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Celiac Disease: Current and Investigational Therapies and the Role of the Pharmacist

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This knowledge-based activity is targeted for all pharmacists and is acceptable for 1.0 hour (0.1 CEU) of continuing education credit. This course requires completion of the program evaluation and at least a 70 percent grade on the program assessment questions.

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Objectives

After completion of this program, the reader should be able to:

1. Explain the etiology, patient presentation and diagnosis of Celiac disease.
2. Discuss the current therapy for Celiac disease, highlighting the gluten-free diet.
3. Identify investigational pharmacotherapeutic options for Celiac disease.
4. Define the pharmacist's role in patient education and counseling for Celiac disease.

Abstract

Celiac disease is a genetically-linked autoimmune disease which affects the gastrointestinal tract. It is an inflammatory reaction to ingested gluten-containing substances that produces the most frequent symptoms of abdominal pain, bloating and intermittent or chronic diarrhea. Diagnosis can be made by blood testing for specific IgA autoantibodies and a confirmation duodenal biopsy to look for the characteristic scalloping and villous atrophy that occurs in response to the inflammation. A gluten-free diet, until recently, was the only treatment available and continues to be the mainstay of treatment. Newer adjunct therapies to dietary management include larazotide acetate, peptidases, the use of parasite Necator americanus, a desensitizing vaccine, polymeric binders, cytokine antagonists, tissue transglutaminase inhibitors, probiotics and anti-inflammatory therapy. This review will outline the potential of each of these therapies and discuss the role of the pharmacist in assisting patients with Celiac disease.

Introduction

In recent years, Celiac disease has emerged in society as a common, genetically-linked condition affecting the gastrointestinal (GI) system. It is an autoimmune disease that leads to gastrointestinal side effects as a result of ingestion of gluten-containing substances. The disease has risen in prevalence as physician awareness and diagnosis of the condition has increased. Still, many patients live with the condition and deal with the symptoms while remaining undiagnosed. Celiac disease can negatively affect patient quality of life for a multitude of reasons. These include physical discomfort associated with the disease as well as the inconvenience of maintaining a gluten-free diet, which is currently the only treatment option.

Several new pharmacological therapies and drug targets are under investigation for relief of symptoms and may be viable options for use as adjunct therapy in Celiac disease patients. While none of these products are currently on the market, they have the potential to be realistic additions to therapeutic regimens in the future. Pharmacists have an important role in counseling patients about the disease and how to manage symptoms. They will be sought out as drug experts for the disease state, as well as excellent resources for information about gluten-free foods and medications. The number of patients with Celiac disease will only continue to increase, and it is important to be knowledgeable about the disease state and incorporate patient counseling and education into pharmacists' everyday practice.

Disease Overview

Celiac disease is an increasingly prominent disease state that is highly linked to genetic factors. Such genetic factors are linked to mutations on the human leukocyte antigen (HLA) Class II genes, specifically haplotypes HLA-DQ2 and HLA-DQ8, found on the 6p21 chromosome.[1] Genetic mutations are the most predominant factor in eliciting the immune-mediated response to gluten, as 4 to 12 percent of Celiac disease patients have a first degree relative also suffering from this disease state.[2] It is important to note, however, that 30 to 40 percent of Caucasians have these HLA mutations with only 2 to 5 percent of carriers presenting with Celiac disease signifying that genetic mutations are necessary for disease presentation but are not the sole cause of Celiac disease.[1]

While genetic predisposition is important to consider, other factors may also contribute to the development of Celiac disease. These include environmental factors, such as a past enteric infection or patients who are exposed to gluten prior to 4 months of age.[1] Furthermore, patients who suffer from other immune-mediated genetic disorders that affect the GI tract, such as Crohn's disease and ulcerative colitis, are more susceptible than other individuals to develop this disease state.[2]

Celiac disease is classified as an immune-mediated disorder, as its symptomatic presentation is due to gluten, which triggers immunological reactions.[3] These immunological reactions stimulate an autoimmune response by the cells of the GI tract, stimulating inflammatory mediators.[4] Inflammatory mediators present in Celiac disease may lead to the opening of tight junctions in the intestinal epithelium. Tight junctions

regulate fluid and molecule passage between intestinal epithelial cells to the lamina propria. Proteins known as zonula occludins also regulate the structure and function of the cellular cytoskeleton by linking tight junctions with the actin network. When the tight junctions are not functioning properly, gluten (or gliaden) peptides gain access across the intestinal epithelium and are then modified by the enzyme, tissue transglutaminase (tTG).[1,5] T-cells will then present the modified gluten as an antigen via HLA-DQ2 and HLA-DQ8 proteins. Gluten presentation then initiates both humoral and cell-mediated immune responses, leading to a temporary and reversible remodeling of intestinal mucosa, including scalloping of the small intestine mucosa and villous atrophy leading to malabsorption and symptoms such as abdominal pain, bloating and diarrhea.[1]

Patient Presentation

Celiac disease is prevalent across ethnicities, ages and genders with increasing prevalence not only in the pediatric population but also the adult population. Symptoms present in 1 percent of the U.S. population but may be undiagnosed in up to 85 to 90 percent of cases.[1,2] Celiac disease classically presents with symptoms related to malabsorption of gluten, which can include but are not limited to abdominal pain, bloating and intermittent or chronic diarrhea.[1,3] Chronic diarrhea is due to changes in the gastrointestinal wall leading to malabsorption of gluten, and can cause dehydration, weight loss and muscle wasting. Further signs of Celiac disease include anemia, most commonly iron-deficiency, due to malabsorption. Vitamin D deficiency and Vitamin B_{12} deficiency can also be signs of Celiac disease.[1] Of those patients with Celiac disease, 15 to 25 percent present with the non-traditional symptom of dermatitis herpetiformis, a rash that occurs without the accompaniment of GI symptoms.[2] The inflammatory process associated with dermatitis herpetiformis results from IgA deposition and neutrophil accumulation, which leads to vesicle formation, producing a rash commonly found on the elbows, knees and buttocks, an important clinical observation for patients with suspected Celiac disease.[2]

Due to similar GI symptoms across various GI disorders, it is important to note that some patients who suffer from Celiac disease also have a secondary disorder including lactose intolerance or inflammatory bowel disease (IBD).[1] Those patients suffering from autoimmune diseases including type 1 diabetes mellitus and autoimmune thyroid disorder may be more likely to present with Celiac disease and should be tested regardless of symptom presentation.[1,3] Celiac disease patients may also be more likely to have other immune-mediated diseases that affect the GI tract, such as Crohn's disease or ulcerative colitis.[2] Patients who have been diagnosed with lactose intolerance or diarrhea-predominant IBD and have not showed improvement should consider being tested for Celiac disease. The diagnosis process is an important step for patients because, although death is not a common outcome of this disease state, patients with multiple disease states are at an increased risk for complications such as vitamin deficiencies, malnutrition, ulcerative jejunitis, T-cell lymphoma and an overall decrease in quality of life.[1]

Diagnosis

Diagnosis is vital for patients suffering from Celiac disease due to a fourfold increase in mortality in patients with an untreated disease state.[7] Patients who present with Celiac disease symptoms should be screened via a blood test or intestinal biopsy.[2] Furthermore, asymptomatic patients who have a first-degree or second-degree relative with confirmed Celiac disease, type 1 diabetes, autoimmune thyroid disorders, rheumatoid arthritis or GI associated autoimmune disorder should be tested for Celiac disease. The first step for suspected patients is testing a blood sample for specific IgA autoantibodies via immunofluorescence. For patients undergoing a blood sample, it is important to eat foods containing gluten prior to testing, otherwise the patient may receive a false negative result for Celiac disease.[1] Those patients suffering from Celiac disease will present with elevated IgA to tTG or epithelial membrane antigen (EMA).[2] Most likely, tTG IgA will be screened due to its cost efficiency and comparable accuracy to the EMA IgA test. Another method of testing is via an upper endoscopy with duodenal biopsies to look for scalloping of the folds or cracking of the small intestine as well as villous atrophy linked to inflammatory changes. Due to the biopsy expense, this step in diagnosis should be suggested after blood testing in order to confirm the disease state.[1]

Treatment

Treatment should be started once Celiac disease is suspected. Currently, a gluten-free diet is the only therapeutic option for patients with Celiac disease. Gluten can be found in wheat, barley and rye containing products. Due to cross-contamination in manufacturing, it is very difficult to completely avoid the irritating substances. Due to the difficulty finding specifically gluten-free foods, many Celiac disease patients are exposed to low levels of gluten on a regular basis. Also, many medications have inert ingredients that contain gluten, making total avoidance even more difficult. It is estimated that 30 to 50 percent of patients are not able to strictly adhere to the proper diet, and at any given time 50 percent of all Celiac disease patients have an active disease state.[4] A gluten-free diet will aid in the healing of intestinal mucosa.[1] Those patients who suffer from dermatitis herpetiformis can treat the rash with dapsone, which inhibits neutrophil recruitment and downstream inflammatory processes, if the rash does not resolve after committing to a gluten-free diet.[1,6] About 90 percent of patients will present with no symptoms after five years of a gluten-free diet, and almost all patients will experience some relief from symptoms immediately after beginning the diet.[8] Those patients who follow a strict gluten-free diet have a better, long-term quality of life due to greater and more consistent relief, as well as an overall enhanced state of health (i.e. mental health, pain, vitality, social function, physical function).[9] Overall, relief of Celiac disease symptoms is due to a decrease in IgA specific autoantibody production via removal of the antigen (gluten).[10] Patients continuing to suffer from symptoms can more rigorously utilize pharmacological agents to treat symptoms related to deficiencies in Vitamin B_{12}, Vitamin D and folic acid. Furthermore, nonsteroidal anti-inflammatory agents (NSAIDs) and anti-diarrheals can be used for symp-

tom management. If symptoms persist after symptom management and strict adherence to a gluten-free diet, it is recommended that the patient revisit his or her doctor to determine if the patient is suffering from an additional disorder.[11]

New Pharmacological Therapies

New pharmacological therapies are in development to treat Celiac disease as an adjunct to the gluten-free diet. These novel therapies are necessary to increase the quality of life in patients who are still exposed to gluten even with best efforts to avoid the offending agent.[4] Currently, many different methods of therapy have been investigated, including larazotide acetate, peptidases, the use of parasite Necator americanus, a desensitizing vaccine, polymeric binders, cytokine antagonists, tissue transglutaminase inhibitors, probiotics and anti-inflammatory therapy.[4,12,13]

Cellular exposure to gluten can be reduced by use of larazotide acetate, a therapy in development. Larazotide acetate (ALBA Therapeutics) acts on the cytoskeleton to prevent opening of tight junctions and reduce gluten transport into cells from the intestinal lumen.[4] It also promotes redistribution and reorganization of zonula occludins and other proteins that associate with actin in the cytoskeleton. ALBA Therapeutics conducted a study testing the effects of larazotide acetate on junction assembly in kidney and intestinal cells. This study was conducted in vitro and showed promising results through several mechanisms including promotion of tight junction assembly, actin reorganization for stronger assembly of tight junctions, GTPase regulation of the cytoskeleton and inhibition of tight junction disassembly.[5] Improved tight junctions will lessen intestinal cell exposure to gluten, which can reduce inflammatory reactions in the GI tract.

Furthermore, in a randomized, placebo-controlled study by Kelly et al., the efficacy of larazotide acetate was assessed in patients receiving small amounts of gluten daily (2.7 g of gluten, equivalent to one slice of bread).[14] The primary endpoint of the study was a measure of intestinal permeability known as the lactulose-to-mannitol (LAMA) ratio. Patients with Celiac disease have an increased LAMA ratio. Results showed no statistical differences in LAMA ratio between placebo and treatment groups; however, the study acknowledged flaws in timing of LAMA assay and outpatient testing that may have affected results. Secondary endpoints included measures of serum anti-tTG IgA levels and showed the greatest increase in the placebo group from zero to six weeks, in which 30 percent of patients in the group seroconverted. Serum concentrations of the treatment group remained below levels that qualify a positive antibody test.[14] When compared to placebo, the treatment groups showed significantly lower anti-tTG IgA levels (1 mg dose $p=0.010$, 4 mg dose $p=0.005$, 8 mg dose $p=0.025$). There was also evidence to suggest that patients treated with larazotide acetate had fewer gastrointestinal side effects when compared to placebo. However, only the 1 mg daily dose of larazotide acetate reached statistically significant lower scores in patient-reported abdominal pain, indigestion and diarrhea versus placebo by the end of the treatment period ($p=0.017$).[14]

Another randomized, double-blinded, placebo-controlled study by Leffler et al. also had a primary endpoint of changes in LAMA ratio as well as measures of serum tTG antibodies. Results were similar to the Kelly et al. study, with the changes in LAMA ratio not reaching statistical significance. However, serum tTG did not reach statistically lower levels in this study. This study did show a significant difference in severity of gastrointestinal side effects between the patients receiving larazotide acetate with a gluten challenge versus the gluten challenge control group as evidenced by the Gastrointestinal Symptom Rating Scale ($p<0.05$).[15] Results from all three studies suggest that larazotide acetate has the benefit of inhibiting the opening of tight junctions in intestinal cells. Larazotide acetate may in the future have the possible therapeutic use as an adjunct to a gluten-free diet and relief of some symptoms of Celiac disease.[5,14,15]

Another novel drug therapy for the treatment of Celiac disease is the use of oral peptidases to hydrolyze gluten polypeptides. In this form, the gluten molecules can no longer stimulate damaging intestinal immune responses. Alvine Pharmaceuticals has developed ALV003, a combination of two gluten-sensitive peptidases. The company DSM has also developed a peptidase (AN-PEP), and a third is being tested by Stanford University. A phase I clinical trial showed that the use of ALV003 for pretreatment of gluten ingestion in Celiac disease patients caused a decrease in activation of immunological markers, as well as benefit in breaking down high gluten-containing foods.[4] However, this trial was underpowered and did not achieve statistically significant values for serology or symptom improvement. AN-PEP has showed less success in reaching significant endpoints in trials. However, AN-PEP is being considered as a food supplement as it is particularly active at degrading gluten in the stomach. One drawback of peptidase use is the susceptibility of these peptides to the acidic conditions of the stomach, and modification with polymer substitutes has been considered.[12] Use of oral peptidases has been one of the most investigated therapeutic options for the treatment of Celiac disease; however, its role in clinical practice has yet to be determined.

The use of the parasite Necator americanus is another investigational therapy for Celiac disease patients. Trials are underway to test whether or not this helminth infection can attenuate the autoimmune intestinal inflammation associated with Celiac disease.[16] The theory behind this therapy is derived from the hygiene hypothesis: the notion that increasing numbers of allergic and autoimmune disorders in developed countries may be associated with the decrease of infectious diseases present in society.[16,17] In a prospective, placebo-controlled, randomized, double-blind trial by Daveson et al., Necator americanus infection in Celiac disease patients was evaluated with primary endpoints of duodenal histology scores (for intestinal damage) and systemic interferon-gamma levels (for inflammation). Inoculation with the worm was instituted in patients who subsequently underwent a gluten challenge. A placebo group underwent the same gluten challenge without the worm for comparison. Results showed no statistical difference in duodenal histology scores or interferon-gamma levels between the infected and control

groups. This study in particular shows that helminth infection may not alleviate the need for a gluten-free diet in Celiac disease.[16] Limited studies using this therapy have been investigated at this time, and currently helminth infection therapy is not seen as a therapeutic option used in clinical practice.

Desensitization through the use of a Celiac disease-specific vaccination is also an investigational therapy. The biotechnology company ImmuSanT has developed a vaccine, Nexvax2®, which contains immunogenic gluten peptides from wheat, barley and rye. The vaccine was developed with the goal of restoring gluten-tolerance in Celiac disease patients through use as an immunotherapeutic and prophylactic agent.[12] A phase I study has evaluated the safety and efficacy of weekly intradermal injections of Nexvax2® compared to placebo by measuring immune T-cell response. The study's formally written publication has not yet been released. Thirty-four HLA-DQ2+ Celiac disease patients were randomized to four treatment groups (receiving 9 mcg, 30 mcg, 60 mcg and 90 mcg of Nexvax2® weekly for three weeks) and a placebo group (receiving saline injections on the same schedule). Results showed that the incidence of GI side effects was similar in the treatment and placebo groups. In the treatment group, immunological responses to Nexvax2® were similar to acute exposure to oral gluten (gluten ingestion) in the mobilization of gluten-specific T-cells.[18,19] Patients receiving the vaccine were found to have interferon-gamma-producing Nexvax2®-specific T-cells, which validates the bioactivity of the vaccine through immunological response. The hope is that through repeated vaccinations, a Celiac disease patient will develop tolerance to the immunogenic gluten peptides and be able to incorporate small amounts of gluten into his or her diet.[12] Thus far, data are extremely limited on the efficacy of such a therapy and more trials are needed. This may be a viable option in the future and an additional agent that could improve the quality of life of Celiac disease patients.

Many new therapeutic options for the treatment of Celiac disease are in very early stages of development. It may be some time before viable options are commercially available or before they become standards of practice for treatment. However, the amount of research and development into pharmacological therapies for Celiac disease is promising, and awareness and knowledge of these therapies are critical for pharmacists to be prepared for potential changes in Celiac disease state management in the future.

Pharmacists' Role

Pharmacists have a key role in improving the quality of life for patients suffering from Celiac disease and thus are best able to share important medication-nutrition and nutrition-disease state interactions with patients.[20] Resources for pa-

Table 1. Drug Excipients That are Safe or Require Further Investigation in Celiac Disease Patients[21,22]

Gluten-free Ingredients	Ingredients Needing Further Investigation (if source not specified)
Benzyl alcohol	
Cellulose	
Cornstarch	Caramel coloring
Croscarmellose sodium	Dextrate
Fructose	Dextrimaltose
Gelatin	Dextrin
Glycerin	Maltodextrin
Lactose	Modified starch
Mannitol	Potato
Polysorbates	Pregelatinized modified starch
Silicon dioxide	Pregelatinized starch
Sodium lauryl sulfate	Sodium starch glycolate
Stearates	Starch
Sucrose	Tapioca
Titanium dioxide	

Note: This chart is not an exhaustive list of gluten-free or gluten-containing ingredients used in medications. If there is ever a question about a specific medication ingredient, the drug manufacturer should be contacted for inquiry.

tient advising can be found through the National Foundation for Celiac Awareness (NFCA) at www.celiaccentral.org. Patient resources and brochures include information regarding what is Celiac disease, the choice to be gluten free, Celiac disease and women's health, and a Celiac disease symptoms checklist.[21] This information is free and available for pharmacists to provide to patients and will afford patients a better understanding of the disease.

Another important concern for pharmacists is the identification of gluten in various medications and over-the-counter products including vitamins, supplements and lip balms. These less obvious sources of gluten have been found to exacerbate patients' symptoms and should be monitored.[1] It is important for pharmacists to be aware of the excipients present in medications, especially because generic medications are not required to use the same excipients as the brand name medication. Likewise, not all generics are equal, and even two generics for the same medication may not contain the same excipients. Table 1 provides a list of excipients that are gluten-free and those ingredients that may need further investigation (if source not specified) to ensure safety. A drug manufacturer should be contacted if the pharmacist or patient is unsure of the excipient used, the source of the excipient or the possibility of cross contamination. As medication experts, pharmacists should know how to obtain this information for an inquiring patient.[22] Pharmacists and patients can find extensive lists of brand and generic prescription medications as well as over-the-counter medications that do not contain gluten at glutenfreedrugs.com. This website is kept up to date by a clinical pharmacist who continually updates the information for public access.[23]

Pharmacists are also an accessible resource for patients to approach about gluten-free food options and healthy living while on this restricted diet. It is important for pharmacists to counsel on the extra cost associated with preparing gluten-free foods and for patients to consider this in their budget. Equally important is directing patients to the aforementioned resources about Celiac disease for additional assistance. In order to help those patients on a gluten-free diet, labeling requirements have been added that mandate food labels to identify wheat and other common food allergens, as a result of a rising prevalence of patients suffering from Celiac disease and gluten intolerance. Additional requirements include regulations by the U.S. Food and Drug Administration (FDA) to control rules for the use of the term "gluten-free" on products. The FDA has standardized their definition of "gluten-free" such that foods containing this term or claiming to contain "no gluten," "free of gluten" and "without gluten" must contain less than 20 parts per million of gluten, an amount not seen to harm patients with Celiac disease.[24]

Conclusion

Celiac disease is gaining more and more recognition by health care professionals as the prevalence of the disease state increases. It is a genetically-linked disease whose diagnosis and treatment can lead to improved patient quality of life. While current practice only champions the gluten-free diet for treatment, newer investigational pharmacotherapy may emerge in the near future. Pharmacists will remain an important resource for patient education about Celiac disease. Pharmacists will be called upon to investigate medications and foods that may be appropriate or inappropriate in Celiac disease. Patient care is always a number one goal, and knowledge of this condition will allow pharmacists to be a primary resource for the treatment of Celiac disease.

References

1. Boettcher E, Crowe SE. Celiac Disease. *Prim Care Rep.* 2012:18(12);153-67.
2. Celiac disease. National Digestive Diseases Information Clearinghouse. U.S. Department of Health and Human Services, NIH Publication 2008:No. 08–4269.
3. Rivera E, Assiri A, Guandalini S. Celiac Disease. *Oral Dis.* 2013:19:635-41.
4. Perez LC, Catillejo de Villasante G, Ruiz A, Leon F. Non-dietary therapeutic clinical trials in celiac disease. *Eur J Intern Med.* 2012:23;9-14.
5. Gopalakrishnan S, Tripathi A, Tamiz A, Alkan S, Pandey N. Larazotide acetate promotes tight junction assembly in epithelial cells. *Peptides.* 2012:35;95-101.
6. Thuong-Nguyen V, Kadunce DP, Hendrix JD, et al. Inhibition of neutrophil adherence to antibody by dapsone: a possible therapeutic mechanism of dapsone in the treatment of IgA dermatoses. *J Invest Dermatol.* 1993:100(4): 349-55.
7. Rubio-Tapia A, Kyle RA, Kaplan EL, et al. Increased prevalence and mortality in undiagnosed celiac disease. *Gastroenterology.* 2009:137:88-93.
8. Wahab PJ, Meijer JWR, Mulder CJJ. Histologic follow-up of people with celiac disease on a gluten-free diet. *Am J Clin Pathol.* 2002:118:459-63.
9. Nachman F, Planzar del Campo M, Gonzalez A, et al. Long-term deterioration of quality of life in adult patients with celiac disease is associated with treatment noncompliance. *Dig Liver Dis.* 2010:42(10): 685-91.
10. Fabiani E, Taccari LM, Ratsch I, et al. Compliance with gluten-free diet in adolescents with screening-detected celiac disease: a 5-year follow-up. *J Pediatr.* 2000:136(6):841-43.
11. Rubio-Tapia A, Hill ID, Kelly CP, et al. ACG clinical guidelines: diagnosis and management of celiac disease. *Am J Gastroenterol.* 2013:108 (5):656-76.
12. Matoori S, Fuhrmann G, Leroux J. Celiac disease: A challenging disease for pharmaceutical scientists. *Pharm Res.* 2012:30;619-26.
13. Sanz Y. Novel perspectives in celiac disease therapy. *Mini Rev Med Chem.* 2009:9;359-67.
14. Kelly C, Green H, Murray J, DiMarino A, Colatrella A, Leffler D, et al. Larazotide acetate in patients with celiac disease undergoing a gluten challenge: a randomized placebo-controlled study. *Aliment Pharmacol Ther.* 2013:37;252-62.
15. Leffler D, Kelly CP, Abdallah HZ, Colatrella AM, Harris LA, Leon F, et al. A randomized double-blind study of Larazotide acetate to prevent the activation of celiac disease during gluten challenge. *Am J Gastroenterol.* 2012;107:1554–62.
16. Daveson AJ, Jones DM, Gaze S, McSorley H, Clouston A, Pascoe A, et al. Effect of hookwork infection on wheat challenge in celiac disease- a randomized double-blinded placebo controlled trial. *PLos ONE.* 2011:6;1-8.
17. Okada H, Kuhn C, Feillet H, Bach JF. The 'hygiene hypothesis' for autoimmune and allergic diseases: an update. *Clin Exp Immunol.* 2010:160;1-9.
18. Brown GJ, Daveson J, Marjason JK, Ffrench RA, Smith D, Sullivan M, et al. A phase I study to determine safety, tolerability and bioactivity of Nexvax2 in HLA DQ2+ volunteers with celiac disease following a long-term, strict gluten-free diet [Abstract]. *Gastroenterology.* 2011:140;437-38.
19. Safety study of Nexvax2 in subjects with celiac disease. Available from: clinicaltrials.gov/show/NCT00879749.
20. Position of the American Dietetic Association: Integration of medical nutrition therapy and pharmacotherapy. *J Am Diet Assoc.* 2010:110;950-56.
21. Celiac Central [homepage on the Internet]. Ambler (PA). National Foundation for Celiac Awareness. c2012-2013 [updated 2013 Oct 16; cited 2013 Oct 16]. Available from: www.celiaccentral.org.
22. Plogsted S. Medications and celiac disease - tips from a pharmacist. *Pract Gastroenterol.* Jan 2007;58-64.

23. GLUTENFREEDRUGS [homepage on the Internet]. Anonymous [updated 2013 Sep 30; cited 2013 Nov 1]. Available from: www.glutenfreedrugs.com.
24. U.S. Food and Drug Administration [homepage on the Internet]. Silver Spring (MD): U.S. Department of Health and Human Services; [updated 2013 Nov 26; cited 2013 Dec 1]. Gluten-free Labeling Final Rule. Available from: www.fda.gov/Food/GuidanceRegulation/Guidance DocumentsRegulatoryInformation/ Allergens/ucm362880.htm.

Assessment Questions

Etiology

1. Development of Celiac disease is genetically linked to which two haplotypes found on the mutated HLA Class II gene?
   A. HLA-DQ2
   B. HLA-DQ8
   C. HLA-DQ21
   D. Both A and B
   E. Both A and C

Patient Presentation

2. Symptoms of Celiac disease include all of the following EXCEPT:
   A. Abdominal pain
   B. Bloating
   C. Cyanosis
   D. Diarrhea
   E. Iron deficiency

Diagnosis

3. What counseling should be provided to a patient who is having a blood test for Celiac disease diagnosis?
   A. Eat gluten prior to the blood test
   B. Do not eat gluten prior to the blood test
   C. Fast for 12 hours prior to the blood test
   D. Exercise one hour prior to the blood test
   E. None of the above

Treatment

4. Relief of symptoms in Celiac disease patients is rooted in a decrease in which autoantibody?
   A. IgA
   B. IgD
   C. IgE
   D. IgG
   E. All of the above

5. After five years of following a gluten-free diet, about _____ of Celiac disease patients will be completely symptom free.
   A. 1%
   B. 10%
   C. 25%
   D. 50%
   E. 90%

6. Which of the following is NOT true about following a strict gluten-free diet?
   A. Following a gluten-free diet will improve patient quality of life.
   B. Patients who follow a gluten-free diet and no longer have symptoms do not need to visit their doctor for reevaluation.
   C. Patients who follow a gluten-free diet have a better health status.
   D. Patients who follow a gluten-free diet have a greater and more consistent relief of symptoms.

Investigational Therapy

7. Larazotide acetate is a novel therapeutic option for Celiac disease whose mechanism of action includes:
   A. Manipulation of the cytoskeleton to facilitate tight junction opening
   B. Actin reorganization for better assembly
   C. Inhibition of tight junction disassembly
   D. Both A and B
   E. Both B and C

8. Therapeutic use of gluten peptidases show the advantage of:
   A. Decrease in activation of immunologic markers
   B. Use as monotherapy for treatment of Celiac disease
   C. Gluten peptides are unsusceptible to acidic conditions in the stomach
   D. All of the above

9. The desensitization vaccine, Nexvax2®:
   A. Is currently on the market and available for patient use
   B. Targets three gluten peptides found in wheat, barley and rye
   C. Has an increased incidence of GI side effects compared to ingestion of gluten
   D. Recently completed phase III clinical trials

Pharmacists' Role

10. If a patient has a question about gluten in medications, a pharmacist should:
    A. Tell the patient to check the medication ingredients on their own.
    B. Explain that all medications are gluten-free and they should not worry.
    C. Contact the drug manufacturer about questionable ingredients or with concerns about cross-contamination.
    D. Assure patients that a small amount of gluten will not effect their condition.

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Raabe College of Pharmacy Continuing Education Evaluation Form

Program Title: **Celiac Disease: Current and Investigational Therapies and the Role of the Pharmacist**
UAN: 0048-0000-14-032-H01-P CEUs: 0.1

All information must be printed CLEARLY to ensure accurate record keeping for attendance and the awarding of continuing education credit. Certificates will be distributed as a PDF document to a valid email address.

Name:				
Address:				
City:	**State:**	**Zip:**		
Phone:	**Email:**			
Pharmacy License #:	**State:**	**ONU Alumni?**	**Y**	**N**

Program Content:	Strongly Disagree				Strongly Agree
The program objectives were clear.	1	2	3	4	5
The program met the stated goals and objectives:					
Explain the etiology, patient presentation and diagnosis of Celiac disease.	1	2	3	4	5
Discuss the current therapy for Celiac disease, highlighting the gluten-free diet.	1	2	3	4	5
Identify investigational pharmacotherapeutic options for Celiac disease.	1	2	3	4	5
Define the pharmacist's role in patient education and counseling for Celiac disease.	1	2	3	4	5
The program met your educational needs.	1	2	3	4	5
Content of the program was interesting.	1	2	3	4	5
Material presented was relevant to my practice.	1	2	3	4	5

Comments/Suggestions for future programs:

Thank you!

Answers to Assessment Questions—Please Circle Your Answer

1. A B C D E	4. A B C D E	7. A B C D E	10. A B C D
2. A B C D E	5. A B C D E	8. A B C D	
3. A B C D E	6. A B C D	9. A B C D	

Any questions/comments regarding this continuing education program can be directed to Lauren Hamman, Advanced Administrative Assistant for the Office of Continuing Education (email: l-hamman@onu.edu, phone 419-772-2280).

Ohio Northern University is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This program is eligible for credit until 02/25/2017.