MAYO CLINIC LABORATORIES

Test Definition: NUTHR

Hazelnut-Food, IgE with Reflex to Hazelnut-Food Components, IgE, Serum

Overview

Useful For

Evaluation of patients with suspected hazelnut-food allergy

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
NUTHX	Hazelnut-Food Components, IgE, S	No	No

Testing Algorithm

Testing begins with analysis of hazelnut-food-specific total IgE. If the hazelnut food-specific total IgE is negative (<0.10 kU/L), testing is complete.

If the hazelnut food-specific total IgE is 0.10 kU/L or more, then the four hazelnut-food components (Cor a 1, Cor a 8, Cor a 9, and Cor a 14) will be performed at an additional charge.

Special Instructions

- Allergens - Immunoglobulin E (IgE) Antibodies

Highlights

The determination of the relative amount of IgE antibody to total hazelnut-food, and IgE antibodies to specific hazelnut-food components, may aid in assessment of the potential strength and type of allergenic response to hazelnut-food.

IgE antibody to total hazelnut-food will be initially tested.

If detectable total specific hazelnut-food IgE antibody is present, additional component hazelnut-food allergen antibody testing will be performed. This is comprised of testing for IgE antibodies to the potential allergens Cor a 1, Cor a 8, Cor a 9, and Cor a 14.

Method Name

Fluorescent Enzyme Immunoassay (FEIA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Ordering Guidance

For a listing of allergens available for testing, see Allergens - Immunoglobulin E (IgE) Antibodies.

Specimen Required

Supplies: Sarstedt Aliquot Tube 5 mL (T914)
Collection Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Submission Container/Tube: Plastic vial
Specimen Volume: 1 mL Serum
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send an Allergen Test Request (T236) with the specimen.

Specimen Minimum Volume

Serum: 0.6 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	14 days	
	Frozen	90 days	

Clinical & Interpretive

Clinical Information

Allergies to tree nuts are relatively prevalent and can result in severe reactions. The main culprits in tree nut allergies include: walnut, almond, pistachio, cashew, pecan, hazelnut, macadamia, Brazil nut, and pine nuts. Tree nut allergy often appears in young children and estimates of prevalence range from 0.1% to greater than 5% of the population dependent on geographical region.

In the case of nut-induced allergic reactions, as with many other foods, symptoms usually present within minutes of

ingestion. Over 80% of reactions to tree nuts involve allergy related respiratory symptoms. Tree nut allergies are one of the most dangerous types of allergic reaction with 20% to 40% of cases of related anaphylaxis and 70% to 90% of fatalities attributable to nut exposure, including peanut exposure.

Hazelnut allergy can occur upon ingestion as a systemic food allergy that can be associated with severe reactions or as oral allergy syndrome, often associated with pollen allergy (pollen-food allergy syndrome). It is the most common tree nut allergy in Europe. Sensitization to birch pollen is strongly associated with hazelnut sensitization, with 84% of those with birch pollen allergy being sensitized to hazelnuts.

Components of hazelnut allergy can be used to stratify risk of severe systemic reactions. Hazelnut allergy can be severe or can be pollen related and less severe. The component protein Cor a 1 is heat and digestion labile and is often cross-reactive with birch pollen sensitivity due to cross-reactivity between homologous allergens of hazelnut and birch pollens (PR-10 proteins Cor a 1 and Bet v 1). Sensitization to Cor a 1 component protein is mainly associated with local reactions, posing a lower risk of severe systemic reaction. Pollen-related hazelnut allergy is often observed in adults, with symptoms limited to the oropharyngeal cavity. However, systemic symptoms and even anaphylaxis have been infrequently reported with sensitivity to Cor a 1.

Cor a 8 is a heat and digestion stabile nonspecific lipid transfer protein that exhibits sensitization in 8% to 17% of hazelnut allergy cases in the United States, with high prevalence in areas that lack birch trees. Cor a 8 sensitization can be associated with clinically silent hazelnut tolerant individuals, oral allergy syndrome or in some cases severe allergy. Peach allergy may be associated with sensitivity for Cor a 8.

Cor a 9 and 14 are heat and digestion stable protein components that are associated with higher risks or severe, systemic reaction. Cor a 9 and Cor a 14 sensitization serve as excellent diagnostic markers for identifying direct hazelnut allergy and for prediction of potentially severe symptoms. Sensitization to Cor a 9 (a legume like globulin) was observed in 10% of hazelnut allergic individuals and has been established to be associated with severe systemic reactions. Other studies have put the sensitization rate or Cor a 9 to be as much as 35%. Cor a 9 may show crossreactivity to 11S globulin protein components of walnut (Jug r 4), peanut (Ara h 3), Brazil nut (Ber e 2), soybean (Gly m 6), cashew (Ana o 2), almond (Pru du 6) and pistachio (Pis v 2). Sensitization to Cor a 14 (a 2S albumin allergen) has been observed in 6% of allergic individuals and is associated with moderate and severe systemic reactions. Cor a 14 is highly heat and digestion resistant and serves as an excellent predictor for clinical allergy. Cor a 14 sensitization has been reported in 15% of individuals with severe symptoms, 5.6% of individuals with moderate symptoms, and 4% of those with localized symptoms. Its cross reactivity is limited to walnut (Jug r 1) and pecan (Car i 1) protein components. Cor a 14-sIgE determination was a better predictor of oral food challenge sensitivity than other hazelnut component allergens (Cor a 1, Cor a 8, and Cor a 9).

Reference Values

Class	IgE kU/L	Interpretation
0	<0.10	Negative
0/1	0.10-0.34	Borderline/equivocal
1	0.35-0.69	Equivocal
2	0.70-3.49	Positive
3	3.50-17.4	Positive

4	17.5-49.9	Strongly positive
5	50.0-99.9	Strongly positive
6	> or =100	Strongly positive

Concentrations of 0.70 kU/L or more (class 2 and above) will flag as abnormally high.
Reference values apply to all ages.

Interpretation

When detectable total hazelnut-food IgE antibody is present (> or =0.10 IgE kUa/L), additional specific component IgE antibody testing will be performed. If at least one potential specific allergenic hazelnut-food component IgE is detectable (> or =0.10 IgE kUa/L), an interpretive report will be provided.

When the sample is negative for total hazelnut-food IgE antibody (<0.10 IgE kUa/L), further testing for specific hazelnut-food component IgE antibodies will not be performed. Negative IgE results for total hazelnut-food antibody may indicate a lack of sensitization to potential hazelnut-food allergenic components.

Cautions

Clinical correlation of results from in vitro IgE testing with patient history of allergic or anaphylactic responses to hazelnut is recommended.

Negative results for IgE antibodies against hazelnut extract or allergenic components do not completely exclude the possibility of clinically relevant allergic responses upon exposure.

Positive results for IgE to hazelnut or any potential hazelnut allergenic components are not diagnostic for allergy and only indicate patient may be sensitized to hazelnut or a cross-reactive allergen.

Testing for IgE antibodies may not be useful in patients previously treated with immunotherapy to determine if residual clinical sensitivity exists or in patients whose medical management does not depend upon the identification of allergen specificity.

False-positive results for IgE antibodies may occur in patients with markedly elevated serum IgE (>2500 kU/L) due to nonspecific binding to allergen solid phases.

Cross-reacting carbohydrate determinants may also result in positive total hazelnut specific IgE testing.

Clinical Reference

1. Salo PM, Arbes SJ Jr, Jaramillo R, et al. Prevalence of allergic sensitization in the United States: results from the National Health and Nutrition Examination Survey (NHANES) 2005-2006. J Allergy Clin Immunol. 2014;134(2):350-359. doi:10.1016/j.jaci.2013.12.1071
2. Waserman S, Watson W. Food allergy. Allergy Asthma Clin Immunol. 2011;7 Suppl 1(Suppl 1):S7
3. Abrams EM, Sicherer SH. Diagnosis and management of food allergy. CMAJ. 2016;188(15):1087-1093. doi:10.1503/cmaj.160124
4. Weinberger T, Sicherer S. Current perspectives on tree nut allergy: a review. J Asthma Allergy. 2018;11:41-51. doi:10.2147/JAA.S141636
5. Lomas JM, Jarvinen KM. Managing nut-induced anaphylaxis: challenges and solutions. J Asthma Allergy. 2015;8:115-123. doi:10.2147/JAA.S89121

6. Maloney JM, Rudengren M, Ahlstedt S, Bock SA, Sampson HA. The use of serum-specific IgE measurements for the diagnosis of peanut, tree nut, and seed allergy. J Allergy Clin Immunol. 2008;122(1):145-151. doi:10.1016/j.jaci.2008.04.014
7. Sicherer SH, Burks AW, Sampson HA. Clinical features of acute allergic reactions to peanut and tree nuts in children. Pediatrics. 1998;102(1):e6. doi:10.1542/peds.102.1.e6
8. Crespo JF, James JM, Fernandez-Rodriguez C, Rodriguez J. Food allergy: nuts and tree nuts. Br J Nutr. 2006;96 Suppl 2:S95-S102. doi:10.1017/bjn20061869
9. Yang L, Clements S, Joks R. A retrospective study of peanut and tree nut allergy: Sensitization and correlations with clinical manifestations. Allergy Rhinol (Providence). Published online February 27, 2015. doi:10.2500/ar.20105.6.0108
10. Masthoff LJ, Hoff R, Verhoeckx KC, et al. A systematic review of the effect of thermal processing on the allergenicity of tree nuts. Allergy. 2013;68(8):983-993. doi:10.1111/all.12185
11. Ebo DG, Verweij MM, Sabato V, Hagendorens MM, Bridts CH, De Clerck LS. Hazelnut allergy: a multi-faced condition with demographic and geographic characteristics. Acta Clin Belg. 2012;67(5):317-321. doi:10.2143/ACB.67.5.2062683
12. Calamelli E, Trozzo A, Di Blasi E, Serra L, Bottau P. Hazelnut Allergy. Medicina (Kaunas). 2021;57(1):67. doi:10.3390/medicina57010067
13. Uotila R, Kukkonen AK, Pelkonen AS, Makela MJ. Cross-sensitization profiles of edible nuts in a birch-endemic area. Allergy. 2016;71(4):514-521. doi:10.1111/all.12826
14. Datema MR, van Ree R, Asero R, et al. Component-resolved diagnosis and beyond: Multivariable regression models to predict severity of hazelnut allergy. Allergy. 2018;73(3):549-559. doi:10.1111/all.13328
15. Hofmann C, Scheurer S, Rost K, et al. Cor a 1-reactive T cells and IgE are predominantly cross-reactive to Bet v 1 in patients with birch pollen-associated food allergy to hazelnut. J Allergy Clin Immunol. 2013;131(5):1384-92.e6. doi:10.1016/j.jaci.2012.10.037
16. Nilsson C, Berthold M, Mascialino B, Orme M, Sjolander S, Hamilton R. Allergen components in diagnosing childhood hazelnut allergy: Systematic literature review and meta-analysis. Pediatr Allergy Immunol. 2020;31(2):186-196. doi:10.1111/pai.13110
17. Inoue Y, Sato S, Takahashi K, et al. Component-resolved diagnostics can be useful for identifying hazelnut allergy in Japanese children. Allergol Int. 2020;69(2):239-245. doi:10.1016/j.alit.2019.10.001
18. Faber MA, De Graag M, Van Der Heijden C, et al. Cor a 14: missing link in the molecular diagnosis of hazelnut allergy?. Int Arch Allergy Immunol. 2014;164(3):200-206. doi:10.1159/000365050
19. Costa J, Mafra I, Carrapatoso I, Oliveira MB. Hazelnut Allergens: Molecular Characterization, Detection, and Clinical Relevance. Crit Rev Food Sci Nutr. 2016;56(15):2579-2605. doi:10.1080/10408398.2013.826173
20. Buyuktiryaki B, Cavkaytar O, Sahiner UM, et al. Cor a 14, Hazelnut-Specific IgE, and SPT as a Reliable Tool in Hazelnut Allergy Diagnosis in Eastern Mediterranean Children. J Allergy Clin Immunol Pract. 2016;4(2):265-72.e3. doi:10.1016/j.jaip.2015.12.012
21. Brough HA, Caubet JC, Mazon A, et al. Defining challenge-proven coexistent nut and sesame seed allergy: A prospective multicenter European study. J Allergy Clin Immunol. 2020;145(4):1231-1239. doi:10.1016/j.jaci.2019.09.036
22. Datema MR, Zuidmeer-Jongejan L, Asero R, et al. Hazelnut allergy across Europe dissected molecularly: A EuroPrevall outpatient clinic survey. J Allergy Clin Immunol. 2015;136(2):382-391. doi:10.1016/j.jaci.2014.12.1949
23. Masthoff LJ, van Hoffen E, Mattsson L, et al. Peanut allergy is common among hazelnut-sensitized subjects but is not primarily the result of IgE cross-reactivity. Allergy. 2015;70(3):265-274. doi:10.1111/all.12554
24. Bastiaan-Net S, Batstra MR, Aazamy N, et al. IgE cross-reactivity measurement of cashew nut, hazelnut and peanut using a novel IMMULITE inhibition method. Clin Chem Lab Med. 2020;58(11):1875-1883. doi:10.1515/cclm-2019-1083
25. Carraro S, Berardi M, Bozzetto S, Baraldi E, Zanconato S. COR a 14-specific IgE predicts symptomatic hazelnut allergy in children. Pediatr Allergy Immunol. 2016;27(3):322-324. doi:10.1111/pai.12526

26. Buyuktiryaki B, Cavkaytar O, Sahiner UM, et al. Cor a 14, Hazelnut-Specific IgE, and SPT as a Reliable Tool in Hazelnut Allergy Diagnosis in Eastern Mediterranean Children. J Allergy Clin Immunol Pract. 2016;4(2):265-72.e3. doi:10.1016/j.jaip.2015.12.012
27. Uotila R, Rontynen P, Pelkonen AS, Voutilainen H, Kaarina Kukkonen A, Makela MJ. For hazelnut allergy, component testing of Cor a 9 and Cor a 14 is relevant also in birch-endemic areas. Allergy. 2020;75(11):2977-2980. doi:10.1111/all.14430

Performance

Method Description
Specific IgE from the patient's serum reacts with the allergen of interest, which is covalently coupled to an ImmunoCAP. After washing away nonspecific IgE, enzyme-labeled anti-IgE antibody is added to form a complex. After incubation, unbound anti-IgE is washed away, and the bound complex is then incubated with a developing agent. After stopping the reaction, the fluorescence of the eluate is measured. Fluorescence is proportional to the amount of specific IgE present in the patient's sample (ie, the higher the fluorescence value, the more IgE antibody is present).(Package insert: ImmunoCAP System Specific IgE FEIA. Phadia; Rev 06/2020)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
Same day/1 to 3 days

Specimen Retention Time
14 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per

manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

86003

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
NUTHR	Hazelnut-Food Component Reflex, S	6136-6

Result ID	Test Result Name	Result LOINC® Value
NUTH1	Hazelnut-Food, IgE, S	6136-6