

1 **Update on Egg Allergy and Influenza Vaccine (Nov 2011)**

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5 **Background**

6  
7 Influenza vaccines are grown in eggs and there has been concern that residual egg protein  
8 (ovalbumin) could cause allergic reactions in egg-allergic recipients. However, all studies to  
9 date have suggested that this risk is very low,<sup>1-7</sup> and the vaccine provides substantial  
10 protection against the morbidity and mortality associated with influenza disease.<sup>8</sup> This  
11 update reflects changes to recommendations for administration of trivalent influenza vaccine  
12 (TIV) to egg-allergic patients based on several studies, most published in the last 2 years.<sup>1-7</sup>  
13 New guidelines have also been issued by the Centers for Disease Control and Prevention's  
14 (CDC) Advisory Committee on Immunization Practices (ACIP)<sup>9</sup> (see Figure) and the  
15 American Academy of Pediatrics' (AAP) Committee on Infectious Diseases ("Red Book"  
16 committee).<sup>10</sup>

17  
18 **Conclusions:**

19  
20 **1. The risks of vaccinating egg-allergic patients with influenza vaccine are outweighed**  
21 **by the risks of not vaccinating.**

22  
23 In 7 published studies, over 1600 patients with egg allergy have been vaccinated without any  
24 serious reactions.<sup>1-7</sup> 0-6.3% of vaccinations have involved reactions confined to the skin, e.g.  
25 hives. 0-4.8% of vaccinations have involved mild respiratory or gastrointestinal symptoms. No  
26 reactions have involved symptoms of hypotension. None of these reactions required  
27 treatment with epinephrine. One study using an adjuvanted H1N1 vaccine included an  
28 additional 3,640 patients with reported, but not proven, egg allergy given influenza vaccine;  
29 1.2% had skin reactions, 0.7% had respiratory reactions including 2 that were given  
30 epinephrine, although the authors conclude that these were not anaphylactic reactions.<sup>3</sup> In  
31 studies that included non egg-allergic controls, similar rates of reactions are reported.<sup>1, 3, 4, 6</sup>

32  
33 On average 294,128 people, including 21,156 children under 5 years of age, are hospitalized  
34 each year in the United States due to influenza,<sup>11</sup> and an average of 23,607 die.<sup>12</sup> Much of  
35 this morbidity and mortality can be prevented by vaccination<sup>13</sup> and it is likely that some of  
36 these preventable hospitalizations and deaths include patients not vaccinated because they  
37 are egg-allergic.

38  
39 **2. Patients who believe they are allergic to eggs should be evaluated by an allergist**  
40 **but, for those with a history of hives only after egg ingestion, this need not delay**

41 **influenza vaccination.**

42  
43 Persons with a history of suspected egg allergy should be evaluated by an allergist <sup>14</sup> where  
44 history and prick skin testing or specific in vitro IgE antibody testing for egg can determine  
45 whether or not they are egg allergic. Even patients with confirmed egg allergy can receive  
46 influenza vaccine. <sup>9, 10</sup> For those with a history of hives only after egg ingestion, the vaccine  
47 can be administered in a primary care setting with appropriate precautions as below, and  
48 such immunization can proceed even prior to additional evaluation of the egg allergy. <sup>9, 10</sup> For  
49 those with more severe reactions after egg ingestion, egg allergy evaluation and influenza  
50 vaccination can both be accomplished in the allergist's office. <sup>9, 10</sup>

51  
52 **3. In all studies to date, even patients with a history of anaphylaxis to egg ingestion**  
53 **have been safely administered the influenza vaccine.**

54  
55 The studies on influenza vaccine in egg-allergic patients have included 185 patients with  
56 histories of anaphylaxis to egg ingestion, and all have tolerated the vaccine without serious  
57 reactions. <sup>1, 3, 4, 6, 7</sup>

58  
59 **4. Skin testing with the influenza vaccine itself in egg-allergic individuals does not**  
60 **identify patients who are at increased risk of reacting to the vaccine and is not**  
61 **recommended.**

62  
63 When influenza vaccine skin testing was done in egg-allergic patients, subjects with positive  
64 skin test results had no reactions, or no greater rate of reactions, than those with negative  
65 skin test results. <sup>1, 2, 4, 6, 7</sup> The rate (low) of reactions (minor) is the same whether skin testing  
66 is included in the protocol or not. <sup>2</sup> Skin testing has greater utility when evaluating patients  
67 with allergic reactions to influenza vaccine itself. <sup>15</sup>

68  
69 **5. Influenza vaccine can be administered as a single dose to egg-allergic patients.**

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71 Some studies of influenza vaccine in egg-allergic patients have given 10% of the dose and, if  
72 no reaction in 30 minutes, given the remaining 90%. The vast majority of patients ultimately  
73 tolerate the entire dose, <sup>1-7</sup> and studies giving the vaccine as a single dose also report no  
74 serious reactions. <sup>3, 4, 6, 7</sup> The CDC and AAP have stated that persons who have experienced  
75 hives only following ingestion of egg should receive influenza vaccine and that vaccine skin  
76 testing and dividing the dose are not necessary or recommended. <sup>9, 10</sup> They recommend that  
77 patients with a history of more severe reactions be referred to an allergist before receipt of  
78 vaccine. <sup>9, 10</sup> Studies support a single dose even in these patients; of the 185 patients  
79 reported with a history of anaphylaxis or severe reaction to egg ingestion who have been  
80 vaccinated with TIV, 119 receive a divided dose and 66 received a single dose, all without

81 developing serious reactions.<sup>1, 3, 4, 6, 7</sup>

82  
83 **6. Egg-allergic individuals should receive influenza vaccine in a setting where**  
84 **anaphylaxis can be recognized and treated and should be observed for 30 minutes**  
85 **after vaccination.**

86  
87 Given the possibility of allergic reactions to any vaccine, and the theoretically increased risk  
88 for influenza vaccine in egg-allergic patients, providers who administer vaccinations should  
89 have proper resuscitative equipment available in the office to manage anaphylaxis.<sup>16</sup> Those  
90 with a history of hives only after egg ingestion can receive the vaccine in a primary care  
91 provider's office, while those with a history of more severe reactions should receive the  
92 vaccine in an allergist's office, where additional expertise is available should it be required.<sup>9,</sup>  
93 <sup>10</sup> All egg-allergic patients receiving influenza vaccine should be observed for 30 minutes  
94 after vaccination, similar to the waiting period after allergen immunotherapy.<sup>9, 10</sup> Egg allergic  
95 individuals should not receive their influenza vaccine from a pharmacy or other non-medical  
96 office setting.

97  
98 **7. All influenza vaccines available in the US contain low amounts of ovalbumin.**

99  
100 Vaccines used in studies on administration of influenza vaccine to egg-allergic recipients  
101 have contained as much as 0.7 mcg of ovalbumin per 0.5 mL dose without serious reactions.  
102 <sup>7</sup> It is not known if there is an amount of ovalbumin per dose that would be associated with a  
103 higher rate of reactions or more severe reactions.

104  
105 All of the manufacturers of injectable influenza vaccines report the maximum amount of  
106 ovalbumin per 0.5 mL dose in their package inserts or will provide the information on request  
107 (Table). All of the claimed amounts are below 1 mcg per 0.5 mL dose. When the actual  
108 amount of ovalbumin in the vaccines has been measured in independent laboratories, the  
109 levels have been much lower than the claimed amounts.<sup>17-19</sup>

110  
111 **8. All studies to date have evaluated injectable trivalent inactivated vaccine (TIV) and**  
112 **thus TIV, rather than intranasal live attenuated influenza vaccine (LAIV) should be**  
113 **used for egg-allergic patients.**<sup>9, 10</sup>

114  
115 **Summary**

116  
117 The risk of an allergic reaction to influenza vaccine in patients with egg allergy is very low,  
118 likely due to the very low amount of ovalbumin in the vaccines. Any such theoretical risk is  
119 far outweighed by the very real risk of such patients remaining unvaccinated. Thus all  
120 patients with egg allergy of any severity, including anaphylaxis, should receive influenza

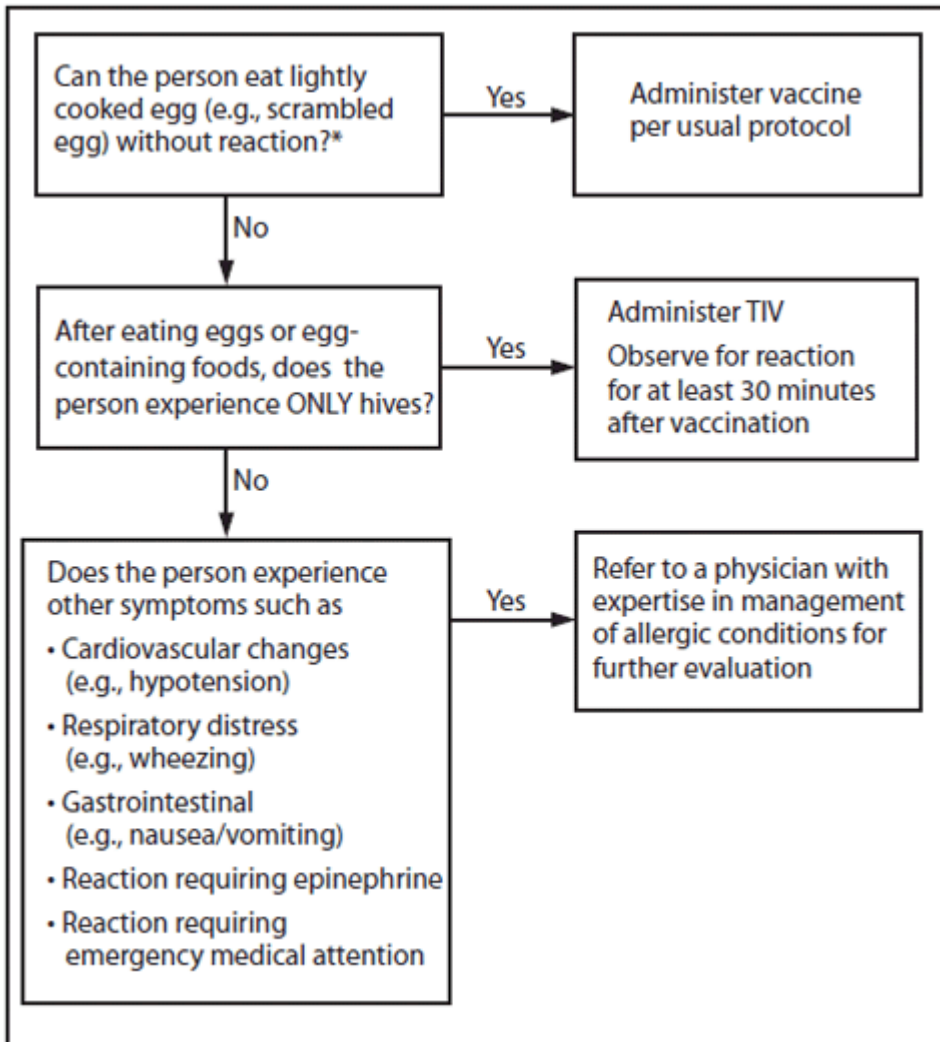
121 vaccine. Skin testing with the vaccine and dividing the dose are not necessary. The  
122 injectable vaccine should be administered in a medical setting where anaphylaxis can be  
123 recognized and treated should it occur. For those with a history of hives only after egg  
124 ingestion, the vaccine can be administered in the primary care provider's office. For those  
125 with more serious reactions to egg ingestion, the vaccine should be administered in an  
126 allergist's office.

## 127 REFERENCES

- 128 1. James JM, Zeiger RS, Lester MR, Fasano MB, Gern JE, Mansfield LE, et al. Safe administration of  
129 influenza vaccine to patients with egg allergy. *J Pediatr* 1998; 133:624-8.
- 130 2. Chung EY, Huang L, Schneider L. Safety of influenza vaccine administration in egg-allergic patients.  
131 *Pediatrics* 2010; 125:e1024-30.
- 132 3. Gagnon R, Primeau MN, Des Roches A, Lemire C, Kagan R, Carr S, et al. Safe vaccination of patients  
133 with egg allergy with an adjuvanted pandemic H1N1 vaccine. *J Allergy Clin Immunol* 2010; 126:317-23.
- 134 4. Greenhawt MJ, Chernin AS, Howe L, Li JT, Sanders G. The safety of the H1N1 influenza A vaccine in egg  
135 allergic individuals. *Ann Allergy Asthma Immunol* 2010; 105:387-93.
- 136 5. Owens G, Macginnitie A. Higher-ovalbumin-content influenza vaccines are well tolerated in children  
137 with egg allergy. *Journal of Allergy and Clinical Immunology* 2011; 127:264-5.
- 138 6. Howe LE, Conlon AS, Greenhawt MJ, Sanders GM. Safe administration of seasonal influenza vaccine to  
139 children with egg allergy of all severities. *Ann Allergy Asthma Immunol* 2011; 106:446-7.
- 140 7. Webb L, Petersen M, Boden S, Labelle V, Bird JA, Howell D, et al. Single-dose influenza vaccination of  
141 patients with egg allergy in a multicenter study. *Journal of Allergy and Clinical Immunology* 2011;  
142 128:218-9.
- 143 8. Fiore AE, Uyeki TM, Broder K, Finelli L, Euler GL, Singleton JA, et al. Prevention and control of influenza  
144 with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010.  
145 *MMWR Recomm Rep* 2010; 59:1-62.
- 146 9. Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on  
147 Immunization Practices (ACIP), 2011. *MMWR Morb Mortal Wkly Rep* 2011; 60:1128-32.
- 148 10. Recommendations for prevention and control of influenza in children, 2011-2012. *Pediatrics* 2011;  
149 128:813-25.
- 150 11. Thompson WW, Shay DK, Weintraub E, Brammer L, Bridges CB, Cox NJ, et al. Influenza-Associated  
151 Hospitalizations in the United States. *JAMA: The Journal of the American Medical Association* 2004;  
152 292:1333-40.
- 153 12. Estimates of deaths associated with seasonal influenza --- United States, 1976-2007. *MMWR Morb*  
154 *Mortal Wkly Rep* 2010; 59:1057-62.
- 155 13. Fiore AE, Uyeki TM, Broder K, Finelli L, Euler GL, Singleton JA, et al. Prevention and control of influenza  
156 with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010.  
157 *Morbidity & Mortality Weekly Report* 2010; 59:1-62.
- 158 14. Boyce JA, Assa'ad A, Burks AW, Jones SM, Sampson HA, Wood RA, et al. Guidelines for the diagnosis  
159 and management of food allergy in the United States: report of the NIAID-sponsored expert panel.  
160 *Journal of Allergy and Clinical Immunology* 2010; 126:S1-58.
- 161 15. Kelso JM, Li JT, Nicklas RA, Blessing-Moore J, Cox L, Lang DM, et al. Adverse reactions to vaccines. *Ann*  
162 *Allergy Asthma Immunol* 2009; 103:S1-14.
- 163 16. General recommendations on immunization --- recommendations of the Advisory Committee on  
164 Immunization Practices (ACIP). *Morbidity & Mortality Weekly Report* 2011; 60:1-64.
- 165 17. Li JT, Rank MA, Squillace DL, Kita H. Ovalbumin content of influenza vaccines. *J Allergy Clin Immunol*  
166 2010; 125:1412-3.
- 167 18. Waibel KH, Gomez R. Ovalbumin content in 2009 to 2010 seasonal and H1N1 monovalent influenza  
168 vaccines. *J Allergy Clin Immunol* 2010; 125:749-51, 51 e1.
- 169 19. McKinney KK, Webb L, Petersen M, Nelson M, Laubach S. Ovalbumin content of 2010-2011 influenza  
170 vaccines. *Journal of Allergy and Clinical Immunology* 2011; 127:1629-32.

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FIGURE. Recommendations regarding influenza vaccination for persons who report allergy to eggs ---  
Advisory Committee on Immunization Practices (ACIP), 2011--12 influenza season



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\* Persons with egg allergy might tolerate egg in baked products (e.g., bread or cake). Tolerance to egg-containing foods does not exclude the possibility of egg allergy.

179 TABLE. Ovalbumin content of injectable trivalent Influenza vaccines (TIV) approved for the 2011-12 season  
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Brand name	Manufacturer	Approved ages	Ovalbumin content (mcg per 0.5 mL dose*)†
Afluria	CSL Biotherapies (Merck)	≥ 9 years	≤ 1
Fluarix	GlaxoSmithKline	≥ 3 years	≤ 0.05
FluLaval	ID Biomedical Corporation of Quebec (GlaxoSmithKline)	≥ 18 years	≤ 1
Fluvirin	Novartis	≥ 4 years	≤ 1
Fluzone	Sanofi Pasteur	≥ 6 months	~0.1
Fluzone High-Dose	Sanofi Pasteur	≥ 65 years	~0.1
*Dose 0.25 mL 6-35 months, 0.5 mL ≥ 3 years			
† Information in package inserts except Fluzone and Fluzone High-Dose from Sanofi Pasteur by telephone (1-800-822-2463) or e-mail ( <a href="mailto:MIS.Emails@sanofipasteur.com">MIS.Emails@sanofipasteur.com</a> )			

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