Gluten Related Disorders: People Shall Not Live on Bread Alone

WEBINAR

Faculty

Alessio Fasano, MD
Visiting Professor of Pediatrics
Harvard Medical School
Chief of Pediatric Gastroenterology and Nutrition
MassGeneral Hospital for Children
Director, Center for Celiac Research
Director, Mucosal Immunology and Biology
Research Center
Massachusetts General Hospital
Boston, Massachusetts

Pam Cureton, RD, LDN
Chair, Dietitians in Gluten Intolerance Diseases (DIGID)
Center for Celiac Research at MassGeneral
Boston, Massachusetts
University of Maryland Celiac Program
Baltimore MD

Objectives

Suggested CDR Learning Codes: 3000, 5000, 5110, 5220; Level 2

1. Identify clinical, epidemiological, and diagnostic characteristics of celiac disease, wheat allergy, and gluten sensitivity

2. Learn the most cost effective means of testing for gluten related disorders

3. List similarities and differences in implementing a gluten free diet for the three different forms of gluten-related disorders
Celiac Disease

- The most common genetically—induced food intolerance worldwide, with a prevalence around 1% (and growing!)
- An autoimmune condition triggered and sustained by the ingestion of gluten (wheat, rye, barley) in genetically predisposed individuals
- Causes an inflammatory damage of the mucosa of the small intestine resulting in a variety of clinical presentations
- Left untreated may lead to complications and increased mortality

Celiac Disease: Pathogenesis of a Model Immunogenetic Disease

HLA-DQ2, DQ8 Are Necessary But Not Sufficient

USA General Population

Individuals with Celiac Disease

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“Typical” Celiac Children

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The Gastrointestinal Presentation

- Diarrhea
- Vomiting
- Failure to thrive or weight loss
- Abdominal bloating/pain
- Constipation
The Extra-Intestinal Presentations

- Dermatitis Herpetiformis and other skin disorders
- Short Stature (15% of our pts!)
- Delayed Puberty
- Dental enamel hypoplasia
- Osteopenia
- Iron-deficient anemia resistant to oral Fe
- Liver and biliary tract disease (High transaminases)
- Arthritis
- Neurological problems
  - Headaches
  - Peripheral Neuropathy
  - “Gluten Ataxia”
- Fatigue
- Behavioral changes/Psychiatric Disorders
- Reduced female fertility or pregnancy adverse events

Current Classification of Celiac Disease Presentations

<table>
<thead>
<tr>
<th>Type</th>
<th>Serology</th>
<th>Age affected</th>
<th>Symptoms</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal</td>
<td>Positive</td>
<td>Toddler, Young Child</td>
<td>Abdominal Pain, Diarrhea, Vomiting</td>
<td>Marsh 2-3</td>
</tr>
<tr>
<td>Extra-Intestinal</td>
<td>Positive</td>
<td>Older Child Adult</td>
<td>None</td>
<td>Marsh 1-3</td>
</tr>
<tr>
<td>Silent</td>
<td>Positive</td>
<td>All Ages</td>
<td>None</td>
<td>Marsh 2-3</td>
</tr>
<tr>
<td>Latent</td>
<td>Positive or Negative</td>
<td>Mostly Adults</td>
<td>None</td>
<td>Marsh 3-1 (may or may not develop enteropathy if left on gluten)</td>
</tr>
</tbody>
</table>

Celiac Disease Is More Frequent In:

- Autoimmune disorders
  - Type 1 diabetes
  - Autoimmune Thyroiditis...
- Relatives of a celiac
- Genetic syndromes
  - Down
  - Turner
  - Williams
Who Should Be Screened?

- Subjects with suggestive GI complaints
  - Diarrhea (+FTT)
  - Vomiting
  - Anorexia
  - Abdominal distention
  - Recurrent abdominal pain
  - Constipation

- Subjects with extra-intestinal manifestations
  - Dental enamel dysplasia
  - Short stature
  - High Transaminases
  - Fe-deficient anemia (unexplained)
  - Fatigue
  - Arthritis....

Gluten Related Disorders Webinar

Wheat Allergy

IgE-Mediated Wheat Allergy

- Food allergy, by definition, depends on an underlying immune-mediated process for its occurrence
- Food allergy is most common in the first year of life, decreasing in adolescence and adulthood
- Wheat is among the 10 most common allergens responsible for food allergy
- Prevalence rates in the first 3 years of life range 3-8%
- Most common allergens are milk, egg, corn and peanuts
- Discrepancy between parent’s reports of suspected allergy and objective tests
- Clinical manifestations include: abdominal pain, nausea, vomiting, diarrhea, skin rashes, rhinitis, conjunctivitis

Gluten Related Disorders Webinar

Non-Celiac Gluten Sensitivity

The Gluten Free Diet: Not Only Celiac Disease

Gluten Free Diet Consumers

Medical Necessity

No Medical Necessity

Wheat Allergy (IgE-mediated) (~0.1%)

Celiac Disease (Autoimmune-based) (~1%)

Gluten Sensitivity (Immune?) (~?%)

Cases of gluten reaction in which both allergic and autoimmune mechanisms have been ruled out (diagnosis by exclusion criteria)

• Negative immuno-allergy tests to wheat;
• Negative CD serology (EMA and/or tTG) and in which IgA deficiency has been ruled out;
• Negative duodenal histopathology;
• Presence of biomarkers of gluten immune-reaction (AGA+);
• Presence of clinical symptoms that can overlap with CD or wheat allergy symptomatology;
• Resolution of the symptoms following implementation of a GFD (double blind)

Symptoms:

- Abdominal pain: 68%
- Eczema and/or rash: 40%
- Headache: 35%
- "Foggy mind": 34%
- Fatigue: 33%
- Diarrhea: 33%
- Depression: 22%
- Anemia: 20%
- Numbness legs/arms/fingers: 20%
- Joint pain: 11%

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Proposed New Classification of Gluten Related Disorders

**Biomarkers**

- YES
- NO

**Pathogenesis**

- Autoimmune
- Allergic
- Not Autoimmune
- Not allergic

(Celiac Disease)

Gluten-Related Disorders

Gluten-Ataxia

Dermatitis Herpetiformis

Wheat Allergy

Gluten Sensitivity

Respiratory Allergy

Food Allergy

Contact Urticaria

Typical

Atypical

Latent

Silent

Potential

Diagnosis of Celiac Disease vs. Wheat Allergy vs. Non Celiac Gluten Sensitivity
Poll Question

• In a patient with symptoms of celiac disease but negative serological tests, would you advise a trial of a gluten free diet?

A. Yes
B. No

Serological Tests

- Antigliadin – IgA & IgG
- Endomysium – IgA (IgG)
- Tissue Transglutaminase – IgA (IgG)
- Deamidated Gliadin Peptides – IgA & IgG
Poll Question Results

- In a patient with symptoms of celiac disease but negative serological tests, would you advise a trial of a gluten free diet?

A. Yes
B. No

How to Test?

- tTG - IgA
- AGA tests
- Serum IgA
- IgA - deficiency
- HLA tests

The young child

Intestinal Biopsy

Serology Positive
Serology Negative

Differential Diagnosis Between CD, GS, & WA

<table>
<thead>
<tr>
<th>Time interval between gluten exposure and onset</th>
<th>Celiac Disease</th>
<th>Gluten Sensitivity</th>
<th>Wheat Allergy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weeks-Years</td>
<td>Autoimmunity (Innate + Adaptive immunity)</td>
<td>Autoimmunity? (Innate?)</td>
<td>Allergic Immune Response</td>
</tr>
<tr>
<td>Pathogenesis</td>
<td>HLA DQ2/8 restricted (~97% positive cases)</td>
<td>Not-HLA DQ2/8 restricted (50% DQ2/8 positive cases)</td>
<td>Not-HLA DQ2/8 restricted (35-40% positive cases as in the general population)</td>
</tr>
<tr>
<td>Autoantibodies</td>
<td>Always present</td>
<td>Always absent</td>
<td>Always absent</td>
</tr>
<tr>
<td>Enteropathy</td>
<td>Almost always present</td>
<td>Always present</td>
<td>Always absent</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Both intestinal and extraintestinal (not distinguishable from CD and WA with GI-symptoms)</td>
<td>Both intestinal and extra-intestinal (not distinguishable from CD and WA with GI-symptoms)</td>
<td>Both intestinal and extra-intestinal (not distinguishable from CD and WA when presenting with GI symptoms)</td>
</tr>
<tr>
<td>Complications</td>
<td>Co-morbidities Long-term complications</td>
<td>Absence of co-morbidities and long-term complications (long follow-up studies needed to confirm it)</td>
<td>Absence of co-morbidities. Short-term complications (including anaphylaxis)</td>
</tr>
</tbody>
</table>
Treatment

Gluten Free Diet: Overview

<table>
<thead>
<tr>
<th>Treatment: GFD</th>
<th>Celiac Disease</th>
<th>Gluten Sensitive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Strict adherence to GFD</td>
<td>&lt;10 mg / day</td>
<td>?</td>
</tr>
<tr>
<td>Life Long</td>
<td>Yes</td>
<td>?</td>
</tr>
<tr>
<td>Improvement of symptoms on GFD</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Consequence of non-compliance:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical symptoms</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Intestinal damage</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Monitored by bio marker</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Co morbidities</td>
<td>Yes</td>
<td>?</td>
</tr>
</tbody>
</table>

Gluten Containing Ingredients to Avoid

Wheat
Barley
Rye
Wheat Bran
Wheat Starch
Wheat Germ
Barley Malt / Extract

Other Types of Wheat:
Spelt
Kamut
Emmer
Einkorn
Semolina
Faro
Bulgur
Couscous
Triticale

Durum
Frequently Overlooked Foods That May Contain Gluten

- Broth
- Candy
- Communion wafers
- Imitation bacon
- Imitation seafood
- Marinades
- Processed meats

Gluten Free Food Labeling

In 2004, the Food Allergen Labeling and Consumer Protection Act (FALCPA) requires that companies identify in “plain English” the eight most prevalent food allergens:

- egg, fish, milk, peanuts, shell fish, soybean, tree nuts and WHEAT

Including the ingredient list with parentheses

- Ingredients: Enriched flour (wheat flour, malt flavoring, niacin, reduced iron, thiamin mononitrate, riboflavin, folic acid), sugar, partially hydrogenated soybean oil, high fructose corn syrup, whey (milk), eggs, salt, leavening

Use a “Contains” statement

- Contains Wheat, Milk, Egg, and Soy

FALCPA Does Not Include...

1. Barley (malt), rye or oat (but not “hidden” ingredients)

2. Meat products covered by USDA, including meats, poultry and certain egg products (although 90% of manufactures follow FALCPA-guidelines)

3. FALCPA covers ingredients not the contamination of the product (oats)

4. Over the counter or prescription medications (www.glutenfreendrugs.com)

5. Alcoholic beverages (Distilled beverages are gluten free)
FALCPA...Shopping Made Easier!

- For foods regulated by the FDA, the consumer should look for the terms in products not labeled gluten free:
  - Wheat
  - Barley
  - Malt
  - Rye
  - Oats
  - Brewer’s yeast

Poll Question

Do you advise your patients not to purchase an item with the statement: Manufactured in a facility that contains wheat?

A. Yes
B. No

Allergen Advisory Statements

“Manufactured in a plant that contains wheat”

- Voluntary statements manufacturers use in labeling their products that could indicate the “potential” unintended presence of a food allergen

- Not reliable way to determine whether a food product is contaminated with gluten.
  
  Products with this statement have been tested to less than 5 ppm while other products with no statement test above 20 ppm
**Poll Question Results**

Do you advise your patients not to purchase an item with the statement: Manufactured in a facility that contains wheat?

A. Yes
B. No

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**The Gluten Free Rule is Finally Here!**

Summary of the FDA Gluten Free Label Rules enacted August 2013

- A food label gluten free must:
  - Be inherently gluten free (raw vegetables, water, 100% juice)
  - Does not contain an ingredient that is a gluten containing grain such as wheat, rye, barley
  - Does not contain an ingredient derived from a gluten containing grain that has not been processed to remove gluten
  - May contain an ingredient derived from a gluten containing grain that has been processed to remove gluten (wheat starch) as long as the food does not contain more than 20 ppm gluten
  - The food product contains less than 20 parts per million gluten
- Any unavoidable presence of gluten in the food is less than 20 ppm gluten

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**Summary of the FDA Gluten Free Label Rules**

- Terms synonymous with gluten free are:
  - No gluten
  - Free of gluten
  - Without gluten
- Oats are not considered a gluten containing grain
- Applies to foods that are regulated by the FDA
  - Does not cover pet food, cosmetics, drugs, foods regulated by the USDA and beverages regulated by Alcohol Tobacco Tax and Trade Bureau (TTB)
- Manufacturers are not required to test either the ingredients or the end product.
- Manufacturers must be in compliance with the rule by August 2014
Relationship Between Gluten Amount and Disease Activity

<table>
<thead>
<tr>
<th>0</th>
<th>10</th>
<th>500 mg</th>
<th>1g &gt; 1 g of gluten/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal biopsy</td>
<td>Normal serology</td>
<td>Minor/small intestinal Damage</td>
<td>Altered biopsy</td>
</tr>
<tr>
<td>Normal serology</td>
<td>Symptoms generally absent (beside some “hypersensitive” cases)</td>
<td>Normal serology or rarely altered</td>
<td>Abnormal serology</td>
</tr>
<tr>
<td>Symptoms generally absent</td>
<td>Altered biopsy</td>
<td>Symptoms generally absent</td>
<td>Symptoms sometimes present</td>
</tr>
</tbody>
</table>

Translating 20 ppm

20 parts per million = 2 mg/100 gm (<0.002%)

1 slice of Bread = 2500 mg of gluten or 125,000 ppm gluten

One minute in two years

Tolerable Daily Intake of Gluten and ppm of Gluten in Food for Celiacs

<table>
<thead>
<tr>
<th>50 g</th>
<th>100 g</th>
<th>200 g</th>
<th>300 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>200 ppm</td>
<td>10 mg</td>
<td>20 mg</td>
<td>40 mg</td>
</tr>
<tr>
<td>100 ppm</td>
<td>5 mg</td>
<td>10 mg</td>
<td>20 mg</td>
</tr>
<tr>
<td>50 ppm</td>
<td>2.5 mg</td>
<td>5 mg</td>
<td>10 mg</td>
</tr>
<tr>
<td>20 ppm</td>
<td>1 mg</td>
<td>2 mg</td>
<td>4 mg</td>
</tr>
</tbody>
</table>
Nutritional Aspects of the GFD

- The GFD can be missing important nutrients needed for optimal health and wellness
  - Lacks fiber
  - Lacks iron
  - Lacks B vitamins - folate, niacin, B12
  - Lacks calcium
  - Phosphorus
  - Zinc
- Nutrition deficiencies lead to:
  - Iron deficiency anemia
  - Reduced bone mineral density
  - Constipation
- Many gluten free foods are not enriched or fortified as their wheat counterpart
- Weight gain on GFD can be due to high fat, sugar and calorie content

Relevant Standard CD Labs

- CBC (hemoglobin, hematocrit, etc)
- 25 OH Vitamin D
- B12
- Folate
- Iron and Ferritin
- Zinc
- Lipids
- Total IgA, IgA-tTG
- Magnesium
- Calcium

<table>
<thead>
<tr>
<th>As Needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parathyroid hormone</td>
</tr>
<tr>
<td>Folate</td>
</tr>
<tr>
<td>Other B vitamins</td>
</tr>
</tbody>
</table>

Common Nutritional Problems on GFD

- Lactose intolerance
  - 30-60% in newly diagnosed
  - Caused by intestinal injury in untreated CD
  - May resolve on GF diet
- Constipation
  - Change in diet, low fiber from high fiber can cause constipation: abdominal pain, cramping, bloating
- Weight gain
Weight Gain Research

Dr. Dan Leffler and colleagues showed that weight does change on the gluten-free diet:
- 679 subjects, whose diet adherence was scored by an expert dietitian
  - Type of presentation, i.e. GI vs non-GI, was not linked to average baseline BMI or diet adherence
  - 15.8% of subjects who began the study at a low or normal BMI increased to an overweight BMI
  - 22% of subjects who were overweight at the time of diagnosis also gained weight
  - The more closely subjects followed the gluten-free diet, the more likely they were to gain weight…however, there is a link between obesity at diagnosis and subsequent poor dietary adherence


Reasons for Weight Gain

- Weight gain on a gluten-free diet is due to a number of factors:
  - Better absorption and healing of the intestine
  - Patients feel better, and therefore eat more
  - Higher calorie food items on the gluten-free diet, i.e. packaged, processed foods
  - “Portion distortion” - patients who were undiagnosed were often able to eat larger portions without gaining weight

“Non-responsive” Celiac Disease

Persistent or recurrent signs/symptoms despite confirmed & treated CD occurs in ~10% of patients (range 10 – 30%)

- Gluten Exposure 36 – 51%
- IBS 18%
- Refractory 2%
  - Type 1 benign prognosis, more common
  - Type 2 refractory very rare, associated with T-cell lymphoma
- Diimnosaccharidase Deficiency 9%
- Microscopic Celitis 7%
- Small Intestinal Bacterial Overgrowth 6%
- Eating Disorder 6%
- Other 8% Peptic ulcer disease, Crohn’s disease, Food allergy, Gastroparesis
Gluten Exposure

- Recheck labels of favorite everyday foods as ingredients can change. Check label of foods not labeled gluten free for ingredients.
- Look for sources of contamination at home and away from home.
  - Toaster, condiment containers, colanders
  - Meal prep: making gluten free along side gluten containing foods
  - Eating at restaurants, school, daycare or social events

Barriers to Compliance

- Diet too restrictive
  - Cross contamination
  - No allowance for occasional “cheating”
- Uncomfortable in social setting
  - Dining away from home
  - Religious considerations
- Too expensive
  - Gluten free foods can be 3-5X more expensive than their wheat counterpart
- Tasteless
- Too difficult
  - Elderly
  - Illiterate
  - Mental/psychological impairment

Academy of Nutrition and Dietetics Resources

- Evidence Analysis Library (EAL) on CD
  - www.adaevidencelibrary.com
- Celiac Disease Toolkit
  - Companion to AND’s EAL on CD
- Dietitians in Gluten Intolerance Diseases (DIGID)
  - a subunit of the Medical Nutrition Practice Group
    - www.mnpdg.org
Books and Guides

• NASPGHAN Foundation Book: A Clinical Guide to Gluten-Related Disorders
  by Alessio Fasano
• Celiac Disease Nutrition Guide
  by Tricia Thompson
• ADA Pocket Guide to Gluten-Free Strategies for clients with Multiple Diet Restrictions
  by Tricia Thompson
• Gluten Free Diet Guide for Families (English and Spanish)
  by NASPGHAN Foundation

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2. Click “Continue” on the webinar description page. Note: You must be logged-in to see the “Continue” button.
3. Select the Evaluation icon to complete and submit the evaluation.
4. Download and print your certificate.

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