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# Gluten Related Disorders: People Shall Not Live on Bread Alone

**WEBINAR**

# Faculty



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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

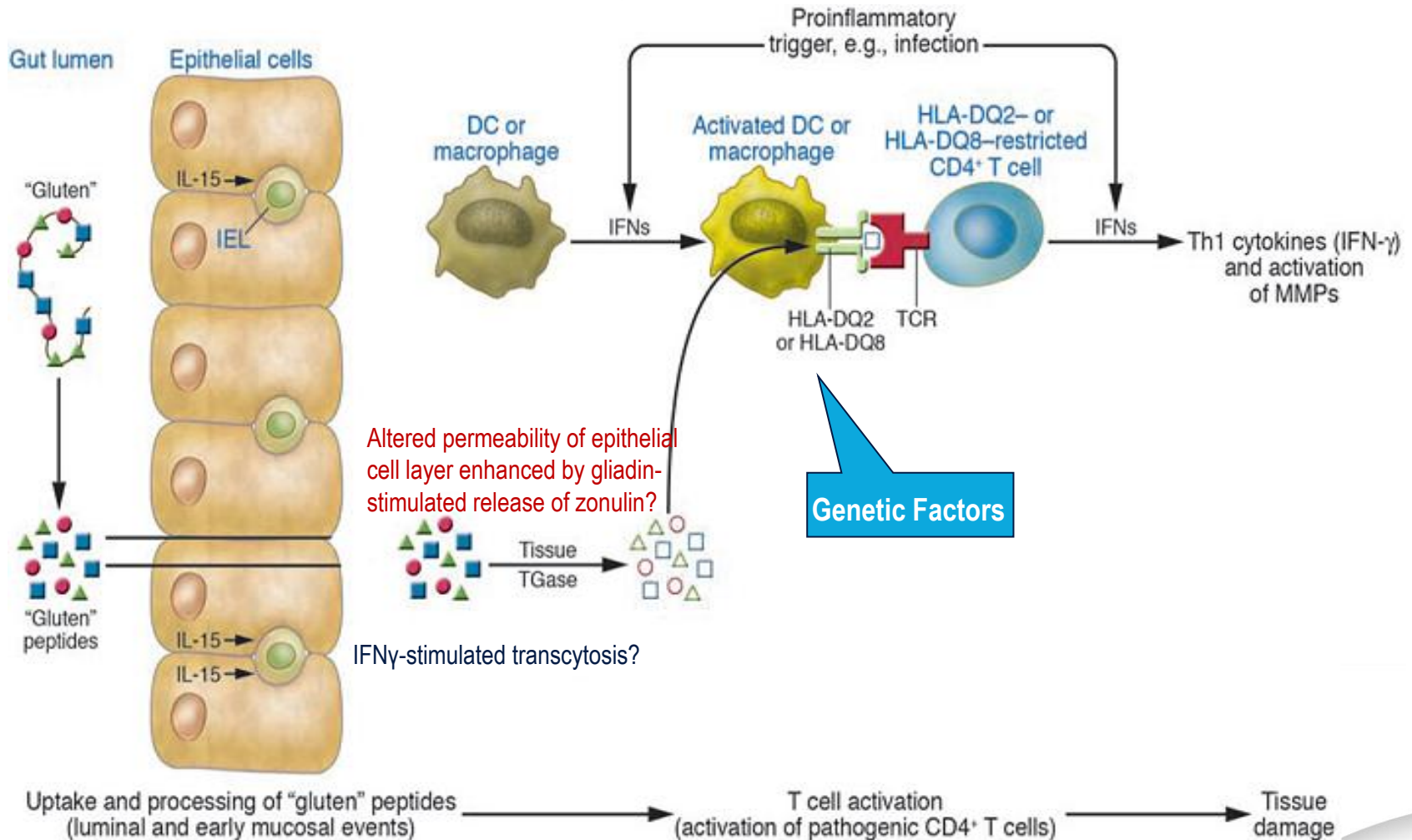
**Gluten Related Disorders Webinar**

# Celiac Disease

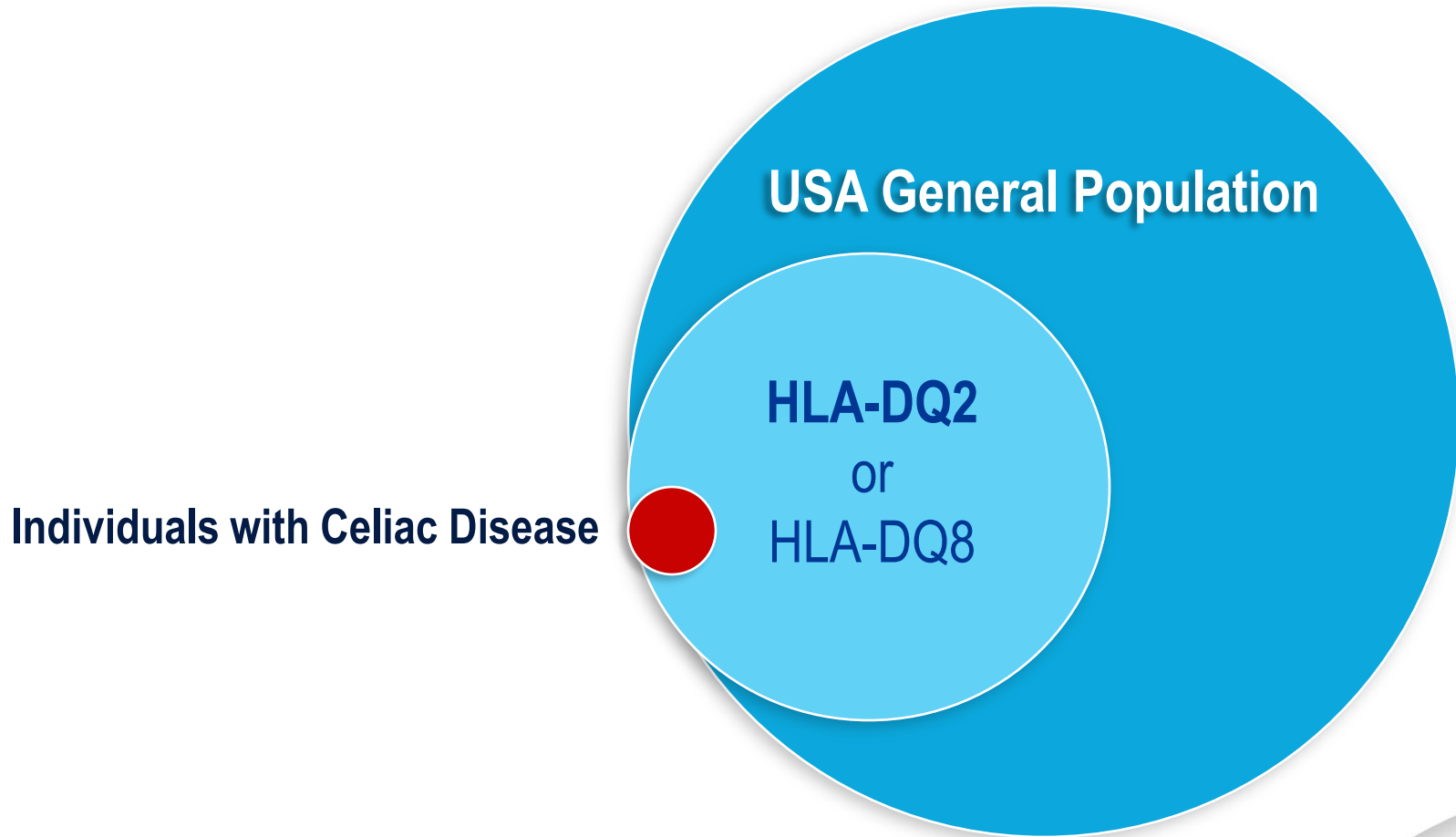
# Celiac Disease

- 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

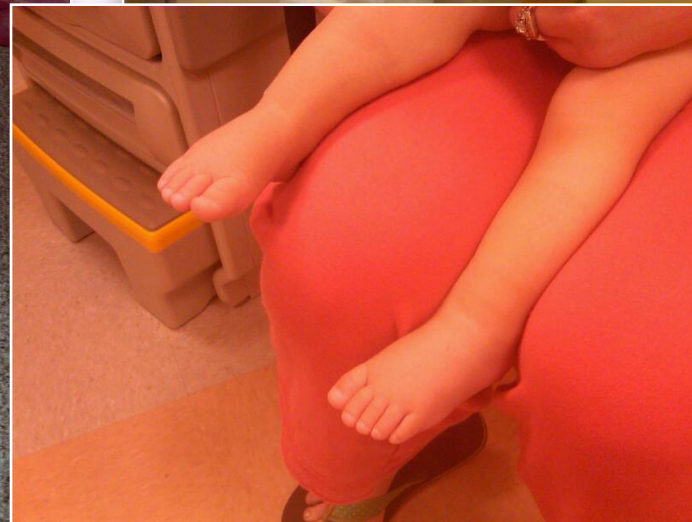
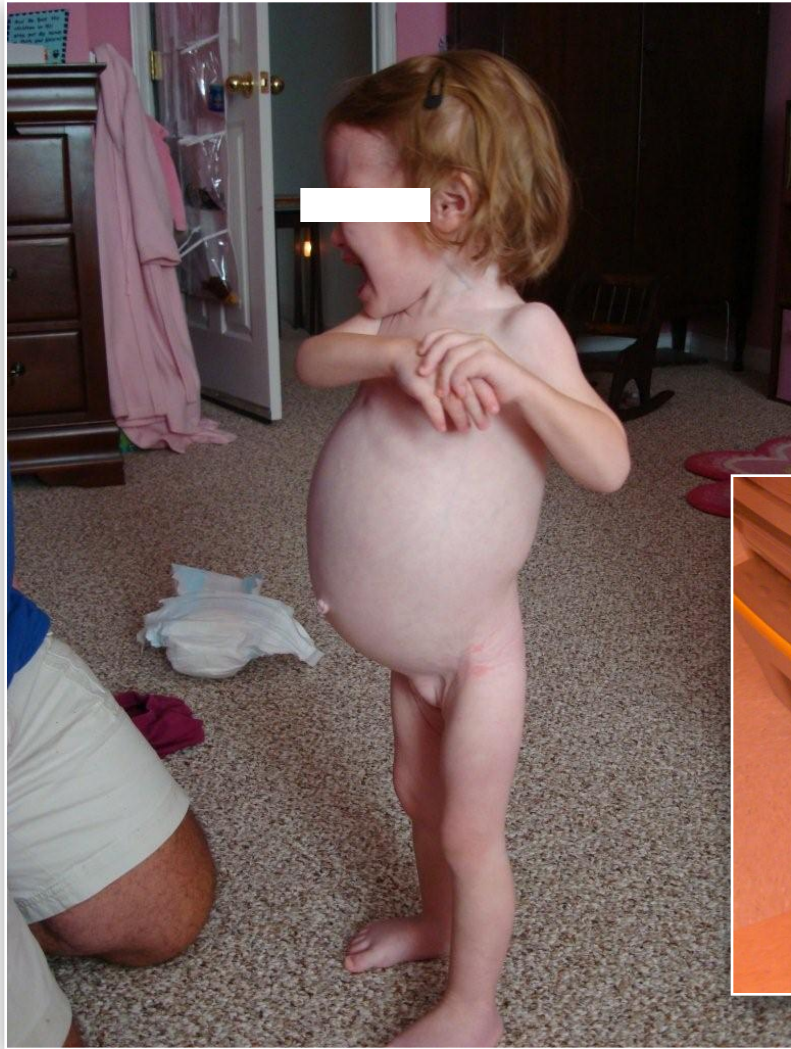


# HLA-DQ2, DQ8 Are Necessary But Not Sufficient





# “Typical” Celiac Children





# 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

Type	Serology (tTG and/or EMA)	Age affected	Symptoms	Pathology
<b>Intestinal</b>	Positive	Toddler, Young Child	Abdominal Pain, Distention Diarrhea Vomiting Anorexia Constipation	Marsh 2-3
<b>Extra-Intestinal</b>	Positive	Older Child Adult	Mostly extra-intestinal	Marsh 1-3
<b>Silent</b>	Positive	All Ages	None	Marsh 2-3
<b>Potential</b>	Positive	Any age	None Gastrointestinal Extra-intestinal	Marsh 0-1 (may or may not develop enteropathy if left on gluten)
<b>Latent</b>	Positive or Negative	Mostly Adults	None Gastrointestinal Extra-intestinal	Marsh 0-1 (previously had gluten-dependent enteropathy)

# 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 ( $\pm$ 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....

# 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

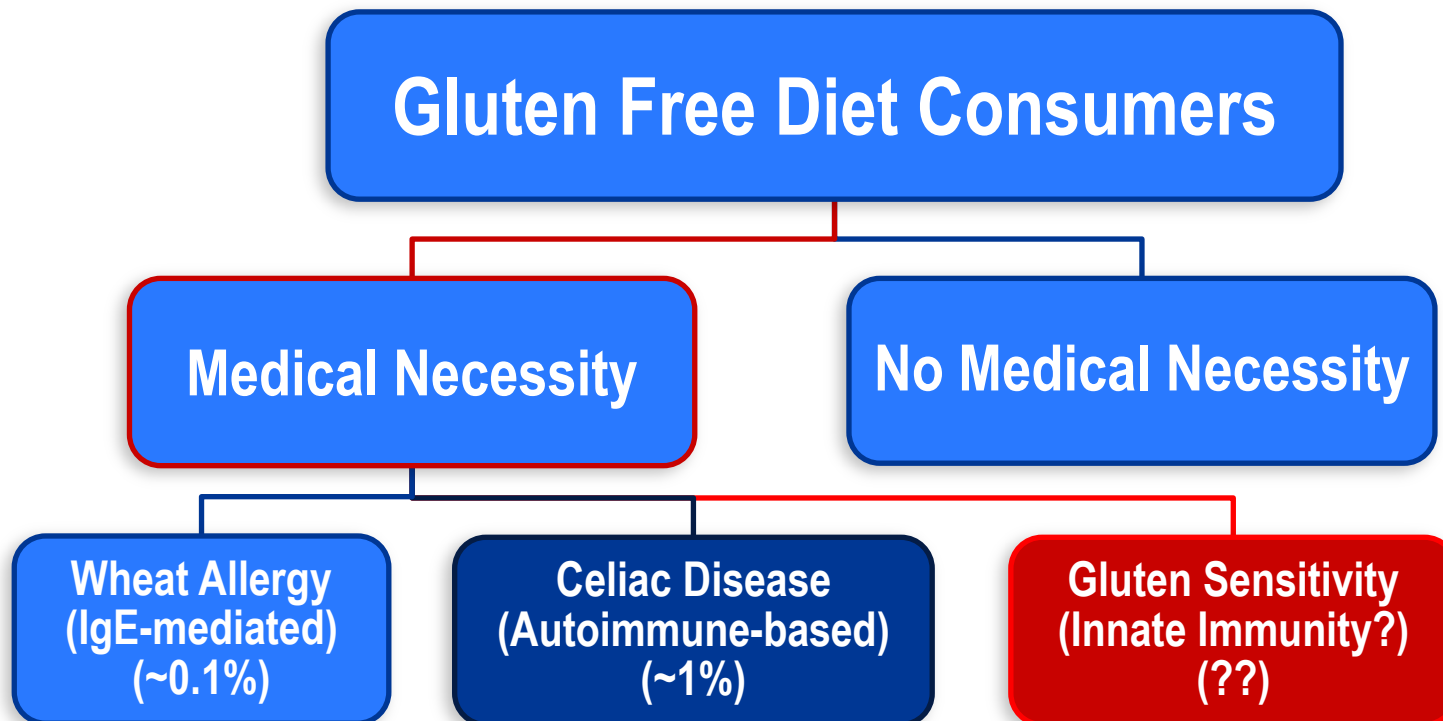
Wang et al. *J Clin Invest.* 2011;121(3):827-35.

Venter et al. *Allergy.* 2008;63(3):354-9.

Inomata et al. *Curr Opin Allergy Clin Immunol.* 2009;9:238-243.

# Non-Celiac Gluten Sensitivity

# The Gluten Free Diet: Not Only Celiac Disease



# Gluten Sensitivity: Definition

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

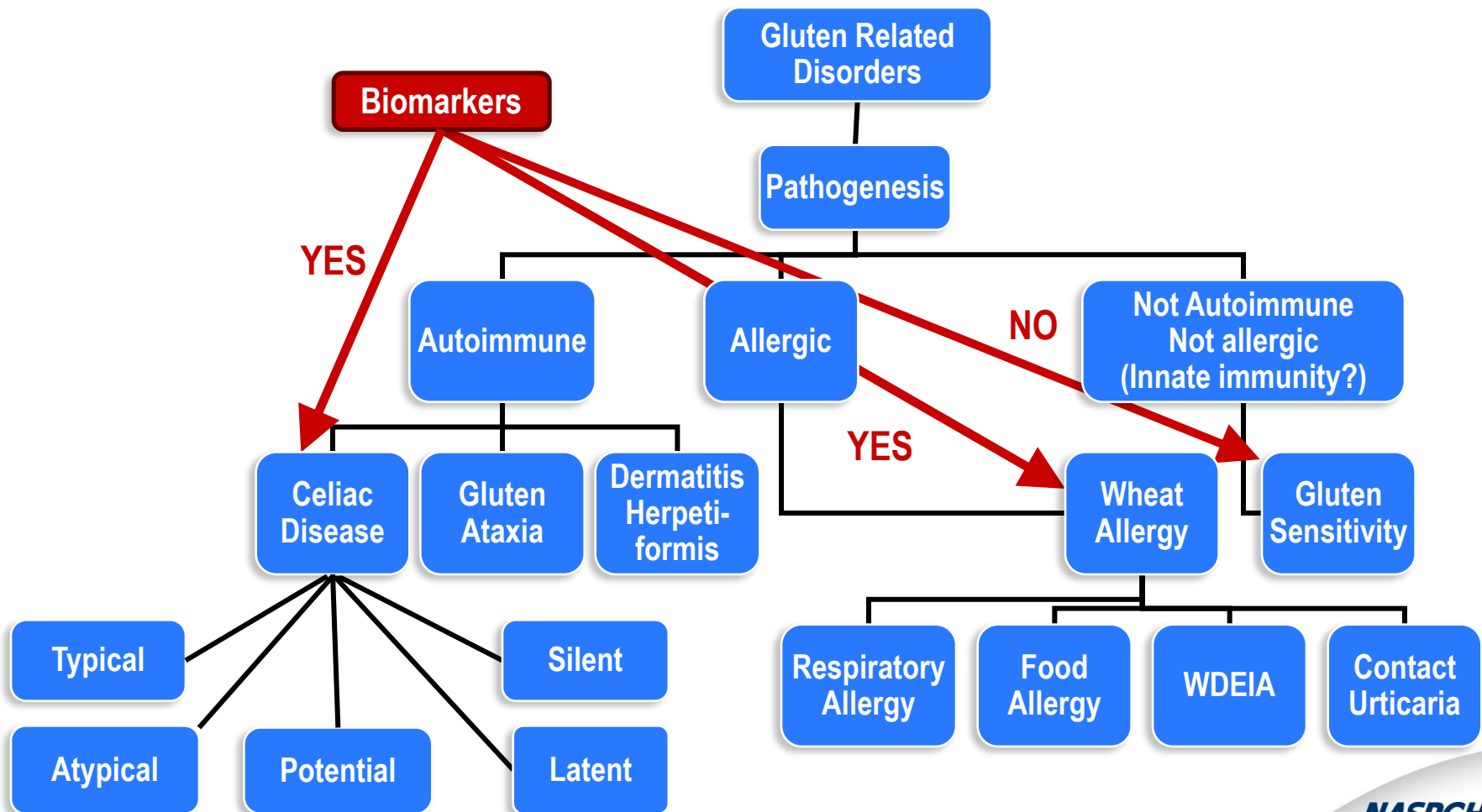
- Negative immuno-allergy tests to wheat;
- Negative CD serology (EMA and/or tTG) and in which IgA deficiency has been ruled out;
- Negative duodenal histopathology;
- Presence of biomarkers of gluten immune-reaction (AGA+);
- Presence of clinical symptoms that can overlap with CD or wheat allergy symptomatology;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

# Gluten Sensitivity: What Kind Of Symptoms?

## 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%

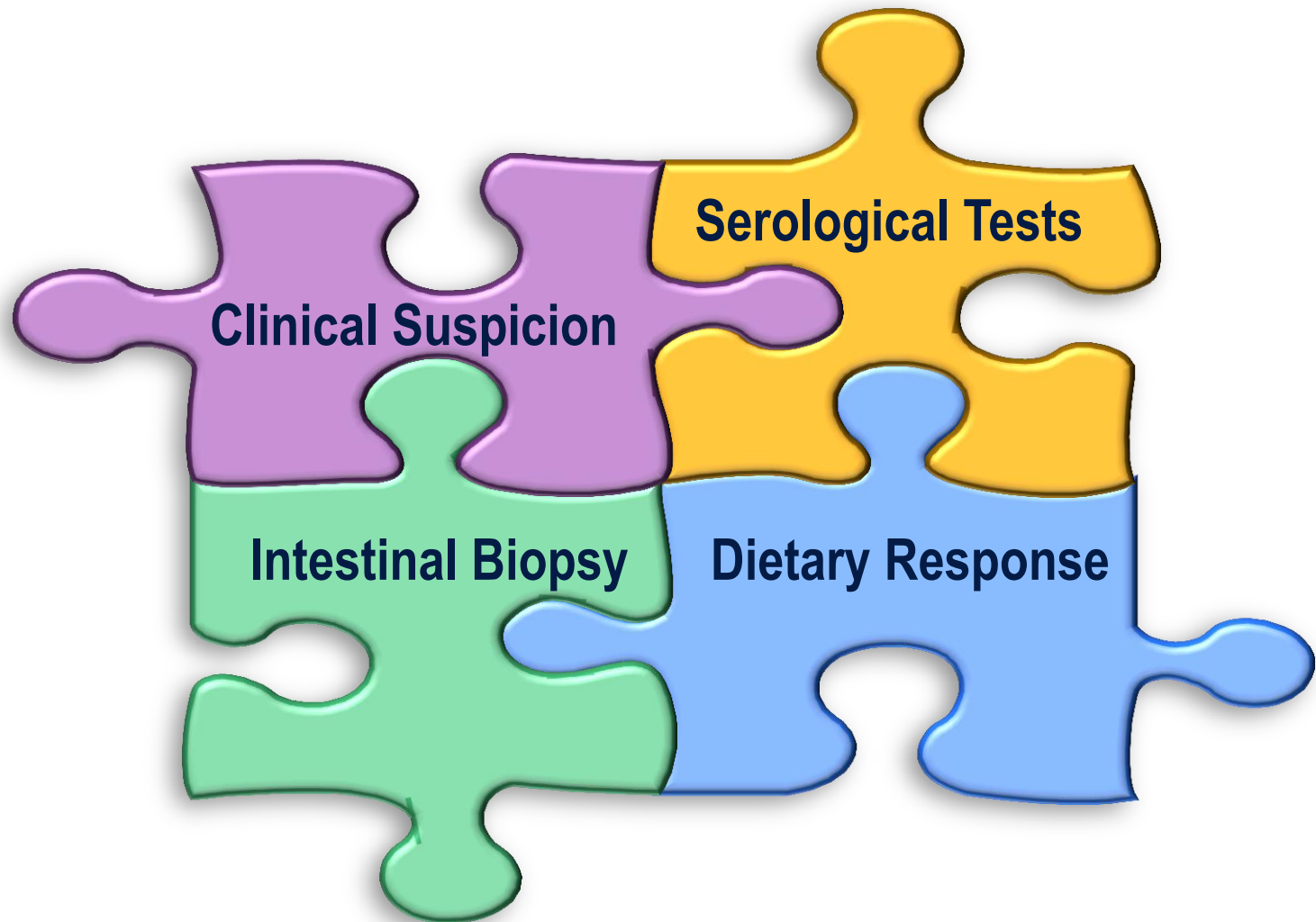
# Proposed New Classification of Gluten Related Disorders





**Diagnosis of Celiac Disease vs.  
Wheat Allergy vs.  
Non Celiac Gluten Sensitivity**

# Celiac Diagnosis



Rubio-Tapia et al. *J Gastroenterol.* 2013; 108:656–676; doi:10.1038/ajg.2013.79; published online 23 April 2013. Hill et al. *J Pediatr Gastroenterol Nutr.* 2005;40:1-19. Husby et al. *J Pediatr Gastroenterol Nutr.* 2012;54:136-160. AGA Institute. *Gastroenterology.* 2006;131:1977-1980.

# 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

Rubio-Tapia et al. *J Gastroenterol.* 2013; 108:656–676; doi:10.1038/ajg.2013.79; published online 23 April 2013. Hill et al. *J Pediatr Gastroenterol Nutr.* 2005;40:1-19. Husby et al. *J Pediatr Gastroenterol Nutr.* 2012;54:136-160. AGA Institute. *Gastroenterology.* 2006;131:1977-1980.

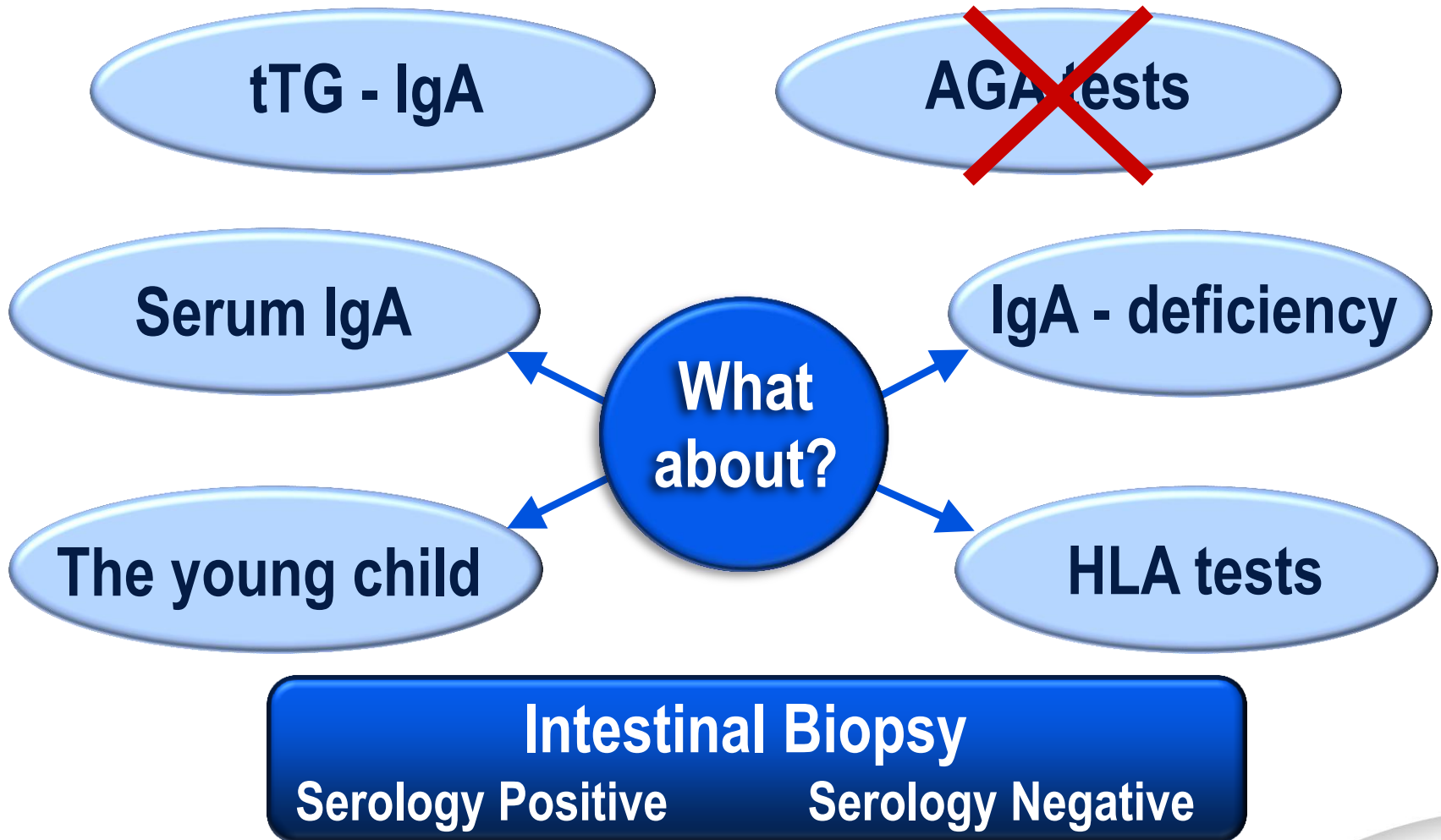
# Poll Question Results

- 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?



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# Differential Diagnosis Between CD, GS, & WA

	<b>Celiac Disease</b>	<b>Gluten Sensitivity</b>	<b>Wheat Allergy</b>
<b>Time interval between gluten exposure and onset of symptoms</b>	Weeks-Years	Hours-Days	Minutes-Hours
<b>Pathogenesis</b>	Autoimmunity (Innate+ Adaptive Immunity)	Immunity? (Innate Immunity?)	Allergic Immune Response
<b>HLA</b>	HLA DQ2/8 restricted (~97% positive cases)	Not-HLA DQ2/8 restricted (50% DQ2/8 positive cases)	Not-HLA DQ2/8 restricted (35-40% positive cases as in the general population)
<b>Auto-antibodies</b>	Almost always present	Always absent	Always absent
<b>Enteropathy</b>	Almost always present	Always absent (slight increase in IEL)	Always absent (eosinophils in the lamina propria)
<b>Symptoms</b>	Both intestinal and extra-intestinal (not distinguishable from GS and WA with GI symptoms)	Both intestinal and extra-intestinal (not distinguishable from CD and WA with GI symptoms)	Both intestinal and extra-intestinal (not distinguishable from CD and GS when presenting with GI symptoms)
<b>Complications</b>	Co-morbidities Long term complications	Absence of co-morbidities and long term complications (long follow up studies needed to confirm it)	Absence of co-morbidities. Short-term complications (including anaphylaxis)

.....

## Gluten Related Disorders Webinar

# Treatment

# Gluten Free Diet: Overview

	Celiac Disease	Gluten Sensitive
Treatment: GFD	Yes	Yes
Strict adherence to GFD	<10 mg / day	?
Life Long	Yes	?
Improvement of symptoms on GFD	Yes	Yes
Consequence of non -compliance:		
Physical symptoms	Yes	Yes
Intestinal damage	Yes	No
Monitored by bio marker	Yes	No
Co morbidities	Yes	?

# Gluten Containing Ingredients to Avoid

Wheat

Wheat Bran

Barley

Wheat Starch

Rye

Wheat Germ

Barley Malt /Extract

## Other Types of Wheat:

Spelt

Einkorn

Bulgur

Kamut

Semolina

Couscous

Emmer

Faro

Durum



Triticale

# Frequently Overlooked Foods That May Contain Gluten

- Broth
- Candy
- Communion wafers
- Imitation bacon
- Imitation seafood
- Marinades
- Processed meats
- Roux
- Sauces
- Soup base
- Soy sauce
- Thickeners
- Medications



# 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

- *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,*
- C*ontains **Wheat**, Milk, Egg, and Soy*

<http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/Allergens/default.htm>



# 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)



FIGURE 2.

3. FALCPA covers ingredients not the contamination of the product (oats)
4. Over the counter or prescription medications ([www.glutenfreedrugs.com](http://www.glutenfreedrugs.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 ppms

# 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

# 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

# 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)
- Manufactures are not required to test either the ingredients or the end product.
- Manufactures must be in compliance with the rule by August 2014

# Relationship Between Gluten Amount and Disease Activity

0	10	50	500 mg	1g	> 1 g of gluten/day
<b>Normal biopsy</b>					
<b>Normal serology</b>					
<b>Symptoms generally absent (beside some “ipersensitive” cases)</b>					
		<b>Minor/small intestinal Damage</b>			
		<b>Normal serology or rarely altered</b>			
		<b>Symptoms generally absent</b>			
					<b>Altered biopsy</b>
					<b>Abnormal serology</b>
					<b>Symptoms sometime present</b>



# 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

	<i>50 g</i>	<i>100 g</i>	<i>200 g</i>	<i>300 g</i>
<i>200 ppm</i>	10 mg	20 mg	40 mg	60 mg
<i>100 ppm</i>	5 mg	10 mg	20 mg	30 mg
<i>50 ppm</i>	2.5 mg	5 mg	10 mg	15 mg
<i>20 ppm</i>	1 mg	2 mg	4 mg	6 mg

# 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
  - Phosphorous
  - 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

# Recommended Standard CD Labs

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

<b>As Needed</b>	
Parathyroid hormone	Fat soluble vitamins A,E,K
Folate	Lipids
Other B vitamins	Selenium, Copper

# 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 food, 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
- Di/monosaccharidase Deficiency 9%
- Microscopic Colitis 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 -5 X 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](http://www.adaevidencelibrary.com)

- Celiac Disease Toolkit

Companion to AND's EAL on CD

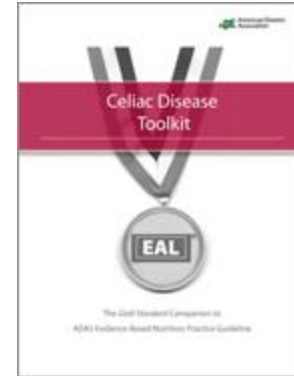
- Dietitians in Gluten Intolerance Diseases (DIGID)

– a subunit of the Medical Nutrition Practice Group

– [www.mnpgdpg.org](http://www.mnpgdpg.org)

## Medical Nutrition Practice Group

a dietetic practice group of the  
Academy of Nutrition  
and Dietetics



# Books and Guides

- *NASPGHAN Foundation Book: A Clinical Guide to Gluten –Related Disorders*

by Alessio Fasano

- *Celiac Disease Nutrition Guide*

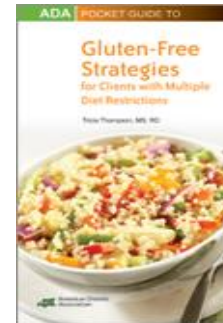
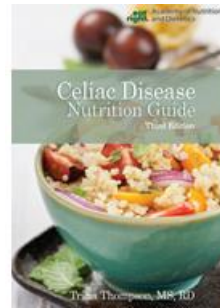
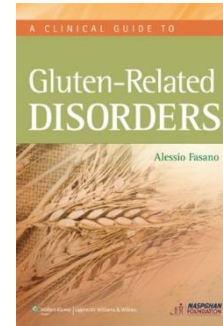
by Tricia Thompson

- *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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1. Go to [www.CE.TodaysDietitian.com/GlutenDisorders](http://www.CE.TodaysDietitian.com/GlutenDisorders) **OR** Log in to [www.CE.TodaysDietitian.com](http://www.CE.TodaysDietitian.com) and go to My Account→ My Activities→ Courses (in Progress) and click on the webinar title.
2. Click “Continue” on the webinar description page. Note: You must be logged-in to see the “Continue” button.
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