



Food intolerances

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Abstract: Food intolerances are prevalent and often confused with food allergies. This article reviews the complex landscape of adverse reactions to food, distinguishing between immune-mediated responses (food allergies) and nonimmune reactions (food intolerances). It also explores specific food intolerances such as lactose intolerance, nonceliac gluten sensitivity, fructose intolerance, and salicylate sensitivity.

Keywords: food intolerance, food sensitivity, fructose intolerance, lactose intolerance, nonceliac gluten sensitivity, salicylate sensitivity

Case study

A 25-year-old female presented to the clinic for an annual physical examination. During the initial interview, she complained of abdominal pain and increased bloating over the past year. She reported diarrhea but also complained of occasional constipation. In addition to the gastrointestinal (GI) complaints, the patient stated she felt “in a fog” and had difficulty focusing on work and remembering things. She attributed the fog-like feeling to a lack of sleep related to abdominal pain.

The patient tried over-the-counter calcium carbonate and omeprazole without much relief. She stated that she recently decreased her intake of bread products, which seemed to help. She asked for recommendations to treat her symptoms.

During the encounter, a thorough health history was obtained, and physical assessments were performed. The patient was advised to maintain a food diary. After 4 weeks, the food diary showed a diet high in processed foods. This raised the concern for gluten sensitivity, and

the patient was advised to eliminate foods containing gluten for 4 weeks. She continued her food diary and noticed a reduction in bloating, abdominal pain, diarrhea, and brain fog. The patient was ultimately diagnosed with nonceliac gluten sensitivity.

Adverse reactions to food can result from food intolerances (also known as food sensitivities) or food allergies; however, food intolerances are often mistakenly attributed to a food allergy.¹

Unlike food allergies, which involve the immune system, food intolerances are non-immune-mediated reactions. Food intolerance refers to difficulty digesting or metabolizing a particular food. It may be secondary to metabolic, toxic, pharmacologic, or undefined mechanisms such as a lack of an enzyme or the inability of the body to break down a substance.² A food intolerance typically causes GI symptoms and is directly related to the amount of exposure to the offending food, whereas an allergic reaction can occur after the consumption of a small amount of the triggering food.^{3,4} Up to an estimated 20% of the global population has a food intolerance.³

Select food intolerances

Lactose intolerance

Lactose intolerance (LI) occurs in individuals unable to absorb lactose.⁵ An estimated 57% of the global population has LI; however, rates range widely across ethnicities and geographic regions.⁶

Lactase-phlorizin hydrolase, or “lactase,” is essential to hydrolyze lactose into digestible molecules.⁶ The reduced ability to break down and absorb lactose increases bacterial fermentation, producing short-chain fatty acids, hydrogen, carbon dioxide, and methane. Over time, individuals can experience downregulation of lactase, resulting in LI. Signs and

symptoms of LI may appear when lactase activity is less than 50%.

There is a growing understanding of LI's etiology; a clear, complex genetic link has been established.⁷ Lactase is encoded by the gene LCT on chromosome 2q21, and mutations are associated with LI.¹² Lactase persistence (LP) is an autosomal dominant trait; lactase nonpersistence is linked to many polymorphisms in the LCT gene and the exact pathway is still not well understood.^{6,7}

Epigenetics is also believed to play an important role. For example, communities with access to fresh milk tend to have LP compared with those without. However, gaps in understanding remain as disease phenotypes do not always align with genetic findings.⁷

Signs and symptoms of LI are not life-threatening but are distressing and negatively impact quality of life.⁵ Food combinations, one's gut microbiome, and orocecal transit time influence signs and symptoms such as bloating, flatulence, pain, diarrhea, and constipation.⁶ Children are less able to reabsorb water in the colon and may more commonly experience diarrhea.⁵

Anxiety, depression, and fatigue are also commonly reported. Memory loss, headache, musculoskeletal pain, rhythm disturbances, oral mucosa ulcers, eczema, asthma, and menstrual cycle disturbances may be reported as well.⁶

LI is commonly diagnosed using the hydrogen breath test, which measures the hydrogen content of exhaled air after fasting and ingesting 25 g to 50 g of lactose.⁶ The test is appropriate for adults and children.

Genetic testing is available, but a positive finding may not correlate to the phenotype nor be prognostic since genetic mapping to LI is incomplete.

The quick lactase test involves a biopsy of the postbulbar duodenal mucosa.

A lactose tolerance test involves ingesting a liquid containing lactose and assessing blood glucose levels. The lactose tolerance test is not commonly used due to fluctuations in postprandial glucose and low sensitivity and specificity.⁶

The mainstay of managing LI in adults and children is the reduction, not elimination, of lactose-containing foods. Lactose is in many medications and foods, making it difficult to eliminate completely, and many individuals can tolerate small amounts of lactose, up to 25 g, particularly if combined with other foods.^{5,6} Exogenous lactase supplementation can be taken in pill or liquid form with each lactose ingestion to minimize symptoms.⁶

Dairy provides a rich source of calcium; therefore, dairy-free diets are not recommended. If dairy elimination is desired, patients should work with a dietitian to ensure they intake adequate amounts of calcium, magnesium, vitamin A, and zinc for bone health.⁶

Probiotic supplementation is recommended to reduce signs and symptoms. Likewise, lactose-containing foods with probiotics, such as yogurt, tend to be better tolerated.⁶

Nonceliac gluten sensitivity

Celiac disease (CeD), also known as gluten-sensitive enteropathy, is an inflammatory disorder of the small intestines caused by a T-cell immune-mediated response to the ingestion of dietary gluten.^{8,9} CeD signs and symptoms include bloating, flatulence, diarrhea, constipation, and nausea.⁸

Nonceliac gluten sensitivity (NCGS), also known as nonceliac wheat sensitivity, is also characterized by intestinal and extraintestinal signs and symptoms that may mimic CeD. The extraintestinal signs and symptoms more often seen in NCGS include headache, brain

High- and low-fructose foods¹⁵

High-fructose foods			Low-fructose foods
Fruits	Vegetables	Other	Fruits
Most fruits	Artichoke	Wheat breads and pastas	Avocado
Dried fruits	Asparagus	Yogurts	Bananas
Canned fruits in juices or syrups	Broccoli	Flavored milk	Cranberries
Tomato products	Chutney	High-fructose corn syrup	Cantaloupe
	Leeks		Lemons
	Mushrooms		Limes
	Okra		Mandarin oranges
	Onions		Pineapple
	Peas		Strawberries
	Red pepper		
	Shallots		

fog, joint pain, neuropathy, fatigue, anemia, depression, and autoimmune diseases.^{8,9}

The prevalence of NCGS in the general population is between 0.6% and 13%.⁸ The lack of specific biomarkers renders diagnosing NCGS difficult.⁹ Overall, young women between 30 and 40 years of age are more likely to self-diagnose and self-treat with a nongluten diet.⁸

One may also differentiate NCGS from CeD by observing microcytic or hypochromic anemia, a feature of the former, or enteropathy, a feature of the latter.^{9,10} Furthermore, altered iron metabolism is associated with NCGS.¹¹

Although data are unclear, NCGS may be associated with autoimmune diseases.⁸ Approximately one-third of individuals diagnosed with NCGS have a positive antinuclear antibody with a high prevalence of Hashimoto's thyroiditis.¹¹

The data on the pathophysiology of NCGS are conflicting.¹¹ The components in wheat that may cause GI or extraintestinal signs and symptoms include fermentable short-chain carbohydrates (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) and amylase-trypsin inhibitors.^{8,12}

The Salerno Diagnostic Criteria,⁸ developed in 2015, defined the

diagnostic criteria for NCGS, including the causality of wheat ingestion and GI or extraintestinal signs and symptoms.^{8,12} Diagnosis is based on a 30% reduction of GI or extraintestinal signs and symptoms on a gluten-free diet (GFD) for 6 weeks, followed by a double-blind, randomized, placebo-controlled challenge with gluten.¹² It is important to note that if an individual begins a GFD before being tested for CeD, Human Leukocyte Antigen genotyping for CeD may not be effective. A false-negative result may occur due to a change in microbiome composition due to a lack of gluten.^{9,13} Additionally, individuals may be reluctant to stop a GFD due to fear of a rebound onset of severe signs and symptoms and, therefore, may not complete the trial non-GFD for diagnostic purposes.⁹

Traditional dietary advice of ad-

hering to a strict GFD continues to be the first treatment choice.^{1,10} In 2013, the FDA developed a requirement that packaged gluten-free foods contain less than 20 parts per million (ppm) of gluten to protect individuals with CeD.¹⁴ Replacing highly processed foods and refined carbohydrates such as white bread with fruits and vegetables can decrease signs and symptoms.¹⁴ Treatments other than GFD are being researched, including ingested supplemental enzymes to accelerate proteolysis and hydrolysis of toxic gliadin to reduce intestinal exposure to gluten and wheat components.⁸

Fructose intolerance

Fructose is a natural sugar found in various foods, including fruits, vegetables, and honey, and can be produced from corn as high-fructose corn syrup (see *High- and low-fructose foods*).¹⁵ A fructose intolerance (also known as fructose malabsorption) may occur when intestinal cells cannot break down this sugar, possibly due to a hereditary lack of the requisite protein or enzyme.¹⁶

Individuals with a fructose intolerance are more likely to be intolerant to other fermentable sugars such as glucose, maltose, and sucrose.¹⁷ Signs and symptoms include increased flatulence, bloating, diarrhea, and abdominal pain. Foods with a lower fructose content may be tolerable as signs and symptoms can be none to minimal.

Foods highest in salicylates¹⁸

Fruits	Vegetables	Legumes	Other
Plums	Cauliflower	Lentils	Herbs (curry, paprika, oregano, mustard, cayenne)
Strawberries	Pickled vegetables	Beans	Spices
Watermelons			Buckwheat
Raspberries			Oat
			Corn

A fructose intolerance diagnosis can be made through an elimination diet or a breath test detecting levels of hydrogen.¹⁵ A high level of hydrogen indicates difficulty digesting fructose. Those with fructose intolerance should keep a food diary, in which they document dietary intake and associated signs and symptoms such as flatulence, bloating, diarrhea, and abdominal pain with timing to help eliminate foods with high fructose. They should also undergo an elimination phase where they consume up to 5 g of fructose per day for the first 2 weeks.¹⁵ Then, they reintroduce foods with slightly higher fructose to determine their tolerance threshold.¹⁵ Most patients with fructose intolerance can usually tolerate 10 g to 15 g of fructose daily.¹⁵

Salicylate sensitivity¹⁸

Salicylates are derived from salicylic acid and are found naturally in certain foods (see *Foods highest in salicylates*). Legumes, fruits, vegetables, some cereals, ground coffee, spices, and herbs are high in salicylates. The etiology of this sensitivity is thought to be related to the inhibition of cyclooxygenase, resulting in an overproduction of leukotrienes.

Clinical manifestations of salicylate sensitivity can vary; however, respiratory signs and symptoms are the most common, including nasal congestion, rhinorrhea, nasal polyps, chronic sinusitis, and asthma.²³ These respiratory signs and symptoms may be misinterpreted as allergic reactions.

GI signs and symptoms may include flatulence, abdominal pain, diarrhea, or colitis.

Dermatologic symptoms may vary from localized tissue swelling to hives.

The most important part of diagnosing salicylate intolerance is obtaining a thorough history to



Nurses should educate patients to avoid prematurely eliminating foods unless there is a strong suspicion of food intolerance.

establish a link between signs and symptoms and salicylate consumption. The gold standard for diagnosing salicylate sensitivity is an exposure or provocation test in which acetylsalicylic acid is administered orally or nasally. Such tests should be conducted cautiously due to possible reactions such as asthmatic reactions. Treatment includes eliminating salicylate-rich foods from the diet, particularly spices and processed foods.

Nursing implications

Nurses must understand the differences between food sensitivities, intolerances, and allergies. Overdiagnosis of food allergies can lead to unnecessary food avoidance, anxiety, and social limitations.^{26,27} Food intolerances and sensitivities are not life-threatening and do not require the complete avoidance of foods.

Nurses should educate patients to avoid prematurely eliminating

foods unless there is a strong suspicion of food intolerance. Patients need instructions to complete a thorough food diary containing foods consumed throughout the day as well as the timing of when symptoms occur.

A food intolerance diagnosis may take 2-3 months because of the timing of the food diary, eliminating or reducing foods, and follow-up evaluations. Patients will need to be encouraged to complete the entire diagnostic process while enduring a host of food intolerances including GI and extraintestinal symptoms.

Conclusion

Food intolerances are the result of nonimmunologic mechanisms that contribute to GI and extraintestinal signs and symptoms. A reproducible adverse reaction to a food or food component that does not have an established or likely immunologic mechanism is a food intolerance, not a food allergy. A variety of substances can cause food intolerances, leading to varying reactions.

A comprehensive health history is critical to selecting appropriate testing for accurate diagnosis. If test results are inconclusive, evaluation of other nonallergy causes should be explored. ■

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