



# Don't Just Go Gluten-Free – Why You Need to be Tested First

*With Benjamin Lebwohl, MD, MS  
Herbert Irving Assistant Professor of Medicine and Epidemiology  
Celiac Disease Center  
Columbia University*





## Join us on our new mission!

The National Foundation for Celiac Awareness advances widespread understanding of celiac disease as a serious genetic autoimmune condition that can be easily diagnosed and effectively managed. We empower our community to live life to the fullest, and serve as a leading and trusted resource that inspires hope, accelerates innovation and forges pathways to a cure.





# Important Reminders!

## ① Will this information be available at a later date?

- Yes, always!
- Webinar recording will be posted along with the webinar slides within **72 hours** after the live webinar ends at [CeliacCentral.org/webinars/archive/](http://CeliacCentral.org/webinars/archive/)

## ② Are continuing education credits available?

- Yes!
- Attendees must **complete the follow-up survey** in order to access this certificate.
  - **The follow-up survey will be sent on Tuesday, February 3<sup>rd</sup> through an email from NFCA.**
- To ensure that you receive this email, make sure that NFCA ([National Foundation for Celiac A@gmail.vresp.com](mailto:NationalFoundationforCeliacA@gmail.vresp.com)) is on your **allowed senders list**.
  - Accidentally unsubscribed? Register for the webinar with a new email address
  - Be sure your email address is spelled correctly when registering
- Continuing education credits given **for live viewers only**
  - We encourage you to check out our archived webinars, but note that continuing education credit will not be given
- In the case of group viewing, **only the registered and logged in participant will receive credit**





# Learning Objectives

- 1) Understand the many reasons to get tested
- 2) Recognize the downside of not getting a proper diagnosis
- 3) Learn about proper testing methods
- 4) Find out what to do if you've already gone gluten-free
- 5) Know what to do if testing is negative



# Welcome!

## Benjamin Lebwohl, MD, MS

- MD from Columbia College of Physicians and Surgeons in 2003
- Joined the faculty of the Celiac Disease Center at Columbia University in 2010
- Irving Scholar (2013-2016)
- Gerstner Scholar (2014-2017)
- Recipient of the American Gastroenterology Association Research Scholar Award (2014-2017)
- Associated scholar at the Karolinska Institute in Stockholm, Sweden





# Quick Poll

If you are already eating gluten-free but feel better, are you interested in getting a blood test?



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# Celiac Disease is Common and Serious

- 0.7-1.0% of the general population
- Affects children and adults
  - Can develop celiac disease at any age
- Can affect multiple organ systems outside of the gastrointestinal tract
  - Can have celiac disease and not have diarrhea
  - Can have celiac disease and be overweight
- Children generally don't "grow out of it"







# Classical Celiac Disease

- Abdominal distension
- Abdominal pain
- Chronic diarrhea
- Anorexia
- Weight loss
- Muscle wasting



Fig. 2.—Photograph of five cases of coeliac disease showing the general clinical features.

Reference: A summary of NASPGHAN, AGA and WHO Guidelines



## Not all patients have GI symptoms

- Even if a person doesn't have digestive symptoms, he or she may still be at risk for celiac disease
- In addition to digestive symptoms, it is important to consider:
  - Family history
  - Medical history
  - Non-classical symptoms





# Non-Classical Celiac Disease

- Iron or folate deficiency
- Chronic constipation
- IBS
- Dental enamel defects
- Neurological (ataxia, neuropathy, epilepsy)
- Short stature
- Elevated liver enzymes
- Infertility
- Osteoporosis
- Delayed puberty
- Fatigue

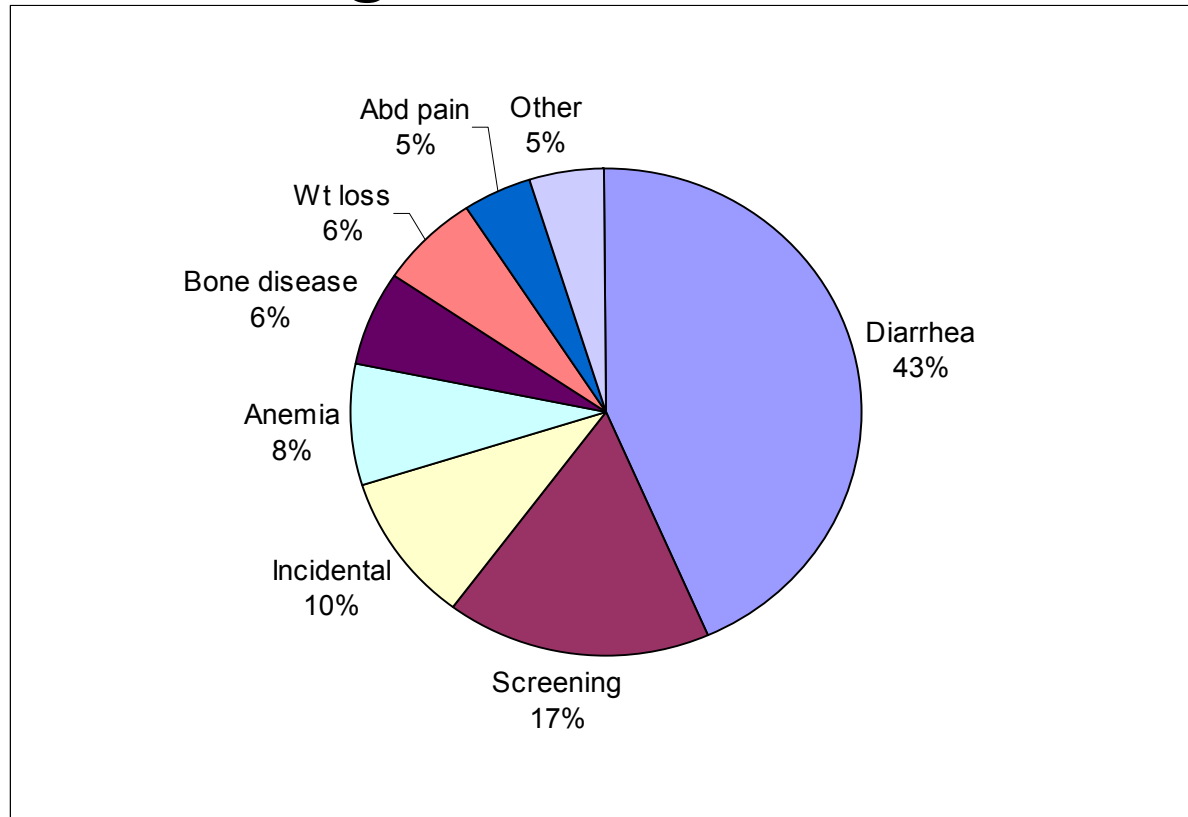


# “Silent” Celiac Disease

- Screening
  - First degree relatives
  - Type 1 diabetes
- Laboratory abnormalities
- Some symptoms only become obvious in retrospect



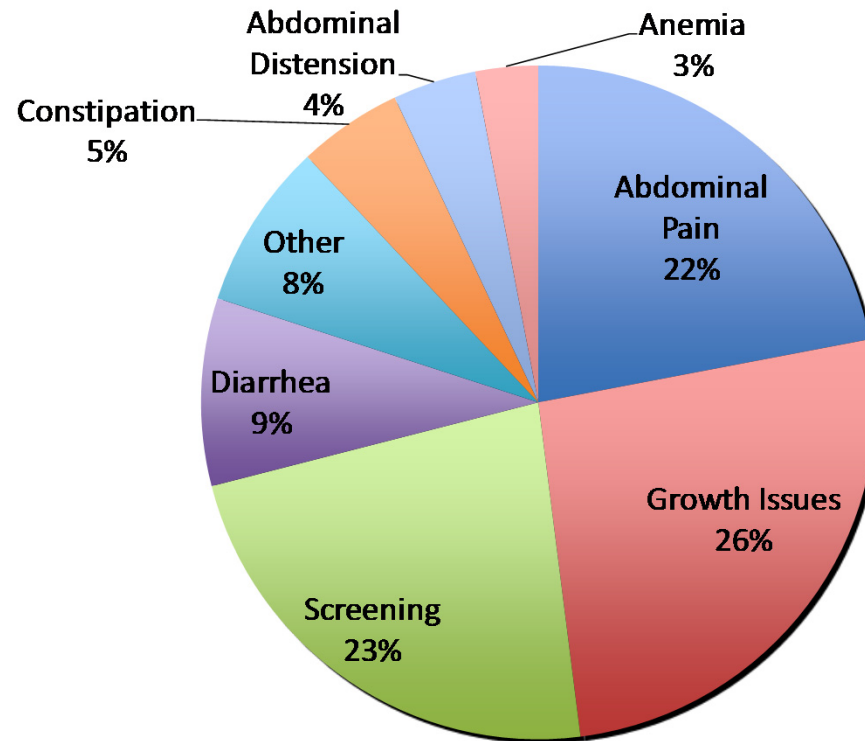
# Adult Presentation Diagnosed after 1993



Lo et al, Dig Dis Sci, 2003;48: 395



# Childhood Presentation



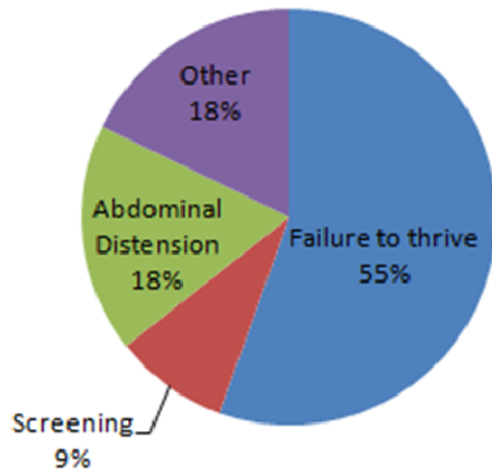
Green P et al. DDW Abstract 2009



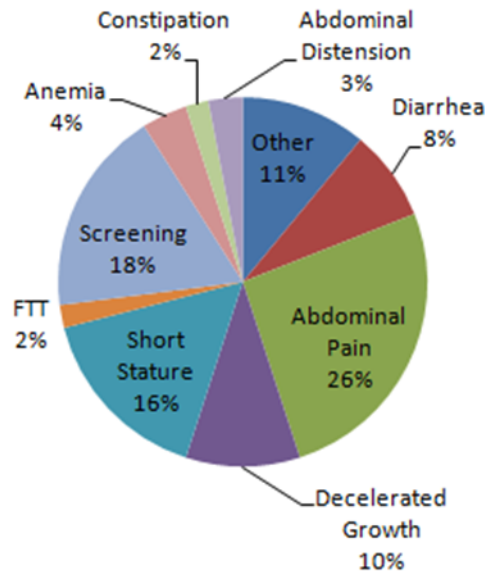


# Most Patients with Celiac Disease Are Not Underweight

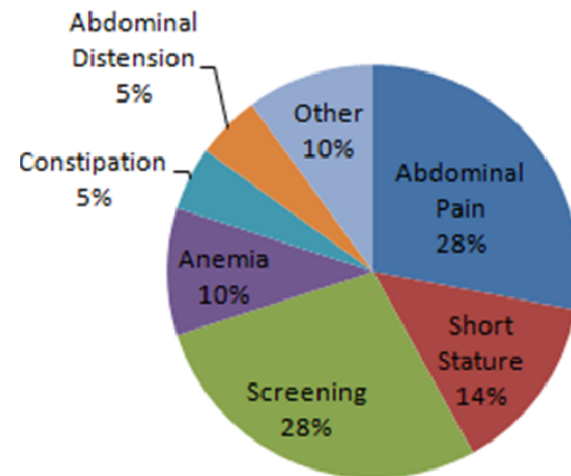
### Underweight



### Normal BMI



### Overweight

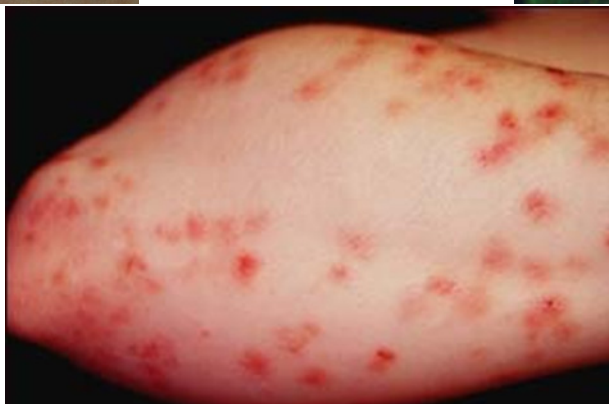
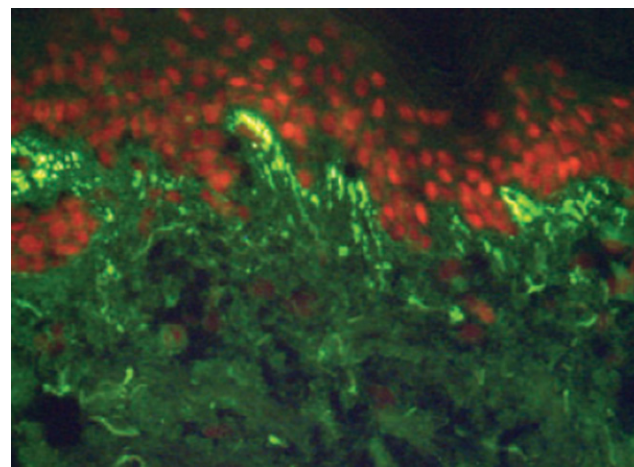


Reilly et al, JPGN 2011;53:528-31







# Dermatitis Herpetiformis



Flann et al. *Clin Exp Dermatol.* 2009  
[www.nlm.nih.gov/medlineplus](http://www.nlm.nih.gov/medlineplus)

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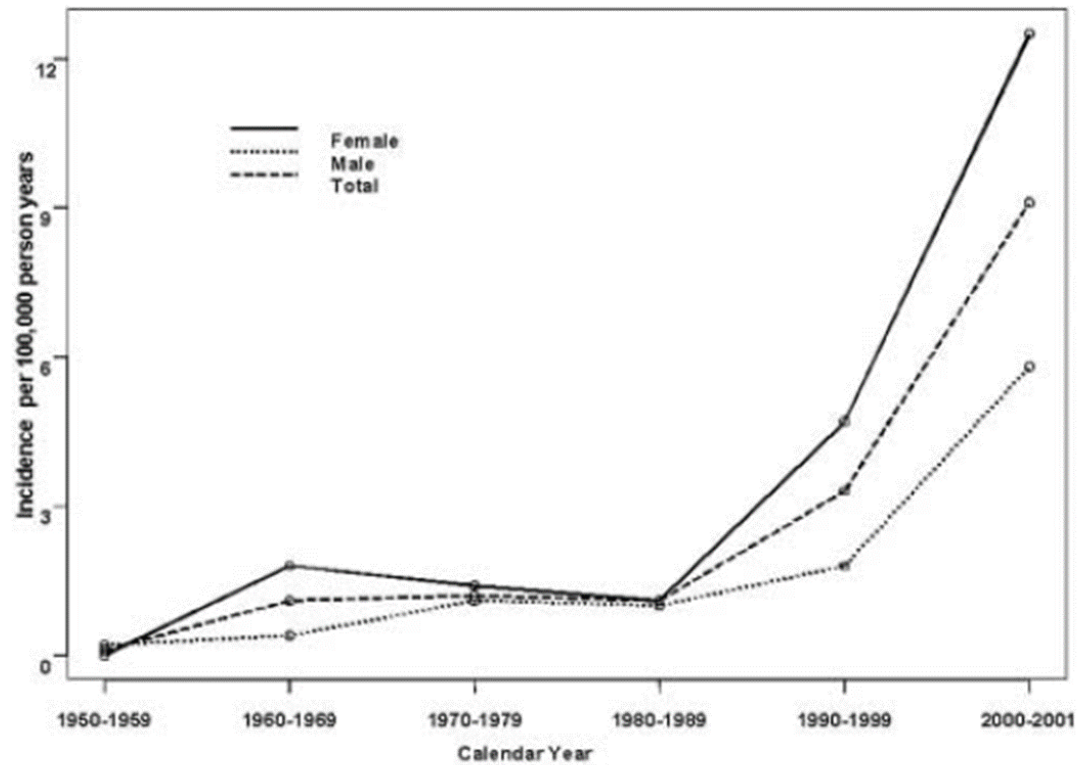


# Dermatitis Herpetiformis

- Blistering rash, intense itchiness
- Elbows, knees, elsewhere
- Skin biopsy
- Most have positive blood test and bowel biopsy
- Treated with gluten-free diet
  - Dapsone



# Celiac Disease: More Diagnoses



Murray, et al. *Clin Gastro Hep* 2003;1:19-27



# Celiac Disease is More Common Today: Increasing Prevalence by Blood Test (Seroprevalence)

Setting	Rise
Air Force Base (US)	0.2% in 1950 → 0.9% in 2006
Finland	1.05% in 1978 → 1.99% in 2000
Maryland (US)	0.21% in 1974 → 0.45% in 1989

Rubio-Tapia, et al. *Gastroenterology* 2009 137:88-93.

Lohi, et al. *Aliment Pharmacol Ther* 2007 26:1217-25.

Catassi, et al. *Ann Med* 2010 42:530-8.





## Problem:

### Most U.S. Patients With Celiac Disease Are Undiagnosed

- Seroprevalence: 0.7%-1.0%
  - Seroprevalence is the percentage of individuals in a population who test positive for a disease based off of serum blood tests
- Percentage undiagnosed:
  - Olmsted County (2001): 95%
  - Wyoming (2003): 90%
  - Washington County, Maryland (1989): 89%
  - NHANES (2009-2010): 83%

*Rubio-Tapia, et al. Am J Gastroenterol 2012;107:1538-44.*

*Murray, et al. Clin Gastro Hep 2003;1:19-27*

*Catassi et al. Ann Med 2010; 42: 530-8*

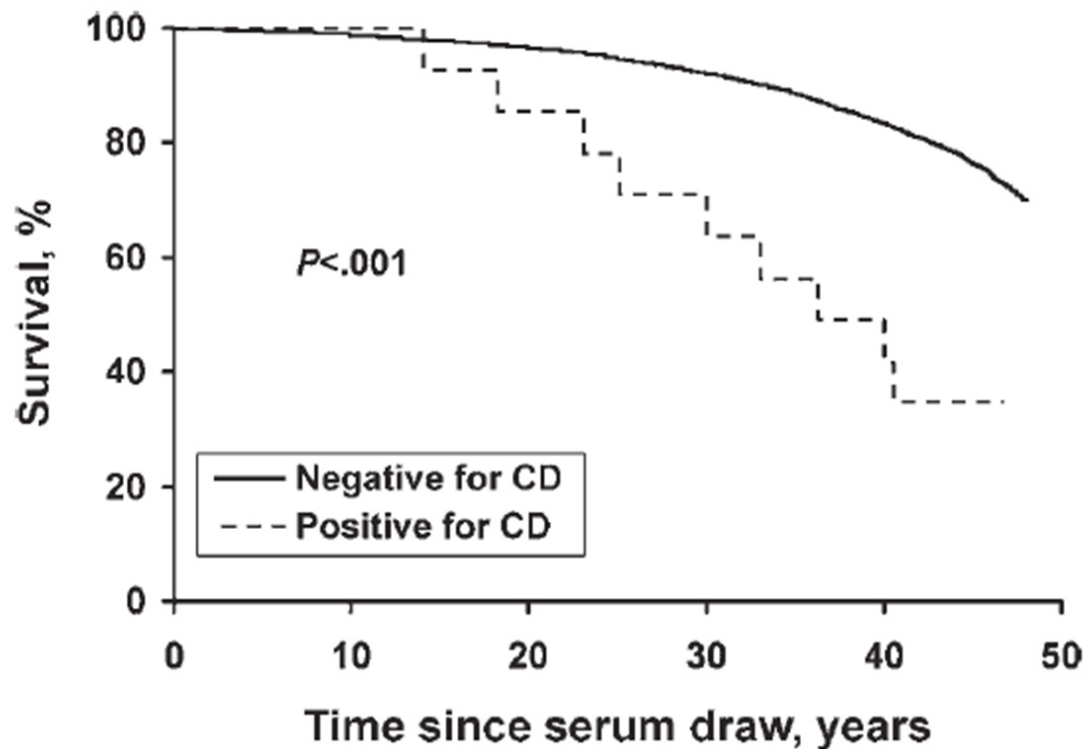
*Fasano, et al. Arch Intern Med. 2003;163:286-92*

*Katz, et al. Am J Gastroenterol 2010; 106:1333-9*



# Undiagnosed Celiac Disease and Mortality

- The death rate in undiagnosed celiac disease may be increased.
- One study saw a nearly 4-fold mortality increase in undiagnosed patients with celiac disease compared to those without celiac disease.



Rubio-Tapia, et al. *Gastroenterology* 2009 137:88-93.



# Mortality Risk is Reduced After Diagnosis

Once diagnosed and treated, people with celiac disease in the long-term have a life-expectancy similar to the general population.

Years since diagnosis	Total (n = 653)		
	Observed deaths	Expected deaths	O:E
<1	16	3.89	4.1 <sup>a</sup>
1-2	12	3.80	3.2 <sup>b</sup>
3-4	26	11.66	2.2 <sup>a</sup>
5-9	28	18.33	1.5
10-14	19	12.45	1.5
15+	14	11.64	1.2
<b>Total</b>	<b>115</b>	<b>61.78</b>	<b>1.9</b>
<b>95% CI</b>	—	—	<b>1.5-2.2</b>

Logan, et al. *Gastroenterology* 1989 97:265-71.



# Celiac Disease is Associated with Other Chronic and Potentially Fatal Conditions

System	Associated Conditions
Cardiovascular	Ischemic heart disease Stroke Atrial fibrillation Dilated cardiomyopathy Type 1 diabetes
Malignancy	Gastrointestinal Lymphoma
Respiratory Disease	COPD Asthma Tuberculosis Influenza



## Why We Need to Spread the Word About Celiac Disease

- It's prevalence has increased nearly 5-fold since 1950
- Associated with increased likelihood of dying early, a risk that is reduced after diagnosis
- Most Americans with celiac disease remain undiagnosed or misdiagnosed







# Learning Objectives

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- 5) Know what to do if testing is negative



## Testing: What Difference Does it Make?

- Gluten-free diet is a life-long prescription (for now)
- Need for medical follow-up
- Implications for family screening
- Delay of other diagnoses
- Cost and consequences of the gluten-free diet
- Difficulty if/when symptoms recur



# Lifelong Medical Follow-Up

Intervention	Frequency	Comment
Dietician	At least once	Gluten avoidance Calories Vitamins Fiber
Check symptoms	3-4 times during first year Annually	
TTG, confirm adherence	3-4 times during first year Annually	Should normalize in 6-12 months
Nutritional status	At diagnosis Annually	CBC, iron studies, B12 folate, 25-hydroxy Vitamin D
Bone density	At diagnosis	(Adults)





## Significant Impact on Emotional and Social Aspects of Daily Life

- Eating out and other concerns related to cross-contact
- Occasional purposeful ingestion of gluten
- Vitamin deficiencies inherent to the gluten-free diet and celiac disease diagnosis, along with unnecessary diet restrictions
- Accommodations/benefits eligibility



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# Celiac Disease Diagnosis: A Multi-Step Process



Clinical  
Suspicion

Blood test  
(serology)

Biopsy

Start gluten-  
free diet

Undiagnosed celiac disease (false negatives) – those who have celiac disease but have been told that they don't have it

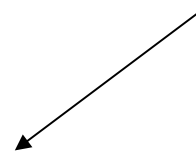
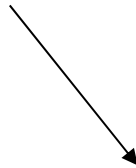
Not celiac disease (false positives) – those who do not have celiac disease but have been told that they have it



# Diagnosis of Celiac Disease

**Clinical Suspicion**

**Positive Serologies**



**BIOPSY**

**Endoscopy for any Reason  
(reflux, abdominal pain, etc.)**





# Quick Poll

**If you have been diagnosed with celiac disease, how were you tested?**





# Serologies

Test	What it Stands For	Characteristics
<b>TTG IgA</b>	Tissue transglutaminase	Sensitive and specific
<b>DGP IgG</b>	Deamidated gliadin peptide antibody	Useful in IgA deficiency
EMA IgA	Endomysial antibody	Highly specific in theory Reproducibility?

## Quick Definitions:

- Sensitive: Will be positive in most patients who have celiac disease
- Specific: Will be negative in most patients who do not have celiac disease



# Why Can't We Rely on Just One Blood Test?

- No blood test is perfect
  - Therefore, panels, or multiple tests, are offered
  - Panel results can be misinterpreted
- Selective IgA deficiency is common in celiac disease patients
  - Detected by checking total IgA level



# Less Helpful Serologies

Test	What it Stands For	Characteristics
DGP IgA	Deamidated gliadin peptide antibody	Role?
TTG IgG	Tissue transglutaminase	Useful in IgA deficiency(?)
AGA IgA/IgG	Anti-gliadin antibody	Not as sensitive or specific



# Unproven Tests for Diagnosis Celiac Disease

- Stool
- “Gluten sensitivity test”
- Saliva
  - Genetic testing can be done via cheek swab
- So what does it mean when we say a scientifically validated test?
  - Definition: Has been shown to correlate with biopsy-verified celiac disease in peer-reviewed studies



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## Role of Genetic Testing: HLA DQ2/DQ8

- Presence of DQ2/DQ8 genes:
  - Celiac disease: 100%
  - General population: 40%
- Genetic testing is **used to exclude celiac disease** in the following cases:
  1. Determining risk of family members
  2. Questionable diagnosis
  3. Already on gluten-free diet



## “Test First, Test Right”

- Once the gluten-free diet is started, celiac markers normalize
  - Serologies: 6-12 months
  - Duodenal biopsy: months to years
    - It is important to make sure that your doctor performs a biopsy in the appropriate locations, with an adequate number of biopsy samples



# Quick Poll

**If you have been tested for celiac disease, were you eating gluten-free at the time of your testing?**





# Going Gluten-Free Without Testing?

- Response is non-specific, meaning it doesn't necessarily indicate celiac disease
  - There are other reasons you may feel better, such as FODMAPS or other food sensitivities, as well as eating healthier in general
- Ability to detect celiac disease is changed
  - Serologies
    - Lack of gluten in the diet alters autoimmune response
  - Biopsy
    - The healing process begins after a gluten-free diet is started, and signs of celiac disease normalize



## Patients Already on a Gluten-Free Diet

- How long have you been eating gluten-free?
- Test for HLA DQ2/DQ8
  - Negative predictive value of ~100%
- Willing to undergo a gluten challenge?



# Quick Poll

**How would you feel if you had to undergo a gluten challenge?**



# Quick Poll

If you are already gluten-free but feel better, are you interested in getting a blood test?



# Healing Takes Time

Setting	Percentage Healed
Olmstead County, MN	
<2 years	35%
2-5 years	43%
>5 years	40%
Sweden	
6-11.99 months	50%
1-1.99 years	62%
2-5 years	56%

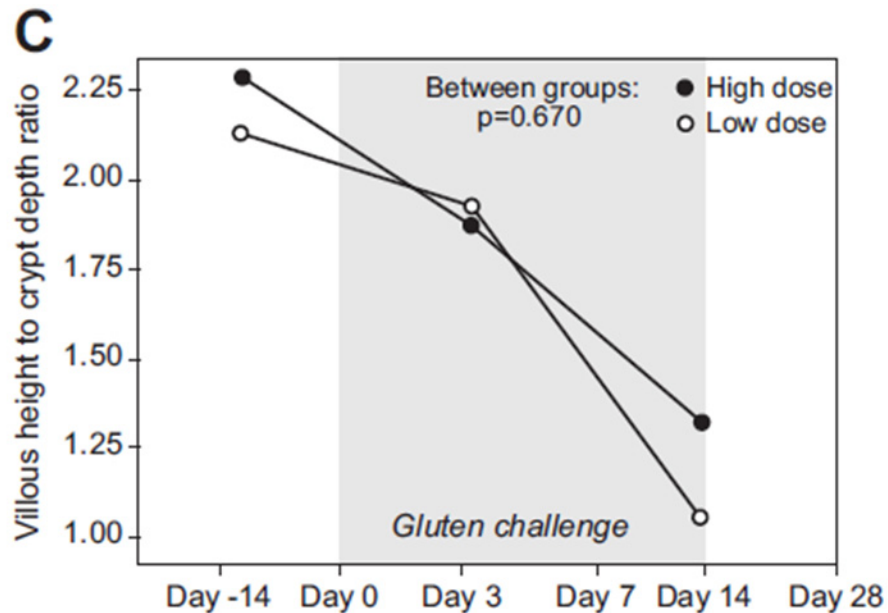
Without an official diagnosis, there is no way to determine how much damage has been done as a result of gluten exposure

*Rubio-Tapia, et al. Am J Gastroenterol 2010;105:1412-20.*

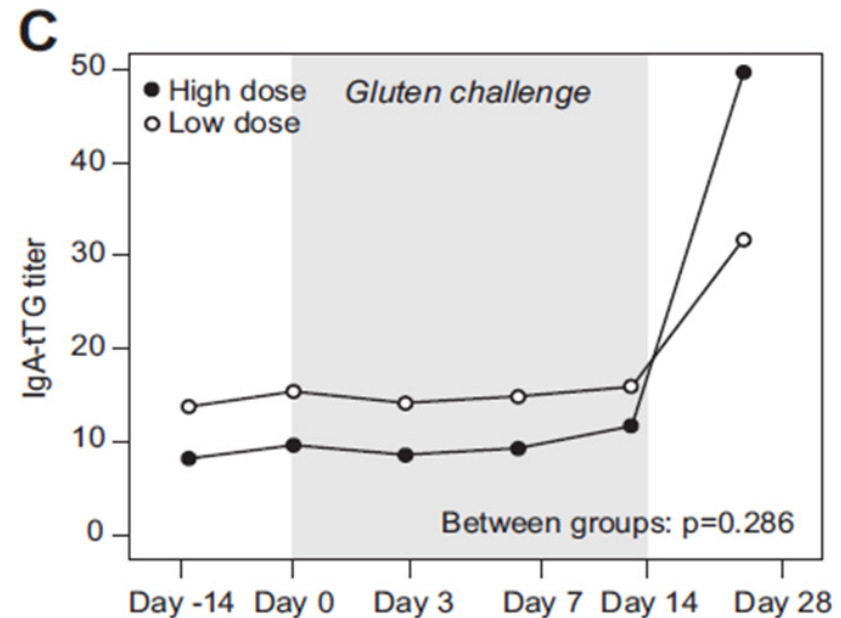
*Lebwohl, et al. Aliment Pharmacol Ther 2014;39:488-95.*



# Two Week Gluten Challenge



At the end of the gluten challenge (shaded area), the height of the villi on intestinal biopsy is decreased.



After the gluten challenge (shaded area), celiac antibody levels rise.

Leffler, et al. Gut 2013;62:996-1004.



## Possible to Modify the Gluten Challenge

- This is one proposed method to test for celiac disease by reintroducing gluten for a shorter period of time than the traditional 8 weeks

*This information is not intended nor suited to be a replacement or substitute for professional medical treatment or for professional medical advice relative to a specific medical question or condition. Please share this with your physician.*

Leffler, et al. Gut 2013;62:996-1004.

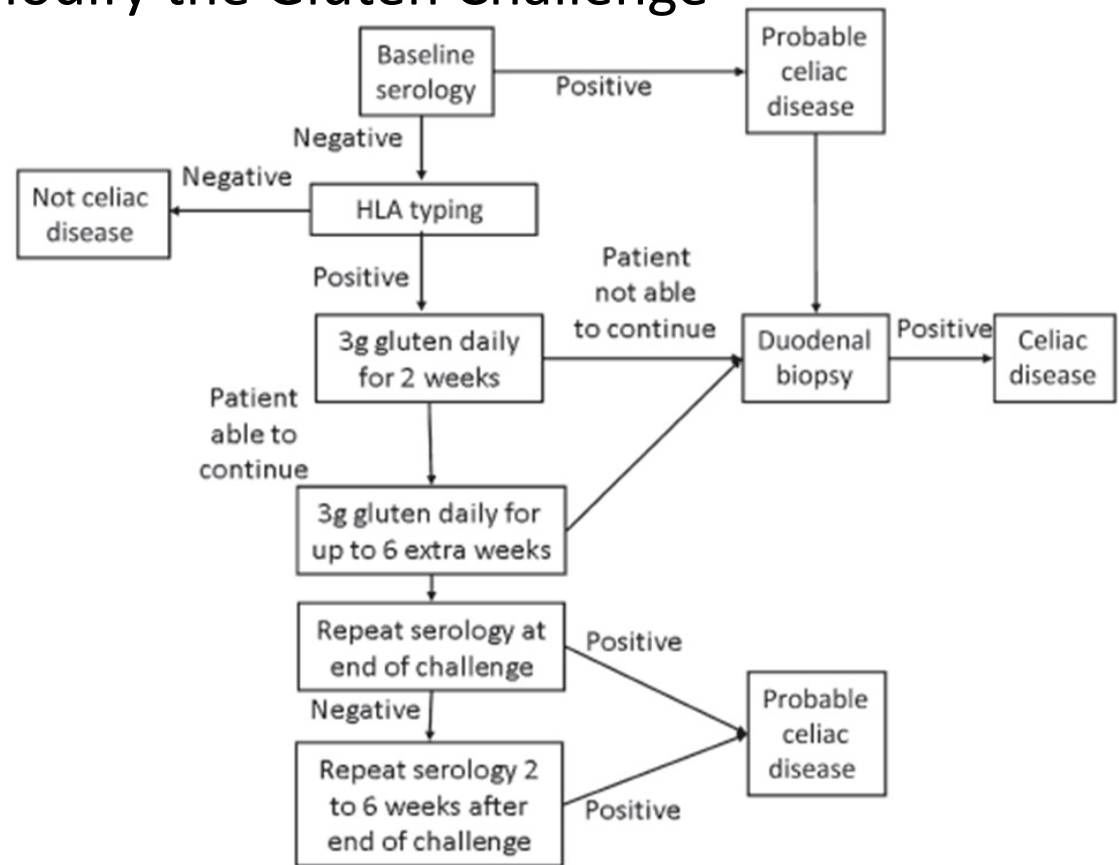


Figure 5 Proposed modified gluten challenge algorithm.





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## Make Sure the Testing Was Proper

- On a gluten-containing diet?
- Duodenal biopsy performed during endoscopy?
- Number of specimens?
- Pathologist interpretation?






## Most Gluten-Sensitive Patients Were Not Fully Tested for Celiac Disease – But Should Have Been

- Survey (n=147)
- Mean age 43
- 88% female
- 62% were not properly excluded for celiac disease
  - Many who underwent biopsy were already on the gluten-free diet during the procedure
  - 15% had no serological/HLA testing or small bowel endoscopy
- 27% were not strictly following the gluten-free diet

*Biesiekierski JR, et al. Nutr Clin Pract 2014;29:504-509.*






## Pathologist Experience Matters: Comparison of “Celiac Pathologists” to Other Pathologists

Institution	Institution	Agreement (Kappa)
	University Hospitals	0.89 (good)
	Community Hospitals	0.46 (moderate)
	Commercial Laboratories	0.42 (moderate)

Kappa statistic ranges from 0 (no agreement) to 1.0 (perfect agreement).

Argulles-Grande, et al. *J Clin Pathol.* 2012;65:242-7.

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## What Else Could It Be?

- Non-celiac gluten sensitivity
- FODMAPs
- IBS (gluten-responsive)
- Other conditions



## It's Common for Patients without Celiac Disease to Have Other Diagnoses and Avoid Wheat and/or Gluten

- N=84
- 79% female, mean age 43
- Additional food intolerances common
- Alternative diagnosis: 30%
  - Small intestinal bacterial overgrowth (SIBO)
  - Fructose/lactose intolerance
  - Microscopic colitis
  - Gastroparesis

*Tavakkoli, et al. Dig Dis Sci 2014;59:1255-61.*





# Final Question

What is the ideal time you would be willing to participate in a gluten challenge?



As we finish...

Questions from the audience?





# NFCA Free Resources

- Check out our website for more information on getting tested including our new handout, “5 Reasons You Need to be Tested for Celiac Disease”
  - <http://www.celiaccentral.org/gettested>
- “Best Practices in Celiac Disease Diagnosis” webinar with Drs. Leffler and Verma
  - <http://www.celiaccentral.org/webinars/archive/>
- Download our Getting Started Guide
  - <http://www.celiaccentral.org/gettingstarted/>







*celiac disease*<sup>TM</sup>  
center at | *columbia university medical center*

BL114@columbia.edu

celiacdiseasecenter.org  
@BenjaminLebwohl





# Save the Date!

## CeliacCentral.org/webinars

**Topic:** “The GREAT (Kitchens) Solution to Dining Out”

**Date:** Tuesday, February 24<sup>th</sup>

**Time:** 8 p.m. Eastern/5 p.m. Pacific

**Speakers:** Beckee Moreland, Director of NFCA’s GREAT Kitchens Program and Bob Strate, COO at GREAT Kitchens accredited TaMolly’s Mexican Restaurants

**Topic:** “Gluten-Free Travel: Making Your Own Rules for the Road”

**Date:** Thursday, March 19<sup>th</sup>

**Time:** 8 p.m. Eastern/5 p.m. Pacific

**Speakers:** Anna Sonnenberg, creator of the blog “Gluten-Free Jet Set” and Erin Smith, creator of the blog “Gluten-Free Globetrotter”





# Thank You!

- Webinar questions, comments, feedback: [webinars@CeliacCentral.org](mailto:webinars@CeliacCentral.org)
- Connect with NFCA:

