- Loss of appetite
- Nausea
- Stomach pain

**JOINT/MUSCLE**
- Ataxia
- Back pain
- Burning sensation in the joints
- Joint pain/stiffness/swelling
- Leg cramps
- Muscle spasms
- Swelling in hands and feet

**MISCELLANEOUS**
- Asthma
- Bladder infections
- Blurred vision
- Chills & fevers
- Chronic fatigue
- Dandruff
- Coughing
- Dizziness/vertigo
- Fatigue
- Fluctuating weight
- Gerd
- Hair loss
- Headaches
- Heartburn
- Hemorrhoids
- High blood pressure
- Hypothyroidism
- Irregular heartbeat
- Low blood sugar
- Migraines
- Night sweats
- Racing heart
- Seizures
- Sinus pressure
- Sleeping issues

**VITAMIN DEFICIENCIES**
- Anemia (low iron)
- Low calcium
- Low vitamin B12
- Low vitamin D

* Symptoms in red were mentioned the most often

Source:
These symptoms were provided by over 180 people currently living with celiac disease. Only symptoms that were mentioned more than once were listed. To see all of the responses, go to: http://glutendudefoods.com/ideas/your-specific-celiac-symptoms/
CELIAC DISEASE: CLINICAL MANIFESTATIONS

- **May be confused with IBS due to non-specific symptoms**
- Malabsorption (diarrhea, foul smelling stools, weight loss, cramps, fatigue)
- Multisystemic
  - Oral (dental enamel, apthous ulcerations)
  - Labs (IDA, elevated transaminases ALT>AST (~42% of pts with celiac and normalize with gluten free diet, low albumin)
  - Dermatitis herpetiformis
  - Neuropsychiatric disease (HA, peripheral neuropathy, ataxia, depression, anxiety, epilepsy)
CELIAC DISEASE: CLINICAL MANIFESTATIONS

- Higher prevalence osteoarthritis (relationship unknown)
- Metabolic bone disease (osteopenia and osteoporosis)
  - Secondary hyperparathyroidism likely d/t vit D deficiency
- Hyposplenism (mechanism unknown)
  - Prophylactic pneumococcal vaccination suggested
- Kidney disease- glomerular IgA deposition, but rarely have manifestations
- Idiopathic pulmonary hemosiderosis (Lane-Hamilton syndrome)
  - Introduction of gluten-free diet assoc with remission of pulmonary symptoms
DENTAL ENAMEL HYPOPLASIA
DERMATITIS HERPETIFORMIS

- Intensely pruritic papulovesicular rash
- Typically on extensor surface
- Represents intestinal sensitivity to gluten
- Biopsy show granular IgA deposits in the papillary dermis (pathognomonic)
- Responds to gluten-free diet
- Dapsone may help with healing of skin
DERMATITIS HERPETIFORMIS
CELIAC DISEASE: LABORATORY STUDIES

- Anti Gliadin IgG: 75% sensitivity, 97% specificity
  - May also be found in 10-20% of patients with other disease that affect the small intestinal mucosa
  - Helpful for monitoring outcome: always becomes negative with the regrowth of jejunal villi in patients after gluten-free diet

- Anti Endomysial IgA: 97-100% specificity, 85% sensitivity (untreated patients)
  - Can persist in low titers in 10-25% of patients who are treated despite normal histology, or become negative with adherence to gluten-free diet
CELIAC DISEASE: LABORATORY STUDIES

- Anti-transglutaminase IgA (tTG IgA): 100% specificity, 90% sensitivity - best sensitivity and specificity

- Endomysial and transglutaminase can be false negative in those with IgA deficiency (approximately 2.5% of the population; therefore IgA level should always be ordered with serology) and children less than 2 years old

- Any serological tests for celiac disease should be confirmed with a small bowel biopsy
Patient presents with symptoms of celiac disease and is not on a gluten-free diet

Perform serologic IgA tTG antibody testing

Positive result

Small bowel biopsy

Positive result

Diagnosis confirmed; begin gluten-free diet and monitor

Negative result

Follow up on patient; consider other diagnoses; consider repeat biopsy

Negative result

High clinical suspicion for celiac disease?

Yes

Small bowel biopsy

Positive result

Treat as celiac disease and monitor for improvement

Negative result

Diagnosis eliminated; look for other causes that mimic celiac disease

Improvement in symptoms?

Yes

Diagnosis confirmed

No

Evaluate for possible secondary cause of symptoms

Low probability of celiac disease; consider total IgA test to rule out IgA deficiency
CELLIAC DISEASE ENDOSCOPY AND HISTOLOGY
**The Marsh–Oberhuber Classification**

<table>
<thead>
<tr>
<th>Marsh Type</th>
<th>Intraepithelial Lymphocytes per 100 Enterocytes</th>
<th>Crypts</th>
<th>Villi</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&lt;40</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>1</td>
<td>&gt;40</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>&gt;40</td>
<td>Increased</td>
<td>Normal</td>
</tr>
<tr>
<td>3a</td>
<td>&gt;40</td>
<td>Increased</td>
<td>Mild atrophy</td>
</tr>
<tr>
<td>3b</td>
<td>&gt;40</td>
<td>Increased</td>
<td>Marked atrophy</td>
</tr>
<tr>
<td>3c</td>
<td>&gt;40</td>
<td>Increased</td>
<td>Absent</td>
</tr>
</tbody>
</table>

Type 0: Normal mucosa; CD highly unlikely.

Type 1 (Infiltrative lesion): Seen in patients on a gluten-free diet (suggesting minimal amounts of gliadin are being ingested); patients with DH; and family members of patients with CD. However, these patients need to be followed because they may convert to a Type 3 lesion.

Type 2 (Hyperplastic type): Very rare; seen occasionally in DH.

Type 3 (Destructive lesion): Spectrum of changes seen in symptomatic CD (38, 39).
CELIAC DISEASE: HISTOLOGY

- Modified Marsh Classification
  - Type 1: increased intraepithelial lymphocytes but no villous atrophy
  - Type 2: villi still present but shortened
  - Type 3: mild to marked villous atrophy
  - Type 4: lamina propria hypoplasia; no villi
CELIAC DISEASE: TREATMENT

- Gluten-free diet: removal of wheat, rye and barley; Nutrition consult for education
  - Oats do not contain gluten but are often contaminated with gluten during processing
  - Rice, corn, and millet do not contain gluten
- Lactose-free diet initially (the brush border contains lactase which is not functional with sprue)
- Those with continued diarrhea should be examined for other causes of diarrhea
- DDX of non-responders:
  - Incorrect diagnosis (IBS), Continuing gluten intake (restaurants), SBBO, IBD/Microscopic colitis, Pancreatic insufficiency, Lactase deficiency, Lymphoma, Autoimmune enteropathy, Refractory sprue (rare)
CELIAC DISEASE: COMPLICATIONS

- Malignancy: Squamous cell cancer of esophagus, Small bowel adenocarcinoma, Intestinal and Extraintestinal lymphoma (T-cell)
- Rarely asplenia can occur, consider Pneumovax
- Risk of untreated Celiac disease: Infertility, Miscarriage, Epilepsy, Intestinal Lymphoma
CELIAC DISEASE: COMPLICATIONS

- Conditions to consider if previously responsive patients begin to deteriorate:
  - Noncompliance: with gluten-free diet (most common)
  - Lymphoma (T-Cell): most common malignancy complicating celiac disease; Requires high index of suspicion
    - Think about in patients not responding to diet therapy or recurrent weight loss despite diet therapy
    - EGD, CT & exploratory laparotomy may be necessary
Refractory Sprue: Patients do not respond to gluten-free diet, either at onset of diagnosis or becoming refractory with diet adherence.

- No other cause found after thorough investigation
- Some respond to steroids, azathioprine and cyclosporine
- Severe complications include ulcerative jejunitis, collagenous sprue, and lymphoma
Collagenous Sprue: subset of Refractory Sprue; Usually refractory to all forms of therapy other than parenteral alimentation
- Characterized by development of thick band of collagen-like material

Other malignancies with increased risk
- Non-Hodgkin’s lymphoma
- Small bowel adenocarcinoma
- Oropharyngeal and esophageal cancers
LEARN MORE ABOUT CELIAC DISEASE

https://celiac.org

Celiac Disease Symptoms and Conditions Checklist
What is Celiac Disease?
Dermatitis Herpetiformis
Gluten Sensitivity
Diagnosing Celiac Disease
Screening Diagnosis
Treatment and Follow Up
Poorly Responsive Celiac Disease

Celiac Disease and Vaccinations
Celiac Disease and Diabetes
Celiac Disease and Crohn’s Disease
Future Therapies for Celiac Disease
Research
Research Studies
Celiac Disease in the News
CELIAC DISEASE FOR PRACTITIONERS

- [https://celiac.org/celiac-disease/provider-directory](https://celiac.org/celiac-disease/provider-directory)
  - Be Listed in the CDF Healthcare Practitioner Directory
  - Earn CME in Celiac Disease
  - Earn CME in Gluten-Related Disorders

- [https://stanfordhealthcare.org/content/dam/.../pdf-lowfodmapdiet.pdf](https://stanfordhealthcare.org/content/dam/.../pdf-lowfodmapdiet.pdf)
  - Download fodmaps diet for patients
Shopping

- **Allergy & Gluten Free Diet Tracker by Fooducate**: Use your smart device to automatically scan a product barcode, search for products, or browse by category. See if a product contains one of the following allergens: gluten, peanuts, tree nuts, fish, shellfish, egg, milk, lactose or soy. The “One Click” button option to directly call the manufacturer for additional product information is an added bonus.

- **Gluten-Free Groceries by Triumph Dining**: Touted as the “yellow pages of gluten-free food,” this app allows you to find gluten-free groceries with the flick of a finger. The app lists more than 30,000 gluten-free products from popular brands to smaller specialty companies.

- **Is That Gluten Free?**: Grocery shop safely with a database of more than 20,000 manufacturer-verified gluten-free products from more than 660 brands. Easily search by categories, brands, ingredients, or keyword.
CELIAC APPS

Eating Out

- **AllergyEats Mobile**: This user-friendly resource provides valuable peer-based feedback about how well (or poorly) restaurants accommodate the needs of food-allergic diners. You can customize your search by selecting from the top 10 allergens (gluten, wheat, corn, dairy, eggs, fish, peanuts, shellfish, soy and tree nuts), entering a specific location, or choosing the “Find Near Me” option. Free, allergyeats.com

- **Dine Gluten Free**: Find and read detailed peer reviews of thousands of “gluten-free-friendly” businesses in the U.S. and around the world. The reviews are searchable by location and include restaurants, bakeries, markets, hotels, B&Bs, cruises and even colleges. Free, glutenfreetravelsite.com

- **Find Me Gluten Free**: Search for gluten-free dining options by entering a specific location or browse the “Popular Chains” option, which includes links to the chain restaurants’ websites and gluten-free menus. The “User Reviews” share valuable information and tips. Free, findmeglutenfree.com

- **iCanEat OnTheGo Gluten Free & Allergen Free**: This app is perfect for those seeking quick-service meals. With 34 U.S. chains from Boston Market, Chick-fil-A and Chipotle to Pei Wei, Qdoba and more; you enter your allergen concerns into the 3,900-plus-item fast food menu database.

- **iEatOut Gluten & Allergen Free**: This “ethnic restaurant” focused gluten-free and allergy-friendly app allows you to explore seven ethnic restaurant cuisines including Chinese, French, Indian, Italian, Mexican, steak and seafood, and Thai. Browse menu choices, ingredients, sauces, food preparation and cross-contamination considerations to avoid any combination of food allergens.
Celiac disease affects 1% of healthy average Americans. That means at least 3 million people in our country are living with celiac disease. 97% of them are undiagnosed.
THANK YOU
clepane@hotmail.com