

Biphasic reactions in children undergoing oral food challenges

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ABSTRACT

Literature regarding biphasic reactions in the pediatric population is sparse. We aimed to determine the prevalence of biphasic reactions in children with food allergies undergoing oral food challenges (OFCs) and examine whether any clinical or treatment factors are associated with biphasic reactions. A retrospective chart review of OFCs conducted between July 2007 and March 2011 was performed. Charts were reviewed from time of challenge to 48 hours after challenge to capture data on any biphasic reactions. Uniphasic and biphasic reactions were compared in terms of specific clinical features and treatments. Of 614 positive challenges, 9 resulted in a biphasic reaction (1.5%). Six of the biphasic reactions occurred in challenges where the initial reaction met anaphylaxis criteria. The biphasic reactions were to eggs (4), peanuts (3), and milk (2). The symptom-free interval ranged from 2 to 24 hours. There were no statistically significant differences in clinical features between uniphasic and biphasic reactions, but there appeared to be a higher percentage of initial reactions with multiple organ involvement and meeting anaphylaxis criteria in the biphasic group. Biphasic reactors were significantly more likely to have received steroids for their initial reaction. A higher percentage of biphasic reactors also appeared to have received epinephrine, multiple doses of epinephrine, and antihistamines for their initial reactions. Biphasic reactions are rare in children undergoing OFCs and may be associated with more severe allergic reactions. Children with severe reactions may benefit from a 24-hour period of observation.

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Food allergies affect 3.9–8% of children in the United States^{1–3} and are most commonly triggered by cow's milk, eggs, peanuts, tree nuts, wheat, soy, fish, and shellfish.^{1–4} As the most common cause of anaphylaxis in children,^{5–7} food allergies contribute to the nearly fourfold increase in rates of children requiring hospitalization due to anaphylaxis.⁸

Biphasic anaphylaxis was first described by Popa and Lerner⁹ in three patients with recurrence of systemic symptoms hours after exposure to an allergen, subsequent to resolution of initial reaction. They recommended observing anaphylaxis patients for 24 hours and suggested that steroids may potentially prevent a biphasic reaction. Rates of 2–20% have since been reported for biphasic reactions^{10–22} with few studies focusing on children.^{15,20,21} No consistent clinical features have been associated with biphasic reactions, but potential risk factors include oral exposure to allergen,¹⁰ longer time between exposure and initial reaction,¹⁰ and longer duration of initial reaction.¹⁸ The relationship between epinephrine and biphasic reactions is unclear. Two studies found that inadequate or delayed treatment with epinephrine may increase the

likelihood of a biphasic reaction,^{15,18} and two different studies suggested that more administrations and higher cumulative dosages (mg/kg) of epinephrine are associated with biphasic reactions.^{14,21} Three other studies found no relationship between epinephrine and biphasic reactions.^{10,17,22} There is similarly conflicting data for steroids, as two studies found positive benefit,^{12,18} but most have found no significant effect of steroids.^{10,15,17,21,22} There is also lack of consensus on observation time for patients with anaphylaxis, with recommendations ranging from 2 to 24 hours.^{9–11,13,15,17,18,21}

Pediatric literature regarding this subject is significantly limited.^{15,20,21} Furthermore, given the serious nature of anaphylaxis and lack of consistent information on the characteristics of biphasic reactions, it appears critically important to work toward developing a clear set of guidelines regarding biphasic reactions. Our study aimed to (1) determine the prevalence of biphasic reactions and biphasic anaphylaxis in children with food allergies undergoing an oral food challenge (OFC), (2) examine whether any clinical features distinguish uniphasic reactions from biphasic reactions, and (3) examine whether any treatment differences are associated with biphasic reactions.

METHODS

A retrospective chart review was performed on 1843 OFCs performed between July 2007 and March 2011. Of these, 155 challenges were excluded: 33 were equivocal, 72 were consistent with food protein-induced enterocolitis reactions as opposed to IgE-mediated re-

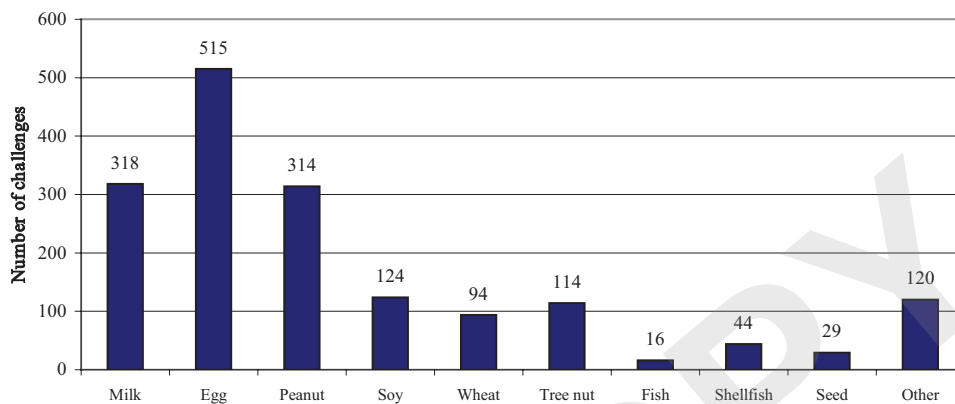
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Figure 1. Distribution of foods challenged. A total of 1688 oral food challenges (OFCs) were analyzed. Egg challenges were the most common. Other foods challenged were milk, peanuts, soy, tree nuts, wheat, shellfish, seeds (sesame, mustard, flax, or sunflower), and fish. One hundred twenty challenges were performed to various other foods, including chicken, beef, oat, and barley.



actions, and 50 were not completed because the children were unwilling to cooperate.

Children were eligible for an OFC if they had a history consistent with an allergic reaction, a positive skin-prick test, or specific IgE to a food based on established criteria.^{23–25} All challenges were performed at the Children’s Hospital of Philadelphia under standardized design protocol.²⁶ Epinephrine, if necessary, was administered per standard dosing (0.01 mg/kg per dose intramuscularly, with a maximum dose of 0.5 mg). Oral steroids were administered when reactions appeared more significant or prolonged. Patients were monitored for 2.5 hours after completion of last dose. On discharge, parents were instructed to call the clinic or allergist on call to report any new symptom development after leaving the OFC.

Electronic medical records were reviewed from OFC to 48 hours after OFC to capture documentation of biphasic reactions from any calls or emergency room visits. The following data were collected: sex, age, history of asthma, history of prior anaphylaxis to challenged food, outcome of OFC, symptoms during OFC, treatment of initial reaction at OFC, time from last dose completed in OFC to onset of initial reaction, time from onset of initial reaction to administration of epinephrine, symptoms during any second reactions, and treatment of second reactions. Approval for the study was obtained from the Institutional Review Board of the Children’s Hospital of Philadelphia.

Biphasic reactions were defined as those involving recurrence of any symptoms after resolution of the initial reaction, and biphasic anaphylaxis was defined as the recurrence of symptoms after resolution of an initial anaphylactic reaction.^{9,16,19,27} Symptoms were categorized into the following groups: skin (including hives, pruritus, angioedema, flushing, eczema flare, and conjunctivitis), respiratory (including rhinorrhea, sneezing, congestion, nasal pruritus, stridor, cough, wheezing, shortness of breath, hypoxemia, and decreased or coarse breath sounds), gastrointestinal (including abdominal pain, nausea, vomiting, and diarrhea), cardiovascular (including hypotension and tachycardia), multiple organ

systems (any constellation of symptoms involving more than one system, whether or not anaphylaxis criteria were met), and anaphylaxis (as defined by Sampson *et al.*²⁷). Any one challenge could be coded for multiple categories of symptoms.

Statistical analysis was performed using JMP Version 10 (SAS, Inc., Cary, NC). All analyses were two-tailed. Chi-square analysis was used to compare categorical variables, and unpaired *t*-tests were used to compare continuous variables. A value of $p \leq 0.05$ was considered statistically significant. Ninety-five percent confidence intervals were calculated for outcomes reported as mean values.

RESULTS

A total of 1688 OFCs were included in the final analysis (Fig. 1). Six hundred fourteen challenges (36.4%) were positive, and nine resulted in biphasic reactions (1.5% of positive challenges). Of the 310 positive challenges meeting anaphylaxis criteria, six resulted in biphasic reactions (1.9%).

Male patients accounted for 65.8% ($n = 1110$) of challenges. Patients ranged in age from 5 months to 20 years (Figure 2) and had a history of asthma in 65.2% ($n = 1101$) of challenges. For the 1634 challenges for which data were available, 159 challenges were performed in patients with a history of prior anaphylaxis to challenged food.

Positive Challenges

Initial reactions for the 614 positive challenges manifested as follows: 77.9% ($n = 478$) involved skin symptoms, 64.3% ($n = 395$) involved respiratory symptoms, 60.9% ($n = 374$) involved gastrointestinal symptoms, and 1.6% ($n = 10$) involved cardiovascular symptoms. Multiple organ systems were affected in 473 challenges (77%). In 310 challenges (50.5%), reactions met criteria for anaphylaxis. Not all multisystemic reactions were anaphylactic. For example, a reaction that manifested with rhinorrhea or sneezing and vomiting was coded as involving multiple organ systems but not as ana-

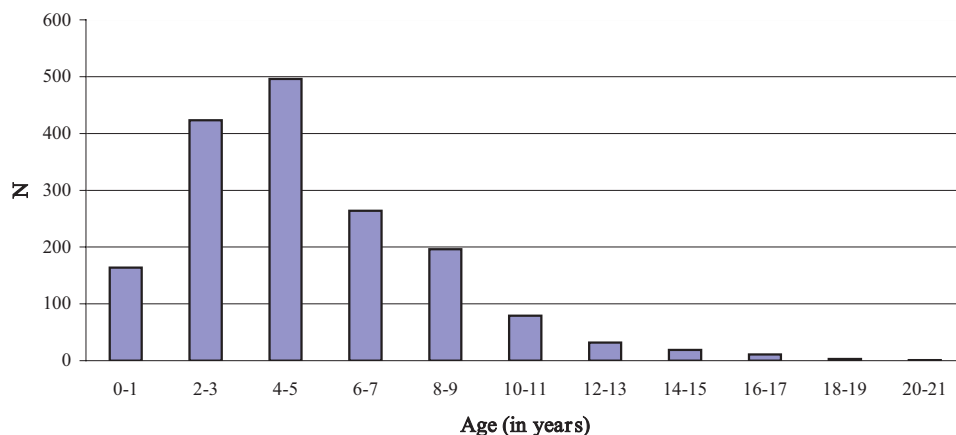


Figure 2. Age distribution for all challenges. Patients ranged in age from 5 months to 20 years (mean 5 ± 3 years).

phylactic as defined by Sampson *et al.*²⁷ because rhinorrhea and sneezing were not considered respiratory compromise.

Treatment of initial reactions included steroids in 167 challenges (27.2%), epinephrine in 262 challenges (42.7%), antihistamines in 463 challenges (75.4%), albuterol in 90 challenges (14.7%), oxygen in 3 challenges (0.5%), and i.v. fluids in 15 challenges (2.4%). Forty-eight of 310 anaphylactic reactions were not documented as being treated with epinephrine. This discrepancy is possibly secondary to a combination of incomplete documentation and clinical judgment of the allergist that the reaction, although meeting anaphylaxis criteria in hindsight, did not appear significant enough to warrant epinephrine at time of OFC. None of these cases resulted in a biphasic reaction. Epinephrine was given for 53% of multisystemic initial reactions. There was no association between epinephrine and biphasic reactions among these challenges.

Biphasic Reactions

Nine challenges resulted in biphasic reactions (1.5% of positive challenges). Six of 310 positive challenges meeting anaphylaxis criteria had biphasic reactions, resulting in a biphasic anaphylaxis rate of 1.9%. The patients with biphasic reactions ranged in age from 14 months to 13 years, and five were male subjects. Four biphasic reactions were to eggs, three were to peanuts, and two were to milk. The time interval between resolution of the initial reaction and onset of the second reaction ranged from 2 to 24 hours. As illustrated in Table 1, the severity and treatment of both initial and second reactions varied widely. Five initial reactions were treated with steroids, six were treated with epinephrine, and two were treated with albuterol. All were treated with antihistamines. The severity of the second reaction ranged from urticaria in one case to multisystemic reactions or anaphylaxis in five cases. Although three of these late-occurring reactions required no treatment, two were treated with epinephrine,

and two required care at an emergency department. For two biphasic cases, detailed documentation of treatment of the second reaction was not available, because they were treated at a hospital outside of our network.

Uniphasic Reactions versus Biphasic Reactions

There were no significant differences in mean age, sex, history of asthma, or history of prior anaphylaxis to challenged food between the uniphasic and biphasic groups (Table 2). The percentages of challenges to milk, eggs, peanuts, soy, wheat, tree nuts, fish, shellfish, seeds, and other foods were similar. The groups did not differ significantly in the type of symptoms during initial reaction or the time from last dose of challenged food to onset of initial reaction. However, biphasic reactors were significantly more likely to have received steroids for their initial reaction ($p = 0.05$). We also observed several trends that were not statistically significant; a higher percentage of initial reactions in the biphasic group involved multiple organ systems ($p = 0.10$), met anaphylaxis criteria ($p = 0.10$), received epinephrine ($p = 0.14$), and received antihistamines ($p = 0.08$). Furthermore, although the two groups were comparable in the time from onset of initial reaction to administration of the first dose of epinephrine, a higher percentage of biphasic reactors appeared to have received multiple doses of epinephrine at initial reaction ($p = 0.11$). Similar percentages were treated with albuterol, oxygen, and i.v. fluids at OFC.

DISCUSSION

We found that biphasic reactions were rare, occurring in 1.5% of all positive OFCs and 1.9% of anaphylactic reactions. The interval from resolution of initial reaction to onset of second reaction ranged from 2 to 24 hours. Our rates were similar to the 2% recently reported by Jarvinen *et al.*²⁰ The two other pediatric-specific rates previously reported were higher: 6% in

Table 1 Biphasic cases

Age	Sex	Hx of Asthma	Hx of Anaphylaxis	Food	Symptoms at Initial Reaction	Treatment of Initial Reaction	Interval*(hr)	Symptoms at Second Reaction	Treatment of Second Reaction
14 mo	M	Yes	No	Milk	Hives, pruritus, erythema, rhinitis, cough, and emesis#	Antihistamine, steroid, and epinephrine	2	Emesis, cough, sneezing, wheezing, and shortness of breath	Antihistamine and steroid
26 mo	M	No	No	Egg	Hives, pruritus, and anaphylaxis (no other details)#	Antihistamine, steroid, albuterol, and epinephrine	11	Hives and shortness of breath	Epinephrine and steroid
4 yr	M	Yes	No	Peanut	Hives, pruritus, cough (once), rhinitis, and conjunctivitis	Antihistamine and steroid	4.5	Cough and hives	Epinephrine ED (further treatment unknown; treated at another institution)
3 yr	F	No	No	Egg	Hives, pruritus, sneezing, coarse breath sounds, and emesis#	Antihistamine, steroid, and epinephrine	12	Emesis and abdominal pain	None
6 yr	M	Yes	No	Peanut	Tongue tingling, hives, abdominal pain, and emesis	Antihistamine	2	Emesis and pallor	Antihistamine, steroid, i.v. fluids, ED (other treatment unknown; treated at another institution)
9 yr	F	Yes	No	Peanut	Itchy throat, decreased breath sounds, wheezing, flushing, hives, and abdominal pain#	Antihistamine, steroid, albuterol, and epinephrine	4.5	Cough, pruritus, and chest tightness	Antihistamine, steroid, albuterol, and Flovent
5 yr	M	No	Yes	Milk	Sneezing, nasal congestion, hives, eye swelling, and cough#	Antihistamine and epinephrine	12-24	Emesis and diarrhea	None
3 yr	F	Yes	No	Egg	Hives, pruritus, abdominal pain, emesis, diarrhea#	Antihistamine and epinephrine	6	Hives	Antihistamine
13 yr	F	Yes	No	Egg	Itchy throat, abdominal pain, and emesis	Antihistamine	3	Emesis	None

*Interval from resolution of initial reaction to onset of second reaction.

#Initial reactions that met anaphylaxis criteria.

ED = emergency department.

Table 2 Uniphasic vs biphasic reactions

	Uniphasic <i>n</i> = 605	Biphasic <i>n</i> = 9	<i>p</i> Value
Mean age (95% CI)	5 yr (4.8–5.3)	5.1 yr (3.3–7.0)	0.91
Sex	30.1% Female	44.4% Female	0.35
History of asthma	67.3%	66.7%	0.97
History of anaphylaxis to challenged food	14.3%	11.1%	0.79
Characteristics of initial reaction at OFC			
Skin symptoms	77.9%	89.9%	0.43
Respiratory symptoms	64.1%	77.8%	0.40
Gastrointestinal symptoms	60.8%	66.7%	0.72
Cardiovascular symptoms	1.7%	0%	0.70
Multiple organ systems	76.7%	100.0%	0.10#
Anaphylaxis	50.1%	77.8%	0.10#
Treatment of initial reaction at OFC			
Steroids	26.8%	55.6%	0.05*
Epinephrine	42.3%	66.7%	0.14#
>1 dose of epinephrine	2.5%	11.1%	0.11#
Antihistamines	75.0%	100.0%	0.08#
Albuterol	14.6%	22.2%	0.52
Oxygen	0.5%	0%	0.83
i.v. fluids	2.5%	0%	0.63
Time from last dose to first reaction onset	18.0 min	13.1 min	0.51
Time from first reaction onset to first epinephrine dose	23.0 min (<i>n</i> = 256)	28.5 min (<i>n</i> = 6)	0.60

Similar percentages of uniphasic and biphasic reactions were treated with albuterol, oxygen, and i.v. fluids at initial reaction.

*Biphasic reactors were significantly more likely to have received steroids for treatment of their initial reaction.

#Although not statistically significant, there were also notable differences in that a greater percentage of initial reactions in the biphasic group appeared to involve multiple organ systems or meet anaphylaxis criteria and require treatment with epinephrine, multiple doses of epinephrine, and antihistamines.

OFC = oral food challenge.

the Lee and Greenes¹⁵ study and 11% in the Mehr *et al.*²¹ study. The rates in adult studies were also higher, ranging from 3 to 20%.^{10–14,16–19,22}

There may be several reasons why our rates of biphasic reactions were low. First, epinephrine is likely administered earlier in OFCs than in spontaneous anaphylactic reactions because of the close supervision of patients. Second, the quantity of allergen exposure was potentially lower in our study, as patients undergoing OFCs are administered gradually increasing amounts of food with a very low initial dose as opposed to children in the natural setting who may ingest a much larger amount of an allergen. Finally, children undergoing OFCs may represent a less severe group compared with children with anaphylaxis in other studies, as many patients already start with a 50% probability of having a negative OFC.²⁵

We saw no statistically significant clinical features that distinguished uniphasic reactions from biphasic reactions, but there was a trend toward a higher percentage of biphasic reactors having initial reactions that were multisystemic or anaphylactic. Unlike Smit *et al.*,¹⁷ whose biphasic reactors were less likely to have

had dyspnea during their initial reaction, our uniphasic and biphasic groups were similar in the percentage of initial reactions involving respiratory symptoms. They were also similar in the percentage of initial reactions involving skin, gastrointestinal, and cardiovascular symptoms. And unlike Confino-Cohen and Goldberg,²² who reported a trend toward a higher percentage of asthmatic patients in their biphasic group, we found no association between asthma and biphasic reactions.

We are the first to report that biphasic reactors were significantly more likely to have received steroids, unlike most previous studies^{10,15,17,21,22} that found no association between steroids and biphasic reactions. This finding contrasts specifically to Ellis and Day,¹⁸ who reported a trend toward a lower rate of steroid use in biphasic reactors, as well as to Douglas *et al.*,¹² who reported that rates of biphasic reactions were potentially decreased in their cohort because of early intervention with steroids. We also observed trends toward a higher percentage of initial reactions in the biphasic group receiving epinephrine, multiple doses of epinephrine, and antihistamines. Our results potentially

support previous findings by Brazil and McNamara¹⁴ and Mehr *et al.*²¹ for whom biphasic reactors required more administrations of epinephrine and higher cumulative dosages (mg/kg) of epinephrine, respectively, at initial reaction; however, unlike Lee and Greenes,¹⁵ whose biphasic reactors had a longer time interval between onset of initial symptoms and the first dose of epinephrine, we saw no difference in this variable. Furthermore, this interval was generally shorter in our study: 23 minutes for the uniphasic group and 28.5 minutes for the biphasic group compared with 48 minutes for the uniphasic group and 190 minutes for the biphasic group reported by Lee and Greenes.¹⁵ This is likely because the close supervision of symptoms in OFCs may lead to earlier administration of epinephrine than in natural settings. Finally, unlike Smit *et al.*,¹⁷ who found that biphasic reactors were less likely to be treated with a bronchodilator at initial reaction, and Mehr *et al.*,²¹ who found that the biphasic group was more likely to have required an i.v. fluid bolus for the initial reaction, we found no differences in the percentages treated with albuterol or i.v. fluids.

Our finding that biphasic reactors were more likely to have received steroids at initial reaction and the trends toward a higher percentage of initial reactions in the biphasic group affecting multiple systems and meeting anaphylaxis criteria in addition to requiring epinephrine (including multiple doses of epinephrine) suggest that the severity of the initial reaction may be associated with biphasic reactions. This is consistent with the results of Mehr *et al.*,²¹ whose biphasic patients more frequently needed i.v. fluids, evidence of a more severe reaction. Steroids are usually administered at OFCs for more severe reactions, as assessed by the allergist. Similarly, epinephrine is administered when reactions appear anaphylactic, and multiple doses of epinephrine are given when an anaphylactic reaction appears prolonged or more severe in nature. Therefore, steroids, epinephrine, and multiple doses of epinephrine may serve as markers of increased severity of a reaction, which may then indicate an increased likelihood of developing a biphasic reaction. The trend toward a higher percentage of initial reactions receiving antihistamines in the biphasic group also supports the theme of biphasic reactors being generally more symptomatic at initial reaction.

There are several potential limitations to our study. First, our study was a retrospective chart review. A prospective, multicenter randomized controlled trial would more definitively explore risk factors associated with biphasic reactions. Additionally, because we relied on parental calls to gauge the occurrence of biphasic reactions, we may have potentially missed biphasic cases for patients who received care outside of our network. We feel that this was not a significant limitation, however, as parents are clearly instructed to call

our clinic with any issues after an OFC, and we did have patients who received care at another hospital but whose parents still called before seeking care. There is also limited generalizability of our study results, because we focused on children with food allergies undergoing food challenges, who comprise just a subset of all children at risk for biphasic reactions.

In conclusion, biphasic reactions appear to be rare in children with food allergies undergoing OFCs. Initial reactions that are more severe may potentially be associated with biphasic reactions. Most children are safe to be discharged soon after resolution of the initial reaction. Those who have more severe reactions may benefit from a more prolonged period of observation to watch for biphasic reactions, but no more than 24 hours may be necessary. In all cases, it is vital that patients know of the potential risk of a biphasic reaction and have an emergency plan and an epinephrine autoinjector available in case a biphasic reaction occurs after discharge.

REFERENCES

1. Branum AM, and Lukacs SL. Food allergy among children in the United States. *Pediatrics* 124:1549–1555, 2009.
2. Liu AH, Jaramillo R, Sicherer SH, et al. National prevalence and risk factors for food allergy and relationship to asthma: Results from the National Health and Nutrition Examination Survey 2005–2006. *J Allergy Clin Immunol* 126:798–806, 2010.
3. Gupta RS, Springston EE, Warrier MR, et al. The prevalence, severity, and distribution of childhood food allergy in the United States. *Pediatrics* 128:e9–e17, 2011.
4. Chafen JJ, Newberry SJ, Riedl MA, et al. Diagnosing and managing common food allergies: A systematic review. *JAMA* 303: 1848–1856, 2010.
5. Dibs SD, and Baker MD. Anaphylaxis in children: A 5-year experience. *Pediatrics* 99:e7, 1997.
6. Novembre E, Cianferoni A, Bernardini R, et al. Anaphylaxis in children: Clinical and allergologic features. *Pediatrics* 101:e8, 1998.
7. Liberman DB, and Teach SJ. Management of anaphylaxis in children. *Pediatr Emerg Care* 24:861–866, 2008.
8. Lin RY, Anderson AS, Shah SN, and Nuruzzaman F. Increasing anaphylaxis hospitalizations in the first 2 decades of life: New York State, 1990–2006. *Ann Allergy Asthma Immunol* 101:387–393, 2008.
9. Popa VT, and Lerner SA. Biphasic systemic anaphylactic reactions: Three illustrative cases. *Ann Allergy* 53:151–155, 1984.
10. Stark BJ, and Sullivan TJ. Biphasic and protracted anaphylaxis. *J Allergy Clin Immunol* 78:76–83, 1986.
11. Sampson HA, Mendelson L, and Rosen J. Fatal and near fatal anaphylactic reactions to food in children and adolescents. *N Engl J Med* 327:380–384, 1992.
12. Douglas DM, Sukenick E, Andrade WP, and Brown JS. Biphasic systemic anaphylaxis: An inpatient and outpatient study. *J Allergy Clin Immunol* 93:977–985, 1994.
13. Brady WJ Jr, Lubner S, Carter CT, et al. Multiphasic anaphylaxis: An uncommon event in the emergency department. *Acad Emerg Med* 4:193–197, 1997.
14. Brazil E, and MacNamara AF. “Not so immediate” hypersensitivity—The danger of biphasic anaphylactic reactions. *J Accid Emerg Med* 15:252–253, 1998.
15. Lee JM, and Greenes DS. Biphasic anaphylactic reactions in pediatrics. *Pediatrics* 106:762–766, 2000.

16. Lieberman P. Biphasic anaphylactic reactions. *Ann Allergy Asthma Immunol* 95:217–226, 2005.
17. Smit DV, Cameron PA, and Rainer TH. Anaphylaxis presentations to an emergency department in Hong Kong: Incidence and predictors of biphasic reactions. *J Emerg Med* 28:381–388, 2005.
18. Ellis AK, and Day JH. Incidence and characteristics of biphasic anaphylaxis: A prospective evaluation of 103 patients. *Ann Allergy Asthma Immunol* 98:64–69, 2007.
19. Tole JW, and Lieberman P. Biphasic anaphylaxis: Review of incidence, clinical predictors, and observation recommendations. *Immunol Allergy Clin North Am* 27:309–326, 2007.
20. Jarvinen KM, Amalanayagam S, Shreffler WG, et al. Epinephrine treatment is infrequent and biphasic reactions are rare in food-induced reactions during oral food challenges in children. *J Allergy Clin Immunol* 124:1267–1272, 2009.
21. Mehr S, Liew WK, Tey D and Tang ML. Clinical predictors for biphasic reactions in children presenting with anaphylaxis. *Clin Exp Allergy* 39:1390–1396, 2009.
22. Confino-Cohen R, and Goldberg A. Allergen immunotherapy-induced biphasic systemic reactions: Incidence, characteristics, and outcome: A prospective study. *Ann Allergy Asthma Immunol* 104:73–78, 2010.
23. Sampson HA, and Ho DG. Relationship between food-specific IgE concentrations and the risk of positive food challenges in children and adolescents. *J Allergy Clin Immunol* 100:444–451, 1997.
24. Sampson HA. Utility of food-specific IgE concentrations in predicting symptomatic food allergy. *J Allergy Clin Immunol* 107:891–896, 2001.
25. Perry TT, Matsui EC, Conover-Walker MK, and Wood RA. The relationship of allergen-specific IgE levels and oral food challenge outcome. *J Allergy Clin Immunol* 114:144–149, 2004.
26. Spergel JM, Beausoleil JL, Fiedler JM, et al. Correlation of initial food reactions to observed reactions on challenges. *Ann Allergy Asthma Immunol* 92:217–224, 2004.
27. 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. □

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