



# ***When the Gluten Free Diet is Not Enough***

*Difficult Cases of Celiac Disease*

CDDW 2020  
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Sickkids and U of T



## ***Learning Points***

- ▶ Be able to develop an approach to the patient with Celiac Disease that despite compliance still has symptoms and positive serology.
- ▶ Understand the challenges that face some of the patients with Celiac Disease and suggestions for intervention.
- ▶ Looking at how to approach the patient with refractory Celiac Disease.

## ***Conflict of Interest***

- None to declare except I do eat gluten!



# **Most common reason for persistent serology**

- ▶ Always review the diet
- ▶ Often compliance rating differs between parent and child



Case 1:  
Persistent  
symptoms  
and  
serology  
and very  
compliant!

14 yo / 28 yo male

Presented with abdominal pain, fatigue and mild iron deficiency anemia.

Initial serology: TTG IGA 3200 CU

Histology: Marsh 3b (although meets the ESPGHAN guidelines for NO biopsy)

Still abdominal pain and fatigue, with minimal improvement although anemia has resolve. Very compliant.

Two years later TTG 95 CU with EMA still positive at 1/10 (Tittered no further). Marsh 2

# WHAT COULD BE THE ISSUE

- 
- ▶ Review compliance at each visit (patient +/- parents)
  - ▶ On going exposure:
    - ▶ 34% of children and adolescents eat fast food on any given day.
    - ▶ Gluten detected in 32% of GF restaurant food. (Detection of Gluten in Gluten-Free Labeled Restaurant Food: Analysis of Crowd-Sourced Data. [Am J Gastroenterol](#). 2019 May;114(5):792-797)
    - ▶ The “great and varied choice” of packaged GF product:  
Gluten contamination in foods labeled as “gluten free” in the United States. [J Food Prot](#). 2014 Oct;77(10):1830-3.

# Packaged food!

- Everyone eats too much
- By law has less than 20 ppm of gluten
- But several servings of “ < 20ppm ” adds up to gluten exposure
- Many do not take this into account

*Your chance to preach  
healthy eating*





# “Testing” for gluten exposure

- Urine and stool testing for gluten are available
  - Not covered by provincial health plans
  - Limited because have limited time span for detection
    - Urine: 1–2 days
    - Stool: 2–4 days
  - Are available by mail order
- 



# Gluten Contamination Elimination Diet

- ▶ Those with non-responsive CD may be reacting to inadvertent exposure to small amounts of gluten
- ▶ Most of the time good dietary review solves the problem
- ▶ When it doesn't
  - ▶ All processed and packaged foods are removed for a period of 3 months
  - ▶ Re biopsy
  - ▶ If successful can usually go back to the typical GF diet
    - ▶ Trace gluten contamination may play a role in mucosal and clinical recovery in a subgroup of diet-adherent non-responsive celiac disease patients. [BMC Gastroenterol.](#) 2013 Feb 28;13:40.

# THE OUTCOME

- Patient became well
- Serology became negative
- The family found this so healthy they all stayed on this diet!



Much more a whole food based diet!



## Case 2

14 yo or 24 yo female

Presented with weight loss, significant abdominal pain and diarrhea, fatigue and iron deficiency anemia.

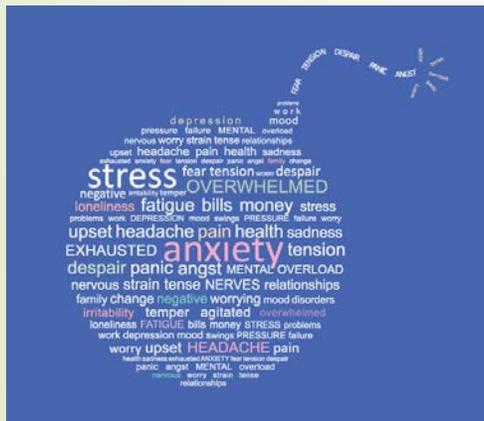
TTG IgA 4960 CU / Marsh 3b

Gets gluten free diet teaching

In follow up is very compliant but has lost more weight and continues with fatigue

## Case 2

- Serology is now normal
- Anemia corrected
- Lost additional 2 kgs
- In review – has had issues with anxiety
- No issues with body image, excessive exercise or “vomiting” after meals
- Mother is “very careful” about gluten exposure
- ***Could you have predicted this?***





# Avoidant/restrictive food intake disorder

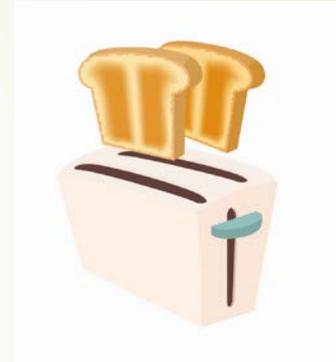
- ▶ ARFID is an eating disorder that occurs when one does not eat enough to meet their energy or nutritional needs.
  - ▶ In CD there can be an overwhelming concern about getting gluten contamination.
  - ▶ This can result in significant weight loss or a failure to gain weight.
  - ▶ Many times there has already been an underlying anxiety disorder
  - ▶ This anxiety can be shared by parents / spouse
    - ▶ Sometimes the parental anxiety is worse than the child's
- 
- ▶ Eating disorders in adolescents with chronic gastrointestinal and endocrine diseases. [Lancet Child Adolesc Health](#). 2019 Mar;3(3):181-189.

# Approaches

- ▶ Ease up on the compliance talk
- ▶ Ensure they understand it takes a while for the serology to become normal
- ▶ Maybe a bit of cross contamination is okay

- ▶ Preparation of Gluten-Free Foods Alongside Gluten-Containing Food May Not Always Be as Risky for Celiac Patients as Diet Guides Suggest.

[Gastroenterology](#). 2020 Jan;158(1):273-275.



- ▶ Often the GF diet is just one more added stressor
- ▶ Refer for professional help



# Resources



- [About Kids Health \(SICKKIDS\)](#)
- [NEDIC – National Eating Disorder Information Centre](#) (Canada)(UHN)
- [NEDA – National Eating Disorder Association](#) (United States)
- American Academy of Pediatrics – [Eating Disorders in Children](#)
- [BEAT – Beating Eating Disorders](#) (United Kingdom)
- [Kelty Eating Disorders](#) (Kelty Mental Health Resource Centre, BC Children's Hospital)
- Children's Hospital of Eastern Ontario – [Eating Disorders](#)
- [ANEB Québec: https://anebquebec.com](https://anebquebec.com)



## Case 3

10 yo

Presented with significant abdominal pain and constipation and fatigue.

Mildly elevated IgA TTG in community and begun on GFD

Serology here negative

Did not want a gluten challenge

In follow up is "very compliant" but feels she is only slightly better



## Case 3

Re biopsy plus colonoscopy /  
Mild lymphocytic infiltrate, microcytic colitis

Mom felt everyone was very compliant

Significant psychosocial issue and missing school  
Significant pain issues / Followed in the Pain Program

Much better at summer camp

# Can Other GI issues Complicate Celiac Disease?

## ➤ IBS – is CD more common?

- Celiac disease is uncommon in irritable bowel syndrome in the USA. [Eur J Gastroenterol Hepatol](#). 2018 Feb;30(2):149-154.
- Screening for Celiac Disease in Irritable Bowel Syndrome: An Updated Systematic Review and Meta-analysis. [Am J Gastroenterol](#). 2017 Jan;112(1):65-76.

## ➤ Can you have IBS in CD

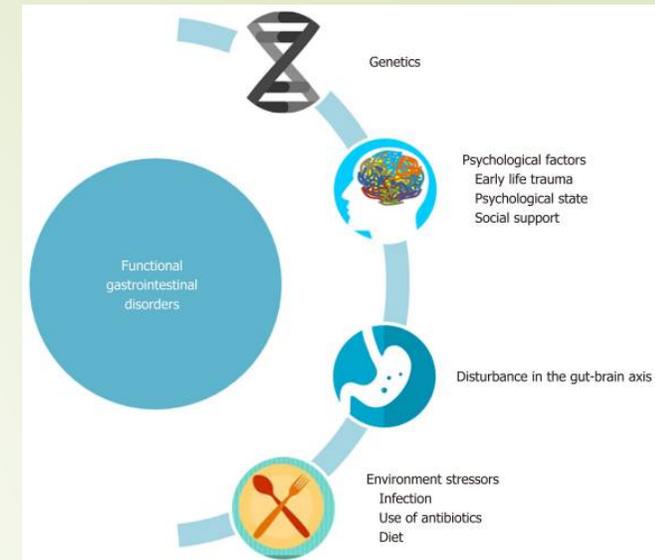
- Clinical features and symptom recovery on a gluten-free diet in Canadian adults with celiac disease. [Can J Gastroenterol](#). 2013 Aug; 27(8): 449–453.
- Gluten and Functional Abdominal Pain Disorders in Children. [Nutrients](#). 2018 Oct 12;10(10).
- Abdominal Pain-Associated Functional Gastrointestinal Disorder Prevalence in Children and Adolescents with Celiac Disease on Gluten-Free Diet: A Multinational Study. [J Pediatr](#). 2017 Mar;182:150-154.

## ➤ *Dysmotility*

- [Dig Dis](#). 2015;33(2):200-7. Motility alterations in celiac disease and non-celiac gluten sensitivity.

# Disorders of Brain / Gut Interaction (DBGI)

- ▶ This is the new name for functional disorders of the GI tract
- ▶ Celiac Disease could be the cause of these symptoms
  - ▶ Sometimes the symptoms will resolve fully on the GFD
- ▶ May be the triggering inflammation
  - ▶ Patients may continue with symptoms despite GFD
  - ▶ Can sometimes be difficult to sort out from dietary compliance / non responsive Celiac Disease
  - ▶ Need patient (parent) buy in





# DBGI “Overlay”

- ▶ Were you suspicious of DBGI at the initial visit?
  - ▶ One reason I often biopsy these patients even if they would meet ESPGHAN criteria for NO Biopsy
  - ▶ It is always easier to have the discussion up front
- ▶ All of the symptoms may NOT go away on the GFD
  - ▶ **Symptoms of Functional Intestinal Disorders Are Common in Patients with Celiac Disease Following Transition to a Gluten-Free Diet.** [Dig Dis Sci](#). 2017 Sep;62(9):2449-2454. (12 mo f/u)
- ▶ My patient took years of “therapy” to be better
- ▶ For sure if you don’t address the DBGI – symptoms will linger



# Interventions

- Add what you do for DBGI to the GFD
- FODMAP Diet – just be aware that you are making the diet even more restrictive
  - **Beyond Irritable Bowel Syndrome: The Efficacy of the Low Fodmap Diet for Improving Symptoms in Inflammatory Bowel Diseases and Celiac Disease.** [Dig Dis.](#) 2018;36(4):271-280.
- Mindfulness
  - **Mindfulness training reduces the severity of irritable bowel syndrome in women: results of a randomized controlled trial.** [Am J Gastroenterol.](#) 2011 Sep;106(9):1678-88.
- See someone who practices **Psychogastroenterology**



Case 3  
What  
happen?

Much better at summer  
camp

Eventually sent to  
inpatient pain program

Years later well in follow

# Case 4: Type 1 Celiac Disease

## *Pediatric*

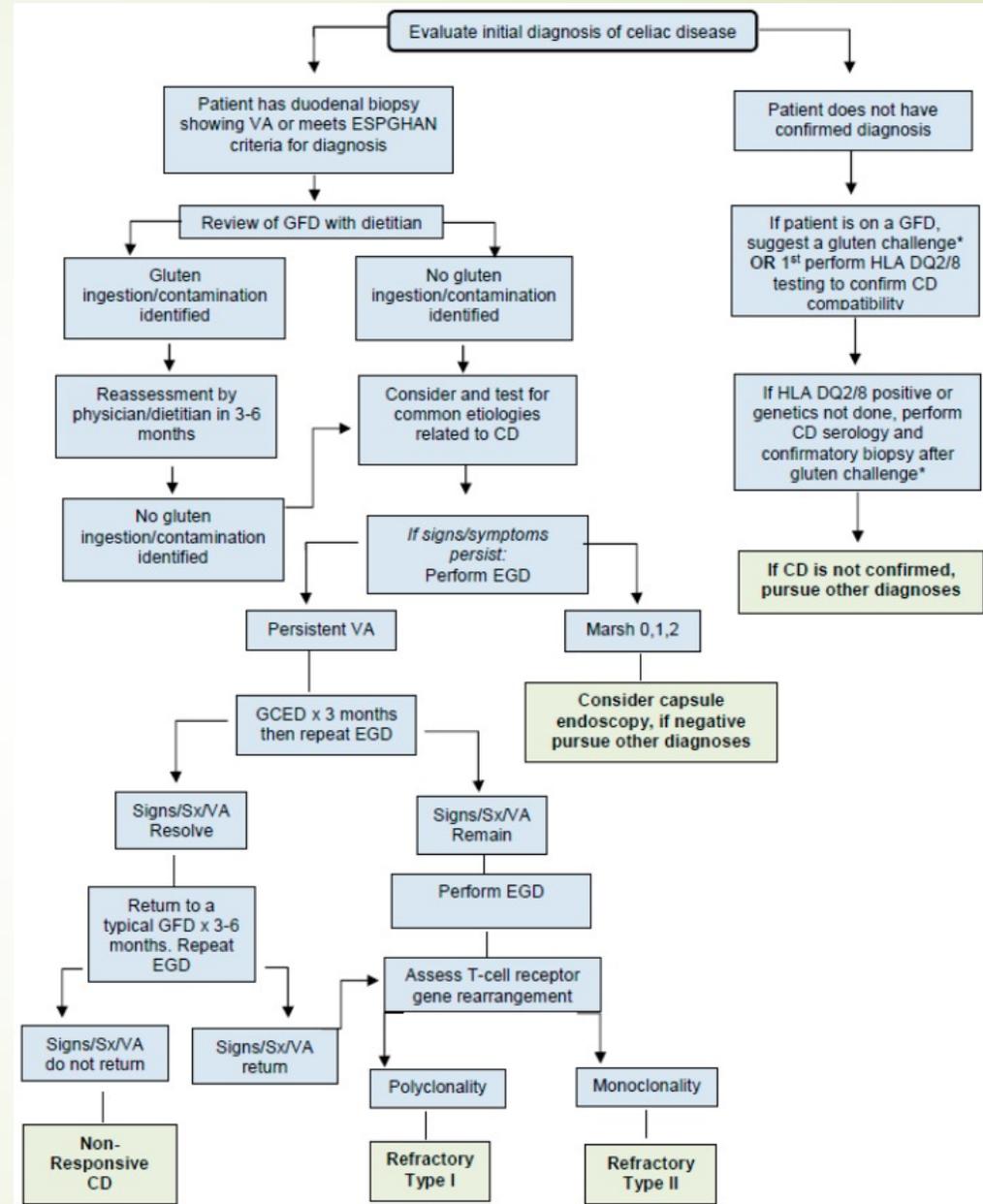
- ▶ 13yo female
- ▶ Trisomy 21
- ▶ 2015 Presented with anemia (Hgb 43) / TTG >100, IgA 8.39
- ▶ C-spine instability to treated re ESPGHAN Guidelines – no biopsy
- ▶ Started GFD – but TTG stayed >100
- ▶ Biopsy Marsh 3a / TTG > 100
- ▶ 2016, 2017, 2018 biopsy and serology the same but she is asymptomatic

## *Adult*

- 49 yr old male
- PMH: recurrent sinus infections – high dose NSAIDs
- Trip Mexico: severe diarrhea - infectious gastroenteritis? Improved with 7 days ATB Tx
- 2 weeks later, symptoms recurred and persisted for >2 Mo
- Investigations: tTG >100 ; Marsh 3c
- GFD but continued severe weight loss
- TPN

# Algorithm

- Refractory Celiac Disease is quite uncommon
- Almost all are in the adult population





# Refractory Celiac Disease

- ▶ Refractory coeliac disease (RCD):
  - ▶ persistent or recurrent malabsorptive symptoms and villous atrophy despite strict adherence to a gluten-free diet (GFD) for at least 6-12 months.
  - ▶ No other cause for non-response
  - ▶ No overt malignancy
  - ▶ May occur after a respond to a GFD or after a relapsed despite adherence and initial response to the GFD.
- ▶ Type 1 (normal intraepithelial lymphocyte phenotype)
  - ▶ usually improves after treatment with a combination of aggressive nutritional support, adherence to a GFD, and alternative pharmacological therapies
- ▶ Type 2 (defined by the presence of abnormal (clonal) intraepithelial lymphocyte phenotype)
  - ▶ response to alternative therapies is less certain and the prognosis is poor. Severe complications such as ulcerative jejunitis and enteropathy-associated T cell lymphoma may occur in a subgroup of patients with RCD.



# Type 2 rather than Type 1

- ▶ Intraepithelial lymphocytes with abnormal immunophenotype (CD3, CD8, by immunochemistry or flow cytometry respectively)
- ▶ Clonal T-cell receptor gene rearrangement by molecular analysis
- ▶ Type 1 – usually respond to diet therapy plus steroids or immunotherapy
- ▶ Malignant risk with Type 2 quite high



# Pediatric patient

- In 2019
- ***Placed on MMF (600mg bid)***
- TTG declines nicely to 9
- Last biopsy still abnormal but no clonality
- Patient remains well
  
- Next biopsy is pending



# Adult patient

- ▶ 3 months of TPN
- ▶ Budesonide and azathioprine
- ▶ Azathioprine stopped due to ↑ bilirubin
- ▶ Then issues with budesonide so azathioprine restarted at a lower dose
  
- ▶ Next biopsy pending – with immunophenotypes
- ▶ Patient is well



# Therapies used for Type 1

- ▶ Oral Steroids – prednisone / prednisolone
- ▶ Oral budesonide – open capsule or crush tablet or use ampules
- ▶ Azathioprine – either alone or in combination with steroids (budesonide)
- ▶ Infliximab may be useful
  
- ▶ Monitor closely
- ▶ May become Type 2



# Review

- ▶ Be a gluten detective and try a clean diet
- ▶ Address the psychosocial issues in Celiac Disease – know resources for your patients
- ▶ If they don't get better with GFD (symptoms and histology and serology) – and they are compliant – only then think of Refractory Celiac Disease
  - ▶ Very rare / usually adults
- ▶ [Published: 23 July 2019](#) BMC MEDICINE
- ▶ **Celiac disease: a comprehensive current review**