Allergol Immunopathol (Madr). 2022;50(SP1):37-45 eISSN:1578-1267, pISSN:0301-0546

Allergologia et immunopathologia

Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica

www.all-imm.com

REVIEW ARTICLE

Nutritional management of immediate hypersensitivity to legumes in vegetarians

Anne Jardim-Botelho[a†*], Lucila Camargo Lopes de Oliveira[b†], Jackeline Motta-Franco[a], Dirceu Solé[b]

[a]Universitary Hospital of Sergipe, Federal University of Sergipe (FUSE), Aracaju, Brazil
[b]Departament of Pediatrics, Division of Allergy, Clinical Immunology and Rheumatology, Escola Paulista de Medicina—Federal University of São Paulo (EPM-UNIFESP), São Paulo, Brazil

[†]Anne Jardim-Botelho and Lucila Camargo Lopes de Oliveira contributed equally to this manuscript.

Received 1 December 2021; Accepted 6 May 2022
Available online 22 June 2022

KEYWORDS
Allergy to Legumes;
Food Allergy;
Nutrition;
Vegan

Abstract
Vegetarianism is becoming a common practice among people. Products of vegetable origin are also on the rise, such as vegetable "milk" and legume-based snacks, which may lead to legume sensitivity and allergies in vegetarian diet followers. Furthermore, products derived from legumes, such as lupin flour or fenugreek powder, are often used as food additives. They function as hidden allergens, not always evident on the precautionary labeling, favoring allergic reactions. As dietary allergen restriction is the fundamental pillar in managing patients with food allergies, this review aims to reflect on practical aspects—diagnosis and nutritional management—in managing legume allergies in vegetarians, aiming to reduce the negative nutritional impact of an even more restrictive diet.

Introduction

For many years, vegetarian food was considered as an unsafe alternative that could generate health risks. Currently, nutrition societies in various countries and expert groups, such as the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN),[1] and the Academy of Nutrition and Dietetics (AND), in America,[2] have been endorsing well-planned and carefully monitored vegetarian diets.

A vegetarian diet is defined as one that does not include any type of meat, fish, mollusks, or crustaceans. Dairy products, eggs, and honey may or may not be included in this type of diet.[3] Lacto-ovo vegetarians have a plant-based diet but sometimes consume dairy products, eggs, and honey—foods that help supplement their nutritional

***Corresponding author:** Anne Jardim-Botelho, Universitary Hospital of Sergipe, Federal University of Sergipe (FUSE), Aracaju, Brazil.
Email address: annejbotelho@gmail.com

https://doi.org/10.15586/aei.v50iSP1.554

needs. On the other hand, a strict vegetarian diet consists of plants as the only food source, which imposes a greater need for dietetic planning and monitoring.[4]

Over the years, allergic reactions to food and rates of hospitalization due to food-related anaphylaxis have increased.[5,6] Among the leading foods commonly related to food allergy, some are from the plant kingdom. Peanuts and soybeans are the legumes commonly implicated in food allergies.[5] Manifestations of legume allergies are likely to increase because plant-based diets are increasing, and prepackaged products and vegetable drinks[7] based on these protein sources are commonly available.

Studies have been conducted on manifestations of hypersensitivity to other legumes such as lentils, peas, lupin, and chickpeas.[8-13] A recent review showed that, despite most of these studies being European, the number of North American publications has increased in the last decade.[14] Lupin, for example, is considered a food source with mandatory label declaration in Europe and as an emerging food allergen in the United States.[15] IgE-mediated manifestations (i.e., anaphylaxis), and non-IgE-mediated, usually Food Protein-Induced Enterocolitis Syndrome (FPIES) by soy,[16] are the most common hypersensitivity reactions when it comes to legumes.

The veganism and food allergy binomial raise greater concerns on the adequate intake of macro- and micronutrients. As legumes are significant bases of the vegetarian diet, this article aims to address the aspects related to the nutritional management of strict vegetarian patients with manifestations of immediate hypersensitivity to legumes.

Legume Allergies—Diagnosis

The legume family (*Leguminosae*) consists of plants that produce a pod with seeds inside.[17] In this article, the term "legumes" is used to describe the seeds of these plants, basically the dried seeds of beans, chickpeas, lentils, lupini beans, peas, soybeans, and peanuts. The World Health Organization (WHO) considers this food group essential due to its high protein content and low cost.[18]

In recent years, high legume consumption rates have resulted in higher rates of sensitization and allergic reactions. In Spain, where legumes are popular, legumes represent the fifth most common cause of food allergy in children under 5 years of age.[19] The high rate of cross-reactivity between different legumes—individuals allergic to one are often allergic to others but not necessarily to all—makes accurate diagnosis essential to avoid extensive dietary restrictions with nutritional loss.[19,20]

The clinical history is essential when attempting to establish a causal relationship between the food and symptoms presented and when making the etiological definition of the immunological mechanism involved.[21] In IgE-mediated allergies, the signs and symptoms have a rapid onset, and the allergic reactions occur within minutes to 2 hours after exposure to the allergen. The causal relationship becomes more evident in these cases, and sensitization can be confirmed using tests capable of detecting specific IgE.[22]

The pattern of sensitization to legumes varies geographically according to consumption pattern and exposure to pollens.[23,24] For many of them, commercial tests are already available to measure specific serum IgE *in vitro* and *in vivo* (skin prick test [SPT]). Routine skin tests for legumes are limited to chickpeas, mixed beans, lentils (not specified), and peas.[25] When inaccessible, the test can be carried out using the legume itself in diluted legume flour.[24,25] Serum IgE and SPT values for lupini beans were not able to predict lupin allergy.[26] As for peanuts, the most studied legume, a papilla size greater than or equal to 8 mm and a specific serum IgE ≥ 15 kU_A/L showed a predictive value above 90% for the diagnosis of allergy in individuals with a suggestive history.[27]

With Component-resolved diagnosis, it was easier to estimate the genuine sensitization than the cross-reactivity. Even though new legume components have been identified,[28] not many genuine sensitization markers are currently commercially available (Table 1).

Although there is *in vitro* reactivity among several legumes, clinical reactivity is not always correlated (5–20%), coallergy with nuts is more frequent (~33%).[29] Therefore, the oral food challenge (OFC) is almost always necessary for this differentiation, especially when the food being tested for had not been consumed previously. In a study comprising 69 children sensitized to multiple legumes, only 2 had allergies to two legumes, which was confirmed using OFC.[30]

The cross-reactivity of soybean with peanuts was also observed in a study with 140 patients allergic to peanuts. Seven percent (7%) of them were also allergic to soybeans.[31] People who are allergic to peanuts have a 25–40% greater chance of being allergic to oilseeds and becoming sensitive to sesame seeds.[32] It must be emphasized that if a child is already consuming foods that present a chance of cross-reactivity with peanuts and does not show a reaction, these foods do not need to be excluded from the diet, and no investigation is required.

Clinical cross-reactivity between peanuts and lupine is often more common,[11,25,33] estimated at 20%.[29]

The OFC is essential to differentiate allergy from sensitization, considered the "gold standard" in food allergy diagnosis. Laboratory test results should never be an absolute indication or contraindication for performing an OFC. They should always be interpreted in the patient's individual clinical context.[34]

Thermal processing can alter the allergenicity of foods, even legumes. Roasting increases the allergenicity of peanuts by up to 90 times, while boiling them decreases it.[11] On the other hand, the allergens in lentils, chickpeas, green beans, and peas maintain great stability even after cooking.[11]

Guidance for Reading Labels

Except for peanuts, soybeans, and lupini beans, legumes are rarely covered by precautionary labeling in most European countries. It is also necessary to be alert of legumes being used as food additives. Fenugreek, a legume used for Indian curry production and as an additive in food and beverages,[35,36] has already been related to the manifestation of anaphylaxis in patients allergic to peanuts.[35] Lupin flour

Table 1 Identified legume and allergen components. In grey, the components identified as primary sensitization markers to currently commercially available legumes.

Legume	Component	Biochemical name
Needle bush	Aca f 1	Ole e 1-like protein
(Acacia farnesiana)	Aca f 2	Profilin
Amendoim	Ara h 1	Cupin (vicilin-type, 7S globulin)
(Arachis hypogaea)	Ara h 2	Conglutin (2S albumin)
	Ara h 3	Cupin (Legumin-type, 11S globulin, Glycinin)
	Ara h 4	Renamed to Ara h3.02
	Ara h 5	Profilin
	Ara h 6	Conglutin (2S albumin)
	Arah 7	Conglutin (2S albumin)
	Ara h 8	Pathogenesis-related protein, PR-10
	Ara h 9	Nonspecific lipid-transfer protein type 1
	Ara h 10	Oleosin
	Ara h 11	Oleosin
	Ara h 12	Defensin
	Ara h 13	Defensin
	Ara h 14	Oleosin
	Ara h 15	Oleosin
	Ara h 16	Nonspecific lipid transfer protein 2
	Ara h 17	Nonspecific lipid transfer protein 1
	Ara h 18	Cyclophilin
Chickpea	Cic a 1	Late embryogenesis protein 4
(Cicer arietinum)		
Soy	Gly m 1	Hydrophobic protein from soybean
(*Glycine max*)	Gly m 2	Defensin
	Gly m 3	Profilin
	Gly m 4	Pathogenesis-related protein, PR-10, Bet v 1 family member
	Gly m 5	Beta-conglycinin (vicilin, 7S globulin)
	Gly m 6	Glycinin (legumin, 11S globulin)
	Gly m 7	Seed biotinylated protein
	Gly m 8	2S albumin
Lentil	Len c 1	Gamma-vicilin subunit
(Lens culinaris)	Len c 2	Seed-specific biotinylated protein
	Len c 3	Seed-specific biotinylated protein
White lupine	Lup a 5	Profilin
(Lupinus albus)		
Narrow-leaved blue lupin	Lup an 1	Conglutin beta (7S seed storage globulin, vicilin)
(Lupinus angustifolius)	Lup an 2	Nonspecific lipid transfer protein
Green bean	Pha v 3	Nonspecific lipid transfer protein type 1
(*Phaseolus vulgaris*)		
Pea	Pis s 1	Vicilin
(Pisum sativum)	Pis s 2	Convicilin
	Pis s 3	nsLTP
Mesquite		
(Prosopis juliflora)	Pro j 1	Ole 1-like protein
	Pro j 2	Profilin
Mung bean	Vig r 1	Pathogenesis-related protein, PR-10, Bet v 1 family member
(Vigna radiata)	Vig r 2	8S Globulin (Vicilin)
	Vig r 3	Renamed to Vig r 2.0201
	Vig r 4	Seed albumin
	Vig r 5	Identified as fragment of Vig r 2
	Vig r 6	Cytokinin-specific binding protein (CSBP), Bet v 1 family member

WHO/IUIS Allergen Nomenclature Sub-Committee website (visited 11.03.2021).

Table 2 Lysine content in plant foods.

Food (100 g)	Lysine (mg)
Cereals and Pseudocereals	
Cooked rice	86
Cooked noodles	130
Cooked corn	282
Oatmeal	700
White bread	224
Whole-grain bread	166
Cooked quinoa	240
Legumes	
Cooked lentils	624
Cooked peas	490
Cooked chickpeas	593
Cooked beans (average)	560
Cooked soybeans	1,100
Soy drinks	439
Tofu	462
Oilseeds	
Roasted peanuts	205
Almonds	575
Hazelnuts	420
Cashews	823
Walnuts	428
Seeds	
Roasted pumpkin seeds	1200
Toasted sesame	540
Linseed	860

Source: USDA Table, 2016.

and flour from other legumes such as peas are used as food additives or are found in gluten-free foods,[13,36,37] especially in vegan foods.

Nutritional Management of Legume Allergies for Vegans

Legumes are known for their high protein content (25%), and soybeans can contain up to 40% protein. As such, legumes are significant components in the diet of people who cannot acquire animal proteins or in the diet of those who choose to be vegetarians. In addition to proteins, legumes are good sources of carbohydrates and fiber and contain vitamins and minerals such as iron, zinc, magnesium, potassium, tocopherols, folic acid, riboflavin, and other B-complex vitamins.[38,39]

The biggest concern about protein adequacy in the vegan diet is the bioavailability of plant proteins,[3] primarily with the physiologically available concentration of essential amino acids. Animal proteins have optimal levels of essential amino acids for the human body to grow and maintain itself. Vegetable proteins have some essential amino acids in lower concentrations. Therefore, the dietary supplementation of these proteins is necessary to obtain quality protein intake.[40] For example, cereal proteins have a lower concentration of the amino acid lysine, and legume proteins have a lower concentration of the amino acid methionine. Combining these foods helps to complement a diet with amino acids. This combination does not need to be in the same meal, as the liver can store essential amino acids.[41,42]

The American Dietetic Association and Dietitians of Canada state that plant proteins can meet the amino acid needs of a vegetarian diet if there is a variety of plant foods and if energy needs are met for adequate nitrogen retention.[43] However, it is estimated that the vegan diet limits more of the amino acid lysine due to the consumption of a greater proportion of cereal proteins.[3,44,45] Therefore, the dietary assessment of vegans with legume allergies must also include the amino acid intake or ensure the intake of foods such as quinoa, walnuts, nuts, and pumpkin seeds, which are also sources of lysine, in addition to an adequate medical evaluation to certify the safe intake of other individually tolerated legumes.

As shown in Table 2, with a well-planned diet, vegan individuals with an allergy to legumes can achieve the estimated mean recommendation of 30 mg/kg of lysine[46] from other tolerated vegetables and/or legumes.

The lower digestibility of proteins in plant foods is another concern about protein adequacy in vegetarian diets, although there is still a debate on this topic.[45] It may be appropriate for vegans to consume a greater amount of protein than what is recommended for the general population, primarily individuals who cannot consume legumes (the most traditional protein source in vegetarian diets). This is not considered a problem because the protein intake tends to exceed dietary requirements for omnivorous individuals and vegetarians.[45,47]

The most limiting micronutrients in the vegan diet are iron, zinc, calcium, riboflavin, vitamin B12, n-3 series fatty acids, and iodine (Table 3).[42,48] Although vitamin D body status depends primarily on sun exposure, low vitamin D levels and reduced body bone mass have been observed in some northern latitude vegan populations who did not consume supplements or fortified foods.[42]

To ensure adequate total protein and lysine intake in the diet of vegans allergic to legumes, special attention is required in the intake of iron, zinc, and riboflavin, as legumes contribute to the supply of these micronutrients. Given the greater risk of vegan diets presenting insufficient energy intake and a greater amount of empty calories, energy intake must also be carefully monitored when managing the diet of vegans with legume allergies.[49]

Table 4 describes the amount of iron, zinc, calcium, and n-3 series fatty acids per portion of commonly consumed foods.

Future Perspectives

Vegetarianism has recently become prominent whether for promoting good health, economic factors, or concerns for environmental impact or animals. Likewise, there has been increased awareness and diagnoses for plant-origin food allergies, particularly legumes, the primary protein-rich food group for complementing micronutrients in vegetarian diets.

Table 3 Nutrients most at risk of deficiency in the vegan diet.

Nutrient	Particularities in veganism	Vegan food sources
Iron	Vegetables contain only nonheme iron, which is more sensitive to absorption inhibitors such as phytates, calcium, teas, coffee, cocoa, and fiber. Of these, phytates are the primary inhibitors of iron absorption. According to the Institute of Medicine (2001), the recommendation for iron intake for vegetarians is 1.8 times the recommendation for nonvegetarians, given the bioavailability.	Legumes, leafy vegetables, broccoli, pumpkin seeds, almonds, cashews, tahini (sesame paste), sunflower seeds, quinoa, and fortified foods. Vitamin C and some organic acids found in fruits and vegetables reduce the effect of absorption inhibitors when consumed together with vegetable sources of iron. Some food preparation techniques, such as soaking, germination, and fermentation of grains and seeds, can hydrolyze the phytate and favor iron absorption.
Zinc	Vegans may experience a compromised zinc intake, given that in a standard diet, meat, fish, and poultry contribute 40% of this nutrient, and dairy products contribute 20%. Although zinc deficiency is not observed in vegetarians, the effects of marginal deficiency are poorly understood, and the serum dosage of this nutrient is not reliable for verifying the body status of zinc. As phytate bonds to zinc and animal protein appear to favor absorption, zinc bioavailability appears to be lower in vegetarian diets.	Legumes, almonds, peanuts, cashews, pumpkin seeds, tahini (sesame paste), sunflower seeds, wheat germ, and fortified foods. The techniques indicated to increase iron absorption also apply to zinc.
Calcium	Calcium intake by vegans tends to be lower than that by lactovegetarians and nonvegetarians.[42,49]	Tahini (sesame paste), dehydrated figs, bok choy, broccoli, collard greens, okra, turnip leaves, kale, sugarcane syrup, and fortified products. In some foods, such as spinach, beetroot, and Napa cabbage, oxalate and phytate can significantly reduce calcium absorption. Factors that increase calcium absorption include vitamin D and protein. Leaves and inflorescences with low oxalate content, such as bok choy, broccoli, collard greens, okra, kale, and turnip leaves, provide high bioavailable calcium (50–60%),. Excessive sodium intake can promote urinary calcium loss. Therefore, sodium intake should also be considered in dietary guidance, despite the vegan diet having lower levels of this nutrient.[42,49]
Riboflavin	Studies have shown that vegans have a low intake of riboflavin compared to nonvegetarians.	Asparagus, bananas, legumes, broccoli, figs, collard greens, seeds, tahini (sesame paste), sweet potatoes, tofu, sprouted wheat, tempeh. These foods provide 1 mg of riboflavin per serving, on average.
Vitamin B12	No single vegetable contains significant amounts of vitamin B12. Marine vegetables, spirulina, and tempeh may contain inactive vitamin B12 analogues and therefore cannot be considered sources of this vitamin.[50] Because they compete for the same absorption site, these analogs can lead to more rapid vitamin B12 deficiency. Vegetarian diets typically have high folic acid content, which can mask the hematologic symptoms of vitamin B12 deficiency. Therefore, if B12 deficiency is suspected, serum homocysteine, methylmalonic acid, and holotranscobalamin II should be measured. Assessing only vitamin B12 levels and hematological parameters does not usually establish the diagnosis of deficiency.[51,52]	Fortified foods such as nutritional yeast, cereals, and soybean products fortified with this vitamin. Vegans should be encouraged to consume reliable sources of vitamin B12, such as fortified foods or supplements. Depending on the status of vitamin B12 and the age of the individual, oral vitamin B12 supplements 5–25 μg/day are recommended; recommendations of 1–3 μg/day refer only to individuals who have sufficient reserves.[51] In cases of overt vitamin B12 deficiency,[53] it is advised to initially treat with a single intramuscular injection of 1000 μg,[43] although several treatment protocols are described. Treatment with high oral doses (e.g., 1000 μg/day for 10 days and then weekly for 4 weeks) is also effective and has been increasingly adopted due to it being noninvasive and less expensive.[47,54] Several studies show that infants of vegan mothers are at increased risk of developing vitamin B12 deficiency with irreversible neurological damage.[43,55] Therefore, vegan mothers need to receive vitamin B12 supplementation during pregnancy and lactation.[51]

(continues)

Table 3 Continued

Nutrient	Particularities in veganism	Vegan food sources
n-3 Fatty acids	Individuals with increased requirements such as infants, pregnant women, nursing mothers, and individuals at risk for low conversion (e.g., the elderly, diabetes, and other chronic diseases) may benefit from the consumption of direct vegan sources of DHA or supplementation.[47,53] Furthermore, the diet influences the conversion of α-linolenic acid to EPA and DHA: a high concentration of linoleic acid (n-6 series), inadequate intake of energy, protein, and some micronutrients such as calcium, copper, magnesium, zinc, and biotin can reduce conversion.[47]	The only n-3 series fatty acid found in proper amounts in plant foods is α-linolenic acid (ALA). Its primary sources are walnuts, flaxseed, chia seeds, and their oils.[47] Some marine vegetables are direct sources of EPA and DHA.[53] Vegans can improve the conversion of ALA to EPA and DHA by reducing the consumption of linoleic acid sources, such as corn and sunflower oil, and with adequate protein-energy intake. There are vegan sources of DHA supplements derived from microalgae in nongelatin capsules.
Iodine	Vegans who do not consume iodized salt may have a deficient intake of iodine. Sea salt and kosher salt are generally not iodized.	Marine vegetables and iodized salt.
Vitamin D	Vitamin D3 (cholecalciferol) is of animal origin, and vitamin D2 (ergocalciferol) is acceptable for vegans. Vitamin D2 appears to be less effective than vitamin D3 in raising the total serum concentration of 25(OH)D,[53,56] which may increase the requirements of vegetarians who depend on D2 supplements to meet their vitamin D needs.[42]	Fortified foods such as cereals and vegetable drinks fortified with ergocalciferol. Sun exposure represents the primary source of vitamin D via body synthesis.

Source: Elaborated by the authors.
DHA: Docosahexaenoic acid; EPA: Eicosapentaenoic acid

Table 4 Amounts of iron, zinc, calcium, and n-3 series fatty acids per portion of commonly consumed foods.

Food	Commonly consumed portion	Weight (g)/volume (ml)	Amount of nutrient per serving
Iron			**mg**
Legumes (average)	½ cup	125 ml	2.3
Almonds	¼ cup	60 ml	1.5
Cashews	¼ cup	60 ml	2.1
Roasted pumpkin seeds	¼ cup	60 ml	5.2
Tahini	2 Tbs	30 ml	2.7
Roasted sunflower seeds	¼ cup	60 ml	2.3
Cooked quinoa	½ cup	120 ml	2.1
Boiled potato, with skin	1 medium unit	170 g	2.3
Cooked broccoli	1 cup	95 g	0.5
Cooked collard greens	½ cup	95 g	1.1
Zinc			**mg**
Legumes (average)	½ cup	120 ml	1.4
Almonds	¼ cup	60 ml	1.2
Cashews	¼ cup	60 ml	1.9
Roasted peanuts	¼ cup	60 ml	1.2
Roasted pumpkin seeds	¼ cup	60 ml	2.6
Tahini	2 Tbs	30 ml	1.4
Sunflower seeds	¼ cup	60 ml	1.8
Wheat germ	2 Tbs	14 g	1.8

(continues)

Table 4 Continued

Food	Commonly consumed portion	Weight (g)/volume (ml)	Amount of nutrient per serving
Calcium			**mg**
Tahini	2 Tbs	30 ml	128
Dehydrated figs	2 units	100 g	162
Cooked bok choy	1 cup	250 ml	167-188
Broccoli	1 cup	95 g	95
Cooked collard greens	1 cup	250 ml	239
Cooked kale	1 cup	250 ml	181
Cooked okra	1 cup	250 ml	107
Cooked turnip leaves	1 cup	250 ml	208
Sugarcane syrup	1 Tbs	15 ml	172
α-linolenic acid			**g**
Canola oil	1 Tbs	15 ml	1.3-1.6
Linseed flour	1 Tbs	15 ml	1.9-2.2
Linseed oil	1 Tbs	15 ml	2.7
Soybean oil	1 Tbs	15 ml	0.9
Cooked soybeans	½ cup	120 ml	1.0
Walnuts	¼ cup	60 ml	2.7
Walnut Oil	1 Tbs	15 ml	1.4-1.7

Source: adapted from the ADA, 2003; USDA table, 2016.

Conclusion

Both legume allergy and consumption of vegetarian diet could increase the risk of nutritional deficiencies, particularly in calories, proteins, iron, zinc, riboflavin, vitamins B12 and D, and calcium from n-3 series fatty acids. Therefore, an allergist must evaluate and monitor vegetarians with legume allergies to accurately diagnose and define allergens to be excluded from their diet. A clinical dietitian must also carefully manage their nutritional status and dietary planning to promote an adequate supplementary intake of nutrients and vitamin B12 from reliable sources.

Conflict of Interest

The authors declare no conflict of interest for this article.

References

1. Fewtrell M, Bronsky J, Campoy C, Domellöf M, Embleton N, Fidler Mis N, et al. Complementary feeding: A position paper by the European Society for Paediatric Gastroenterology, hepatology, and Nutrition (ESPGHAN) Committee on Nutrition. J Pediatr Gastrenterol Nutr. 2017;64(1):119-32. https://doi.org/10.1097/MPG.0000000000001454
2. American Dietetic Association, Dietitians of Canada. Position of the American Dietetic Assocation and Dietitians of Canada: Vegetarian diets. Can J Diet Pract Res. 2003;64(2):62-81. https://doi.org/10.3148/64.2.2003.62
3. Agnoli C, Baroni L, Bertini I, Ciappellano S, Fabbri A, Papa M, et al. Position paper on vegetarian diets from the working group of the Italian Society of Human Nutrition. Nutr Metab Cardiovasc Dis. 2017;27(12):1037-52. https://doi.org/10.1016/j.numecd.2017.10.020
4. Hargreaves SM, Nakano EY, Han H, Raposo A, Ariza-Montes A, Vega-Muñoz A, Zandonadi RP. Quality of life of Brazilian vegetarians measured by the WHOQOL-BREF: Influence of type of diet, motivation and sociodemographic data. Nutrients. 2021 Jul 30;13(8):2648. https://doi.org10.3390/nu13082648
5. Sicherer SH, Sampson HA. Food allergy: A review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. J Allergy Clin Immunol. 2018;141(1):41-58. https://doi.org/10.1016/j.jaci.2017.11.003
6. Kivistö J, Protudjer JLP, Karjalainen J, Wickman M, Bergström A, Mattila V. Hospitalizations due to allergic reactions in Finnish and Swedish children between 1999 and 2011. Allergy. 2016;71(5):677-83. https://doi.org/10.1111/all.12837
7. Sethi S, Tyagi SK, Anurag RK. Plant-based milk alternatives an emerging segment of functional beverages: A review. J Food Sci Technol. 2016;53(9):3408-23. https://doi.org/10.1007/s13197-016-2328-3
8. Bansal AS, Sanghvi MM, Bansal RA, Hayman GR. Variably severe systemic allergic reactions after consuming foods with unlabelled lupin flour: A case series. J Med Case Rep. 2014;8:55. https://doi.org/10.1186/1752-1947-8-55
9. Bar-El Dadon S, Pascual CY, Reifen R. Food allergy and cross-reactivity-chickpea as a test case. Food Chem. 2014;165:483-8. https://doi.org/10.1016/j.foodchem.2014.05.138
10. Richard C, Jacquenet S, Sergeant P, Moneret-Vautrin DA. Cross-reactivity of a new food ingredient, dun pea, with legumes, and risk of anaphylaxis in legume allergic children. Eur Ann Allergy Clin Immunol. 2015;47(4):118-25.
11. Cabanillas B, Jappe U, Novak N. Allergy to peanut, soybean, and other legumes: Recent advances in allergen characterization, stability to processing and IgE cross-reactivity. Mol Nutr Food Res. 2018;62(1). https://doi.org/10.1002/mnfr.201700446
12. Smits M, Le TM, Welsing P, Houben G, Knulst A, Verhoeckx K. Legume protein consumption and the prevalence of legume sensitization. Nutrients. 2018;10(10):1545. https://doi.org/10.3390/nu10101545

13. Jappe U, Karstedt A, Warneke D, Hellmig S, Böttger M, Riffelmann FW, et al. Identification and purification of novel low-molecular-weight lupine allergens as components for personalized diagnostics. Nutrients. 2021;13(2):409. https://doi.org/10.3390/nu13020409
14. Hildebrand HV, Arias A, Simons E, Gerdts J, Povolo B, Rothney J, et al. Adult and pediatric food allergy to chickpea, pea, lentil, and lupine: A scoping review. J Allergy Clin Immunol Pract. 2021;9(1):290-301.e2. https://doi.org/10.1016/j.jaip.2020.10.046
15. Bingemann TA, Santos CB, Russell AF, Anagnostou A. Lupin: An emerging food allergen in the United States. Ann Allergy Asthma Immunol. 2019;122(1):8-10. https://doi.org/10.1016/j.anai.2018.09.467
16. Leonard SA, Pecora V, Fiocchi AG, Nowak-Wegrzyn A. Food protein-induced enterocolitis syndrome: A review of the new guidelines. World Allergy Organ J. 2018;11(1):4. https://doi.org/10.1186/s40413-017-0182-z
17. Kouris-Blazos A, Belski R. Health benefits of legumes and pulses with a focus on Australian sweet lupins. Asia Pac J Clin Nutr. 2016;25(1):1-17.
18. Leterme P. Recommendations by health organizations for pulse consumption. Br J Nutr. 2002;88:239-42. https://doi.org/10.1079/BJN2002712
19. Martinez SIM, Ibanez MD, Fernandez Caldas E, Carnes J. In vitro and in vivo cross-reactivity studies of legume allergy in a Mediterranean population. Int Arch Allergy Immunol. 2008; 147:222-30. https://doi.org/10.1159/000142045
20. Andreae DA, Grishina G, Sackesen C, Ibáñez MD, Sampson HA. High similarity between lentil and other lentil-like-proteins (dal) complicates recommendations on avoidance in lentil allergic patients. J Allergy Clin Immunol Pract. 2015;3(5):808. https://doi.org/10.1016/j.jaip.2015.05.010
21. Eigenmann PA, Oh JW, Beyer K. Diagnostic testing in the evaluation of food allergy. Pediatr Clin North Am. 2011;58:351-62. https://doi.org/10.1016/j.pcl.2011.02.003
22. Gupta M, Cox A, Nowak-Wegrzyn A, Wang J. Diagnosis of food allergy. Immunol Allergy Clin North Am. 2018;38(1):39-52. https://doi.org/10.1016/j.iac.2017.09.004
23. Verma AK, Kumar S, Das M, Dwivedi PD. A comprehensive review of legume allergy. Clin Rev Allergy Immunol. 2013;45(1):30-46. https://doi.org/10.1007/s12016-012-8310-6
24. Villa C, Costa J, Mafra I. Lupine allergens: Clinical relevance, molecular characterization, cross-reactivity, and detection strategies. Compr Rev Food Sci Food Saf. 2020;19(6):3886-915. https://doi.org/10.1111/1541-4337
25. Peeters KA, Nordlee JA, Penninks AH, Chen L, Goodman RE, Bruijnzeel-Koomen CA, et al. Lupine allergy: Not simply cross-reactivity with peanut or soy. J Allergy Clin Immunol. 2007;120(3):647-53. https://doi.org/10.1016/j.jaci.2007.05.032
26. Kakleas K, Luyt D, Foley G, Noimark L. Is it necessary to avoid all legumes in legume allergy? Pediatr Allergy Immunol. 2020;31(7):848-51. https://doi.org/10.1111/pai.13275
27. Roberts G, Lack G. Diagnosing peanut allergy with skin prick and specific IgE testing. J Allergy Clin Immunol. 2005;115(6):1291-6. https://doi.org/10.1016/j.jaci.2005.02.038
28. Popp J, Trendelenburg V, Niggemann B, Randow S, Völker E, Vogel L, et al. Pea (*Pisum sativum*) allergy in children: Pis s 1 is an immunodominant major pea allergen and presents IgE binding sites with potential diagnostic value. Clin Exp Allergy. 2020;50(5):625-35. https://doi.org/10.1111/cea.13590
29. Cox AL, Eigenmann PA, Sicherer SH. Clinical relevance of cross-reactivity in food allergy. J Allergy Clin Immunol Pract. 2021;9(1):82-99. https://doi.org/10.1016/j.jaip.2020.09.030
30. Bernhisel-Broadbent J, Sampson HA. Cross-allergenicity in the legume botanical family in children with food hypersensitivity. J Allergy Clin Immunol. 1989;83(2 Pt 1):435-40. https://doi.org/10.1016/0091-6749(89)90130-9
31. Green TD, LaBelle VS, Steele PH, Kim EH, Lee LA, Mankad VS, et al. Clinical characteristics of peanut-allergic children: Recent changes. Pediatrics 2007;120(6):1304-10. https://doi.org/10.1542/peds.2007-0350
32. Stutius L, Sheehan WJ, Rangsithienchai P, Bharmanee A, Scott JE, Young MC, et al. Characterizing the relationship between sesame, coconut, and nut allergy in children. Pediatr Allergy Immunol. 2010;21(8):1114-8. https://doi.org/10.1111/j.1399-3038.2010.00997.x
33. Chan ES, Greenhawt MJ, Fleischer DM, Caubet JC. Managing cross-reactivity in those with peanut allergy. J Allergy Clin Immunol Pract. 2019;7(2):381-6. https://doi.org/10.1016/j.jaip.2018.11.012
34. Andrew Bird J, Leonard S, Groetch M, Assa'ad A, Cianferoni A, Clark A, et al. Conducting an oral food challenge: An update to the 2009 Adverse Reactions to Foods Committee Work Group Report. J Allergy Clin Immunol Pract. 2020;8:75-90. https://doi.org/10.1016/j.jaip.2019.09.029
35. Singletary KW. Fenugreek. Nutr Today. 2017;52(2):93-111. https://doi.org/10.1097/NT.0000000000000209
36. Skypala IJ. Food-induced anaphylaxis: Role of hidden allergens and cofactors. Front Immunol. 2019;10:673. https://doi.org/10.3389/fimmu.2019.00673
37. Claver A, Morales M, Elduque C, Navarro B, Botey E, Fernandez MC, et al. Fenugreek: A hidden allergen to consider in peanut allergic patients. J Allergy Clin Immunol 143(2): AB241. https://doi.org/10.1016/j.jaci.2018.12.737
38. Ornellas HL. Técnica Dietética. 8th ed. São Paulo: Editora Atheneu; 2013.
39. Jukanti AK, Gaur PM, Gowda CL, Chibbar RN. Nutritional quality and health benefits of chickpea (Cicer arietinum L.): A review. Br J Nutr. 2012;108 Suppl 1:S11-26. https://doi.org/10.1017/S0007114512000797
40. Cozzolino SMF. Biodisponibilidade de Nutrientes. 4th ed. São Paulo: Manole; 2012. p.1334.
41. Young VR, Pellett PL. Plant proteins in relation to human protein and amino acid nutrition. Am J Clin Nutr. 1994;59(5 Suppl):1203S-12S. https://doi.org/10.1093/ajcn/59.5.1203S
42. American Dietetic Association; Dietitians of Canada. Position of the American Dietetic Association and Dietitians of Canada: Vegetarian diets. J Am Diet Assoc. 2003;103(6):748-65. https://doi.org/10.1053/jada.2003.50142
43. Irevall T, Axelsson I, Naumburg E. B12 deficiency is common in infants and is accompanied by serious neurological symptoms. Acta Paediatr. 2017;106(1):101-4. https://doi.org/10.1111/apa.13625
44. Souza ECG, MSL, Duarte, LL Conceição, editors. Alimentação vegetariana: Atualidades na abordagem nutricional. Rio de Janeiro: Editora Rubio; 2016.
45. Mariotti F, Gardner CD. Dietary protein and amino acids in vegetarian diets—A review. Nutrients. 2019;11(11):2661. https://doi.org/10.3390/nu11112661
46. Joint FAO/WHO/UNU Expert Consultation on Protein and Amino Acid Requirements in Human Nutrition (2002: Geneva, Switzerland), Food and Agriculture Organization of the United Nations, World Health Organization & United Nations University. Protein and amino acid requirements in human nutrition: Report of a joint FAO/WHO/UNU expert consultation. Geneva: World Health Organization; 2007.
47. Bolaman Z, Kadikoylu G, Yukselen V, Yavasoglu I, Barutca S, Senturk T. Oral versus intramuscular cobalamin treatment in megaloblastic anemia: A single-center, prospective, randomized, open-label study. Clin Ther. 2003;25(12):3124-34. https://doi.org/10.1016/s0149-2918(03)90096-8
48. Weikert C, Trefflich I, Menzel J, Obeid R, Longree A, Dierkes J, et al. Vitamin and mineral status in a vegan diet. Dtsch

Arztebl Int. 2020;117(35–36):575–82. https://doi.org/10.3238/arztebl.2020.0575
49. Clarys P, Deliens T, Huybrechts I, Deriemaeker P, Vanaelst B, De Keyzer W, et al. Comparison of nutritional quality of the vegan, vegetarian, semi-vegetarian, pesco-vegetarian and omnivorous diet. Nutrients. 2014;6(3):1318–32. https://doi.org/10.3390/nu6031318
50. Watanabe F, Yabuta Y, Tanioka Y, Bito T. Biologically active vitamin B12 compounds in foods for preventing deficiency among vegetarians and elderly subjects. J Agric Food Chem. 2013;61(28):6769–75. https://doi.org/10.1021/jf401545z
51. Rudloff S, Bührer C, Jochum F, Kauth T, Kersting M, Körner A, et al. Vegetarian diets in childhood and adolescence: Position paper of the nutrition committee, German Society for Paediatric and Adolescent Medicine (DGKJ). Mol Cell Pediatr. 2019;6(1):4. https://doi.org/10.1186/s40348-019-0091-z
52. Hannibal L, Lysne V, Bjørke-Monsen AL, Behringer S, Grünert SC, Spiekerkoetter U, et al. Biomarkers and algorithms for the diagnosis of vitamin B12 deficiency. Front Mol Biosci. 2016;3:27. https://doi.org/10.3389/fmolb.2016.00027
53. Martineau AR, Thummel KE, Wang Z, Jolliffe DA, Boucher BJ, Griffin SJ, et al. Differential effects of oral boluses of vitamin D2 vs vitamin D3 on vitamin D metabolism: A randomized controlled trial. J Clin Endocrinol Metab. 2019;104(12):5831–9. https://doi.org/10.1210/jc.2019-00207
54. Sezer RG, Bozaykut A, Akoğlu HA, Özdemir GN. The efficacy of oral vitamin B12 replacement for nutritional vitamin B12 deficiency. J Pediatr Hematol Oncol. 2018;40(2):e69–e72. https://doi.org/10.1097/MPH.0000000000001037
55. Stabler SP. Clinical practice. Vitamin B12 deficiency. N Engl J Med. 2013;368(2):149–60. https://doi.org/10.1056/NEJMcp1113996
56. Shieh A, Chun RF, Ma C, Witzel S, Meyer B, Rafison B, et al. Effects of high-dose vitamin D2 versus D3 on total and free 25-hydroxyvitamin D and markers of calcium balance. J Clin Endocrinol Metab. 2016;101(8):3070–8. https://doi.org/10.1210/jc.2016-1871