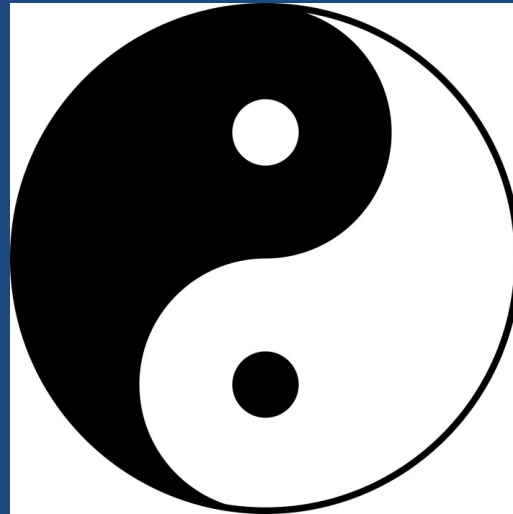


Celiac Disease or Something Else?

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Disclosure

- None



Learning Objectives

1. To describe the varied clinical manifestations of Celiac Disease (Sprue)
2. To define the workup of Celiac Disease especially when a patient is already on a self imposed gluten free diet
3. To recognize the entity of Non Celiac Gluten Sensitivity
4. To identify how the symptoms of Celiac Disease, Non Celiac Gluten Sensitivity and Irritable Bowel Syndrome may be IDENTICAL





What is Gluten?



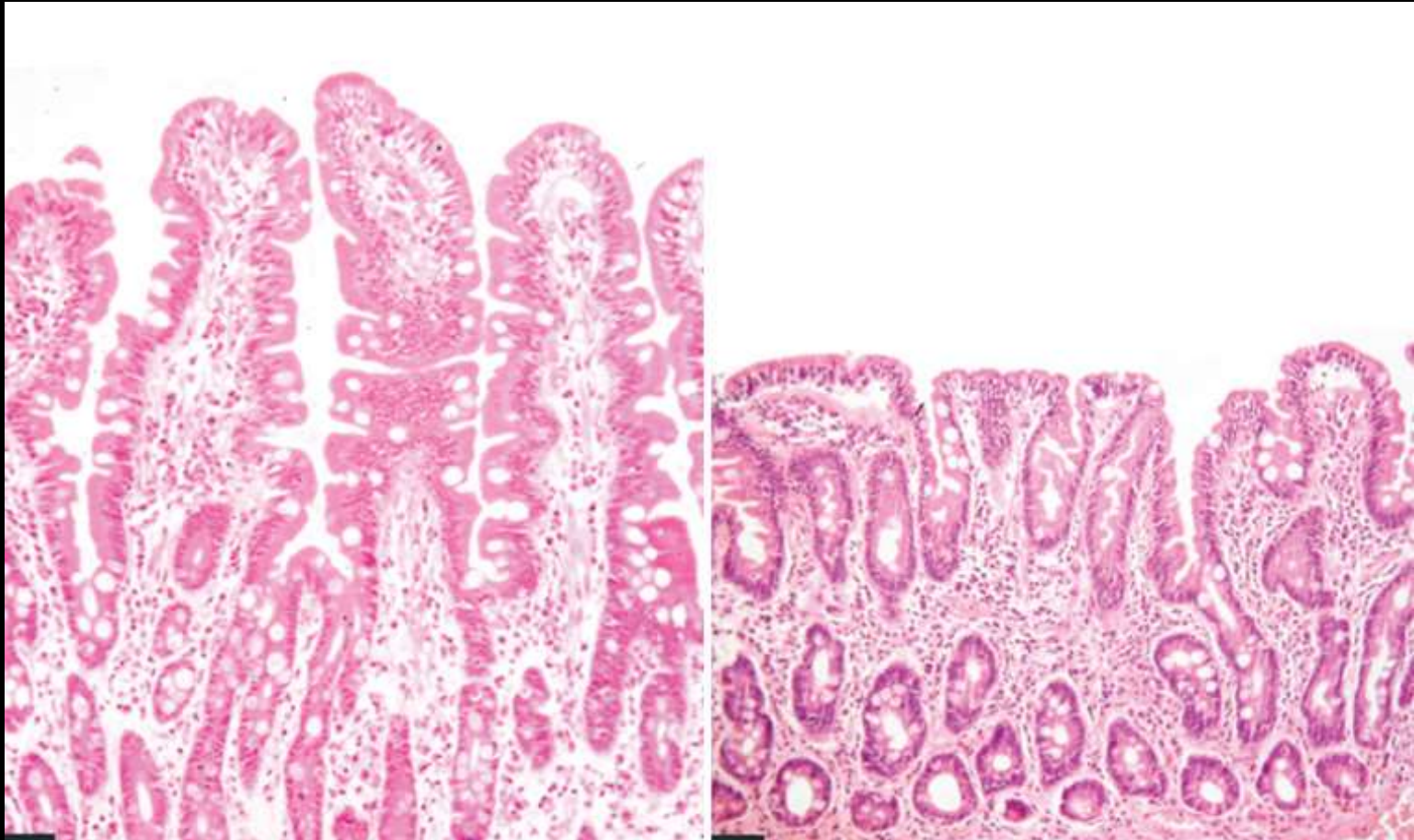
What is Gluten?

A protein in wheat
barley
rye

That gives elasticity to dough
& is also a common filler and
additive

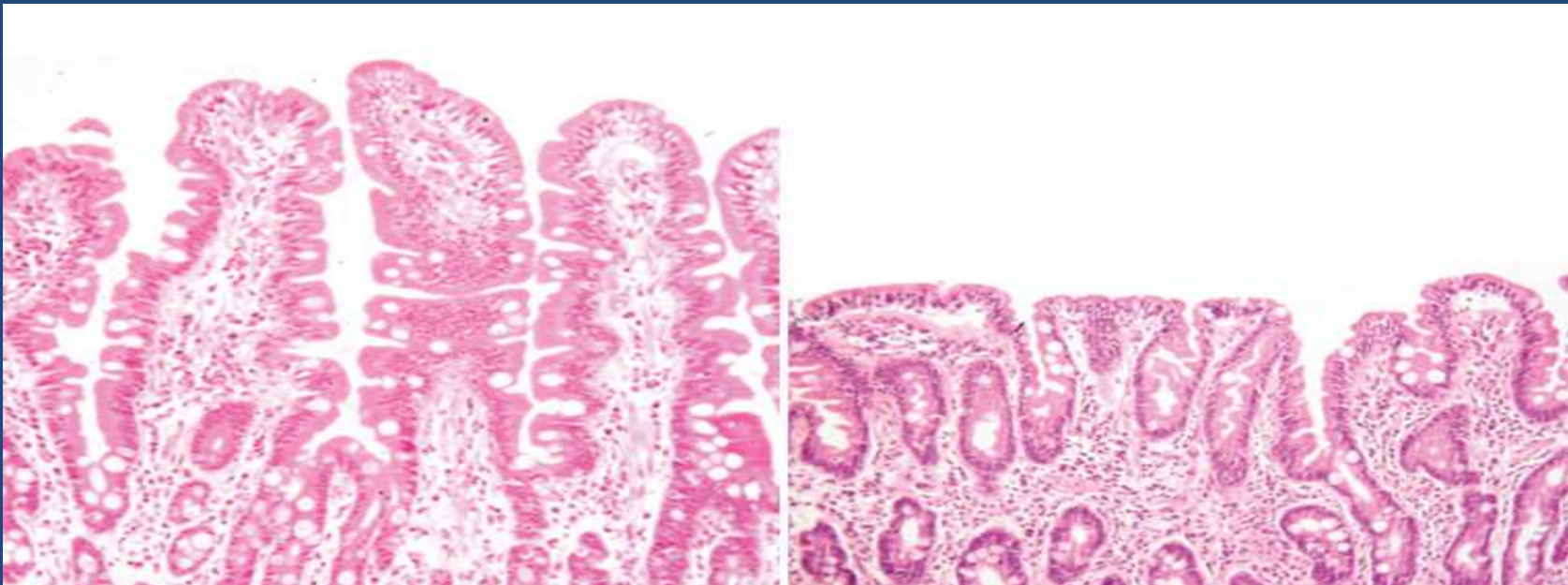


What is Celiac Disease?



What is Celiac Disease?

- The immunological effect of exposure to gluten in predisposed individuals
- This is mostly, but not entirely manifested in the small intestine
- Present in 1% of population



What is the
differential diagnosis
of Celiac Disease?



What is the differential diagnosis of Celiac Disease?

- Lactose Intolerance
- Irritable Bowel Syndrome
- Inflammatory Bowel Disease
- Medication side effects
- Small bowel overgrowth
- Infections
- Microscopic Colitis



What is Non Celiac Gluten Sensitivity?



What is Non Celiac Gluten Sensitivity?

- A variety of poorly understood reactions to gluten or another food element in patients who do NOT have a diagnosis of sprue
- Estimated in .55% of population*
- May be related to fructans rather than gluten
- Fructans are polymers of fructose



Magnitude of the problem

- Celiac Disease approx. 3 million in the US
only 300,000 on gluten free diet*
- Non celiac gluten sensitivity
30% of Americans have tried a gluten free diet**

*Rubio-Tapia A et al
The prevalence of celiac disease in the United States
Am J Gastroenterol 2012;107;1538

**Moore LR
"But we're not hypochondriacs" the changing shape of gluten free dieting and the contested illness experience
Social Sciences & Medicine 2014;105;76



Diagnosis of Celiac Disease

- Sometimes a delay of 4 – 12 years



Rampertab SD et al
Trends in the presentation of celiac disease
Am J Med 2006;119;355





Magnitude

- There has been a fivefold increase in the prevalence of Celiac Disease in the past 50 years

Rubio-Tapia A et al
Increased prevalence and mortality in undiagnosed celiac disease
Gastroenterology 2009;137:88



Why do so many
Americans who do not
have Celiac Disease try
a Gluten Free Diet?



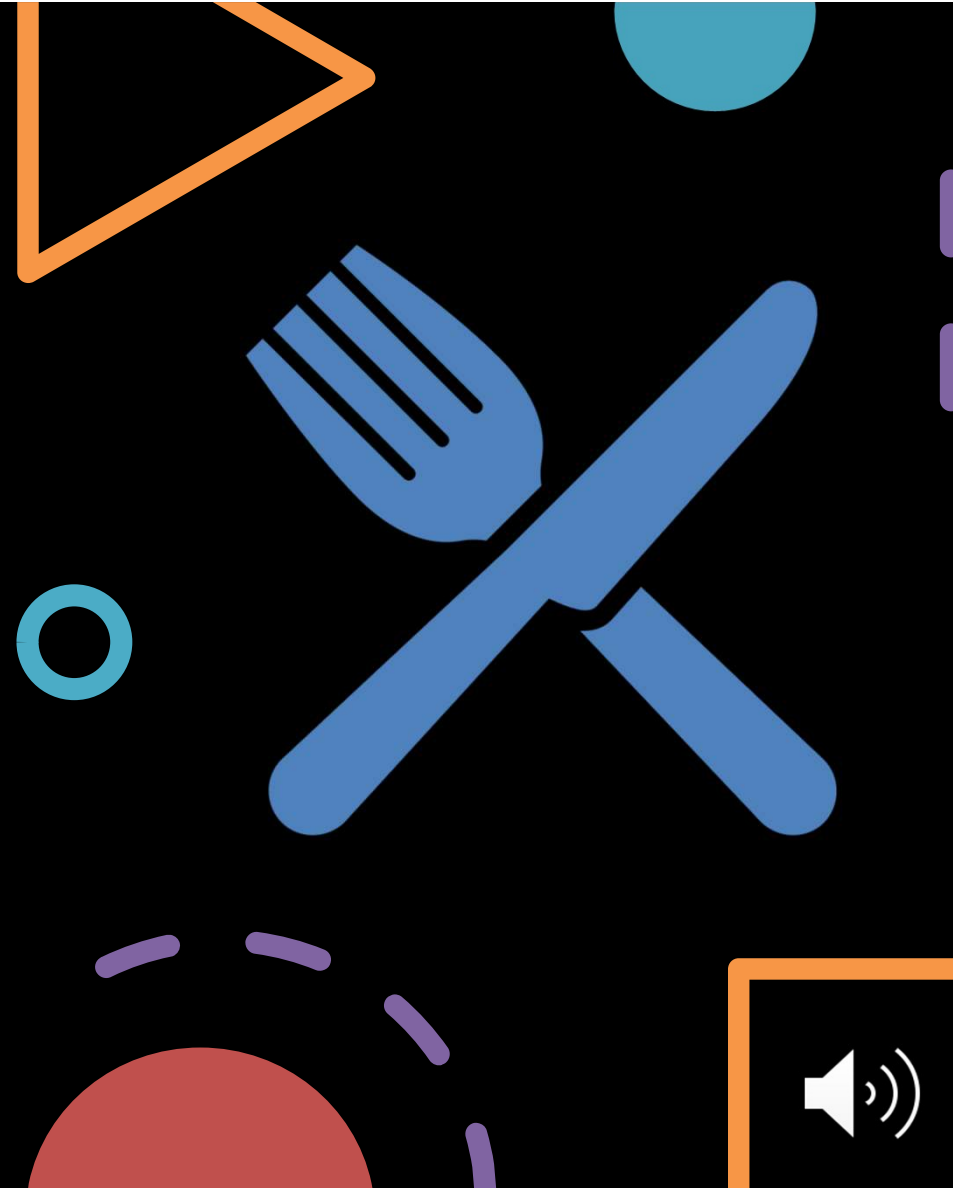
Why do so many Americans who do not have Celiac Disease try a Gluten Free Diet?

- Healthier than regular diet?
- Weight loss?



Risks of Consuming a Gluten Free Diet

- Increased fats and sugars
- Low in fiber, iron and B vitamins
- May have increased heavy metals



Most people in the U.S. With Sprue Are

1. Underweight
2. Normal weight
3. Overweight

Paca L et al
Managing celiac disease: a brief overview
The New Gastroenterologist
Winter 2016:13



Most people in the U.S. With Sprue Are

1. Underweight
2. Normal weight
3. **Overweight**

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All of the following contain gluten **EXCEPT**:

1. Beer
2. Dextrin
3. Rye
4. Oats



All of the following contain gluten **EXCEPT**:

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2. Dextrin
3. Rye
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Which of the following is **NOT** a manifestation of Sprue?

1. Neuro psychiatric issues
2. Autoimmune disease
3. Fever
4. Elevated transaminases



Which of the following is **NOT** a manifestation of Sprue?

1. Neuro psychiatric issues
2. Autoimmune disease
3. **Fever**
4. Elevated transaminases



Shift from Classic to Non Classic Presentations

- Classic diarrhea
 weight loss
- Non Classic **(Increasingly prevalent)**
 chronic fatigue
 peripheral neuropathy
 elevated transaminases
 reduced bone density
 unexplained infertility
 anxiety
 iron deficiency
 autoimmune thyroid disease



What is this?



Dermatitis Herpetiformis

- Diagnostic for Celiac Disease
- Very itchy blisters
- Usually occurring in forearms, elbows, knees, buttocks
- Seen in 10% of patients with Celiac Disease, oftentimes WITHOUT GI symptoms*
- A skin biopsy can confirm the diagnosis/small bowel bx not needed

Alonzo-Llamazares J et al
Clinical, pathologic and immunologic features of dermatitis herpetiformis: review of the Mayo Clinic experience
International Journal of Dermatology 2007;46:910



What is the Relationship of Dapsone and Celiac Disease?

- Dapsone is an immediate treatment for Dermatitis Herpetiformis (DH)
- A gluten free diet takes months to reverse DH



Other Non GI
Manifestations
of Sprue

Delayed puberty

Short stature

Tooth discoloration

Aphthous ulcers



What is the best serum test to evaluate Sprue?

1. Anti-gliadin Antibody
2. Antiendomysial Antibody
3. Transglutaminase Antibody (tTG- IgA)



What is the best serum test to evaluate Sprue?

1. Anti-gliadin Antibody
2. Antiendomysial Antibody
3. Transglutaminase Antibody (tTG- IgA)



Test	Sensitivity	Specificity	Tech	Cost
------	-------------	-------------	------	------

tTG	96-98%	88-100%	Low	\$\$
-----	--------	---------	-----	------

EMA	75-98%	99-100%	High	\$\$\$\$
-----	--------	---------	------	----------



RARE False Positive tTG IgA

- Inflammatory Bowel disease
- Connective Tissue Diseases
- Febrile illnesses
- Type 1 Diabetes



What percentage of Celiac Disease patients are IgA deficient?

1. 2 – 5%
2. 10 – 15%

Crowe S
Celiac disease
Annals of Internal Medicine
2011;154(9):ITC5-1.doi:10.7326/0003-4819-154-9-201105030-01005



What percentage of Celiac Disease patients are IgA deficient?

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Are the Majority of IgA Deficient Patients?

Symptomatic

Asymptomatic



Are the Majority of IgA Deficient Patients?

Symptomatic

Asymptomatic



Take Home Message

- IgA deficiency is 10-15x more prevalent in Celiac Disease than the general population
- Therefore MEASURE IgA





Sarah

- Is a 43 y.o. female with a lifelong hx of diarrhea and abdominal pain.
- She started a strict gluten free diet 8 weeks ago based on information she read on the Internet
- She now feels 50% better and asks you to make a definitive diagnosis



What do you tell
Sarah?



3 Choices

1. Do genetic tests including HLA DQ 2 and 8
If they are **negative** results she definitely does NOT have Sprue*
2. Do a gluten challenge with 3 slices of wheat bread daily for 1 – 3 months
then do a tTG-IgA Ab
3. Stay on the diet

*Husby S et al

AGA clinical practice update on diagnosis and monitoring of celiac disease-changing utility of serology and histologic measures: expert review
Gastroenterology 2019;156;885



HLA DQ 2 and 8

- Carried by 35-40% of American population
- Associated with :
 - Autoimmune diseases
 - Diabetes
- If **NEGATIVE**...no Sprue



What are the risks of
remaining on a Gluten
Free Diet?



A Person With Celiac Disease Can Still Consume:

1. Rice
2. Quinoa
3. Soy
4. All the above



A Person With Celiac Disease Can Still Consume:

1. Rice
2. Quinoa
3. Soy
4. All the above



Non Celiac Gluten Sensitivity

- No serological test yet
- A diagnosis of Non Celiac Gluten Sensitivity should be made only after Celiac Disease has been excluded with appropriate testing*
- 45% of self reported "wheat sensitivity" have Irritable Bowel Syndrome

Rubio-Tapia et al

ACG Clinical Guidelines: diagnosis and management of celiac disease

Am J Gastroenterol 2013;108;656

Potter MDE et al

Wheat intolerance and chronic gastrointestinal symptoms in an Australian population-based study: association between wheat sensitivity, celiac disease and functional gastrointestinal disorders

Am J Gastro 2018;113;1036



Non Celiac Gluten Sensitivity vs Irritable Bowel Syndrome?

- Exclude Celiac Disease
- Follow with gluten free diet for at least 6 weeks

Igbinedion SO et al

Non celiac gluten sensitivity: All wheat attack is not celiac

World J Gastroenterol 2017;23;7201





Sam

- Is a 34 y.o. male who visited his primary care doctor for a routine visit
- Routine bloods found H/H 11/33 with Fe 14
- Endo and colon normal, U/A normal
- What may be causing the anemia?



Anemia in Celiac Disease

- Iron deficiency: 33% men
19% women
- Folate deficiency: 12%
- B 12 deficiency: 5%

Harper JW et al

Anemia in celiac disease is multifactorial in etiology

Am J Hematol 2007;82;996



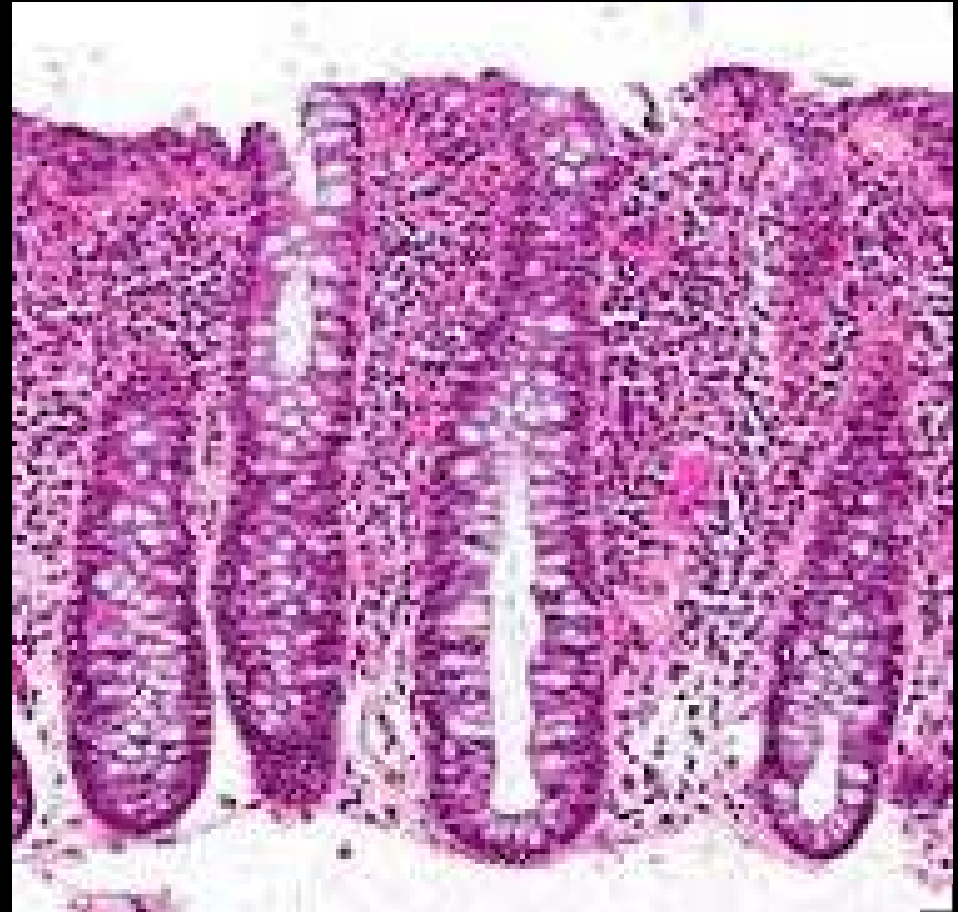
Extra Credit Questions

- Can the filler in pills/capsules exacerbate Sprue?
- Can Irritable Bowel and Sprue co exist?
- You have a patient **already** on a self-imposed gluten free diet. Will duodenal biopsies be useful to check for Sprue?
- Can Sprue and Microscopic Colitis co exist?



Microscopic Colitis

- Chronic inflammation of the colon
- Manifested by watery diarrhea
- Normal colonoscopy, but diagnosed through biopsies
- Higher prevalence in: females
over age 65



How do we treat Sprue in 2021??

1. Diet
2. Peptide Vaccination
3. Enzymes
4. Probiotics
5. All of the above



How do we treat Sprue in 2021??

1. Diet
2. Peptide Vaccination
3. Enzymes
4. Probiotics
5. All of the above



Celiac Disease/Diet

- Two thirds of patients committed to a gluten free diet are regularly exposed to gluten
- There is no regulation for food manufacturers to test their products for gluten



Edy

- Is a 47 y.o. female with a longstanding hx of bloating, constipation and diarrhea who has had a full workup including:
 - CBC
 - Gen Chem
 - CRP
 - T4, TSH
 - tTG-IgA
 - Lactose tolerance test
 - Endo/Colon
- All NEGATIVE



With a negative tTG, can Edy still have Sprue?



With a negative tTG, can Edy still have Sprue?

- Possible, but unlikely
- False negative results may occur with mild disease
- It is much more likely that the patient has Irritable Bowel Syndrome



Do all patients who are tTG + need a small bowel biopsy?

Rubin JE and Crowe S

Celiac Disease

Annals of Internal Medicine 2020;172;ITC1



Do all patients who are tTG + need a small bowel biopsy?

- AGA Guidelines 2019
- “Transglutaminase antibodies, at high levels (greater than 10X upper normal limit) is a reliable and accurate test for diagnosing active Celiac Disease. When such a strongly positive transglutaminase antibody is combined with a positive endomysial antibody in a second blood sample, the positive predictive value for Celiac Disease is virtually 100%.”
- Biopsies are still recommended for confirmation

Husby S et al

AGA Clinical Practice Update on Diagnosis and monitoring of Celiac Disease-Changing Utility of Serology and Histologic Measures: Expert Review
Gastroenterology 2019;156;885



Some additional causes of villous atrophy

- Small bowel bacterial overgrowth
- Malnutrition
- Autoimmune enteropathy
- B and T cell lymphomas
- HIV
- TB
- Eosinophilic enteritis
- Crohn's
- Giardia

Kelly CP et al
Advances in diagnosis and management of celiac disease
Gastroenterology 2015;148;1175

Jansson-Knodell CL et al
Not all that flattens villi is celiac disease: a review of enteropathies
Mayo clinic Proceedings 2018;93;509



Small Bowel Biopsy?

- In the pediatric population, a biopsy is considered optional under certain circumstances
- This approach has not yet been adopted in the adult population

Husby S et al

European Society for Pediatric Gastroenterology, Hepatology and Nutrition guideline for the treatment of coeliac disease

J Pediatric Gastroenterol Nutr 2012;54;136



Extra Credit



Under what circumstances should we use tTG to follow a Sprue patient?



Do patients with a diagnosis of Sprue who are doing well need a gluten re challenge? Or re biopsy?



What should we recommend to **asymptomatic** family members?



More

- Are there false positive tTG results?
- Can Celiac Disease occur in the presence of constipation?
- What should you do for a patient referred to your office with:
 - tTG -
 - Bx -
 - Genetics +



Questions

- Dr Abel has a patient with an antigliadin Ab IgG+ from 1997. The patient is doing very well on a gluten free diet. Any advice?



Advice

1. HLA testing: if negative you're done
2. If positive, then gluten challenge and tTG-IgA



Is there a relationship
between Sprue and
Lymphoma?



Is there a relationship between Sprue and Lymphoma?

- Yes
- 1/8000 patients with Sprue develop lymphoma
- Diet compliance MAY play a role



Joyce

- Age 45 has Celiac Disease for 10 years
- Is it possible for Joyce to develop a thyroid illness?





Is “Leaky Gut” the source of Celiac Disease?



Leaky Gut

- Refers to permeability
- Permeability may be an epiphenomenon
- Has been demonstrated in Celiac Disease and many other health issues
- Leaky Gut may be related to change in microbiota composition
- The clinical significance is still unclear

Camillieri M

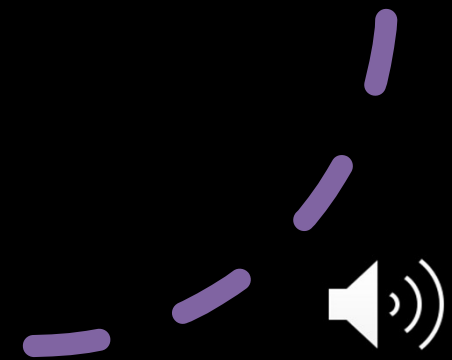
Leaky gut: mechanisms, measurement and clinical implications in humans

Gut 2019;68;1516



Question

- Ron G is a 45 y o patient with diarrhea and cramps. Also + tTG but negative small bowel biopsy sent back to you.
- What can you do now?



Question

What can you do now?

Check to make sure an adequate number of duodenal biopsies done

Two from bulb

Four from second duodenum



Non Response

- About 20% of patients with Celiac Disease have persistent symptoms, despite following a gluten free diet

Leffler DA et al

Etiologies and predictors of diagnosis in nonresponsive Celiac Disease
Clin Gastroenterol Hepatol 2007;5;445



Q: Patient non response to a gluten free diet can be due to:

1. Cheating on the diet
2. Microscopic colitis
3. Irritable bowel syndrome
4. Inflammatory bowel disease
5. All of the above



Q: Patient non response to a gluten free diet can be due to:

1. Cheating on the diet
2. Microscopic colitis
3. Irritable bowel syndrome
4. Inflammatory bowel disease
5. All of the above



What
would you
do?

- 2 physicians recently told me about their patients with Sprue refusing to alter their diet!



Risks

- Lymphoma
- Osteopenia
- 4 – 5 X increase in overall mortality over control population*

*Rubio-Tapia A et al
Increased prevalence and mortality in undiagnosed celiac disease
Gastroenterology 2009;137;88



Harry



- Has abdominal pain, bloating and diarrhea
- Harry is a 54 y.o male with type I diabetes
- He is on Insulin glargine (Lantus)
 - 20u sc daily
 - Insulin aspart (NovoLOG)
 - coverage schedule
- His blood sugars are in the 120 – 140 range
- Hgb A1c 5.9%





What is your
differential
diagnosis?



Thoughts:

- Gastroparesis
- Small intestinal bacterial overgrowth
- Irritable Bowel Syndrome
- Sprue



Conditions Associated With Celiac Disease

- Type 1 diabetes
- Autoimmune thyroid disease
- Autoimmune liver disease
- Down's Syndrome
- Selective IgA deficiency
- Elevated transaminases

Bai J and Ciacci C

World Gastroenterology Organisation Global Guidelines Celiac Disease 2017

J Clinical Gastroenterol 2017;51;755





If serology and biopsy are equivocal, can we do genetic testing to make a definitive diagnosis?





If serology and biopsy
are equivocal, can we
do genetic testing to
make a definitive
diagnosis?

YES



Looking for Answers

- Is genetically modified wheat the source of increased Sprue and Non Celiac Gluten Sensitivity?
- Will we have markers for Non Celiac Gluten Sensitivity in the future?*

Uhde M et al

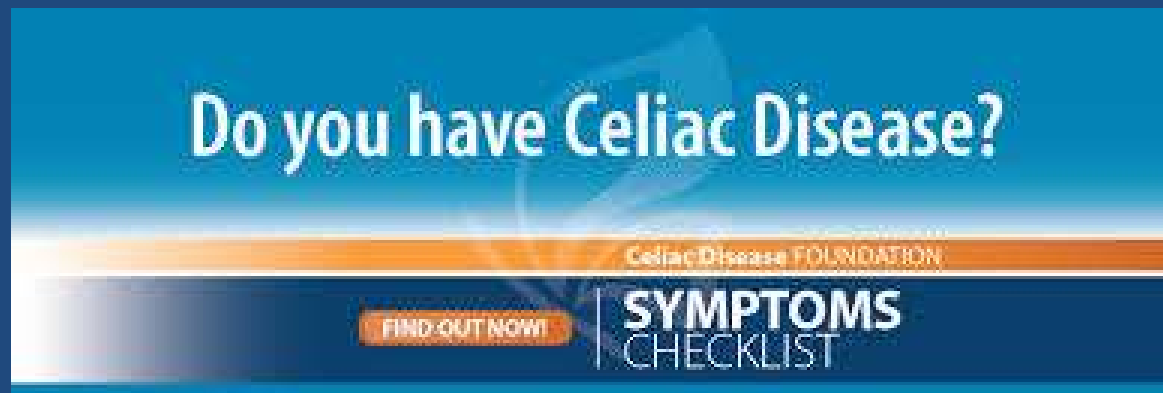
Intestinal cell damage and systemic immune activation in individuals reporting sensitivity to wheat in the absence of coeliac disease

Gut doi:10.1136/gutjnl-2016-311964



Resources

National Institutes of Health
Celiac Disease Awareness
Campaign <https://celiac.nih.gov>



<https://celiac.org>



Summary

- Celiac Disease may have many different presentations
- Non Celiac Gluten Sensitivity is real, but is often confused with Irritable Bowel Syndrome
- Most Americans are overweight; don't just look for Celiac Disease among underweight patients
- Remember HLA DQ2 and 8 negative results mean that the patient does not and never will get Celiac Disease



Thank You
Peter Buch MD
gieducator.com

