A 52 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 a 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 felt better initially but now finds that other foods are also leading to bloating, abdominal pain and loose stools. She is concerned about food allergies and if she might have celiac disease. She also asks if her increasingly restrictive diet will cause nutritional problems.

What do you think is the clinical problem and how can we 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 they eat and/or is it something they are 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.
Good Grains and Bad Grains?

**HIS AND HERS “SEX” CEREAL**

**THE DAILY CONSTITUTIONAL AID**
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

• There is a reported increase in food allergies, celiac disease and seemingly of food sensitivities too
Biological Variables that Influence the Developing Immunophenotype of an Infant

- Atopic (allergic) phenotype
- Epithelial permeability
- Indigenous microbiota
- Exogenous microbial exposure (e.g. LPS, helminths)
- Genetic impact
- Oral tolerance
- Homeostasis
- Productive immunity
- Antigen (nature, timing, dose)
- Dietary factors (lipsids, omega-6, omega-3, vitamin A)
- Breastfeeding
- Nutrition
- Age

Brandtzaeg, Nat Rev Gastroenterol Hepatol, 7: 380-400, 2010
Classification of Adverse Reactions to Food (ARF)

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
- 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 X/day)
Mechanical Problems with Food

• Medical conditions in which foods can be problematic:
  • Strictures
  • Gastric outlet problems
  • Gastroparesis
  • Diverticulitis

• Foods that can cause problems:
  • Insoluble fibers – skins or peel, seeds, nuts, many vegetables
Pharmacological Food Reactions

Reactions to food due to chemical components in foods and food additives such as:

- Histamine
- Swiss cheese
- Tuna and other scombroid fish
- Sulfites
- Tartrazine
- MSG
- Caffeine
- Amines

This form of ARF does not tend to result in GI problems but asthma, headaches, and skin manifestations.
Not All Adverse Reactions to Food Can Be Classified

“Did you say this pizza gave you indigestion?”
Psychological Adverse Reactions to Food

Snow White was poisoned by an apple, Jack found a giant in his beanstalk, and look what happened to Alice when she ate the mushroom! And you wonder why I won’t eat fruits and vegetables?!
Immunological Reactions to Food

- Food hypersensitivity (IgE-mediated allergy)
- Celiac disease (T-cell mediated)
- Food protein enteropathies (mixed)
  - Hypersensitivity
  - Immune complexes
  - T-cells
Food Allergy: Epidemiology

- Of the population have food allergy
- Of the population *think* they have food allergy
- Of patients with FA have asthma/atopic dermatitis
- Of anaphylaxis treated in ED are due to FA
- Of patients with FA have + FHx of atopic diseases

Sicherer SH, Sampson HA, JACI, 125:S116-25, 2010
**Food Allergy – Key Information**

### Definition
- Adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food

### Outgrowing phenomena
- Egg: >50% by age 5
- Milk: >80% by age 5
- Peanut: ~20%

### Big 8
- Milk, soy, eggs, wheat, peanuts, tree nuts, fish and shellfish

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Manifestations of Food Allergy

• GI symptoms (in 30-70%):
  • swelling of oropharyngeal mucosa
  • nausea/vomiting, diarrhea, abdominal pain, bloating

• Other manifestations:
  • hives, eczema
  • asthma, rhinitis, otitis
  • anaphylaxis
Oral Allergy Syndrome

- Localized IgE - Initial sensitization to pollens results in IgE that cross reacts with fruit and vegetables

- Raw fruit and vegetables
  - Birch pollen – apple, peach, pear, almond, hazelnut, potato, carrot
  - Ragweed pollen – melons, banana, gourd family
  - Mugwort pollen – celery, carrot, spices
  - Grass pollen - tomato

- Itching, ± swelling and/or tingling

- Confined to lips, tongue, roof of mouth and throat

- Affects patients with pollen allergy

Latex – Food Allergy Syndrome

- Sensitization to latex results in IgE that cross reacts with fruit and vegetables
- Exposure to foods give same symptoms as latex
- Natural Rubber Latex contains over 200 proteins, 10 bind IgE (HEV b 1-10)
- Food associations:
  - Kiwi (5)
  - Potato, tomato (7)
  - Avocado, chestnut, banana (6)
Treatment – the 4E’s

- Expert
- Elimination
- Epinephrine
- Education

Management of Food Allergy

- Avoidance of food allergens
- Patient education
  - Understand food allergen groups
  - Since Jan 2006 USA labeling for 8 major food allergens
  - Recognize warning symptoms
- Information networks, newsletters
  - Food Allergy Research and Education (FARE) (www.foodallergy.org)
- Treatments
  - Antihistamines, mast cell inhibitors, cromolyn sodium, corticosteroids
  - Injectable epinephrine
  - No proven role for oral desensitization
Lactose Intolerance

• Symptoms due to lactose malabsorption resulting from lactose deficiency
  • Congenital deficiencies - rare
  • Constitutional lactase insufficiency
    • Genetically programmed decreased in lactase synthesis after weaning
    • Common in native NA, Asians, Africans, those from Mediterranean areas
  • Secondary lactase insufficiency
    • Gastroenteritis, Crohn’s disease, celiac disease

• Most common ARF worldwide
Management of Lactose Intolerance

• Most individuals with lactose intolerance can tolerate 12-15 g lactose (8-10 oz of milk)
• Yoghurt, hard cheeses are naturally lactose-free
• Lactose better tolerated when taken in small, more frequent amounts and with other foods
• Lactase supplements helpful
• No proven benefit for probiotics, adaptation programs
• Triacylglycerol content of many milk products can cause GI symptoms unrelated to lactase insufficiency or cows milk protein (CMP) allergy

## Dietary Treatments for IBS and Other Functional GI Disorders

<table>
<thead>
<tr>
<th>Diet</th>
<th>Evidence for use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low fat</td>
<td>Limited</td>
</tr>
<tr>
<td>Gluten-free</td>
<td>Limited</td>
</tr>
<tr>
<td>Specific carbohydrate intolerance</td>
<td>Little to none</td>
</tr>
<tr>
<td>Low FODMAP</td>
<td>Limited</td>
</tr>
<tr>
<td>Paleolithic</td>
<td>Minimal</td>
</tr>
<tr>
<td>Candida</td>
<td>None</td>
</tr>
<tr>
<td>Hypoallergenic</td>
<td>Little to none</td>
</tr>
</tbody>
</table>
# What is Gluten Sensitivity?

<table>
<thead>
<tr>
<th>Oslo Definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gluten Sensitivity Due to Celiac Disease (CD)</td>
</tr>
<tr>
<td>Non-Celiac Gluten Sensitivity (NCGS)</td>
</tr>
</tbody>
</table>

Gluten Causes Symptoms in IBS Patients Without Celiac Disease

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

Fructan and GOS content (g/serve)

- rice-brown
- rice-white
- rice-noodles
- gluten-free bread
- quinoa-pasta
- pasta-gluten free
- rice bubbles
- cornflakes
- wheat-pasta
- wheat-bread
- rye bread
- muesli
- wheat-cous cous
- haricot beans

Categories:
- GOS
- Fructan
- Fructose
- Gluten free products
Proposed Mechanisms of Non-Celiac Gluten or Wheat Sensitivity

Wheat ingestion

- Poorly Absorbed Carbohydrates
- Gluten-mediated
- Nocebo Effect
- Altered Permeability
- Immune Activation/Low grade inflammation

GI Symptoms

- Excess Fructans
- Fermentation
- Gas production & SCFA formation
- Microbiome changes


SCFA = short chain fatty acid
Between Celiac Disease & IBS: The “No Man’s Land” of Gluten Sensitivity

Is it IBS, Celiac Disease or Something in Between?

Non-celiac Gluten Sensitivity

IBS symptoms

Motility / visceral sensation
Brain - gut interactions
Immune activation
Altered gut microbiome

Spectrum of CD

Potential / asymptomatic CD
Symptomatic CD

Back to the Patient

Diagnosis

• Assessment for celiac disease
• Assessment for food allergies
• Assessment for other conditions that might be contributing to her food sensitivities (SIBO, IBS, lactose intolerance)
• Assessment for nutritional status
  - vitamin D, iron are most commonly deficient

Treatment

• Referral to a Registered Dietitian for dietary management
• Additional management according to the diagnosis
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 IBS
• 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 patients

DeGaetani & Crowe, CGH, 8: 755, 2010
Questions?