In the last 3 years, the acceptance of Non-Celiac Gluten Sensitivity (NCGS) in the medical community as a distinct clinical entity has gone from that of being an orphaned child crying in the world for recognition, to an accepted, unique component of the triad of gluten-related disorders. Differentiating among gluten-related disorders, guides clinicians in making an accurate diagnosis and recommending specific dietary, nutritional and other medical advice; however, clinical and laboratory diagnosis is complex and evolving. For example, Irritable Bowel Syndrome (IBS) is the most common abdominal complaint patients suffer from. Although the frequency of IBS with accompanying Celiac Disease (CD) is about 1%, the frequency of IBS with accompanying NCGS is over 30%. Resolution of IBS symptoms occurs in these individuals with a GFD.

Gluten Sensitivity (GS) is a state of heightened immunological responsiveness to ingested gluten in genetically susceptible people. It represents a spectrum of diverse manifestations, of which, the gluten sensitive enteropathy known as CD is one of many. Adverse reactions to the toxic family of gluten proteins found in wheat, barley, rye, and their derivatives may trigger a heterogeneous set of conditions, including wheat allergy (IgE), NCGS, and CD, that, combined, affect between 10–35% of the population. Once believed to fall exclusively into the domain of allergic conditions (e.g., wheat allergy), it is now clear that the intestinal and extra-intestinal manifestations of CD are entities that may differ from allergy, and are mediated by innate and adaptive immune pathways.

**TRUE or FALSE**

1) Even in the presence of negative small bowel biopsy, positive Endomysial antibody (EMA) IgA predicts development of CD.

2) The prevalence of CD varies by race/ethnicity, with a marked predominance among non-Hispanic whites.

3) With more sophisticated diagnostic markers now available, the majority of CD cases are being recognized.

4) Complete histological normalization of the small-intestinal mucosa occurs in the majority of adult patients after commencing a gluten-free diet (GFD).

5) An American College of Gastroenterology Task force recommends that patients presenting with diarrhea-predominant IBS type symptoms should be serologically tested for CD.

6) What percent of individuals with NCGS suspect they may have a problem with wheat?
   - A. 32%
   - B. 76%
   - C. 50%
   - D. 12%

7) Of the following three scenarios, which is the most dangerous for increased mortality in CD?
   - A. Total villous atrophy
   - B. Positive celiac serology with negative villous atrophy
   - C. Increased intraepithelial lymphocytes (IEL) with negative serology and negative villous atrophy
8) In differentiating wheat sensitivity from IBS, which one of the following features is significantly more frequent in wheat sensitive (WS) patients compared to IBS patients?
   A. Anemia
   B. Self-reported fructose intolerance
   C. Weight gain
   D. Self-reported lactose intolerance

9) Compared to patients with CD, what are the characteristic features, other than self-reported wheat intolerance, of patients with wheat sensitivity?
   A. Anemia and family history of CD
   B. Weight loss and increased IEL count
   C. Coexistent atopy and food allergy in infancy
   D. Increased serum C reactive protein and erythrocyte sedimentation rate

Current therapeutic protocols for CD, NCGS and wheat allergy include dietary counseling from a trained professional, nutritional therapy addressing biomarkers of malabsorption and creating a more balanced intestinal environment. Currently, there are no approved pharmaceutical treatments for this silent epidemic, however a number of Phase 3 trials are underway. Promising gluten-based research is currently being done including wheat alternatives and wheat selection, enzymatic alteration of wheat, oral enzyme supplements and polymeric binders as exciting new therapies for treatment of CD.

There appears to be at least two distinct groups of NCGS individuals. There are those who are sensitive to wheat and those who have multiple food sensitivities. In a recent study 75% of NCGS patients with IBS had multiple food sensitivities including cow’s milk protein, eggs and tomato. This may explain the frustration of Clinicians when a GFD is less-than-optimally effective in suspected and/or identified NCGS.

Those NCGS patients with IBS and wheat sensitivity had more features in keeping with CD (higher frequency of anemia, weight loss, and HLA DQ2 or DQ8) than those with multiple food sensitivities. Furthermore, the multiple food sensitivity group had a higher prevalence of coexisting atopy or food allergy in infancy. It is critically important to identify whether a NCGS individual has multiple food sensitivities or exclusively has NCGS. This suggests the world of NCGS is greater than just one mechanism and invites the Clinician to explore its pathophysiology.

**ANSWERS**

1) True. The presence of IgA EMA antibodies predicted deterioration of the microvilli with subsequent development of CD.
2) True. "Our results confirm prior data showing that a substantial burden of CD in the United States predominantly affects the non-Hispanic white population".
3) False. Current estimates from Mayo Clinic are that 1.8 million Americans have celiac disease and a whopping 78 percent of sufferers don't realize they have the condition. Study co-author, gastroenterologist Joseph Murray, in a clinic news release summarizes, "If you detect one person for every five or six [who have it], we aren't doing a very good job detecting CD.”
4) False. In CD, complete histological normalization of the small-intestinal mucosa occurs in only 8 – 20 % of adult patients after commencing a GFD. If you let that sink in, you MUST ask the question, "Why is that?"
5) True. Patients with undetected CD may present with IBS type symptoms. This has led to the recommendation by the American College of Gastroenterology Task Force that patients presenting with diarrhea predominant IBS type symptoms should be serologically tested for CD.
6) C. "It is interesting to note that 50% of the 276 patients self-reported wheat intolerance."
7) C. The incidence of increased mortality in CD with total villous atrophy is 39%.
   The incidence of increased mortality with just positive serology is 35%.
   The incidence of increased mortality with just increased IEL’s is 72%.
8) A. “As regards the clinical characteristics of WS patients and the identification of possible diagnostic markers, our data indicated that the presence of anemia and weight loss and a history of food allergy in infancy and of coexistent atopic diseases are more frequent in WS patients than in IBS controls. Other studies have not shown changes in intestinal permeability and absorption”.xx

9) C. “When we considered the 276 patients suffering from Wheat Sensitivity as a whole group, they showed an anemia (most sideropenic anemia) and weight loss frequency intermediate between the CD and IBS control groups and a higher frequency of coexistent atopic diseases, self-reported wheat intolerance, and history of food allergy in infancy than both the CD and IBS controls”.xx

References

ix Ibid, reference 2
xi Ibid reference 3
xv Mayo Clinic, news release, July 31, 2012