

# The SOY Connection

Health & Nutrition News About Soy



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## ESTIMATING PREVALENCE OF SOY PROTEIN ALLERGY

By Steve L. Taylor, Ph.D.

### A QUICK TASTE

*Soy protein has been designated one of the major allergens by the U.S. Food and Drug Administration. Nevertheless, rigorous prevalence data are not available for soy protein allergy, and indirect evidence suggests it occurs less frequently than other common allergens including shell-fish, peanuts, tree nuts and fish.*

Food allergies are becoming an increasingly important issue. True soybean allergy involves the generation of allergen-specific IgE antibodies in certain individuals upon exposure to soy protein. Soybeans contain several allergenic proteins. IgE-mediated soybean allergy can be a serious condition because of low threshold doses for the offending protein(s) and the possibility of severe reactions in some soy-allergic individuals.

Soybeans are considered by worldwide regulatory authorities as one of the most commonly allergenic foods. Soybean allergy is most common among infants and young children because of exposure to soybean-based infant formula.<sup>1,2</sup> Many infants outgrow soybean allergy, so the prevalence is lower in adults.<sup>3</sup>

Despite widespread acceptance of the notion that soybeans are a commonly allergenic food, solid scientific information on the prevalence of soybean allergy in the overall population does not exist. However, the prevalence of soybean allergy can be estimated by extrapolation from existing information. A rigorous estimate of the prevalence of soybean allergy would need to involve several critical features: 1) a study of the general population; 2) clinical demonstration of adverse reactions to soybean preferably by double-blind, placebo-controlled food challenges (DBPCFC); 3) and clinical documentation of an IgE-mediated mechanism for the adverse reaction. The literature relevant to the prevalence of soybean allergy was screened, and no clinical studies were found that met these rigorous criteria. Thus, the prevalence of soybean allergy must be estimated from a critical examination of existing studies.

Only one study actually attempted to determine the prevalence of soybean allergy

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## AHA ADVISORY ON SOY AND HEART HEALTH

By Mark Messina, Ph.D.

The American Heart Association (AHA) has updated its scientific advisory on soy protein and cardiovascular disease (CVD).<sup>1</sup> The previous advisory on this topic was published in 2000,<sup>2</sup> not long after the U.S. Food and Drug Administration approved a health claim for soy protein and coronary heart disease.<sup>3</sup> A

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## FOCUS ON // SOY ALLERGY

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# SOYBEAN OIL & LECITHIN: ARE THEY ALLERGENIC?

By Steve L. Taylor, Ph.D.

The Food Allergen Labeling & Consumer Protection Act (FALCPA) in the U.S. mandates labeling of all ingredients derived from commonly allergenic foods, including soybeans, with the exception of highly refined oils. Commercially, soybean oil and soy lecithin are two of the most important food ingredients. Are all soybean oils excluded from labeling? Why? What about soy lecithin?

## Highly Refined Soybean Oil

Most soybean oil manufactured in the United States and added to food products is highly refined. FALCPA exempts highly refined oils from the new source labeling provisions because highly refined soybean, peanut and sunflower seed oils have been clinically documented to be safe for consumption by individuals allergic to the source food.<sup>1,5</sup> Commercially, the soybean oil refining process uses extraction with hot solvents, bleaching and deodorization, and these processes serve to eliminate almost all soy protein, and thus allergens, from the oil.<sup>6</sup> Although highly refined soybean oil contains extremely low levels of detectable soy protein, FALCPA provides an exemption from source labeling.

## Cold-Pressed Soybean Oil

Cold-pressed, also known as extruder-pressed, soybean oil is not excluded from source labeling.

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# SOY PROTEIN ALLERGY

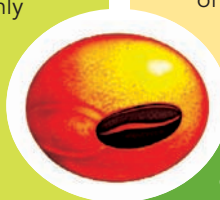
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directly in the general adult population. Bjornsson *et al.* indicated a 2 percent prevalence of soy allergy among 1,397 unselected Swedish adults of ages 20-44 years.<sup>4</sup> However, the diagnosis was based only on serum screening for soy-specific IgE and is thus undoubtedly an over-estimate because no oral challenges were done to confirm that adverse reactions to soy actually occurred in these individuals. It is well known that individuals can have food-specific IgE in their serum without clinical reactivity to oral challenge to that food, especially in the case of legumes, like soybean.<sup>5</sup> In other studies, fewer than 10 percent of patients with positive soy-specific IgE levels reacted adversely on blinded oral challenge<sup>6,7</sup>; however these two studies cannot be used to estimate overall prevalence of soybean allergy because they were confined to food-allergic subpopulations. If we assumed that 10 percent of the Swedish subjects with soy-specific IgE would have been challenge-positive, then the prevalence of soybean allergy is estimated at about 0.2 percent in adults.

Clinical experience would suggest that the prevalence of soy allergy should be higher among infants and young children than among adults. Yet, the prevalence of soybean allergy among unselected Australian children was estimated at only 0.1 – 0.28 percent based upon a unique extrapolation strategy developed initially by Hill *et al.*<sup>8</sup> They determined the prevalence of milk allergy among a cohort of high-risk infants (those born to families with allergies). Then, they corrected this estimate to the general Australian population by estimating the percentage of infants who would be considered high-risk (19.3 percent). Their estimate of the prevalence of milk allergy among Australian infants was 2 percent, which is in agreement with earlier studies of the prevalence of milk allergy in other countries based on challenge trials of the general infant population.<sup>9,10</sup> The prevalence of soy allergy can be estimated from the prevalence of milk allergy based upon data on the subsequent development of soy allergy in milk-allergic infants who were switched to soy formula. Various investigations estimate that 5-14 percent of milk-allergic infants develop soy allergy.<sup>1,10,11,12</sup> Thus, the prevalence of soybean allergy is estimated as 2 percent x 5-14 percent, or 0.1-0.28 percent.

Information from the infant formula industry could be used to confirm these estimates because milk-allergic infants are often switched first to soybean-based infant formula. A study by Cordle<sup>2</sup> can be used to confirm the estimate of Hill *et al.*<sup>8</sup> because it provides information on a large number of milk-allergic infants switched to soybean formula. Cordle indicated that 26

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## AHA ADVISORY *Continued from Page 1*

tremendous amount of research on the cholesterol-lowering effects of soy protein has been published during the intervening years and much of this information was considered by the nutrition committee of the AHA. Its current position is that soyfoods such as tofu, soy nuts and soy burgers are likely to be beneficial to cardiovascular health because of their low saturated fat content and high polyunsaturated fat, fiber, and vitamin and mineral content. In addition to displacing less heart-healthy foods, the AHA also estimated, based on a meta-analysis of 22 trials, that soy protein directly lowered LDL-cholesterol about 3 percent. This decrease is similar to the findings from one,<sup>4</sup> but somewhat lower than another,<sup>5</sup> recently published meta-analysis and is not dissimilar to estimates expressed in other recent publications.<sup>6,7</sup> (See Table 1 on Page 6 to compare findings.) However, it is much lower than the average decrease of 12.9 percent reported in the meta-analysis by Anderson *et al.* published in 1995.<sup>8</sup> This analysis first brought widespread attention to the cholesterol-lowering effects of soy protein. The AHA also found that soy protein modestly lowered triglyceride levels and raised HDL levels, findings which are also in agreement with the other meta-analyses listed in the table. Each of these lipid effects should help to further reduce CVD risk.

The reasons for the revised downward estimates of the cholesterol-lowering effects of soy protein are not clear. In the analysis by Anderson *et al.*, the 12.9 percent decrease was derived from several studies that involved subjects with extremely high cholesterol. Conventional wisdom has been that the effects of soy protein are more pronounced in very hypercholesterolemic individuals. However, the AHA advisory concluded that baseline cholesterol level is unrelated to cholesterol reduction. This finding, while not providing a possible explanation for the discrepancy, is particularly noteworthy because it means all people, regardless of their cholesterol level, will experience at least a small reduction in cholesterol in response to soy protein. This is especially relevant as evidence indicates the optimal cholesterol level is much lower than previously thought. Increasingly, evidence suggests the lower the better.

In contrast to the findings by Anderson *et al.*, the AHA found no evidence of a dose response relationship between soy protein and cholesterol reduction; studies using 50 g/day soy protein were not more efficacious than those studies using smaller amounts. This suggests that less than 25 g/day soy protein – the threshold amount established by the FDA for cholesterol reduction – may also be efficacious. There is evidence in support of this hypothesis,

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## SOY PROTEIN ALLERGY

Steve L. Taylor, Ph.D.

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out of 247 cows' milk-allergic infants (10.5 percent) were unable to tolerate soy-based infant formula. If 10.5 percent of cows' milk-allergic infants have soy allergy, then an estimated prevalence of soy allergy in the infant population would be 0.21 percent (2.0 percent x 10.5 percent).

Of course, this type of approach to estimating the prevalence of soybean allergy has a significant potential flaw. It assumes that only infants with cows' milk allergy will develop soy allergy in infancy. But in all likelihood, at least for young infants (those less than 2 years of age, the age group typically exposed to infant formula), that is probably true for the vast majority of cases.

Many infants with soybean allergy will outgrow their soybean allergy within a few years. Thus, using the prevalence of soy allergy in infants to estimate the prevalence in the overall population would require a significant adjustment for this development of oral tolerance. In studies on a limited number of soy-allergic infants, 50-100 percent of the infants became tolerant of soybeans within 2-3 years.<sup>3,13</sup> It is thought that the development of oral tolerance to soybean follows the same pattern as for milk and egg, where much larger numbers of infants have been followed. In an evaluation of several studies, Eggleston estimated that 70 percent of children who developed food allergies at ages less than 3 years would outgrow the allergy within a few years.<sup>14</sup> Most of these infants were sensitive to milk and egg, although some were allergic to soy or wheat. In a preceding paragraph, the estimated range of soybean allergy in infants was 0.1-0.28 percent. If we assume that 70 percent of these infants will outgrow their soybean allergy, the estimated prevalence in the overall population would be 0.02-0.056 percent. Of course, this assumes that all sensitization to soybeans is initiated in infancy. While this is not true, the majority of soy allergy likely does emanate from sensitization during infancy.



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## SOYBEAN OIL & LECITHIN Continued from Page 2

This type of soybean oil is often found in natural food sections or gourmet sections of retail stores, and typically is not used as an ingredient in further processed foods. Although cold-pressed soybean oil has not been documented to provoke allergic reactions, this type of oil is likely to contain somewhat higher levels of residual protein than highly refined oil. The safety of cold-pressed soybean oil has not been documented by clinical challenge trials beyond one small trial in seven soy-allergic subjects.<sup>3</sup>



### Soy Lecithin

FALCPA also requires the labeling of soy lecithin because it is derived from soybeans and contains residual protein. The Grocery Manufacturers of America and other trade associations are working with the Food & Drug Administration to try to exempt soy lecithin from the source labeling requirement of FALCPA. Soy lecithin is acknowledged to contain residual levels of protein, although the amount of residual protein is uncertain. The Food Chemicals Codex specification for lecithin allows a maximum of 0.3 percent hexane insoluble matter in food-grade lecithin. If all protein, then the upper limit for protein should be 3,000 ppm. No validated method is available for the precise measurement of protein levels in lecithin. Soy allergens have been identified within the residual protein in soy lecithin by various investigators. However, the presence of residual levels of soy protein and soy allergens in soy lecithin is insufficient to document the allergenicity of soy lecithin. Only two reports exist of allergic reactions to soy lecithin among soy-allergic consumers, despite its widespread use.<sup>7,8</sup> The allergenicity of soy lecithin remains unknown, although the very small number of documented episodes and their questionable nature suggest empirically that its allergenicity is quite low.

*Editor's Note: This work is a contribution from the University of Nebraska Cooperative Extension Division, Lincoln, Nebraska, Journal Series No. 1033.*

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## SOY PROTEIN ALLERGY Continued from Page 3

Since most soy allergy is outgrown, the prevalence of soybean allergy should be higher among infants than among adults. The only study of the prevalence of soybean allergy among adults is the estimate of 0.2 percent for Swedish adults – higher than predicted based on this logic.

Despite the continuing uncertainties, the prevalence of soybean allergy in the general population is probably not higher than 0.2 percent and could be as low as 0.1 percent (290-580,000 individuals) among the U.S. population. This likely prevalence for soybean allergy contrasts with prevalence estimates of 1.9 percent for crustacean allergy, 0.6 percent for peanut allergy, 0.5 percent for tree nut allergy, and 0.4 percent for fish allergy.<sup>15,16</sup>

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**F.Y.D.**

From Your Dietitian

# TOP 10 QUESTIONS ON SOY & HEART HEALTH

By Mark Messina, Ph.D.

## 1 Q: Are soyfoods a heart-healthy food?

**A:** Both the American Heart Association (AHA) and U.S. Food and Drug Administration (FDA) agree that soyfoods contribute to a heart-healthy diet. According to a very recent statement from the AHA, "... soy products such as tofu, soy butter, soy nuts, or some soy burgers should be beneficial to cardiovascular and overall health..."<sup>1</sup> In 1999, the FDA approved a health claim for soy protein and coronary heart disease.<sup>2</sup> As a result, foods containing sufficient soy protein can include a statement about the heart benefits of soy on their label.

## 2 Q: If my blood cholesterol is very elevated, will eating soyfoods lower my cholesterol to the recommended level?

**A:** No single food or dietary supplement will lower elevated cholesterol to the target goal. A heart-healthy diet—to substantially lower cholesterol—requires making comprehensive changes. This can mean making small changes in a number of different areas of the diet. Scientific research has conclusively shown that adding soy protein-rich foods to the diet can be an important factor in a overall diet that substantially reduces cholesterol.<sup>3-5</sup>

## 3 Q: How do soyfoods lower cholesterol?

**A:** Soyfoods act to reduce cholesterol in two ways.

1) Traditional soyfoods are high in polyunsaturated fat, low in saturated fat, and cholesterol-free. Because saturated fats raise cholesterol and polyunsaturated fats lower it, consuming foods like soyfoods in place of many traditional sources of protein can reduce cholesterol.<sup>6</sup> 2) Soy protein also directly lowers blood cholesterol levels. This effect has been shown in more than 50 clinical trials.<sup>7,8</sup>

## 4 Q: How much will soyfoods lower cholesterol?

**A:** The degree to which soyfoods lower cholesterol is different among individuals. People respond differently to foods and to dietary changes aimed at cholesterol reduction.<sup>9</sup> Adding soy protein to the diet reduces LDL-cholesterol (the bad cholesterol) by 3 to 5 percent.<sup>1,7</sup> Over a period of many years, this one dietary change can reduce risk for heart disease by as much as 10 percent.<sup>10-12</sup> In addition, if soyfoods replace foods that are high in saturated fats, the reduction in cholesterol and in heart disease risk will be even greater.

## 5 Q: Does soy protein have heart-benefits beyond lowering bad cholesterol?

**A:** Soy protein has been shown to lower blood triglyceride levels by approximately 6 percent.<sup>1,7</sup> Triglycerides, a type of fat, are believed to raise risk for heart disease.<sup>13</sup> Soy protein also very modestly raises levels of HDL-cholesterol,<sup>1,7</sup> the good cholesterol that protects against heart disease.<sup>14</sup>

## 6 Q: What other benefits for heart disease do soyfoods have?

**A:** Studies show that soyfoods may affect a number of risk factors for heart disease. Compounds in soyfoods called isoflavones may directly improve the health of the arteries.<sup>15-19</sup> They also may inhibit clot formation<sup>20</sup> and reduce inflammation,<sup>21</sup> two factors that can lower heart disease risk. More research is needed in these areas, however, before definitive conclusions can be made. Nevertheless, it is clear there are many potential means by which soyfoods can reduce heart disease risk.

## 7 Q: How much soy protein is needed to lower blood cholesterol?

**A:** The exact amount of soy protein needed to lower cholesterol has not been determined. The FDA has established that people who wish to reduce their cholesterol should consume 25 grams per day of soy protein, but there is evidence that lower amounts of soy protein may be just as effective.<sup>22</sup>

## 8 Q: How often do I need to consume soyfoods to lower cholesterol?

**A:** People who participated in studies of cholesterol reduction ate soyfoods every day. It isn't yet known what effect less frequent consumption will have. Eating soyfoods several times a day—as is typical in many parts of Asia—may be more beneficial than consuming a large portion of soy once a day.

## 9 Q: Are some types of soyfoods better for fighting heart disease than others?

**A:** All soyfoods can play a role in a heart-healthy diet, especially if they replace foods high in saturated fat and cholesterol. Soyfoods that are especially protein-rich can make it easier to meet the recommendations for 25 grams of soy protein intake established by the FDA. Since isoflavones may also have coronary benefits, there are benefits to consuming foods that are rich in both soy protein and isoflavones.

## 10 Q: Is too much soy bad for you?

**A:** Studies show that it is safe for healthy adults to consume even large amounts of soyfoods. However, health experts always recommend choosing a diet based on a variety of foods. Soyfoods are most properly viewed as one of many healthful sources of protein in the diet.

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## AHA ADVISORY Continued from Page 3

although the AHA did not provide an opinion on this particular matter. The AHA also found there was insufficient evidence to conclude that soy protein lowers levels of lipoprotein(a) or blood pressure. Unfortunately, the AHA advisory did not have the opportunity to consider recently published research by He *et al.*, who found that soy protein markedly lowered blood pressure in hypertensive patients, although the comparison in this study was to carbohydrate, not another protein.<sup>9</sup>

Importantly, even the modest direct cholesterol-lowering effect of soy protein, while not clinically (i.e., at the individual level) relevant, is still noteworthy. Soy protein alone is certainly not going to bring cholesterol levels down to the target goal in hypercholesterolemics, but the inclusion of sufficient amounts of soy protein will in theory reduce coronary heart disease at the population levels by as much as 10 percent.<sup>10,11</sup> This will lead to a marked reduction in coronary heart disease morbidity and mortality. The modest reductions in triglyceride levels and the increase in HDL, along with a possible reduction in the consumption of higher saturated fat foods, will be of further benefit.

Finally, and surprisingly, the AHA nutrition panel also commented on the effects of soy on health outcomes outside of CVD. Specifically, they concluded that there is little evidence soy alleviates hot flashes or reduces cancer risk, and also that the evidence that soy reduces postmenopausal bone loss is mixed. However, in contrast to their comprehensive review of CVD, the reviews in these other areas were quite limited and cursory. More extensive reviews on these subjects with different conclusions have been published elsewhere.<sup>4, 12, 13</sup>

Table 1: Meta-analysis Findings

Reference	No. of trials*	Subjects*	LDL reduction	Triglyceride reduction	HDL increase
Sacks <i>et al.</i> <sup>1</sup>	22	757	3%	5%	1.5%
AHQ <sup>4</sup>	52	~2,000	~3%	~6%	~1%
Zhan & Ho <sup>5</sup>	33	1,749	5.3%	7%	3%
Anderson <i>et al.</i> <sup>8</sup>	31	564	12.9%	10.5%	2.4%

\* Refers to LDL-related measurements.

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# SOY PROTEIN ALLERGY Continued from Page 4

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# EXCLUSIVE ON-LINE ARTICLE: FOOD ALLERGY & INTOLERANCE: A GUIDE FOR PRACTITIONERS

By Lynn Christie, M.S., R.D., L.D.

Food allergy and food intolerance are adverse food reactions defined as abnormal physiological responses to the ingestion of food. Food allergy relates to immunologic reactions to proteins (allergens) in foods ingested by susceptible individuals that are primarily immunoglobulin E (IgE) mediated. Food intolerance is an abnormal physiological response to an ingested food that does not involve the immune system.

In the United States, eight foods – cows' milk, egg, peanuts, soybeans, wheat, tree nuts, fish and shellfish – cause 90 of allergic reactions. The majority of children are allergic to cows' milk, egg, soybeans and wheat. Most will lose their food allergy by the time they are school age. Peanut, tree nut, fish and shellfish allergies are rarely lost and are responsible for the more severe allergic reactions.<sup>1,2</sup>

IgE-mediated food allergic reactions are triggered when an individual comes in contact with the food allergen.<sup>3</sup> Reactions can begin within seconds after contact or take up to two hours before symptoms begin. The skin, gastrointestinal tract and/or respiratory tract are the target organs involved during an allergic reaction. Skin symptoms may be an itchy rash, hives, redness, swelling or atopic dermatitis (intense itching followed by a red, raised rash). Nausea, abdominal cramping, vomiting, or diarrhea indicate gastrointestinal symptoms. Respiratory involvement includes watery, itchy eyes, rhinitis

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(inflammation of the nasal mucous membranes), sneezing, dry cough, tightness in the chest and wheezing. Any of these symptoms can lead to systemic anaphylaxis involving hypotension, shock and possibly death.

Food protein-induced enterocolitis, enteropathy and proctocolitis are non-IgE mediated malabsorption disorders traditionally diagnosed in infancy.<sup>4</sup> These food allergy disorders usually resolve within 1-2 years of allergen avoidance. Cows' milk, soy, eggs and grains are the primary allergens responsible for symptoms. Symptoms range from diarrhea with/without blood, vomiting, edema, shock and/or poor weight gain. Celiac disease, a specific type of enteropathy, is caused by immune reaction to gluten found in wheat, rye and barley. Celiac disease requires a lifetime gluten avoidance diet. Eosinophilic esophagitis/gastroenteritis may or not be associated with a food allergy component.

Food intolerances are caused by a wide range of disorders.<sup>5</sup> Gastrointestinal symptoms can be caused by structural abnormalities (e.g., hiatal hernia), enzyme deficiencies (e.g., lactase deficiency), gastroesophageal reflux and peptic ulcer disease. Symptoms associated with these disorders include chronic cough and wheezing, recurrent vomiting, diarrhea, abdominal distention and cramping. Unintentional food contaminants (e.g., microbial or fungal toxins, food-borne infectious agents) can cause headache, gastrointestinal symptoms, neurological symptoms, urticaria and potentially paralysis. Naturally-occurring pharmacologic agent (e.g., tyramine, histamine) symptoms are nausea, vomiting and headaches.

Symptoms for food allergy are similar to symptoms for food intolerance. The diagnostic approach to suspected adverse food reactions begins with a medical history, physical examination, testing, diagnostic elimination diet and oral food challenges.<sup>3</sup> A thorough history uncovers suspected food(s), quantity of food(s) ingested, and time between ingestion and symptoms. Prick skin testing (PST) and radioallergosorbent test (RAST) are used to establish whether the patient has IgE antibodies to specific food allergens. These tests indicate the presence of allergen-specific IgE, but they do not indicate if the patient will react upon ingestion of that food. One type of RAST, Pharmacia CAP system FEIA (Pharmacia & Upjohn Diagnostics, Uppsala, Sweden), has been used to demonstrate quantitative values for eggs, milk, peanut and fish that provide predictive information of having an allergic reaction to that allergen.<sup>6</sup>

If the practitioner suspects a food allergy or intolerance triggered by food, the patient is placed on a diagnostic elimination diet that removes the offending food(s). The individual needs to strictly avoid the foods in question for 2-4 weeks. If the symptoms do not subside, the eliminated food(s) are unlikely a strong contributor to the disorder, but it must be considered that food(s) maintained in the diet may be causing symptoms, even if some of the eliminated ones were also responsible for the symptoms. If symptoms discontinue and several foods were eliminated, further evaluation may be needed to verify the offending food(s).

Oral food challenges provide the most definitive means to diagnose an adverse reaction to food, especially food allergies.<sup>7</sup> <sup>8</sup> The selection of foods to be tested by oral challenge is determined by history and test results. Oral food challenges are performed openly (patient and physician aware of the challenge content) or are single-blinded (patient unaware, but physician knows content of challenge) for screening. The gold standard to diagnose food allergy is the double-blind, placebo-controlled oral food challenge (both patient and physician unaware of challenge content).

Current treatment for food allergy is following an allergen(s) avoidance diet with ready access to injectable epinephrine in case of accidental ingestions. Nutrition education for avoidance diets<sup>9</sup> is complex but necessary for an individual to be free of symptoms. Treatment for food intolerances is based upon the cause of the symptoms. Differentiating the symptoms and test results with the correct diagnosis of an adverse food reaction is tedious but essential for the correct treatment.

### ABOUT THE AUTHOR

Lynn Christie, M.S., R.D., L.D. received her master's in nutrition and food science at Florida State University. She practices dietetics and is a clinical coordinator for the Pediatric Allergy and Immunology Division at the University of Arkansas for Medical Sciences and Arkansas Children's Hospital.

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