The Truth Behind Gluten and Other Sensitivities

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An Everyday Case in My Clinic

• A 28 yr old woman comes to see me for food intolerances and gluten sensitivity. She reports abdominal bloating and discomfort after eating various foods, abdominal cramping and loose stools ranging from 2 to 3 per day without blood for the past year. Symptoms are relieved by passage of stool. She also complains of fatigue.

• She went on a gluten free diet two months ago. She feels better but now finds that other foods are also leading to bloating, pain and loose stools. She is concerned about food allergies and asks if she has celiac disease. The patient also asks if her increasingly restrictive diet will cause nutritional problems. She wants to know what type of diet she should eat.

What do you think is the clinical problem and how do you address the patient’s concerns?
What to Eat and What Not to Eat?

• Nearly every patient who sees a GI practitioner wants to know is it something that they eat and/or is there something missing from their diet that is the cause of their GI and other health problems
• The popularity of many types of diets underscore the notion that what we eat is the key to health and well-being
• Marketing of food promoting potential health benefits is becoming more common

Food and the Digestive Tract: Friend or Foe?

• The average human ingests a large amount of food in their lifetime
  – ~ 60,000 pounds - 27,273 kilograms - 30 tons
• The vast majority benefit from this ingestion but a small percentage develop complications:
  – Food poisoning
  – Food allergies
  – Food sensitivities
• However, there is a reported increase in food allergies, celiac disease and seemingly of food sensitivities
Biological Variables that Influence the Developing Immunophenotype of an Infant

Classification of Adverse Reactions to Food

Adapted from Boyce JA et al. JACI.2010;126(6):1105
GI Disorders and ARF

- GI food allergy
- Food protein enteropathies (milk, soy)
- Celiac disease
- Nonceliac gluten sensitivity (NCGS)
- Eosinophilic gastroenteritis, esophagitis
- Lactose and other carbohydrate intolerance
- Irritable bowel syndrome
- Inflammatory bowel disease
- Dyspepsia, GERD, peptic ulcer

Physiological Food Reactions

- Large volume meals (overeating) cause distension, promote regurgitation
- Fatty foods delay gastric emptying, alter motility
- Legumes, cruciferous vegetables, garlic, onions, etc, may lead to flatus (farts)
- Non-absorbable or poorly absorbed sugars and carbohydrates can cause diarrhea, bloating, flatulence, etc
- However, intestinal gas is NORMAL (14 farts/day)
Immunological Reactions to Food

- Food hypersensitivity (IgE-mediated)
  - GI food allergy
  - Oral allergy syndrome
  - Latex-food allergy
- Celiac disease (T-cell mediated)
- Eosinophilic GI disorders (eosinophils)
  - EoE, EGE, Eosinophilic colitis
- Food protein enteropathies (mixed immune)

Food Allergy: Epidemiology

- 4-5% of the population have food allergy
- 20-30% of the population think they have food allergy
- 30-40% of patients with FA have asthma/atopic dermatitis
- 50% of anaphylaxis treated in ED are due to FA
- 70% of patients with FA have + FHx of atopic diseases

Sicherer SH, Sampson HA, JACI, 125:S116-25, 2010
Dietary Response to a Gluten-Free Diet: Is this Diagnostic of Celiac Disease?

- Placebo response in IBS up to 70%
- Gluten (increased prolamines) is hard to digest, increases stool volume
- Gluten-free diet often eliminates other dietary factors (additives, preservatives)
- PPV of symptom improvement after gluten withdrawal for celiac disease only 36% in one study
- What else is improved by a gluten free-diet?
Patients Already on a Gluten Free Diet: How to Test for Celiac Disease?

- Depends on duration and stringency of the GFD
  - if truly on a GFD for years it is difficult to prove CD
  - many patients on a self-taught GFD are not truly gluten-free
- Serology can take over a year to normalize
  - Check TTG IgA +/- DGP IgA, IgG
- Histology can take several years plus to become normal

- Thus, if an undiagnosed patient wants an assessment for possible CD assess with serological tests, HLA DQ2/8 and EGD with biopsies within the first year on a GFD
- Absence of HLA DQ2.2, 2.5 or 8 effectively excludes CD now or in the future

Sugal, E, et al, Digestive & Liver Disease, 42:352, 2010
Crowe, SE. In The Clinic : Celiac Disease, Ann Int Med,2011 154:ITC5-14,

How to Evaluate for Causes of Adverse Reactions to Food

- History - ? co-factors (exercise, drugs)
- Assess for lactose intolerance
- Assess for SIBO
- Skin testing for food allergens
- Diet diary
- Hypoallergenic diet trial
- Endoscopy and biopsy
- CBC, eosinophil count
- Quantitative immunoglobulins
- Specific IgE levels (RAST, ELISA)
- Serum IgG to foods – No longer accepted
- Celiac serology and/or HLA DQ assay
- Other tests for non-IgE mediated reactions

Bischoff & Crowe, Gastroenterology, 128: 1089, 2005
DeGaetani & Crowe, CGH, 8: 755, 2010
Food Antigen Challenges

- Skin prick testing
  - Excellent negative predictive value
  - Poor positive predictive value
- Skin patch testing for food allergens
- Double blinded food challenge (NG tube, capsule)
- GI tract by endoscopic mucosal testing
  - Limited studies but appears useful
- Other sites unproven or not accepted
  - Sublingual
  - Neuromuscular
  - Iridology

Alternate Tests for Food Sensitivity and Non-Celiac Gluten Sensitivity

- LabCorp – NCGS screen = IgG to native gliadin
- ALCAT – Gut Heath Profile (tests specific genetic predisposition to celiac disease as well as antibody testing and immune system activation to food sensitivities), also leukocyte assays for food sensitivities
- Cyrex – Intestinal antigen permeability screen, Wheat/ Gluten proteome reactivity/autoimmunity, Cross-reacting foods & food sensitivities (IgG & IgA)
- Enterolab – various stool panels (food Abs, gene tests, celiac Abs) se
- Genova Diagnostics (Great Smokies Diagnostic Lab) – Blood for IgG4 to food, for celiac & gluten sensitivity, saliva for gliadin sensitivity
Alternate Tests for Food Allergy or Food Intolerance

• **Many labs** – food allergies, IgG to food antigens*
• **Cyrex, ALCAT** – as per previous slide*
• **MRT/LEAP** – Measures release of immune mediators (histamine, cytokines, etc) via changes to the liquid/solids ratio of a blood sample after incubation with specific food, additive, or chemical*
• **Applied kinesiology** – patient holds putative allergenic food while muscle strength is tested by the practitioner*
• **Electrodermal skin testing** - machine measures electrical resistance at acupuncture points when allergen is placed in the electrical circuit*

* Expert NIH panel “recommends not using” this test for routine diagnosis of food allergy

Boyce JA et al. JACI.2010;126(6):1105

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Gluten Causes Symptoms in IBS Patients Without Celiac Disease

[Graphs showing mean change in symptoms over 6 weeks]

Adapted from Biesiekierski JR, et al. Am J Gastroenterol, Jan. 11, 2011 (Epub ahead of print)
Adverse Reactions to FODMAPs

Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols

- Fructose and fructans
- Sorbitol
- Sucrose
- Lactose

Many foods (grains including wheat starch, fruits, vegetables) contain FODMAPs

No Effect of Gluten after Reduced FODMAP Diet in IBS Patients

- 37 subjects with IBS (Rome III) reporting NCGS (celiac disease meticulously excluded) underwent double-blind cross-over study
- 2 wks low FODMAP diet resulted in significant improvement of GI symptoms and fatigue
- Challenge with gluten (high, low or control) did not result in symptomatic or biological changes
- Suggests sensitivity may not be due to gluten

No Effect of Gluten after Reduced FODMAP Diet in IBS Patients


Gluten Coexists with Nonabsorbed Fructans and Other Saccharides
Proposed Mechanisms of Non-Celiac Gluten or Wheat Sensitivity

Wheat ingestion

- Poorly Absorbed Carbohydrates
- Gluten-mediated
- Excess Fructans
- Fermentation
- Gas production & SCFA formation
- Microbiome changes
- Altered Permeability
- Immune Activation/ Low grade inflammation

GI Symptoms

SCFA = short chain fatty acids

Vazquez-Roque MI, et al. Gastroenterology 2013;144:903

Back to the Patient

Lab test results
- Normal CBC & diff, CMP
- Stool studies negative for pathogens
- Celiac serology not elevated
- No HLA DQ susceptibility genes
- Specific IgE to wheat negative
- Glucose breath test – no rise in hydrogen or methane

What to do next?
- Consider endoscopy/biopsy
- Check nutritional parameters
- Diet diary
- Referral to a knowledgeable RD
- Trial of low FODMAP diet
- Other dietary trials within reason
- Consider treating SIBO
Take Home Points

• Lactose intolerance is common and easily treated
• Celiac disease is common and easily screened for
• Food allergies are not rare and can be identified with subsequent dietary elimination providing benefit
• Patients can have a specific ARF and also have a FGID
• The role of gluten, FODMAPs, and other foods in IBS/FGIDs remains unclear. However, identifying specific food intolerances can be beneficial for IBS patients
• The microbiome/SIBO also contribute to food intolerances
• Patients appreciate the assessment even if it turns out to be negative and they have the non-specific food sensitivity common to most IBS/FGID patients

DeGaetani & Crowe, CGH, 8: 755, 2010