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AJG The American Journal of GASTROENTEROLOGY

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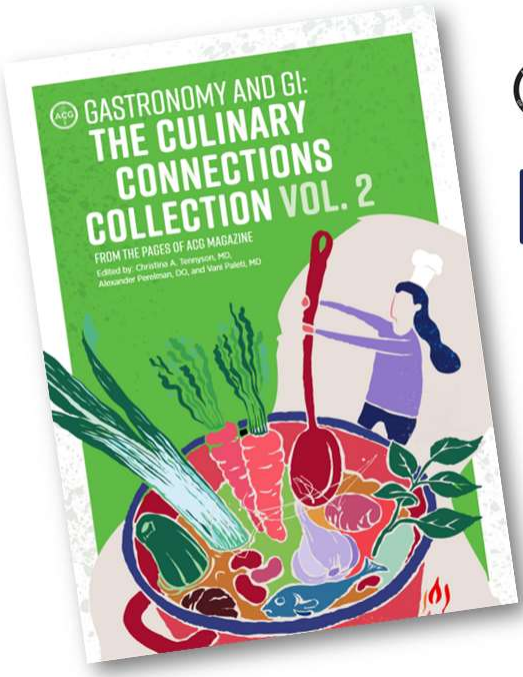
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Wolters Kluwer

ACG INSTITUTE FOR CLINICAL RESEARCH AND EDUCATION

Unrestricted educational grants to support the monograph have been provided to the ACG Institute for Clinical Research and Education from Nestlé Health Science and Seres Therapeutics and Ferring Pharmaceuticals Inc.

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**GASTRONOMY AND GI:
THE CULINARY
CONNECTIONS
COLLECTION VOL. 2**

FROM THE PAGES OF ACG MAGAZINE
Edited by Christina A. Sorrentino, MD,
Alexander Fereimban, MD, and Sara Palfy, MD

ACG **GASTRONOMY AND GI:
FROM ACG MAGAZINE
THE CULINARY
CONNECTIONS
COLLECTION VOLUME 2**
[BIT.LY/ACG-FOODIES-2](https://bit.ly/acg-foodies-2)

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2024 **ACG/LGS REGIONAL
POSTGRADUATE COURSE**

MARCH 1-3, 2024 | DOUBLETREE BY HILTON NEW ORLEANS
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Register online: meetings.gi.org



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2024 **ACG / FGS**
ANNUAL SPRING
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MARCH 8-10, 2024 | NAPLES GRANDE BEACH RESORT
NAPLES, FLORIDA

ACG FGS

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The banner features a central circular image of a fountain at night, surrounded by palm trees and buildings. The ACG logo is in the top right corner. A call-to-action button with a right-pointing arrow is located in the bottom right.

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Special Issue:
WELL-BEING

JOY AND WELL-BEING IN THE PRACTICE
OF MEDICINE - THE IMPORTANCE OF THE
HUMAN CONNECTION

ACG MAGAZINE

[BIT.LY/ACG-MAG-WELLBEING](https://bit.ly/acg-mag-wellbeing)

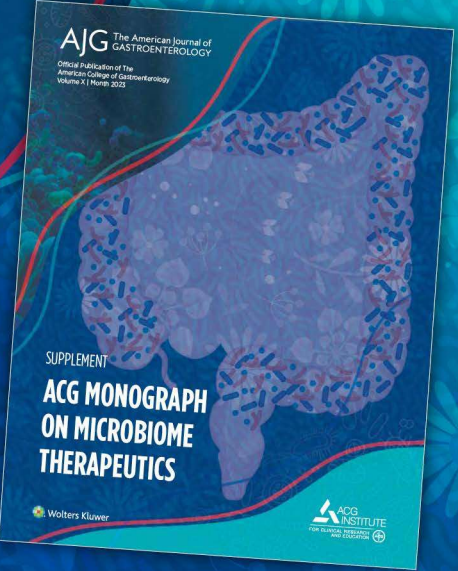
The cover features a blue silhouette of a human figure in a meditative pose, surrounded by colorful paper-cut style plants and butterflies. The background is a dark blue gradient.

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Participating in the Webinar




Moderator:
Isabel Hujuel, MD

All attendees will be muted and will remain in "Listen Only Mode"

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

A handout with the slides and room to take notes can be downloaded from your control panel.



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ACG Virtual Grand Rounds

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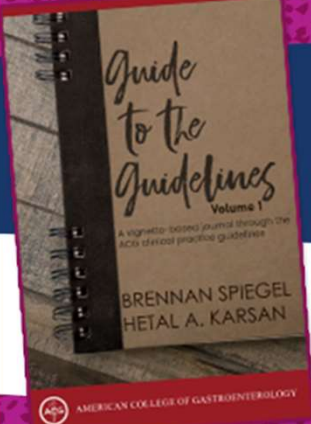



Week 7 – Thursday, February 15, 2024
 A New Organ: The Mesentery and Mesenteric Disease
 Faculty: Monjur Ahmed, MD, FACP
 Moderator: Christian S. Jackson, MD, FACP
At Noon and 8pm Eastern

Week 8 – Thursday, February 22, 2024
 Interpretation and Therapeutic Implications of Physiologic Testing in the Management of Esophageal Disorders
 Faculty: Dustin A. Carlson, MD, MSCI
 Moderator: Fady Haddad, MD
At Noon and 8pm Eastern

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Disclosures



Lucinda A. Harris, MD, MS, FACP:
 AbbVie: Advisor or Review Panel Member; Ardelyx: Advisor or Review Panel Member; Gemelli Biotech: Advisory Committee/Board Member; Mahana: Advisor or Review Panel Member

OFF LABEL USE: May discuss treatments of celiac disease under development. Will discuss treatments of IBS like symptoms with TCAs and Peppermint oil.



Isabel Hujuel, MD:
 No relevant financial relationships with ineligible companies.

**All of the relevant financial relationships listed for these individuals have been mitigated*

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Celiac Disease: What to do after the Diagnosis is Made



Lucinda A. Harris, MD, MS, FACP
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 Mayo Clinic – Alix School of Medicine
 Scottsdale, AZ
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 February 8th, 2024



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Objectives & Disclosures

- Review diagnostic work-up for celiac disease (CeD)
- Discuss follow-up care of the celiac patient
- Differentiate causes- and treatment of persistent symptoms

Disclosures – AbbVie, Ardelyx, Ironwood, Gemelli, QOL Medical, Salix, - consulting. Takeda – Research

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Celiac Disease vs. Gluten Sensitivity

- Celiac Disease – a well-defined autoimmune disorder
- Gluten sensitivity – uncertain disorder that has yet to be fully defined.

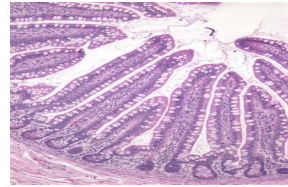
- Certain clinical features and pathways may be shared

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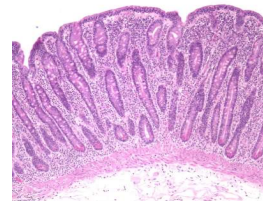


What is celiac disease?

- Occurs in genetically susceptible individuals
- Inflammatory response in small intestine
- Resolves when gluten is removed from the diet.



Normal small intestine



Total villous atrophy

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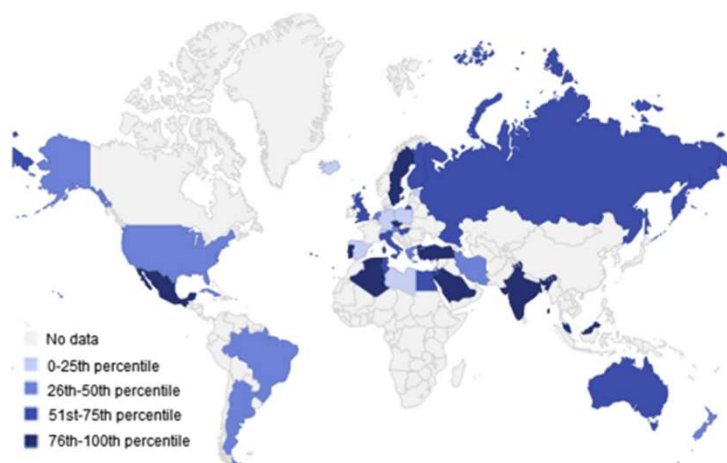


Who gets celiac disease?

Worldwide disorder – Global prevalence 1.4%

Higher in **Females** (0.6 vs. 0.4%)

Higher in **children** (0.9 vs 0.5%) but **ANY AGE**



Seroprevalence data

Singh P, et al. Clin Gastroenterol & Hepatol 2018;16:823-836

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Who gets celiac disease in the USA?

Seroprevalence

- Non-hispanic black population – 0.2%

- Hispanic population – 0.3%

- White individuals – 1.0%

- **Biopsy-based** prevalence is 0.7%
- **Genetics** – HLA DQ2 > HLA DQ8 (present in 35 % of the population)
- Evidence suggests prevalence is increasing!!!!

Singh P, et al. Clin Gastroenterol & Hepatol 2018;16:823-836

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How does celiac disease present?

GI Presentations

- **Classic Malabsorption** (25%)
Diarrhea, steatorrhea, weight loss, multiple vitamin deficiencies
- **Monosymptomatic** (50%)
Anemia, diarrhea, constipation, lactose intolerance, recurrent idiopathic pancreatitis, abnl lfts
- **Acute Abdomen** (Rare)
Perforation, abdominal pain, lymphoma, vomiting, intussusception, obstruction

Non-Classical Presentations

- **Non-GI presentation** (25%)
 - **Cardiac** – myocarditis
 - **Endocrine** – Auto-immune thyroid disease, Type I Diabetes, Infertility
 - **Musculoskeletal** – Bone disease, Sjogren's disease
 - **Neurologic** – Ataxia, neuropathy, epilepsy with occipital calcifications
 - **Psychiatric** – children/teens with depression/irritability

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How is the diagnosis of celiac disease made?

- **Serology**

IgA level
tissue transglutaminase (IgA)
De-amidated gliadin abs (IgA, IgG)
Anti-endomysial abs

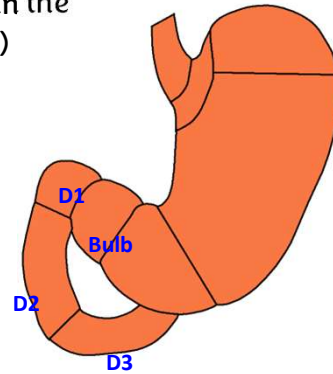
- **Genetics**

HLA - DQ2
HLA - DQ8

Guidelines for adults/children - Bx for confirmation (moderate evidence, strong recommendation)

- **Biopsy - Single pass**

• 4 biopsies pre & post ampulla
• 1-2 biopsies in the Bulb (targeted)



Rubio-Tapia A, et al. Am J Gastroenterol 2023;118: 59-76

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What is seen endoscopically?

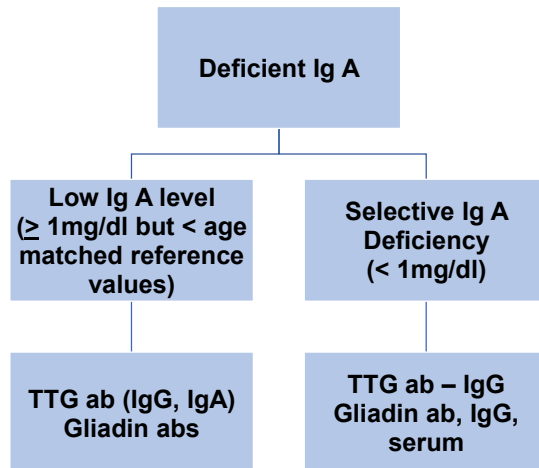


- Normal – at least 3 folds per endoscopic view
- Celiac Disease – may see decreased folds and/or “scalloping” (see photos)
- Gluten sensitivity – looks normal endoscopically, on path may see increased intraepithelial lymphocytes

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Serologic Diagnosis in IgA deficiency



If high pretest probability need EGD with duodenal biopsy

In setting of negative TTG-IgG, role of deamidated IgG gliadin abs is uncertain

Remember though + Endomysial ab is highly specific it is test most operator dependent

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Diagnosis of celiac disease in children

- Combination of high-level TTG IgA (> 10x upper limit of normal) with a + endomysial ab in a 2nd blood sample (moderate quality of evidence, conditional strength)
- May consider this in symptomatic adults unwilling/unable to undergo EGD
- Limitation – not all TTG assays are equal. Also, evidence for children more supportive of “no biopsy” than in adults

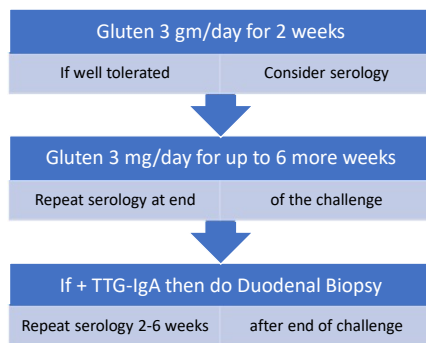
Rubio-Tapia A, et al. Am J Gastroenterol 2023;118: 59-76

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Special Situations

- **PATIENT ALREADY ON A GFD DIET**
- **Check Celiac HLA**
- **If positive HLA - Gluten Challenge¹**
- **BIOPSY DEMONSTRATES LYMPHOCYTIC INFILTRATION ONLY** (>25 intraepithelial lymphocytes/100 epithelial cells)



- Think:
- Helicobacter pylori
- Medications (NSAIDs)
- Small bowel intestinal overgrowth
- Systemic Autoimmune disorders
- Nonceliac wheat/gluten sensitivity

1. Rubio-Tapia A, et al. Am J Gastroenterol 2023;118: 59-76

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What additional blood tests should be done when considering diagnosis of CeD?

- CBC (Indices)
- Comprehensive metabolic profile (Calcium, liver function tests)
- Iron/TIBC/% Saturation
- Ferritin
- B12/Folate
- Vit D
- Trace minerals (copper, ceruloplasmin, selenium, zinc)
- Thyroid cascade/ autoimmune abs

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What's next once CeD is diagnosed?

Referral to dietician **well-versed in celiac disease (AVOID OATS)**

Dexa Scan?

Toothpaste, lipsticks/chapsticks/medications – gluten free

Vitamin supplementation

- Chewable multiple vitamin

- Vitamin D

- Calcium Supplementation

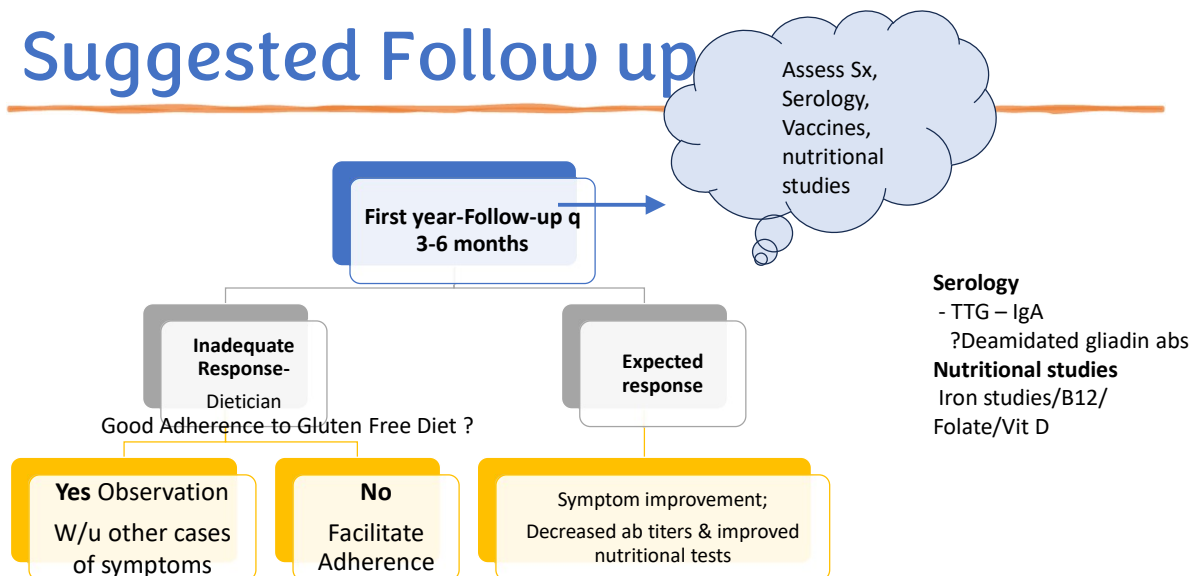
Counseling about testing children & other family members

Vaccines

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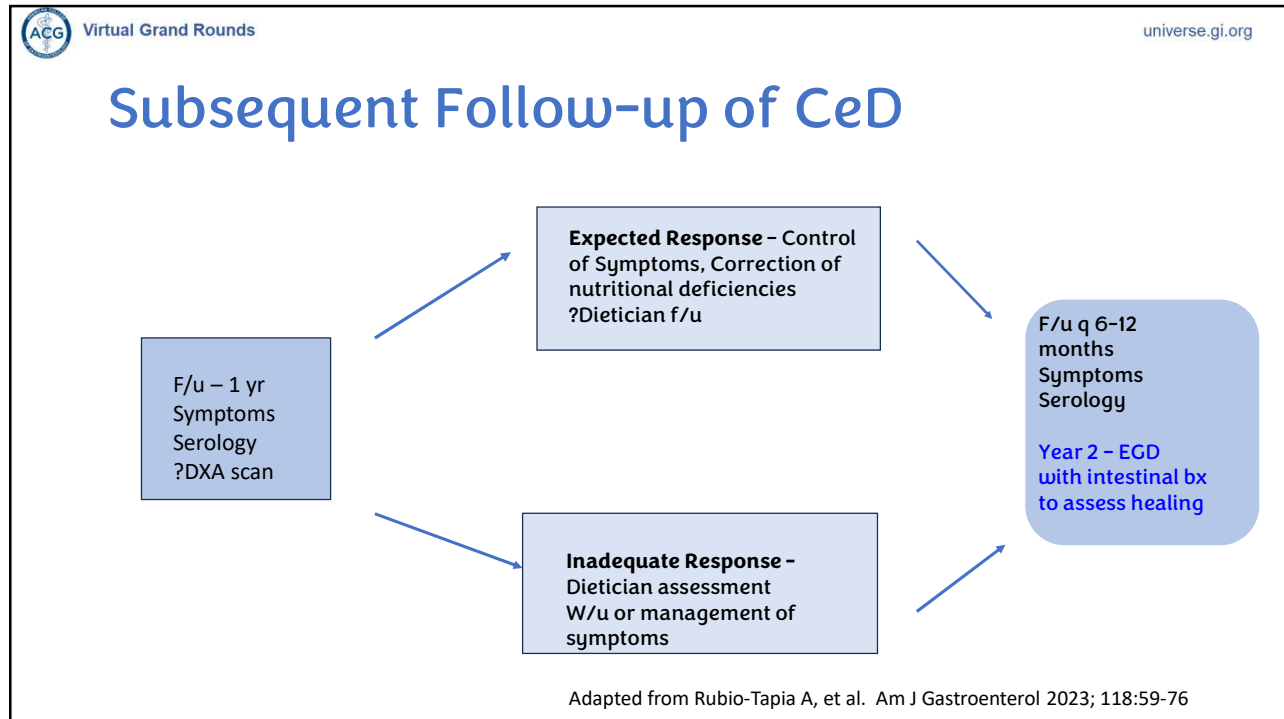


Suggested Follow up



Adapted from Rubio-Tapia A, et al. Am J Gastroenterol 2023; 118:59-76

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What is the goal of treatment?

- Mucosal healing
- Serological remission

➔

To improve long-term outcomes (5 yrs) for mortality, cancer risk and osteoporosis in adults

- Individualized discussion with patient regarding goals of therapy
- F/u biopsy should be considered for assessment of mucosal healing in adults after 2 years of doing GFD (shared decision making btwn pt and provider)
- **Conditional recommendation, low quality of evidence**

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Understanding mucosal healing

- Celiac disease is a patchy disease
- Mucosal healing rate is variable over time but is achievable
- There is poor correlation between serology and mucosal healing
- Negative serology increases the probability of mucosal healing
- Biopsy only reliable way to assess for mucosal healing

Rubio-Tapia A, et al. Am J Gastroenterol 2010;105:1412-20.
Pekki H, et al. Am J Gastroenterol 2015; 110:1078-1085.

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What is non-responsive CeD?

- > 15 % of adults have persistent symptoms on a strict GFD
- Gluten ingestion the most common cause
- Other factors associated with symptomatic persistent villous atrophy include age > 70, use of proton-pump inhibitors, NSAIDs, or SSRIs
- Relatively few have refractory celiac disease (0.04-1.5%)

Silvester J, et al. Am J Gastroenterol 2021;116:1148-1155. van
Wanrooij RL, et al. Clin Transl Gastroenterol 2017;8:e218

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What should be considered if symptoms persist?

- “Gluten, Gluten & Gluten” (Quote from Joe Murray, MD)
(Be careful how you broach this topic)
- Oats
- Other food intolerances (Corn, Lactose, FODMAPs, Sucrose)
- Small intestinal bacterial overgrowth
- Irritable bowel Syndrome & other DGBIs (GERD & Dyspepsia)
- Pancreatic Insufficiency
- Bile Acid Diarrhea
- Microscopic Colitis
- Refractory Sprue
- Mast cell activation Disorder
- Postural Orthostatic Tachycardia Syndrome (POTS) & Dysautonomia
- Malignancy - Lymphoma & Small bowel adenocarcinoma

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What is refractory sprue?

- Two types
 - Type 1 - nl intra-epithelial lymphocytes (IELs)
 - Type 2 - aberrant or pre-malignant population of IELs
- Rare
- Patient may have jejunal ulcers
- High rate of lymphoma
- Usually occur in patients with disease for > 10 yrs
- Diagnosis requires intestinal biopsy, CT of abdomen & pelvis and possibly PETscan

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How is refractory Sprue treated?

• TREATMENT OPTIONS

- Corticosteroids (including budesonide)
- Azathioprine
- Cyclosporine
- Cladribine (synthetic purine nucleoside)
- Biologics
- TPN

Type 2 can regress to Type 1 with treatment.

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What about OATS ?

Controversial

Studies with conflicting results* - Range from - no diff in bx's/sx's to increased sx's/increased IELs.

Guidelines recommendation - recommend gluten free oats for those with CeD. Gluten contamination, variable toxicity in different varieties of oats, risk of immune reactivation to oat protein avenin require monitoring for oat intolerance. Strong recommendation, Moderate quality of evidence.

Avoid in severe disease

Cross-contamination in production

1. Janutinen, et al. Gut 2002;50:332. 2. Peraaho, M. Scand J Gastroenterol 2004;39:27 3. Rubio-Tapia A, et al. Am J Gastroenterol 2023; 118:59-76

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Do probiotics have a role in the treatment of CeD?

- There is insufficient evidence for or against the use of probiotics for the treatment of CeD (**evidence gap in recommendation, very low quality of evidence**)
- Rationale for use is dysbiosis in duodenal microbiome in pts with CeD
- Probiotics are not subject to rigid standards of production and may be a potential source of gluten contamination

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Should gluten detection devices vs. current standard of care be used to monitor adherence to a GFD?

- **Gluten detection** – Commercially available kits to test urine & stool vs. NIMA
- For NIMA – Gluten detection depends on sample containing gluten and amt (>40 ppm)
- urine and stool tests may demonstrate gluten but not when it was ingested and may not detect clinically significant gluten
- Not enough clinical trials to suggest they help adherence to GFD
- **Suggest AGAINST use of gluten detection devices in food or biospecimens, conditional recommendation, low quality of evidence.**



Rubio-Tapia A, et al. Am J Gastroenterol 2023; 118:59-76

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What vaccines do patients with celiac disease need?

- **Pneumococcal Vaccine** is recommended for patients with CeD – it is safe & effective. (**conditional recommendation, low quality of evidence**)
 - Pts with CeD are at increased risk of pneumococcal infection due to hyposplenism (often subclinical)
 - Recommendation is for Prevnar 20 or PVC 15 followed 1 yr later by pneumococcal polysaccharide vaccine (PPSV23).
- **Covid vaccine** is safe and offers good protection for patients with CeD without other contra-indications.

Pts with CeD do not demonstrate increased risk of Covid

1. Rubio-Tapia A, et al. Am J Gastroenterol 2023; 118:59-76

2. Cohen BS, et al. Therap Adv Gastroenterol 2023; 16:17562848231170944

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Why should clinicians and patients care about compliance to a Gluten Free Diet ? Or why do Ce D patients need f/u?

- **Mortality rate in patients with untreated celiac disease is TWO FOLD GREATER at every age**
 - **Gastrointestinal malignancies** (lymphoma, SB adenoca, esophageal cancer, head & neck tumors)
 - **Osteoporosis**
 - Stunted growth
 - Infertility
 - Gluten ataxia and other neurological disturbances
 - Recurrent stomatitis/dental hypoplasia
 - Refractory disease (collagenous colitis)
 - Chronic ill health

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Future Directions: Is a Gluten Free Diet Sufficient Treatment for Ce D

- As emphasized in discussion of non-responsive Ce D and treatment of CeD – achieving a GFD is a real challenge
- New therapies – Allow consumption of small amts of gluten
- Glutenases (lactiglutenase, TAKO62)
- Tight junction regulators (larazotide)
- Nanoparticles inducing tolerance to gliadin (TAK 101, KAN-101)
- Immunotherapies

1. Pultz IS, et al. Gastroenterol 2021; 161:81-93. 2. Kelly CP, et al. Gastroenterol 2021; 161:66-80. 3. Leffler DA, et al. Gastroenterology 2015; 148: 1311-1319. 4. Diekman T et al. Curr Opin Pharmacology 2022; 66:102268

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Questions



Lucinda A. Harris, MD, MS, FACC



Isabel Hujoel, MD

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