



Perspective

Lupin

An emerging food allergen in the United States

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Introduction

Food allergies are on the rise and becoming a global concern.¹ Common food allergens are well recognized and have been studied extensively in the United States and Europe. However, there is a gradual emergence of new food allergens, such as lupin, which are neither as well characterized nor as well studied.

Lupin is a legume, known as the genus *Lupinus*, and white lupin is the form typically used by the food industry, whereas yellow and blue lupin are primarily found in animal feed.²

Most people are unaware of lupin's allergenic potential, including possible cross-reactivity with peanut.³ In Europe, cases of lupin allergy were described after lupin was introduced in food products.³ Lupin is slowly being introduced into more products in the United States.

We describe 2 cases of lupin allergy, highlighting the fact that this emergent food allergy can present both independently (without a prior history of food allergy) and in association with established food allergies, especially peanut.

In our view, lupin is an important emerging food allergen, necessitating increased awareness among allergy and immunology specialists about what is known and unknown with regard to its natural history, allergenic proteins, and potential cross-reactivity. This knowledge will allow better diagnosis and patient education.

Patient Cases of Lupin Allergy

Case 1

A 4-year-old boy with known atopic dermatitis, peanut, tree nut, egg, pea, and sesame allergy presented to the office after a recent anaphylactic reaction. He tried a gluten-free cracker, which did not contain any of his known allergens. He immediately reported throat discomfort followed by stomach pain. Within minutes, he also developed a barking cough and difficulty breathing followed by vomiting. At that point, his parents administered self-injectable epinephrine and called 911. He was treated with a nebulizer in the ambulance. In the emergency department, prednisone and diphenhydramine were administered. Review of the ingredients of the crackers showed that it contained lupin, an allergen that may be cross-reacting in individuals with established peanut allergy. Subsequently, specific IgE testing showed a lupin IgE level of 7.82 kU/L and a peanut IgE level greater than 100 kU/L.

Case 2

An 11-year-old boy with a history of allergic rhinitis and exercise-induced asthma presented to the allergy clinic with a history of an allergic reaction after eating a commercially made waffle given to him by a friend. Soon after eating it, he developed abdominal pain, facial erythema, generalized urticaria, and swelling of his ears. Symptoms responded to 2 doses of antihistamine (1 short acting and 1 long acting). He did not have a prior history of food allergies. He was consuming all foods and had a varied diet, although he ate nuts infrequently because he did not like the taste. Skin testing was performed, the results of which were negative for peanut and tree nuts and positive for lupin (8-mm wheal). The results of tests for common aeroallergens, including grasses, trees, and dust mites, were also negative.

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Lupin was tested because it was on the online list of ingredients for the ready-made waffle.

Lupin and Common Diagnostic Challenges

The diagnosis of lupin allergy can be elusive and presents many challenges to the practicing clinician. A detailed clinical history is paramount in the evaluation of lupin allergy, with special emphasis required on a detailed ingredient list of the product suspected of causing the allergic reaction. Although commercial lupin skin testing reagents are not currently widely available, percutaneous skin testing to the fresh form of lupin, such as with lupin flour or lupin bean, may also be performed and is an acceptable diagnostic method, although it is not standardized or validated. Fresh food skin testing may be performed either by creating a slurry made of the fresh food and sterile saline as the extract used for testing or by the prick-prick method in which the tester first pricks the fresh food and then the skin.⁴ Serum specific IgE testing to lupin is commercially available and may also be used in addition to skin testing. However, diagnostic decision points (eg, 95% positive predictive values) for serum IgE levels and skin prick test sizes that may help predict the likelihood of a clinical reaction to lupin do not exist at present. Once the diagnosis is confirmed, strict avoidance of lupin, and potentially of relevant cross-reactive foods, will likely be advised because of the risk of a severe and potentially life-threatening reaction.

Cross-reactivity between lupin and peanut may be explained after examination of lupin allergenic proteins. The major allergenic proteins associated with lupin sensitization, although not fully characterized, include Lup-1, which is a β -conglutin (vicilin-like protein), and Lup-2, which is an α -conglutin (legumin-like protein). γ -Conglutin (vicilin-like protein) and δ -conglutin (2S albumin) are minor allergenic proteins.⁵ Amino acid sequence homology exists between major lupin allergens and major peanut allergens; cross-reactivity has been described between β -conglutin and Ara h 1 and between δ -conglutin and Ara h 2.⁶ In addition, cross-reactivity between the peanut Bet v 1 homologue Ara h 8 and pathogenesis-related protein 10 of lupin has been reported.⁷

An important consideration for clinicians is the fact that sensitization to lupin may occur primary or because of cross-reactivity with other legumes and therefore may not necessarily result in clinical reactivity on ingestion. Studies evaluating lupin sensitization have reported rates ranging from 34% to 82% of individuals allergic to peanut or other legumes. However, clinically relevant lupin allergy, based on positive oral food challenge results and/or convincing history, has been reported in only 4% to 29% of these individuals.^{8–12} This wide range of reported sensitization rates is likely related to differences in lupin consumption in various countries. Because many patients who are sensitized to lupin may be able to tolerate lupin on ingestion, performing a supervised oral food challenge to lupin is often recommended to confirm lupin allergy and to advise on proper food avoidance measures.

Lupin and Areas of Uncertainty

In addition to the diagnostic challenges described above, the natural history and rate of lupin allergy remain unknown, limiting the information that can be provided to patients in terms of allergy persistence and rates of resolution. Few published studies exist on lupin allergy, and a large number of observations are based on case reports. There is also a clear need for markers that will differentiate between sensitization and true allergy. Currently, oral food challenges will need to be performed to differentiate sensitization from clinical reactivity.

Lupin and Food Labelling

There is a wide range of food products that may contain lupin, but consumers are often not aware of this. Lupin, in roasted and ground powder form, has been used to add protein, fiber, and texture to food

Table 1
Selected Patient Resources

American Academy of Allergy, Asthma & Immunology: What Is Lupin Allergy? http://www.aaaai.org/conditions-and-treatments/library/allergy-library/lupin-allergy
Anaphylaxis Campaign: Lupin Allergy – The Facts https://www.anaphylaxis.org.uk/wp-content/uploads/2015/06/Lupin-allergy-fact-sheet-v3-with-footer-corrected-july-2016.pdf
Australasian Society of Clinical Immunology and Allergy: Lupin Food Allergy https://www.allergy.org.au/patients/food-allergy/lupin-food-allergy
US Food and Drug Administration: Allergies to a Legume Called Lupine: What You Need to Know https://www.fda.gov/forconsumers/consumerupdates/ucm409836.htm
US Food and Drug Administration: Sign Up for Product Recalls, Market Withdrawals & Safety Alerts https://www.fda.gov/safety/recalls
University of Nebraska-Lincoln Food Allergy Research and Resource Program: Legumes https://farpp.unl.edu/informalllegumes

products. Although not an exhaustive list, such products include pasta, baked goods, cake mixes, dairy products, beverages (eg, as milk or coffee substitute), crackers, breaded onion rings, sauces, stews, cereals, mueslis, breads, muffins, spreads, pancakes, pizza, Asian fermented foods, Japanese miso, and vegetarian foods.^{13,14} Lupin does not contain gluten, and therefore lupin flour and lupin protein are increasingly used in gluten-free products.^{14,15} This fact is often unknown to food allergic consumers. Fiber and protein isolates from lupin have been used as vegetable protein extenders and fat replacers in meat products (eg, sausages).¹⁴ Lupin may be used as an egg or soy substitute in food products and has been used in soil fertilizer, poultry feed, and animal feed.^{14,15} Lupin may also be found in a variety of vegetable dishes similar to other types of beans.

Countries may differ on food allergens required by law to be listed on ingredient labels. For example, in Europe, lupin is a more common food, and allergen labeling legislation in the European Union includes lupin as a required allergen to be listed on ingredient labels.¹⁶ In the United States, where lupin is becoming more available, the current Food Allergen Labeling and Consumer Protection Act does not include lupin or lupin-derived ingredients on the list of priority food allergens required to be listed on ingredient labels and it does not mandate precautionary allergen labeling.¹⁷ It is prudent for lupin allergic individuals to still read ingredient labels for the presence of lupin before consuming a food or beverage and to contact food manufacturers with ingredient concerns to avoid unintentional exposure with risk of reaction.

Lupin may be described on an ingredient label in forms that may include lupine, lupini, lupinus, lupin flour, lupin seed, lupin bean, lupines, *Lupinus luteus*, *Lupinus albus*, or *Lupinus albus*.^{16,18} Lupin may or may not be a visible food ingredient and may be undeclared on an ingredient label, especially in the United States, where, as previously described, lupin is not considered a priority allergen under the Food Allergen Labeling and Consumer Protection Act.¹³ As with other food allergens, it is important to instruct lupin allergic patients to carefully read ingredient labels before consuming food products and to avoid consuming a food or beverage when unsure of all its ingredients.¹⁹ Describing risks regarding cross-contact of food proteins and subsequent need for safe practices in handling food, at home and away from home (eg, dining out), is a critical topic to cover during patient education.¹⁹ It is also important to encourage patients to contact food manufacturers with any questions about product ingredients, clarification of label contents, and/or the potential for cross-contact presence of lupin in a specific product.¹⁹ Helpful resources for providers and patients can be found in Table 1.

Conclusion

Dietary habits and consumer preferences are changing around the world, and moving populations with differing cultural food habits

now inhabit various geographic areas. As a result, we are encountering a number of new (emergent) food allergies, such as lupin, more frequently in the United States. The food industry will likely be required to make the necessary adjustments, and labeling laws will need to be reexamined to stay abreast of new developments in the field of food allergies.

In our opinion, health care professionals should be educated on emerging food allergens and remain vigilant in cases where the cause of a food allergic reaction is not directly evident. New food allergens can present many diagnostic challenges, and management pathways are often less clear because the natural history is elusive. However, the basic principles of diagnosis and management can be applied to all food allergies and practice can be adjusted over time as new information and research become available to guide both health care professionals and patients in this multifaceted journey.

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