Is it Gluten Intolerance or is it IBS?

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Conflicts of Interest

- Shares in NexPep (ImmusanT)
  - Developing immunotherapy based treatment for coeliac disease
- Regular consumption of gluten-containing products supplied by pharmaceutical companies
- Home bread making

Clinical Scenario

- 29 year woman, JT attends for her first consultation, having recently moved from Brisbane for work-related reasons (promotion).
- Long history of gastrointestinal symptoms
  - Bloating
  - Intermittent diarrhoea and a few normal bowel actions
  - Crampy lower abdominal pain
- Also
  - Dysmenorrhea (intermittent naproxen)
  - Fatigue
  - Fibromyalgia
  - Iron deficiency
    - GI side effects from oral iron supplements

Clinical Scenario

- Symptoms worse since coming to Melbourne
- Diet
  - Avoided lactose containing foods since childhood
  - Ethical Vegan since 19 years of age
  - Recently commenced gluten free diet on the advice of Naturopath and feels that although this has improved her symptoms, they remain troublesome
  - Now planning to restrict her diet further to control her symptoms and 'work out the cause'
- Questions
  - 'Do I have Coeliac Disease?'
  - 'Why are my symptoms still present on a gluten free diet?'
  - 'What else do I need to eliminate from my diet?'

Synopsis

- What is Gluten Intolerance and how does it differ from Coeliac Disease?
- What is IBS?
- How can we differentiate Gluten Intolerance, Coeliac Disease and IBS?
- What are the therapeutic implications?

What is Gluten Intolerance?

- Symptoms after consumption of gluten, improved by restricting dietary gluten
  - Coeliac disease excluded
- Gastrointestinal
  - Bowel disturbance, pain, bloating
- Extraintestinal
  - Lethargy, brain fog, rheumatological
- Respond to reduction of or removal of gluten from the diet
  - 10% of population on low gluten or gluten free diet (10 x #Coeliacs)
- No underlying structural, histological or immunological abnormality
- Inadvertent gluten exposure not an issue beyond symptoms

Coeliac Disease

- Immunologically mediated disorder affecting primarily small intestine
- Abnormal reaction to gluten resulting in lymphocyte infiltration of the small intestinal mucosa, villus damage, crypt hypertrophy and reduced function
- 1% of population, all are DQ2 or DQ8 positive
- Responds to gluten free diet
  - Strict
  - Lifelong
- Symptoms
  - May be 'asymptomatic'
  - GI Symptoms – malabsorptive
  - Systemic symptoms and other autoimmune manifestations
  - Some become exquisitely sensitive to gluten whilst on GFD

Irritable Bowel Syndrome

- Common (20% of population), female predominance in west
- Specific diagnostic criteria (Rome Criteria)
  - Abdominal pain
  - Altered bowel habit
  - Subtyped by dominant bowel habit
    - Constipation, Diarrhoea, Mixed
- Cause 'unknown' and likely heterogeneous
  - Disorder of the Brain/Gut axis
  - ?microinflammation
  - ?disordered microbiota
- No underlying malabsorptive or inflammatory disease
- Management centres on symptom control

Why Distinguish Coeliac Disease from IBS and Gluten Intolerance?

- Therapeutic implications
  - Coeliac Disease = No Gluten
  - Lifelong, strict gluten free diet
- Prognostic implications
  - Malabsorption
  - Resistant/Refractory Coeliac Dis
  - T cell lymphoma

Distinguishing Coeliac Disease from Gluten Intolerance and IBS

- 'Coeliac Gene Test'
  - HLA typing, DQ2 or DQ8
  - Present in up to 40% of population
  - Useful for excluding, not diagnosing Coeliac Disease
- Serology
  - Tissue Transglutaminase IgA + Total IgA and:
  - Deamidated Gliadin Peptide IgG
  - High titre = Coeliac Disease likely – confirm with duodenal biopsy
- Endoscopy and duodenal biopsy
  - Confirmatory or in equivocal serology/high risk situation
  - On gluten loaded diet (4 slices/day 4 weeks)

Back to the action…….

Investigations

- Hb 105, MCV 78, Ferritin 6
- U&E Normal
- LFT Normal
- ESR, CRP normal
- HLA DQ2, 8 negative
- Faecal MCS, PCR negative
- Faecal Calprotectin normal
- No endoscopic investigations required

What is Going On?

- Iron deficiency
  - Likely dietary/menstrual +/- NSAID
- Contributing to symptoms
- Intolerant of oral iron
- Iron infusion
  - Total dose by infusion (1g Fe Carboxymaltose)
  - Repeated IV boluses (200mg Fe Carboxymaltose)
- Monitoring of iron status and preemptive action

What About The Gut Symptoms?

- Excluded Coeliac Disease, IBD very unlikely (Faecal Calprotectin)
- Fulfils criteria for IBS, Diarrhoea predominant
- Possible lactose intolerance
- Responded to 'Gluten Free Diet'
- So does she have IBS or Gluten Intolerance?

Gluten Intolerance

- Patient with symptoms, where these improve or resolve with removal/reduction of gluten from the diet

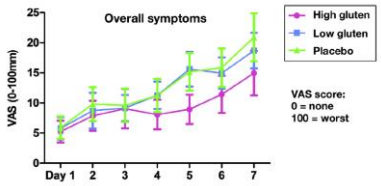
But….

- Gluten does not occur as a pure substance in nature
  - Commonly occurs with other substances that can cause GI symptoms
    - FODMAPs
- Symptoms are nonspecific (and therefore not helpful) and no diagnostic testing is available
- The Placebo Effect is powerful
  - Adoption of a treatment accepted as likely to be helpful by the healer and the patient will be expected to result in improvement
- The Nocebo Effect is also powerful
  - Knowingly consuming the 'toxic' substance will cause symptoms by the same mechanisms as the placebo effect (acting in the opposite direction)

Gluten Intolerance (Non-Coeliac Gluten Sensitivity)

- Contentious diagnosis in Gastroenterology
- Face validity in that removal/reduction in dietary gluten reduces symptoms in some (many) patients
- These diets also reduce other problematic substances (FODMAPs)
  - Poorly or nonabsorbed carbohydrates acted on by colonic bacteria to produce small molecules and gas, thereby increasing colonic volume and reducing stool viscosity, leading to symptoms in susceptible individuals
- Blinded dietary gluten challenges have given conflicting results
  - Background level of FODMAP intake is likely the explanation

Effect of Perceived Gluten Intake in NCGS



Biesiekierski et al 2013

How to Distinguish IBS and Gluten Intolerance?

- Low FODMAP diet
- Blinded, placebo controlled challenge with pure gluten

Is a Breath Test the Answer?

- Disaccharide malabsorption, Small Intestinal Bacterial Overgrowth
- Hydrogen, methane
- Special diet
- Ingestion of the sugar, then regular collections of expired breath
- Symptoms
- Commonly positive control
  - Lactulose
- Test Substances
  - Lactose
  - Fructose

Breath Testing

- Covers only a small range of potential problem substances
- Questionable value in diagnosis of SIBO
- Expensive
- Time consuming
- **Does not predict response to diet**
- On the positive side:
  - May validate patient's symptoms
  - May identify some particularly troublesome foods

What are the Implications of Making a Diagnosis of Gluten Intolerance vs IBS

- Diet (and in particular gluten content) is the primary cause of symptoms
  - Ignores other aspects of diet
    - FODMAPs found in a broader range of foods
    - Fats and spices may cause symptoms
  - No evidence that GFD is 'healthier' in non-coeliacs
- May be OK, provided that diet is effective in controlling symptoms and remains balanced
- Risks – residual symptoms may lead to further exclusions and disordered eating

What are the Implications of Making a Diagnosis of Gluten Intolerance vs IBS

- Framework for explanation of symptoms
  - Common and well recognised/studied disorder of Brain-Gut communication
  - Validates and legitimises symptoms
    - Remove perjorative implications
- Recognises that diet is an important aspect, but not the sole focus of treatment
  - Gluten is not the main offender
    - FODMAPs
    - Fats
    - Spices
    - Manipulation of soluble/insoluble, fermentable/nonfermentable fibres
  - Some online help, but an experienced dietitan is invaluable

What are the Implications of Making a Diagnosis of Gluten Intolerance vs IBS

- Other aspects of treatment are important and may be dominant
- Pharmacological (symptomatic) treatments
  - Antispasmodics
  - Antidiarrhoeals
  - Visceral analgesics (tricyclics)
  - (Bile salt binding agents)
- Psychological therapies
  - Strong evidence for efficacy in short and long term
  - Gut Focussed Hypnotherapy, CBT, Mindfulness
  - Professionally delivered – some cost (reduced with MHCP)
  - Online CBT – ibsclinc.org.au

So What about JT?

- Explanation of symptoms and their contributions
  - Gut Symptoms – IBS-D with FODMAP sensitivity
  - Extraintestinal
    - Fibromyalgia, dysmenorrhea (?? Endometriosis), iron deficiency
- Management
  - Iron infusion
  - Dietitian referral
  - Recognition of likely stress component – move, new job
    - Psychologist for GFH, CBT, Mindfulness
  - Pharmacological
    - Antispasmodic, Antidiarrhoeal
    - ?Tricyclic
    - ?Suppress menstruation

Take Home Messages

- Gut Symptoms are complex and have many causes
- In young patients, simple blood and stool tests are sufficient to exclude underlying 'organic' disorders
- IBS is common, but misunderstood by patients and doctors
- 'Gluten Intolerance' presents with similar symptoms to IBS and likely reflects FODMAP sensitivity
- Treatment of 'Gluten Intolerance' is highly focussed on diet, and may not relieve all symptoms, leading to further unhealthy and ineffective restrictions with the possibility of disordered eating (orthorexia, anorexia)

Take Home Messages

- Making a positive diagnosis of IBS broadens the range of treatment options and recognises the contributions of a variety of factors to symptoms
- The diagnosis of IBS needs to be presented positively, in a way that legitimises and validates the patient's illness
- 'Extra' treatments include a broader dietary focus on potential causes (preferably delivered by a dietitian), as well as psychological and symptomatic pharmacological therapies.