

BÖLÜM 11

ALERJİDE BİLEŞENE BAĞLI TESTLER

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GİRİŞ

Immunglobulin E'nin (IgE) keşfine kadar alerjik hastalıkların tanısında sadece deri testleri kullanılabılırken, 1968'de IgE'nin keşfi, 1973'te spesifik IgE'nin (sIgE) keşfi ile in vitro tanı yöntemleri olan IgE ve sIgE alerjik hastalıkların tanısında kullanılmaya başlamıştır (1). Son yıllarda moleküler alerjideki gelişmeler alerjik hastalıkların tanısında bileşene bağlı tanı testlerin (BBT) kullanılabilmesine olanak sağlamıştır. BBT, saflaştırılmış doğal ya da rekombinant bileşenler kullanılarak alerjik duyarlılığın moleküler düzeyde belirlenmesini sağlayan bir yöntemdir. BBT'de alerjik duyarlanma tek tek (singleplex) veya pek çok bileşenin aynı anda değerlendirildiği (multiplex) yöntemlerle saptanır (2). Tek bileşenin değerlendirildiği test yöntemleri arasında ImmunoCAP TM (Phadia/Thermo Fisher Scientific, Uppsala, Sweden) ve Immulite (Siemens Healthcare Diagnostics, Los Angeles, CA, USA) yöntemleri sayılabilir. Birden fazla bileşene duyarlılığın aynı anda ölçüldüğü yöntemler

arasında; mikroarray yönteminin kullanıldığı 112 alerji komponentine duyarlılığın aynı anda belirlenebildiği ISAC 112 (Immuno Solid phase Allergen Chip) (Phadia/ThermoFisher Scientific, Uppsala, Sweden), 157 alerjen özütü ve 125 alerji bileşenin aynı anda değerlendirildiği ALEX (Allergy Explorer) (MacroArrayDX, Wien, Austria) yöntemleri sayılabilir. Microtest'te de (microtest DX, London, UK) mikroarray yöntemi ile 19 allerjen özüt ve 16 alerjen bileşen değerlendirilirken, EUROline (EUROIMMUN, Lübeck, Germany) yönteminde immünblot ile aynı anda 54 alerjen değerlendirilebilir (3).

Tek test ile bir çok alerjen hakkında bilginin aynı anda elde edilebilmesi, az miktarda kan örneğinin ölçüm için yeterli olması, çoklu duyarlılığı olan hastalarda gerçek duyarlanma ile çapraz duyarlanmayı ayırt edebilmeyi sağlaması, Multiplex testlerin avantajlı yönleridir. Ancak çok fazla veri olması nedeniyle sonuçları yorumlama gerekliliği, test maliyetinin yüksek olması, IgE düzeyi düşük olan hastalarda IgG ve IgG4 blokan antikorlar nedeniyle duyarlılığın düşük olması multipleks testlerin dezavantajdır (3,4).

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KAYNAKLAR

1. Johansson SGO. The discovery of IgE. *J Allergy Clin Immunol.* 2016;137(6):1671-1673. doi:10.1016/j.jaci.2016.04.004
2. Hamilton RG, Hemmer W, Nopp A, Kleine-Tebbe J. Advances in IgE Testing for Diagnosis of Allergic Disease. *J Allergy Clin Immunol Pract.* 2020;8(8):2495-2504. doi:10.1016/j.jaip.2020.07.021
3. Keshavarz B, Platts-Mills TAE, Wilson JM. The use of microarray and other multiplex technologies in the diagnosis of allergy. *Ann Allergy Asthma Immunol.* 2021;127(1):10-18. doi:10.1016/j.anai.2021.01.003
4. Steering Committee Authors; Review Panel Members. A WAO - ARIA - GA²LEN consensus document on molecular-based allergy diagnosis (PAMD@): Update 2020. *World Allergy Organ J.* 2020;13(2):100091. Published 2020 Mar 7. doi:10.1016/j.waojou.2019.100091
5. Sin B, Şahiner ÜM (2016) (ed). Allerjen immünoterapiye başlanmasında çapraz reaksiyon sorunu ve "component-resolved diagnosis" tanıda moleküler allerji testleri. *Allerjen İmmünoterapisi: Ulusal Rehber 2016.* s:50-57.
6. Ferreira F, Hawranek T, Gruber P, Wopfner N, Mari A. Allergic cross-reactivity: from gene to the clinic. *Allergy.* 2004;59(3):243-267. doi:10.1046/j.1398-9995.2003.00407.x
7. McKenna OE, Asam C, Araujo GR, Roulias A, Goulart LR, Ferreira F. How relevant is panallergen sensitization in the development of allergies? *Pediatr Allergy Immunol.* 2016;27(6):560-568. doi:10.1111/pai.12589
8. Gunning PW, Ghoshdastider U, Whitaker S, Popp D, Robinson RC. The evolution of compositionally and functionally distinct actin filaments. *J Cell Sci.* 2015;128(11):2009-2019. doi:10.1242/jcs.165563
9. Tinghino R, Twardosz A, Barletta B, et al. Molecular, structural, and immunologic relationships between different families of recombinant calcium-binding pollen allergens. *J Allergy Clin Immunol.* 2002;109(2):314-320. doi:10.1067/mai.2002.121528
10. Richard C, Leduc V, Battais F. Plant lipid transfer proteins (LTPs): biochemical aspect in panallergen--structural and functional features, and allergenicity. *Eur Ann Allergy Clin Immunol.* 2007;39(3):76-84.
11. Seutter von Loetzen C, Hoffmann T, Hartl MJ, et al. Secret of the major birch pollen allergen Bet v 1: identification of the physiological ligand. *Biochem J.* 2014;457(3):379-390. doi:10.1042/BJ20130413
12. Treudler R, Simon JC. Overview of component resolved diagnostics. *Curr Allergy Asthma Rep.* 2013;13(1):110-117. doi:10.1007/s11882-012-0318-8
13. Sastre J. Molecular diagnosis in allergy. *Clin Exp Allergy.* 2010;40(10):1442-1460. doi:10.1111/j.1365-2222.2010.03585.x
14. Barber D, Diaz-Perales A, Escribese MM, et al. Molecular allergology and its impact in specific allergy diagnosis and therapy. *Allergy.* 2021;76(12):3642-3658. doi:10.1111/all.14969
15. Barber D, de la Torre F, Feo F, et al. Understanding patient sensitization profiles in complex pollen areas: a molecular epidemiological study. *Allergy.* 2008;63(11):1550-1558. doi:10.1111/j.1398-9995.2008.01807.x
16. Barber D, de la Torre F, Lombardero M, et al. Component-resolved diagnosis of pollen allergy based on skin testing with profilin, polcalcin and lipid transfer protein pan-allergens. *Clin Exp Allergy.* 2009;39(11):1764-1773. doi:10.1111/j.1365-2222.2009.03351.x
17. Barber D, Moreno C, Ledesma A, et al. Degree of olive pollen exposure and sensitization patterns. Clinical implications. *J Investig Allergol Clin Immunol.* 2007;17 Suppl 1:11-16.
18. Custovic A, Sonntag HJ, Buchan IE, Belgrave D, Simpson A, Prosperi MCF. Evolution pathways of IgE responses to grass and mite allergens throughout childhood. *J Allergy Clin Immunol.* 2015;136(6):1645-1652.e8. doi:10.1016/j.jaci.2015.03.041
19. Celi G, Brusca I, Scala E, et al. House dust mite allergy in Italy-Diagnostic and clinical relevance of Der p 23 (and of minor allergens): A real-life, multicenter study. *Allergy.* 2019;74(9):1787-1789. doi:10.1111/all.13776
20. Rodríguez-Domínguez A, Berings M, Rohrbach A, et al. Molecular profiling of allergen-specific antibody responses may enhance success of specific immunotherapy. *J Allergy Clin Immunol.* 2020;146(5):1097-1108. doi:10.1016/j.jaci.2020.03.029
21. Casaulta C, Flückiger S, Cramer R, Blaser K, Schoeni MH. Time course of antibody response to recombinant *Aspergillus fumigatus* antigens in cystic fibrosis with and without ABPA. *Pediatr Allergy Immunol.* 2005;16(3):217-225. doi:10.1111/j.1399-3038.2005.00262.x
22. Uriarte SA, Grönlund H, Wintersand A, Bronge J, Sastre J. Clinical and immunologic changes due to subcutaneous immunotherapy with cat and dog extracts using an ultrashort up-dosing phase: a real-life study [published online ahead of print, 2020 Nov 25]. *J Investig Allergol Clin Immunol.* 2020;0. doi:10.18176/jiaci.0656
23. Asarnoj A, Hamsten C, Wadén K, et al. Sensitization to cat and dog allergen molecules in childhood and prediction of symptoms of cat and dog allergy in adolescence: A BAMSE/MeDALL study. *J Allergy Clin Immunol.* 2016;137(3):813-21.e7. doi:10.1016/j.jaci.2015.09.052
24. Uriarte SA, Sastre J. Subcutaneous Immunotherapy With High-Dose Cat and Dog Extracts: A Real-Life Study. *J Investig Allergol Clin Immunol.* 2020;30(3):169-174. doi:10.18176/jiaci.0415
25. Mittermann I, Zidarn M, Silar M, et al. Recombinant allergen-based IgE testing to distinguish bee and wasp allergy. *J Allergy Clin Immunol.* 2010;125(6):1300-1307.e3. doi:10.1016/j.jaci.2010.03.017



26. Hofmann SC, Pfender N, Weckesser S, Huss-Marp J, Jakob T. Added value of IgE detection to rApi m 1 and rVes v 5 in patients with Hymenoptera venom allergy. *J Allergy Clin Immunol.* 2011;127(1):265-267. doi:10.1016/j.jaci.2010.06.042
27. Köhler J, Blank S, Müller S, et al. Component resolution reveals additional major allergens in patients with honeybee venom allergy. *J Allergy Clin Immunol.* 2014;133(5):1383-1389. e13896. doi:10.1016/j.jaci.2013.10.060
28. Ebo DG, Faber M, Sabato V, Leysen J, Bridts CH, De Clerck LS. Component-resolved diagnosis of wasp (yellow jacket) venom allergy. *Clin Exp Allergy.* 2013;43(2):255-261. doi:10.1111/cea.12057
29. Frick M, Fischer J, Helbling A, et al. Predominant Api m 10 sensitization as risk factor for treatment failure in honey bee venom immunotherapy. *J Allergy Clin Immunol.* 2016;138(6):1663-1671.e9. doi:10.1016/j.jaci.2016.04.024
30. Popescu FD. Cross-reactivity between aeroallergens and food allergens. *World J Methodol.* 2015;5(2):31-50. Published 2015 Jun 26. doi:10.5662/wjm.v5.i2.31
31. Andersen MB, Hall S, Dragsted LO. Identification of European allergy patterns to the allergen families PR-10, LTP, and profilin from Rosaceae fruits. *Clin Rev Allergy Immunol.* 2011;41(1):4-19. doi:10.1007/s12016-009-8177-3
32. Borres MP, Maruyama N, Sato S, Ebisawa M. Recent advances in component resolved diagnosis in food allergy. *Allergol Int.* 2016;65(4):378-387. doi:10.1016/j.alit.2016.07.002
33. Altıntaş DU (2017) (ed). *Besin alerjenleri ve çapraz reaktifler. Besin Alerjisi: Türk Ulusal Rehberi 2017.* s:15-22.
34. Ott H, Baron JM, Heise R, et al. Clinical usefulness of microarray-based IgE detection in children with suspected food allergy. *Allergy.* 2008;63(11):1521-1528. doi:10.1111/j.1398-9995.2008.01748.x
35. Nowak-Węgrzyn A, Bloom KA, Sicherer SH, et al. Tolerance to extensively heated milk in children with cow's milk allergy. *J Allergy Clin Immunol.* 2008;122(2):342-347. e3472. doi:10.1016/j.jaci.2008.05.043
36. Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, et al. EAACI Molecular Allergology User's Guide. *Pediatr Allergy Immunol.* 2016;27 Suppl 23:1-250. doi:10.1111/pai.12563
37. Urisu A, Ando H, Morita Y, et al. Allergenic activity of heated and ovomucoid-depleted egg white. *J Allergy Clin Immunol.* 1997;100(2):171-176. doi:10.1016/s0091-6749(97)70220-3
38. Benhamou Senouf AH, Borres MP, Eigenmann PA. Native and denatured egg white protein IgE tests discriminate hen's egg allergic from egg-tolerant children. *Pediatr Allergy Immunol.* 2015;26(1):12-17. doi:10.1111/pai.12317
39. Ando H, Movérare R, Kondo Y, et al. Utility of ovomucoid-specific IgE concentrations in predicting symptomatic egg allergy. *J Allergy Clin Immunol.* 2008;122(3):583-588. doi:10.1016/j.jaci.2008.06.016
40. Ito K, Futamura M, Borres MP, et al. IgE antibodies to omega-5 gliadin associate with immediate symptoms on oral wheat challenge in Japanese children. *Allergy.* 2008;63(11):1536-1542. doi:10.1111/j.1398-9995.2008.01753.x
41. Palosuo K, Varjonen E, Kekki OM, et al. Wheat omega-5 gliadin is a major allergen in children with immediate allergy to ingested wheat. *J Allergy Clin Immunol.* 2001;108(4):634-638. doi:10.1067/mai.2001.118602
42. Mäkelä MJ, Eriksson C, Kotaniemi-Syrjänen A, et al. Wheat allergy in children - new tools for diagnostics. *Clin Exp Allergy.* 2014;44(11):1420-1430. doi:10.1111/cea.12393
43. van Wijk F, Hartgring S, Koppelman SJ, Pieters R, Knipfels LM. Mixed antibody and T cell responses to peanut and the peanut allergens Ara h 1, Ara h 2, Ara h 3 and Ara h 6 in an oral sensitization model. *Clin Exp Allergy.* 2004;34(9):1422-1428. doi:10.1111/j.1365-2222.2004.02062.x
44. Nicolaou N, Poorafshar M, Murray C, et al. Allergy or tolerance in children sensitized to peanut: prevalence and differentiation using component-resolved diagnostics. *J Allergy Clin Immunol.* 2010;125(1):191-7.e13. doi:10.1016/j.jaci.2009.10.008
45. Klemans RJ, Broekman HC, Knol EF, et al. Ara h 2 is the best predictor for peanut allergy in adults. *J Allergy Clin Immunol Pract.* 2013;1(6):632-8.e1. doi:10.1016/j.jaip.2013.07.014
46. Krause S, Reese G, Randow S, et al. Lipid transfer protein (Ara h 9) as a new peanut allergen relevant for a Mediterranean allergic population. *J Allergy Clin Immunol.* 2009;124(4):771-8.e5. doi:10.1016/j.jaci.2009.06.008
47. Beyer K, Grabenhenrich L, Härtl M, et al. Predictive values of component-specific IgE for the outcome of peanut and hazelnut food challenges in children. *Allergy.* 2015;70(1):90-98. doi:10.1111/all.12530
48. Hansen KS, Ballmer-Weber BK, Sastre J, et al. Component-resolved in vitro diagnosis of hazelnut allergy in Europe. *J Allergy Clin Immunol.* 2009;123(5):1134-1141. e11413. doi:10.1016/j.jaci.2009.02.005
49. 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
50. Tuano KS, Davis CM. Utility of Component-Resolved Diagnostics in Food Allergy. *Curr Allergy Asthma Rep.* 2015;15(6):32. doi:10.1007/s11882-015-0534-0
51. Maruyama N, Nakagawa T, Ito K, et al. Measurement of specific IgE antibodies to Ses i 1 improves the diagnosis of sesame allergy. *Clin Exp Allergy.* 2016;46(1):163-171. doi:10.1111/cea.12626