Should I Be Gluten-Free?

Deep Dive Webinars – for **Empower*Ed*** members

Disclaimer

This webinar is not a substitute for medical advice; participants should discuss their health status with a knowledgeable health care provider before making any decisions about care.

What we'll cover

1. What is gluten?
2. Gluten-related disorders
3. Other grain-related issues
4. Who should avoid gluten?
5. What foods must be avoided if I have issues with gluten?
6. Gluten myths and misunderstandings
7. Why are gluten-related disorders on the rise?

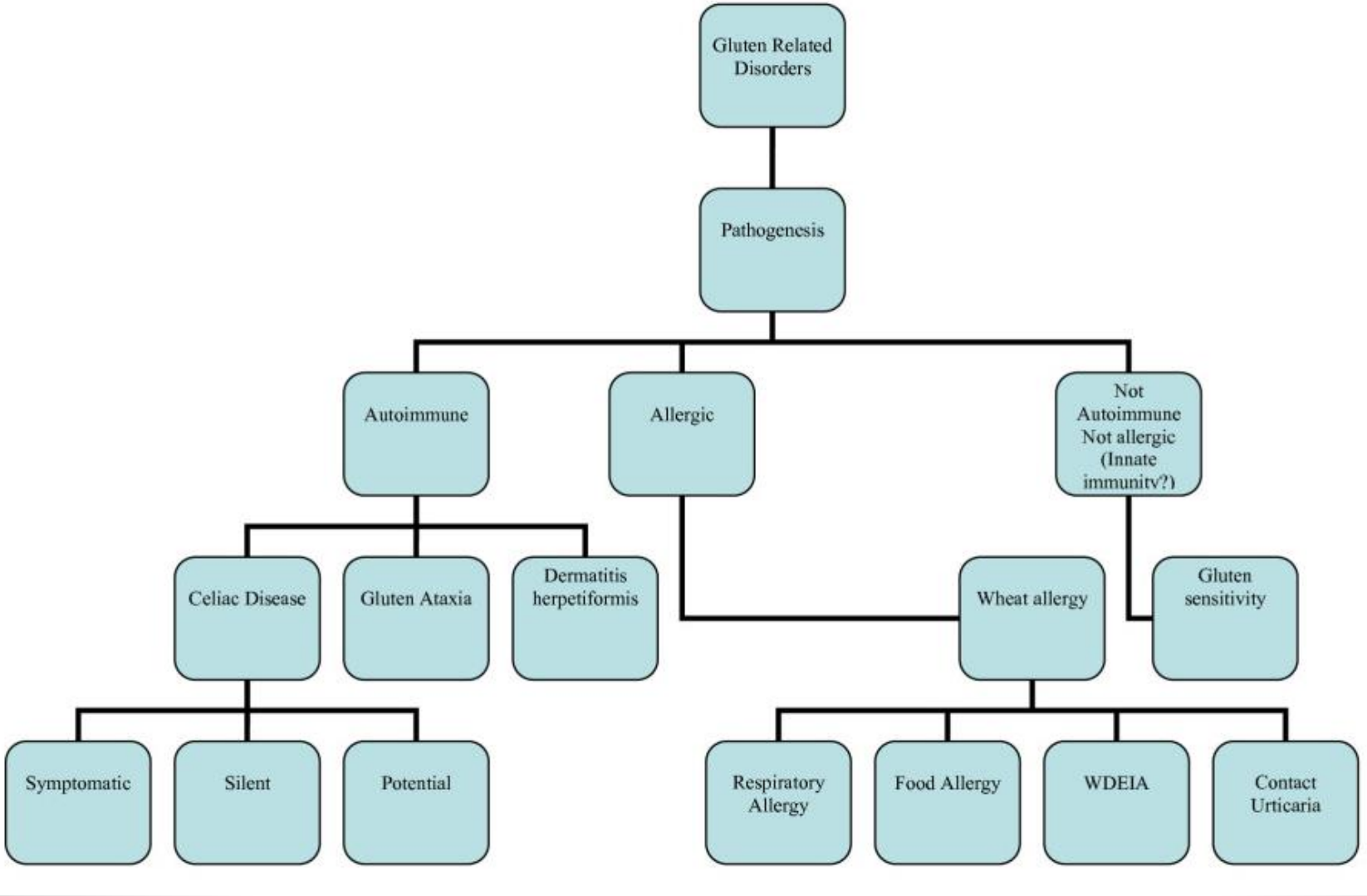
What is gluten?

- Principal storage protein in wheat; very similar proteins found in barley and rye.
- Gluten is the composite of two storage proteins:
  - Gliadin (a prolamine i.e. rich in proline and glutamine) – gives bread the ability to rise properly during baking; and
  - Glutenin – gives dough strength and elasticity.
- Gliadin is highly resistant to digestion by gastric, pancreatic and brush border peptidases (1).

Gluten-related disorders

- Popular interest in gluten-free diets + explosion in market for gluten-free foods (US$2.5 billion global sales in 2010) (1) → convening of panel of 15 experts in London in February 2011 to develop consensus on new nomenclature and classification of gluten-related disorders.
- Panel proposed definitions and developed a diagnostic algorithm:

Diagnostic algorithm



Gluten-related disorders

- Coeliac disease
- Gluten ataxia
- Other autoimmune disorders
- Non-coeliac gluten sensitivity
- Wheat allergy

Coeliac disease

- The most common autoimmune condition.
- In genetically predisposed individuals, undigested gliadin triggers immune response in intestinal mucosa → proliferation of gluten-specific activated cytotoxic T cells → destruction of mucosa in small intestine.
- Symptoms may occur months-years after gluten exposure (2).
- Coeliac sufferers must be medically gluten-free.

Coeliac disease

- Prevalence:
  - Highest in countries populated primarily by people of European origin; also common in North Africa, the Middle East and part of the Asian continent (1).
  - 1.2% in men
  - 1.9% in women (1);
  - Prevalence has quadrupled in last 50 years (2)
  - Strong genetic component to risk; multiple genes involved (4).
    - ~ 95% of CD patients are HLA-DQ2 positive (i.e. express genes encoding the major histocompatibility complex class II protein HLA-DQ2); remaining patients are usually HLA-DQ8-positive.
    - BUT ~ 30% of Caucasian individuals are HLA-DQ2-positive i.e. the presence of HLA-DQ2 and/or HLA-DQ8 is necessary for disease development but not sufficient on its own.
    - Estimated risk effect is 36%-53%.

Coeliac disease

- Symptoms:
  - Classical intestinal: Chronic diarrhoea, indigestion, stomach pain, bloating, gas (frequently malodorous), constipation, loss of appetite, greasy stools, weight loss
  - Non-classical extraintestinal: anaemia, osteoporosis, neurological disturbances, fatigue.
  - Dermatitis herpetiformis (blistering rash and cutaneous IgA deposits).
  - In infants and children, failure to thrive.
  - Silent forms: Many people have no symptoms but are diagnosed through serological screening.
  - Potential forms: Auto-antibodies are detected but autoimmune insult of the intestinal mucosa is not present.
  - Long-term complications if not diagnosed: infertility, lymphoma.
  - In diagnosed coeliacs on long-term GFD, gluten ingestion may occasionally cause immediate acute symptoms, including vomiting and abdominal pain (1).

Testing for coeliac disease

- Initial test: Anti-tTG – IgA antibodies to tissue transglutaminase (tTG)
- Confirmatory tests:
  - IgA anti-EMA.
  - Small intestinal biopsy.
- Additional tests:
  - Deamidated gliadin peptides (DGP) antibodies (especially of the IgG class) – higher sensitivity and specificity than anti-tTG and anti-EMA, but possibly perform better in IgA-deficient subjects and in children < 3 years.
  - IgA deficient CD sufferers will not have abnormally elevated levels of IgA anti-tTG or IgA anti-EMA; IgG-based screening tests are required (1).

Gluten ataxia

- Sporadic ataxia with positive serological markers for gluten sensitisation (1).
- Caused by gluten-induced autoimmune damage to the cerebellum. Antibody cross-reactivity occurs between antigens on Purkinje cells and gluten components.
- Transglutaminase antibodies are deposited around blood vessels in the brain, especially in the cerebellum, pons and medulla.
- Ocular symptoms may also occur.

Who should be tested?

- Adults and children with any of the following should undergo initial testing (1, 2):
  - First-degree relatives of people with coeliac disease
  - Persistent unexplained abdominal or gastrointestinal symptoms
  - Faltering growth
  - Prolonged fatigue
  - Unexpected weight loss
  - Severe or persistent mouth ulcers
  - Unexplained iron, vitamin B12 or folate deficiency
  - Type 1 diabetes, at diagnosis
  - Autoimmune thyroid disease, at diagnosis
  - Irritable bowel syndrome (in adults)
  - IgA deficiency.

Possible indicators for testing

- Any other type of autoimmune disease
- Metabolic bone disorder (reduced bone mineral density or osteomalacia)
- Unexplained neurological symptoms (particularly peripheral neuropathy or ataxia)
- Unexplained subfertility or recurrent miscarriage
- Persistently raised liver enzymes with unknown cause
- Dental enamel defects
- Down's syndrome
- Turner syndrome
- William syndrome.

(1)

Other autoimmune disorders

- Autoimmune sufferers should avoid high-gluten foods, especially those with:
  - Type 1 diabetes
    - Prevalence of CD in T1 diabetics 0.6-16.4%; 10% have CD at some point in the lives (1).
    - < 10% of T1 diabetics who develop CD show gastrointestinal symptoms; most are either asymptomatic or mildly symptomatic (2).

Other autoimmune disorders

- Autoimmune sufferers should avoid high-gluten foods, especially those with:
  - Autoimmune thyroid disease
    - ATD sufferers more likely to develop CD and vice versa (1).
    - Serum antitissue transglutaminase antibodies (present in patients with active coeliac disease) bind and react to thyroid tissue. Anti-tTG antibodies decrease and eventually disappear on a gluten-free diet (2).

Other autoimmune disorders

- Autoimmune sufferers should avoid high-gluten foods, especially those with:
  - Rheumatoid arthritis
    - GFD decreases serum IgG antibodies to gliadin (1).
  - Sjögren's syndrome
    - Increased prevalence of both CD and NCGS in Sjögren's patients (2, 3).

Non-coeliac gluten sensitivity

- Originally described in the 1980s; recently "re-discovered" but still contentious (1, 2).
- Intestinal and extra-intestinal symptoms related to ingestion of gluten-containing food, in subjects who don't have coeliac disease or wheat allergy.
- Symptoms occur soon after eating gluten; disappear if gluten is avoided and relapse within hours or a few days after gluten challenge (3).

Non-coeliac gluten sensitivity

- Symptoms:
  - Abdominal pain/discomfort, bloating, diarrhoea and/or constipation, nausea, epigastric pain, gastroesophageal reflux, aphthous stomatitis;
  - Headache, fibromyalgia-like joint/muscle pain, muscle cramps, bone pain, leg or arm numbness, behaviour changes, 'brain fog', depression, anxiety, weight loss;
  - Dermatitis, ezcema;
  - Fatigue, anaemia (1, 2)
  - Gastrointestinal symptoms + tiredness are major symptoms in children (3).

Non-coeliac gluten sensitivity

- May be involved in some cases of autism and schizophrenia (1, 2)
  - Schizophrenics have higher than average anti-gliadin antibody titres.
  - A subset of autistic children improve on a GFCF diet.

Non-coeliac gluten sensitivity

- May be caused by wheat amylase-trypsin inhibitors (ATIs) triggering innate immune response in intestinal monocytes, macrophages and dendritic cells (1).
- Time lapse between gluten ingestion and appearance of symptoms: from hours to days (2, 3).
- Female:male ratio 5.4:1 (4).
- More common in young/middle age adults (5).
- Prevalence estimates vary from 0.5 - 6% (6).
- 1.15:1 ratio between suspected NCGS and new CD diagnoses (7).

Non-coeliac gluten sensitivity

- ~ 30% of IBS sufferers have NCGS (1, 2).
  - DBPCT of 34 IBS sufferers in whom coeliac disease was ruled out, and who were controlling their own symptoms with GFD, randomised to receive gluten or placebo for ≤ 6 wks (3).
  - 68% of patients in gluten group vs 40% of patients on placebo reported that symptoms (pain, bloating, satisfaction with stool consistency, and tiredness) were not adequately controlled (note nocebo effect).
  - Patients were significantly worse within 1 week of gluten reintroduction.

Non-coeliac gluten sensitivity

- Diagnosis: ‘diagnosis of exclusion’
  - No specific biomarker of NCGS yet established (i.e. no tTG autoantibodies or other specific celiac-related antibodies (1).
  - No damage to intestinal mucosa, no increased IP (2, 3).
- Withdraw all gluten-containing foods and, if symptoms disappear, after ≥ 3 weeks re-challenge (DBPCC if possible) with simple high-gluten foods e.g. wheat pasta, plain bread, freekeh or couscous to avoid errors of attribution from eating high-fat and/or high-sugar gluten-containing foods.

Wheat allergy

- Immune reaction to gluten, occurring minutes-hours after ingestion (1).
- Cross-linking of immunoglobulin E (IgE) by repeat amino acid sequences in gluten peptides (especially repeated glutamine) triggers the release of chemical mediators including histamine, from basophils and mast cells (2).
- Manifestations of wheat allergy (3, 4):
  - Baker's asthma and rhinitis (from inhalation of wheat flour)
  - Atopic dermatitis (skin eruption and itching) which develops shortly after wheat ingestion.
  - Food-dependent exercise-induced anaphylaxis (FDEIA) – wheat is most common cause (WDEIA).
- Prevalence estimates vary from 0.4-9%; mostly < 4% (5).

Other grain-related issues

- FODMAPs malabsorption (fermentable oligo-, di-, and mono-saccharides and polyols)
- Wheat is high in FODMAPs; symptom improvement on GFD in some IBS sufferers may be due to reduced FODMAPs intake (1).
  - DB cross-over trial of 37 subjects (aged 24-61 y, 6 men) with NCGS and IBS (based on Rome III criteria), but not CD (2).
  - 2 weeks on reduced FODMAPs diet, then random assignment to either high-gluten (16 g gluten/d), low-gluten (2 g gluten/d and 14 g whey protein/d), or control (16 g whey protein/d) diets for 1 week, followed by a washout period of at least 2 weeks.
  - 22 participants then crossed over to either gluten (16 g/d), whey (16 g/d), or control (no additional protein) diets for 3 days.
  - GI symptoms consistently and significantly improved in all participants during reduced FODMAP intake, but significantly worsened to a similar degree when given gluten or whey protein.
  - Only 8% of participants showed gluten-specific effects (but did whey cause adverse effects?).

Who should avoid gluten?

- People with:
  - Diagnosed coeliac disease
  - Other autoimmune diseases
  - Wheat allergy
  - Challenge-proven NCGS
  - IBS – re-challenge if symptoms resolve
  - Autism?? – opioid peptides (1)
  - Schizophrenia ?? – elevated antigliadin antibodies (2).
- Everyone else is OK to eat gluten!

Foods to avoid

- Wheat, barley, rye, spelt, kamut/khorasan, einkorn, triticale (1)
  - CD and gluten ataxia – medically gluten-free diet i.e. must avoid even traces of gluten e.g. from toaster.
  - Other gluten-related syndromes – avoiding high-gluten foods is adequate.
- Avenin is a protein found in oats; similar structure to gluten BUT most people with coeliac disease can eat oats (1)
- Coeliac Australia position statement on oats (2):

"It is recommended that individuals who wish to consume oats as part of their gluten free diet do so under medical supervision to ensure appropriate review and safety. Undertaking a gastroscopy and small bowel biopsy before and after 3 months of regular uncontaminated oat consumption can help guide whether an individual with coeliac disease can safely consume oats."

Gluten myths & misunderstandings

- **Claim # 1:** Wheat is problematic because humans have only been consuming it since agriculture began, and that's not long enough for us to adapt to it.
- **Reality:**
  - Everything we now eat, including animals, has only been consumed since agriculture began. Humans have extensively modified all food species (plant and animal) through selective breeding.
  - Wheat was first domesticated in southeastern Anatolia ~ 11,000 years ago (1).
  - Ohalo II archaeological site in Israel shows humans gathered, processed and ate wild grains, including barley and wheat, ~ 23,000 years ago (2).
  - Adaptation to a new food can occur in a few millenia e.g. lactase persistence.
  - Population growth increases speed of adaptation (100 x faster in last 5000 yrs) (3, 4).

Gluten myths & misunderstandings

- **Claim # 2:** Wheat is problematic because it has been hybridised extensively.
- **Reality:**
  - Wheat *has* been extensively hybridised (> 25 000 cultivars worldwide (1))… but so has almost every other plant we eat, especially grapefruit, tomatoes, beets, carrots, corn, cucumbers, eggplant, spinach, squash, and broccoli.
  - Farmed animals are also genetically selected for various characteristics.
  - Hybridisation is completely different to genetic modification.

Gluten myths & misunderstandings

- **Claim # 3:** Wheat is problematic because it has more protein now than a century ago.
- **Reality:**
  - USDA scientist Donald D. Kasarda analysed records of protein content in wheat harvests going back nearly a century and found that they haven't changed (1).

Gluten myths & misunderstandings

- **Claim # 4:** Wheat is problematic because we are eating so much more of it now than in previous generations.
- **Reality:**
  - Wheat intake has fluctuated in Australia (1), but total grain intake decreased by nearly 30% between 2011 and 2014 (2).
  - In the US, consumption of wheat flour rose to ~ 225 lb per capita in 1880, and fell to ~ 110 lb in 1980. Rose to 146.3 lb per capita in 2000, hit a low of 133.4 lb in the mid-2000s, recovered slightly, then dropped back to 132.5 lb per person for 2011 (3).
  - Analysis of serum stored since the mid-20th century suggests that CD incidence was ~ ¼ today's levels, at a time when Americans ate about as much wheat as they do now (4).

Gluten myths & misunderstandings

- **Claim # 5:** Wheat is toxic to all humans.
- **Reality:**
  - If wheat is so toxic, how could populations that eat it have tolerated it for > 10,000 years?
  - Wheat was a dietary staple of ancient Egyptians for millenia (1).
  - 60% of the Bedouin's energy intake in the 1960s came from wheat; rates of obesity, hypertension and diabetes were negligible (2).
  - Genetics of coeliac disease contradict argument that wheat is intrinsically toxic: coeliac-associated genes are abundant in Middle Eastern populations (whose ancestors first domesticated wheat) AND have spread in recent millennia, indicating that they confer a survival advantage – same genes that predispose to autoimmune disease also increase immune defences against infectious disease (3).

Why are gluten-related disorders on the rise?

- All autoimmune diseases are increasing in prevalence.
- Hygiene hypothesis: cleaner environments decrease the risk of infection but increase the risk of immune system malfunction.
  - Karelia: bisected by Finno-Russian border; wheat consumption and genetics are roughly equivalent, but coeliac disease is almost 5x more common in Finnish than Russian Karelians (1).
  - T1DM is 6x less common in Russian Karelians (2).
  - Autoimmune thyroid disease significantly less common (3).
  - Atopy 4x less common (4).
  - Attributed to greater exposure to infections (especially faecal-oral infections) due to poverty and dirty environment in Russian Karelia (5, 6).

Why are gluten-related disorders on the rise?

- Dysbiosis – depletion of bifidobacteria, overabundance of *E. coli* (1).
  - Lack of breastfeeding (breastfed babies have more bifidobacteria (2)), or introduction of gluten after breastfeeding cessation (3).
  - Breastfeeding by overweight mothers (more Staphylococcus, less Bifidobacterium group (4)).
  - Antibiotic use.
  - Diet – high fat, high protein, low fibre (5).

Question time

Emailed questions

- Can gluten free enhance sports performance eg Djokovic is renowned as being gluten free?
- Some gluten free breads include ingredients such as potato flour/starch and rice flour - do you recommend these or are they likely to mess with your health in another way?
- I have found vital wheat gluten as an ingredient in a number of American vegan recipes & after finally sourcing it, have used with pleasing results. I have not looked into the nutritional side though. Is it a healthy addition to a vegan diet if one has no dietary issue with gluten?
- Are you able to check out this article http://www.amymyersmd.com/2016/03/ditch-gluten-autoimmune/ and see what you think? Does it mean I just can't touch gluten if have any AI issues even if gut seems to be healed?