

Egg hypersensitivity in review

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ABSTRACT

Egg hypersensitivity is the second most common food allergy with a prevalence of up to 1.7% and the discovery of information about egg allergy is ongoing. This review aims to summarize the current understanding of the allergens involved, natural history, clinical presentation, diagnostic strategies, treatment options, egg-containing vaccine guidelines, and future therapies for health care providers in managing egg hypersensitivity. Recent clinically applicable articles are reviewed for the allergist as an update for the state of the art management of egg allergy. Approximately 70% of children will outgrow egg allergy by 16 years of age and children are able to tolerate well-cooked eggs sooner than uncooked eggs. Egg-specific IgE of >50 kIU_A/L can be used as a predictor for persistent egg allergy. Double-blind placebo-controlled food challenges are still the gold standard for diagnosis. Oral immunotherapy trials still are not generalizable for routine clinical practice, but the influenza vaccine can be given to most egg-allergic patients. Allergists can now educate, diagnose, and manage egg-allergic patients with state-of-the-art information to improve patient's quality of life as never before.

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Food allergy is increasing in prevalence and affects 2–10% of the pediatric population in the United States.¹ Physicians diagnose food allergy based on clinical history, laboratory data, and oral food challenges.² Novel diagnostic methods, such as evaluating the immune system's response to food proteins, may add to the accuracy of diagnosis.² In IgE-mediated food-allergic reactions, 80% are initiated by cow's milk, egg, soy, peanut, wheat, and tree nuts.³ Egg allergy is the second most common food allergy with a prevalence of up to 1.7% of children and adults in available studies involving double-blind placebo-controlled food challenges (DBPCFCs).⁴ The discovery of information on egg allergy is ongoing and this article aims to summarize the current understanding of the allergens involved, natural history, clinical presentation, diagnostic strategies, treatment options, egg-containing vaccine guidelines, and future therapies for health care providers in managing egg hypersensitivity.

EGG ALLERGENS

Egg white and egg yolk both contain clinically relevant allergens. Five are considered to be of most importance and are named *Gallus domesticus* 1–5 (Gal d 1–5). Ovomucoid (Gal d 1) is the major allergen found in egg white and chicken serum albumin, also known as α -livetin, (Gal d 5) is the immunodominant protein in egg yolk.^{5,6}

Ovalbumin (Gal d 2) comprises 54% of egg white but is not as immunogenic as ovomucoid, which makes up only 11% of egg white.⁵

Food processing can alter the allergenicity of egg proteins by altering the binding sites for IgE. IgE antibodies may recognize two forms of allergenic epitopes. The first is a conformational site that is made by the folding of proteins. This results in specific amino acids that are in close proximity to each other forming a binding cleft for the specific IgE antibody. The second is a sequential site composed of linear amino acids in which a specific IgE antibody binds.⁷ Heating or baking denatures the protein, leading to the loss of conformational epitopes. Therefore, heat-labile proteins are of reduced allergenicity.⁷

Ovalbumin (Gal d 2) is heat labile, and ovomucoid (Gal d 1) is heat resistant. This explains why even though ovalbumin is more prevalent in egg white, it has the least allergenicity.^{7–9} Gal d 3–5 (ovotransferrin, lysozyme, and α -livetin) are also all heat labile.⁷ In sera of patients with egg allergy, no significant difference was found in conformational and linear egg white-specific IgE binding.^{7–9} However, those with persistent egg allergy had higher ovomucoid-specific IgE to linear epitopes.^{7–9} The data suggest that ovomucoid conformational and linear epitopes are both important and that different phenotypes exist among children with egg allergy.⁹ Children who generate IgE antibodies directed primarily to conformational epitopes of ovomucoid in egg white and caseins in cow's milk are likely to have transient allergy; in one study, those with IgE antibodies directed primarily at sequential epitopes were noted to have a more persistent allergy.¹⁰

NATURAL HISTORY

Egg allergy is typically identified in infancy and can manifest with hives, wheezing, acute vomiting, and

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Table 1 Natural history of egg allergy

Author	Subjects	Determination of Tolerance	Age of Tolerance		Percent Tolerant
Boyano-Martinez <i>et al.</i> ¹⁵	58 Children, mean age of 16 mo (11–24 mo)	Challenge test	Well cooked	1 yr	16
			Uncooked	2 yr	28
				3 yr	52
				4 yr	57
				5 yr	66
Savage <i>et al.</i> ¹⁶	881 Children, median age of 14 mo, follow-up 4.9 yr	Tolerating concentrated egg by history and/or challenge	Well cooked	4 yr	4
			Uncooked	6 yr	12
				10 yr	37
				16 yr	68
Clark <i>et al.</i> ¹⁷	95 Children, median age of 12 mo	Open challenges with well-cooked and uncooked egg Challenge to well cooked Challenge to uncooked	Well cooked	5.3 yr	NA
			Uncooked	10.3 yr	
				8 yr	66
				13 yr	96
				6 yr	32
				12 yr	62

anaphylaxis.^{5,11} Egg-allergic patients can develop every disease of the allergic march including eczema, aeroallergen sensitization, and asthma.^{11–13} The initial egg allergy studies were completed in the 1980s and concluded that those with egg allergy developed tolerance by early school age.¹⁴ A more recent study found that, of children who had a diagnosis of egg allergy before 2 years of age, ~66% outgrew their egg allergy within 3 years from onset of symptoms.¹⁵ The latest natural history study by Savage *et al.*¹⁶ included 881 egg-allergic patients referred to a tertiary center. The authors observed that 4% of the study population would outgrow egg allergy by 4 years of age, 12% by 6 years, 37% by 10 years, and 68% by 16 years of age.¹⁶ This report indicated that most children would likely not outgrow their egg allergy by early school age as previously reported, but, instead, had a longer progression to egg allergy resolution with the majority tolerating egg by the late teen years. Factors that led to the delay in resolution included a history of asthma, allergic rhinitis, and other food allergies.¹⁶ However, in this study, a large number of these children were diagnosed without food challenge with only evidence of sensitization so the results may not be generalizable to all children with challenge-proven egg allergy. Interestingly, Savage *et al.*¹⁶ did not find a significant difference in the time of resolution between the patients who had clinical symptoms with egg ingestion and those who were diagnosed with egg sensitization based on an elevated egg-specific IgE alone.

Baked or well-cooked egg (350°F for 20 minutes)^{17,18} ingestion has the potential effect of hastening development of tolerance in egg-allergic patients.¹⁷ Clark

*et al.*¹⁸ conducted a longitudinal study from 2004 to 2010 in which children underwent challenge with well-cooked egg and if negative, uncooked egg. These children had repeat annual challenges. It was found that tolerance to well-cooked egg was achieved approximately twice as fast as tolerance to uncooked egg with the median age at tolerance of 5 and 10 years for well-cooked and uncooked egg, respectively (Table 1.) A prospective study was performed in egg-allergic children who tolerated egg-containing muffins and waffles and introduced egg into their diet versus egg-allergic children who did not tolerate egg-containing baked goods and were challenged with baked goods yearly.¹⁹ The baked egg-tolerant group was three times more likely to develop regular egg tolerance than those who were not initially tolerant of baked egg. Also, the group eating baked goods was 14 times more likely to develop tolerance to regular egg when compared with a nonintervention comparison group. The median age of the development of tolerance in these two groups was 22.0 months versus 66.7 months, respectively ($p < 0.0001$).¹⁹ Immunologic changes noted in children who tolerate baked egg include increased IgG4 antibody levels and decreases in skin-prick testing (SPT) wheal.^{8,20}

CLINICAL PRESENTATION

Egg allergy has been identified as an illness of young children with mild-to-moderate reactions and very few anaphylactic reactions. From 1990 to 2005, egg accounted for 7% of fatal anaphylaxis.⁶ Two children who died were <2 years of age.^{3,21} The majority of

patients present with cutaneous manifestations such as eczema exacerbation, angioedema, or urticaria. About two-thirds of patients with egg allergy present with gastrointestinal symptoms, and about one-third present with respiratory complaints.¹⁶ Each episode varies in severity, and a history of a mild reaction in the past does not negate the possibility of a severe reaction in the future or *vice versa*.²²

DIAGNOSTIC STRATEGIES

The diagnosis of egg allergy must always include a detailed clinical history, but objective measures (egg-specific IgE, SPT, and oral food challenge) have shown to be reliable and help predict prognosis.¹ A physician's decision to incorporate one test over another or in a specific order may be based on several variables. A specific IgE value may also be advantageous in patients with a history of suspected reactivity, and significant dermatographism or eczema, who are unable to discontinue antihistamines, or who have exquisite sensitivity to the food in question in which an SPT would elicit a large cutaneous response, causing prolonged patient discomfort.²³ A DBPCFC is generally not indicated for diagnosis in a patient with a history strongly suggestive of anaphylaxis.¹

Egg-Specific IgE

Egg-specific IgE values have been standardized by the Pharmacia CAP (Thermo Fisher Scientific, Portage, MI) system fluorescence enzyme immunoassay since 1999.²⁴ A CAP fluorescence enzyme immunoassay >2 kU/L in those <2 years of age and a value >7 kU/L in those >2 years of age is correlated with a positive food challenge in >95% of cases.²²⁻²⁴ Caution must be taken in that the decision points only confirm an egg allergy that clinically manifests and should not be used as a means of excluding egg allergy.²² These studies were in referral centers so it is also possible that these decision points may not be accurate in the general population. Also, care providers must be aware that the level of the egg-specific IgE does not correlate with the severity of the clinical reaction if the patient ingests egg,²² although one study by Benhamou *et al.*^{5,24} found that their population had no severe reactions after egg ingestion at a specific IgE level <1.10 kU/L.

Monitoring egg-specific IgE levels over time may predict the onset of egg tolerance or identify those who will have persistent egg allergy. Patients who develop egg tolerance tend to have a lower initial egg-specific IgE value and the rate of decline of the IgE value is faster when compared with those with persistent egg allergy.²⁵ Egg-specific IgE >50 kU/L correlates with persistent egg allergy.¹⁶

Skin-Prick Testing

SPT is a rapid screening tool for patients with food allergies. The results are considered positive if the patient develops a wheal of at least 3 mm greater than that produced by the negative control.²⁵ Patients have greater than a 95% chance of not having a clinical food reaction if the skin test is negative.^{21,25} However, it is suggested that individuals with a convincing history of allergy but a negative SPT should receive an oral food challenge to the food in question. For example, in a study by Sporik *et al.*²⁶ 8 of 15 patients with a 0-mm skin test had a positive food challenge.

SPT results vary by age. In those <2 years of age, a wheal >5 mm in diameter was 100% specific in defining a positive egg food challenge outcome in a cohort from Australia. In those >2 years of age, a cutoff of >7 mm in diameter was sufficient to predict a positive egg oral food challenge.²⁷ Hill *et al.*²⁷ found that the SPT results were superior to egg-specific IgE in identifying patients who do not need an egg food challenge for diagnosis, suggesting that SPTs are more accurate than egg-specific IgE values. In a recent study, patients with low egg white-specific IgE levels (<2.5 kU/L) and a small egg SPT wheal diameter had higher pass rates for the DBPCFC. However, specific cutoffs for the SPT that would lead to a negative DBPCFC could not be determined.²⁸

Patch Skin Test

The atopy patch skin test (APT) is an epicutaneous test that applies allergen directly to the skin for 48 hours to detect late-phase allergic or cell-mediated skin reactions.²⁹ The usefulness of APT in egg allergy is not proven. Niggemann *et al.*²⁹ found that the APT is 76% sensitive and 95% specific in identifying late-phase clinical reactions after egg ingestion in patients with atopic dermatitis. Roehr *et al.*³⁰ found an egg-specific IgE ≥17.5 kU/L alone or in concert with a positive APT increased the positive predictive value to 100%. The authors concluded that for individuals with atopic dermatitis, a DBPCFC would be superfluous if the patients had a positive egg APT and egg-specific IgE ≥17.5 kU/L.³⁰ However, other studies have found that the usefulness of the APT in predicting the need for the DBPCFC is not as advantageous.³¹⁻³³

Food Challenge

A food challenge confirms a history of clinical reaction after ingestion, identifies a sensitized patient who is clinically reactive, or excludes the diagnosis of a specific food allergy.^{34,35} In a food challenge, individuals are given small increments of food, usually in 15- to 20-minute intervals, until a reasonable portion has been consumed. Expert opinion strongly recommends that, in individuals with a convincing history of ana-

phylaxis to the food in question, a food challenge is unnecessary due to the risk of anaphylaxis and death.^{1,24} The DBPCFC remains the gold standard in diagnosing food allergy.^{34,35}

Three forms of food challenge currently exist: open challenge, single-blinded challenge, and DBPCFC.³¹ Timing and type of food challenge depends on several factors. For example, in patients without a convincing history of a specific food allergy and with a negative SPT, an open or single-blinded challenge can be used effectively.^{24,34} In other situations, the use of SPT or specific IgE values may aid the physician in timing when the patient has greater than a 50% chance of passing the food challenge.^{1,5} A patient with an egg-specific IgE < 2 kU/L or an SPT with a wheal diameter of ≤ 3 mm may have a 50% probability in passing the oral food challenge.^{28,36}

CURRENT TREATMENT OPTIONS

Treatment of any food allergy includes recognizing the symptoms of the allergic reactions, promptly treating reactions including providing epinephrine when anaphylaxis is occurring,³⁷⁻⁴⁰ and eliminating continued exposure to the allergen.

Food Avoidance

Food avoidance remains the mainstay in the prevention of food-allergic reactions but does not come without risk of nutritional deficits.⁴¹ There has been a change in expert recommendations regarding the use of food avoidance to prevent the development of food allergy. Previous American Academy of Pediatrics recommendations to delay introduction of complementary foods were based on expert consensus rather than on direct evidence. Since that time, an update in 2008 indicates that it is best left up to each individual parent/care provider to decide when to introduce complementary foods.⁴² However, the experts conclude that exclusive breastfeeding for 4–6 months is beneficial, and beyond that age range, no evidence for preventive effect of dietary restrictions is apparent.⁴³⁻⁴⁷ This paradigm shift is related to recent data that there may be detrimental effects of delayed introduction of food in infants.

Oral Immunotherapy

Oral delivery of proteins to alter the immune system is known as oral immunotherapy (OIT).⁴⁸ In OIT, food protein is given in incrementally increasing doses in attempts to achieve a maintenance dose. The aim is to create tolerance of the ingested allergens.⁴⁸⁻⁵¹ OIT is thought to create a state of tolerance in which the food allergen is ingested without any allergy symptoms even in a period of abstinence from that allergen.⁴⁸ Clinical trials of specific oral tolerance induction have

Table 2 Egg content of 2011–2012 influenza vaccines

Manufacturer/ Distributor	Vaccine	Trade Name	Route	How Supplied	Age Group	Stated Ovalbumin Content*
CSL Behring GlaxoSmithKline	TIV (inactivated)	Afluria Intramuscular	Intramuscular	0.5-mL prefilled syringe	≥ 9 years	≤ 1 µg/0.5-mL dose
	TIV (inactivated)	Fluarix	Intramuscular	0.5-mL prefilled syringe	≥ 36 mo	≤ 0.05 µg/0.5-mL dose
MedImmune# Novartis	LAIV	FluLaval	Intramuscular	5-mL multidose vial	≥ 18 yr	≤ 1 µg/0.5-mL dose
		FluMist	Intranasal	0.2-mL sprayer	2–49 yr	≤ 0.24 µg/0.2-mL dose+
	TIV (inactivated)	Fluvirin	Intramuscular	0.5-mL prefilled syringe	≥ 4 yr	≤ 1 µg/0.5-mL dose
				5-mL multidose vial	≥ 4 yr	≤ 1 µg/0.5-mL dose
Sanofi Pasteur*	TIV (inactivated)	Agriflu	Intramuscular	0.5-mL prefilled syringe	≥ 18 yr	≤ 0.4 µg/0.5-mL dose
			Intramuscular	0.25-mL prefilled syringe	6–35 mo	≤ 2.5 µg/0.25-mL dose
		Fluzone		0.5-mL prefilled syringe	≥ 36 mo	~ 0.1 µg/0.5-mL dose
				0.5-mL single-dose vial	≥ 36 mo	~ 0.1 µg/0.5-mL dose
				5-mL multidose vial	≥ 6 mo§	~ 0.1 µg/0.5-mL dose

*Information in package inserts except Fluzone from Sanofi Pasteur by telephone (1-800-822-2463) or email (MIS.Emails@sanofi-pasteur.com)

#Information from 2010 to 2011 season; insufficient data available for use of LAIV in egg-allergic persons for 2011–2012 season.

Information found in Figure 2 of Ref. 52.

LAIV = live attenuated influenza vaccine; TIV = trivalent influenza vaccine.

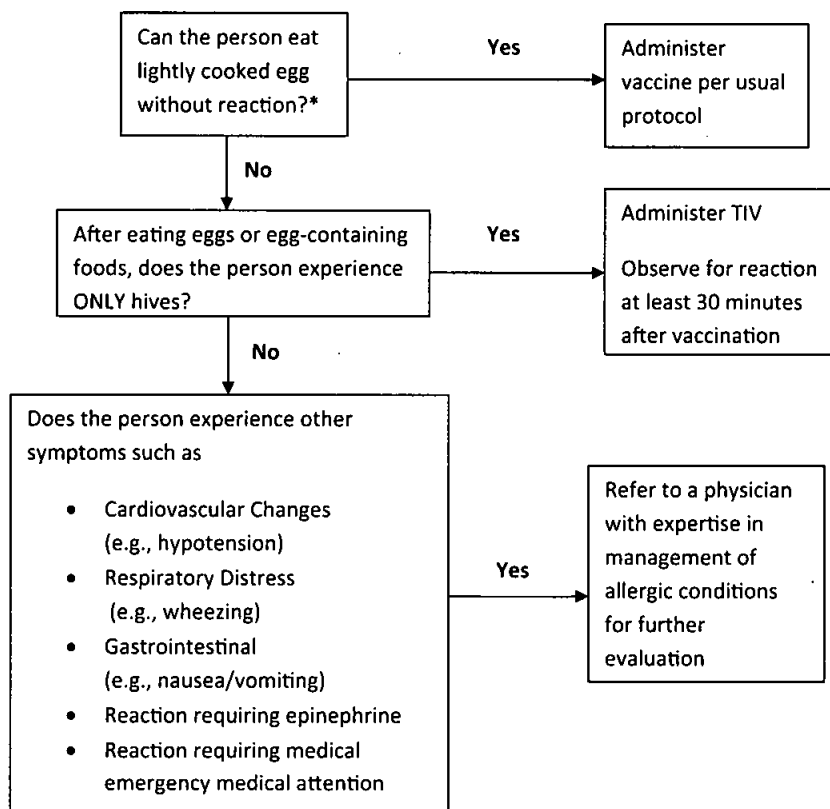


Figure 1. 2011–2012 Recommendations for influenza vaccination in egg-allergic patients.

been performed, but the rate of tolerance induction by OIT was low despite long treatment periods, at least 3 months to several years.^{50,51}

Recently, Burks *et al.* reported a double-blind, randomized, placebo-controlled study with 55 children aged 5–11 years who received egg OIT. Although only 55% of those receiving egg OIT passed food challenge at 10 months, 75% of the children passed at 22 months. After 4–6 weeks of no egg consumption, ~25% of the children receiving OIT passed an oral challenge and had continued desensitization 36 months after beginning OIT.⁴⁹ This work has opened the possibility that individualized desensitization protocols may be more efficacious in the future than standard protocols. However, the rate of allergic reactions during OIT is quite high with up to 78% of patients having allergic reactions during rush protocols.⁵⁰ Therefore, egg OIT still is not generalizable for routine clinical practice.

Egg-Containing Vaccines

Currently available influenza vaccines in the United States contain egg proteins, which raises concerns for their safe administration to egg-allergic patients (Table 2). There is significant variation in vaccines of different manufacturers and within the same manufacturer from lot to lot. James *et al.*^{53,54} showed that vaccines with ovalbumin content <1.2 µg/mL were safe in egg-allergic patients, so practice parameters⁵⁵ recommended administration of vaccines with <1.2 µg/mL until

2011. Historically, the ovalbumin content was not reported by all manufacturers of egg-containing vaccines. There was renewed interest because of the H1N1 pandemic in 2009–2010.^{56–58}

Of 115 egg-allergic patients without anaphylaxis to egg 97% safely received the influenza vaccine in a 2-dose, graded fashion without a vaccine skin test,⁵⁵ and in 2011, a retrospective study of 171 egg-allergic individuals without history of anaphylaxis or severe reactivity attributed to egg-confirmed influenza vaccine safety in this population.⁵⁷ A policy statement by the American Academy of Pediatrics and the Committee on Infectious Diseases indicates that previously used approaches such as skin testing or a two-step graded challenge are no longer recommended.⁵⁸

Fung *et al.*⁵⁹ reported 110 vaccinations in 56 patients with egg-induced anaphylaxis where only 2 patients had a reaction with hives compared with 530 egg-allergic patients without anaphylaxis who had 11 skin-limited reactions. Gagnon *et al.*⁶⁰ indicated that in 4430 patients with egg allergy, the frequency of adverse events was not higher in the 9% of patients vaccinated with divided doses versus those receiving single doses, suggesting that these patients would have tolerated the single-dose vaccine. Nine patients had minor allergic reactions treated with antihistamines. The Advisory Committee on Immunization Practices recommended an algorithm for the

administration of the influenza vaccine for the 2011–2012 influenza season (see Fig. 1).

Measles, mumps, and rubella vaccine administration is safe in egg-allergic patients. Yellow fever vaccine, like influenza, is cultured in chicken embryo and may contain residual chicken and egg proteins. The reported rate of anaphylactic reactions to yellow fever vaccine is 0.8–1.8 per 100,000 injections but some of these reactions were likely caused by gelatin or another vaccine component.^{61,62} Prospective administration of the vaccine in egg-allergic patients has not been reported, so the Centers for Disease Control and Prevention recommends a scratch test or intradermal test be performed before administering the vaccine to egg-sensitive persons. If a person has a severe egg sensitivity or has a positive skin test to the vaccine, but the vaccination is recommended because of their travel destination-specific risk, desensitization can be performed.⁶³ Alternatively, a five-step algorithm published by the American Academy of Pediatrics can be used.⁶⁴

CONCLUSION

Food allergy is increasing in prevalence, and egg remains one of the most common food allergens in children. Clinical reactions may present as mild as angioedema or as severe as anaphylaxis and treatment options range from antihistamines to epinephrine to complete food avoidance. Diagnosis includes clinical history supplemented with objective measures including egg-specific IgE, SPT, patch skin test, and oral food challenge. Treatment options such as OIT are still under investigation, and at this point in time food avoidance is the mainstay of therapy. Allergists can now educate, diagnose, and manage egg-allergic patients with state-of-the-art information to improve patients quality of life as never before.

REFERENCES

1. National Institute of Allergy and Infectious Diseases (NIAID)–Sponsored Expert Panel, Boyce JA, Assa'ad A, Burks AW, Jones SM, Sampson HA, Wood RA, Plaut M, Cooper SF, Fenton MJ, Arshad SH, Bahna SL, Beck LA, Byrd-Bredbenner C, Camargo CA Jr., Eichenfield L, Furuta GT, Hanifin JM, Jones C, Kraft M, Levy BD, Lieberman P, Lucciolli S, McCall KM, Schneider LC, Simon RA, Simons FE, Teach SJ, Yawn BP, and Schwaninger JM. Guidelines for the diagnosis and management of food allergy in the United States: Report of the NIAID-sponsored expert panel. *J Allergy Clin Immunol* 126(suppl):S1–S58, 2010.
2. Sicherer SH. Food allergy. *Mt Sinai J Med* 78:683–696, 2011.
3. Ramesh S. Food allergy overview in children. *Clin Rev Allergy Immunol* 34:217–230, 2008.
4. Rona RJ, Keil T, Summers C, et al. The prevalence of food allergy: A meta-analysis. *J Allergy Clin Immunol* 120:638–646, 2007.
5. Benhamou AH, Caubet JC, Eigenmann PA, et al. State of the art and new horizons in the diagnosis and management of egg allergy. *Allergy* 65:283–289, 2010.
6. Tey D, and Heine RG. Egg allergy in childhood: An update. *Curr Opin Allergy Clin Immunol* 9:244–250, 2009.
7. Nowak-Węgrzyn AA, and Fiocchi AB. Rare, medium, or well done? The effect of heating and food matrix on food protein allergenicity. *Curr Opin Allergy Clin Immunol* 9:234–237, 2009.
8. Lemon-Mule H, Sampson HA, Sicherer SH, et al. Immunologic changes in children with egg allergy ingesting extensively heated egg. *J Allergy Clin Immunol* 122:977–983, 2008.
9. Jarvinen M, Beyer K, Vila L, et al. Specificity of IgE antibodies to sequential epitopes of hen's egg ovomucoid as a marker for persistence of egg allergy. *Allergy* 62:758–765, 2007.
10. Leonard SA, and Nowak-Węgrzyn A. Redefining food allergy phenotypes and management paradigm: Is it time for individualized egg allergy management? *Clin Exp Allergy* 41:609–611, 2011.
11. Dean T, Venter C, Pereira B, et al. Patterns of sensitization to food and aeroallergens in the first 3 years of life. *J Allergy Clin Immunol* 120:1166–1171, 2007.
12. Wolkerstorfer A, Wahn U, Kjellman NI, et al. Natural course of sensitization to cow's milk and hen's egg in childhood atopic dermatitis: ETAC study group. *Clin Exp Allergy* 32:70–73, 2002.
13. Tariq SM, Matthews SM, Hakim EA, et al. Egg allergy in infancy predicts respiratory allergic disease by 4 years of age. *Pediatr Allergy Immunol* 11:162–167, 2000.
14. Wood RA. The natural history of food allergy. *Pediatrics* 111:1631–1637, 2003.
15. Boyano-Martinez T, Garcia-Ara C, Diaz-Pena JM, et al. Prediction of tolerance on the basis of quantification of egg white-specific IgE antibodies in children with egg allergy. *J Allergy Clin Immunol* 110:304–309, 2002.
16. Savage JH, Matsui EC, Skripak JM, et al. The natural history of egg allergy. *J Allergy Clin Immunol* 120:1413–1417, 2007.
17. Huang F, and Nowak-Węgrzyn A. Extensively heated milk and egg as oral immunotherapy. *Curr Opin Allergy Clin Immunol* 12:283–292, 2012.
18. Clark A, Islam S, King Y, et al. A longitudinal study of resolution of allergy to well-cooked and uncooked egg. *Clin Exp Allergy* 41:706–712, 2011.
19. Lieberman JA, Huang FR, Sampson HA, and Nowak-Węgrzyn A. Outcomes of 100 consecutive open, baked-egg oral food challenges in the allergy office. *J Allergy Clin Immunol* 129:1682–1684.e2, 2012.
20. Cortot CF, Sheehan WJ, Permaul P, et al. Role of specific IgE and skin-prick testing in predicting food challenge results to baked egg. *Allergy Asthma Proc* 33:275–281, 2012.
21. Allen CW, Campbell DE, and Kemp AS. Egg allergy: Are all childhood food allergies the same? *J Paediatr Child Health* 43:214–218, 2007.
22. Sampson HA. Utility of food-specific IgE concentrations in predicting symptomatic food allergy. *J Allergy Clin Immunol* 107:891–896, 2001.
23. Sampson HA. Food allergy. Part 2: Diagnosis and management. *J Allergy Clin Immunol* 103:981–989, 1999.
24. Sampson HA. Update on food allergy. *J Allergy Clin Immunol* 113:805–819, 2004.
25. Shek LP, Soderstrom L, Ahlstedt S, et al. Determination of food specific IgE levels over time can predict the development of tolerance in cow's milk and hen's egg allergy. *Allergy Clin Immunol* 30:387–391, 2004.
26. Sporik R, Hill DJ, and Hosking CS. Specificity of allergen skin testing in predicting positive open food challenges to milk, egg and peanut in children. *Clin Exp Allergy* 30:1540–1546, 2000.
27. Hill J, Hosking CS, and Reyes-Benito LV. Reducing the need for food allergen challenges in young children: A comparison of in vitro with in vivo tests. *Clin Exp Allergy* 31:1031–1035, 2001.
28. Knight AK, Shreffler WG, Sampson HA, et al. Skin prick test to egg white provides additional diagnostic utility to serum egg

- white-specific IgE antibody concentration in children. *J Allergy Clin Immunol* 117:842–847, 2006.
29. Niggemann B, Reibel S, and Wahn U. The atopy patch test (APT)—A useful tool for the diagnosis of food allergy in children with atopic dermatitis. *Allergy* 55:281–285, 2000.
 30. Roehr CC, Reibel S, Ziegert M, et al. Atopy patch tests, together with determination of specific IgE levels, reduce the need for oral food challenges in children with atopic dermatitis. *J Allergy Clin Immunol* 107:548–553, 2001.
 31. Osterballe M, Andersen KE, and Bindslev-Jensen C. The diagnostic accuracy of the atopy patch test in diagnosing hypersensitivity to cow's milk and hen's egg in unselected children with and without atopic dermatitis. *J Am Acad Dermatol* 51:556–562, 2004.
 32. Mehl A, Rolinck-Werninghaus C, Staden U, et al. The atopy patch test in the diagnostic workup of suspected food-related symptoms in children. *J Allergy Clin Immunol* 118:923–929, 2006.
 33. Hansen TK, Høt A, and Bindslev-Jensen C. An evaluation of the diagnostic value of different skin tests with egg in clinically egg-allergic children having atopic dermatitis. *Pediatr Allergy Immunol* 15:428–434, 2004.
 34. Nowak-Węgrzyn A, Assa'ad AH, Bahna SL, et al.; Adverse Reactions to Food Committee of American Academy of Allergy, Asthma and Immunology. Work Group report: Oral food challenge testing. *J Allergy Clin Immunol* 123(suppl):S365–S383, 2009.
 35. Kemp AS, Allen CW, and Campbell DE. Parental perceptions in egg allergy: Does egg challenge make a difference? *Pediatr Allergy Immunol* 20:648–653, 2009.
 36. Perry TT, Matsui EC, Conover-Walker MK, et al. The relationship of allergen-specific IgE levels and oral food challenge outcome. *J Allergy Clin Immunol* 114:144–149, 2004.
 37. Sampson HA, Munoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: Summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network Symposium. *J Allergy Clin Immunol* 117:391–397, 2006.
 38. Sampson HA, and Wang J. Food anaphylaxis. *Clin Exp Allergy* 37:651–660, 2007.
 39. Sampson HA. Anaphylaxis and emergency treatment. *Pediatrics* 111:1601–1608, 2003.
 40. Sicherer SH, and Simons ER. Self-injectable epinephrine for first-aid management of anaphylaxis. *Pediatrics* 119:638–646, 2007.
 41. Kirby M, and Danner E. Nutritional deficiencies in children on restricted diets. *Pediatr Clin North Am* 56:1085–1103, 2009.
 42. Fiocchi A, Assa'ad A, and Bahna S. Food allergy and the introduction of solid foods to infants: A consensus document. *Ann Allergy Asthma Immunol* 97:10–21, 2006.
 43. Pali-Scholl I, Renz H, and Jensen-Jarolim E. Update on allergies in pregnancy, lactation, and early childhood. *J Allergy Clin Immunol* 123:1012–1021, 2009.
 44. Sicherer SH, and Burks AW. Maternal and infant diets for prevention of allergic diseases: Understanding menu changes in 2008. *J Allergy Clin Immunol* 122:29–33, 2008.
 45. Høst A, Halken S, Muraro A, et al. Dietary prevention of allergic diseases in infants and small children. *Pediatr Allergy Immunol* 19:1–4, 2008.
 46. Greer FR, Sicherer SH, and Burks AW. Effects of early nutritional interventions on the development of atopic disease in infants and children: The role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. *Pediatrics* 121:183–191, 2008.
 47. Sicherer NY. Food allergy. *J Allergy Clin Immunol* 125(suppl 2):S116–S125, 2010.
 48. Simons FER. Anaphylaxis. *J Allergy Clin Immunol* 125:S161–S181, 2010.
 49. Burks AW, Jones SM, Wood RA, et al.; Consortium of Food Allergy Research (CoFAR). Oral immunotherapy for treatment of egg allergy in children. *N Engl J Med* 367:233–243, 2012.
 50. García Rodríguez R, Urra JM, Feo-Brito F, et al. Oral rush desensitization to egg: Efficacy and safety. *Clin Exp Allergy* 41:1289–1296, 2011.
 51. Mousallem T, and Burks AW. Immunology in the Clinic Review Series; focus on allergies: Immunotherapy for food allergy. *Clin Exp Immunol* 167:26–31, 2012.
 52. Centers for Disease Control and Prevention. Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2011; Figure 2. *MMWR Morb Mortal Wkly Rep* 60:1128–1132, 2011.
 53. James JM, Zeiger RS, Lester MR, et al. Safe administration of influenza vaccine to patients with egg allergy. *J Pediatr* 133:624–628, 1998.
 54. McKinney KK, Webb L, Petersen M, et al. Ovalbumin content of 2010–2011 influenza vaccines. *Allergy Clin Immunol* 127:1629–1632, 2011.
 55. Greenhawt MJ, Li JT, Bernstein DI, et al. Administering influenza vaccine to egg allergic recipients: A focused practice parameter update. *Ann Allergy Asthma Immunol* 106:11–16, 2011.
 56. Chung EY, Huang L, and Schneider L. Safety of influenza vaccine administration in egg-allergic patients. *Pediatrics* 125:1024, 2010.
 57. Webb L, Petersen M, Boden S, et al. Single-dose influenza vaccination of patients with egg allergy in a multicenter study. *J Allergy Clin Immunol* 128:218–219, 2011.
 58. Brady MT, Byington CL, Davies HD, et al. Recommendations for prevention and control of influenza in children, 2011–2012. *Pediatrics* 128:813–825, 2011.
 59. Fung I, and Spergel JM. Administration of influenza vaccine to pediatric patients with egg-induced anaphylaxis. *J Allergy Clin Immunol* 129:1157–1159, 2012.
 60. Gagnon R, Primeau MN, Roches AD, et al. Safe vaccination of patients with egg allergy with an adjuvanted pandemic H1N1 vaccine. *J Allergy Clin Immunol* 126:317–323, 2010.
 61. James JM, Burks AW, Roberson PK, and Sampson HA. Safe administration of the measles vaccine to children allergic to eggs. *N Engl J Med* 332:1262–1266, 1995.
 62. Staples JE, Gershman M, and Fischer M; Centers for Disease Control and Prevention (CDC). Yellow fever vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 30:1–27, 2010.
 63. Kelso JM, Mootrey GT, and Tsai TF. Anaphylaxis from yellow fever vaccine. *J Allergy Clin Immunol* 103:698–701, 1999.
 64. Wood RA, Berger M, Dreskin SC, et al. An algorithm for treatment of patients with hypersensitivity reactions after vaccines. *Pediatrics* 122:e771–e777, 2008. □

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