

BSACI POSITION STATEMENT

Clinical & Experimental Allergy

Swine flu vaccination in patients with egg allergy

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Swine flu, a new subtype of influenza A virus H1N1, not previously detected in pigs or humans has arrived in the United Kingdom in recent months with hundreds and thousands of cases already confirmed in both adults and children. The World Health Organisation (WHO) has raised the threat level to Phase 6 (pandemic) to reflect the ongoing community outbreaks of swine flu throughout the world. So far in the United Kingdom, most cases have been mild but clustering of cases shows infectivity and with an anticipated increase in cases towards the autumn, a potential winter crisis looms. International data show the age profile of affected subjects is predominantly in children especially young children and young adults up to age 30 years. The WHO has reported that fatalities have occurred in pregnant women, those with significant comorbidities and also in previously healthy young individuals. The Department of Health (DoH) is planning a mass vaccination programme as soon as the pharmaceutical industry produces sufficient quantities of an effective vaccine. Swine flu vaccine is likely to be manufactured in a similar manner to the currently available influenza vaccines by inoculating embryonated chicken eggs with the virus. The vaccine will then be extracted from the extra-embryonic fluid by chemically inactivating the virus that is then further treated and purified. Consequently influenza vaccines contain measurable quantities of egg protein [1] with both fatal and non-fatal anaphylaxis reported following administration [2, 3]. Therefore, there is a potential risk of allergic reaction for the 1–2% of children who have egg allergy [4] and a significant number of adults who have either persisting or adult-onset egg allergy.

Each year the European Pharmacopoeia publishes guidance on the maximum allowable ovalbumin content of influenza vaccines. Up to the end of 2005, conventional split and subunit influenza vaccines were allowed to contain a maximum of 1 µg ovalbumin per dose, whereas virosomal influenza vaccines were permitted < 50 ng/dose. In an apparent retrograde step, however, from 2006 all influenza vaccines were permitted a maximum ovalbumin content of up to 1 µg/dose [5, 6]. Therefore, virosomal vaccines can no longer be relied upon to contain safe quantities of egg protein for the egg-allergic population. Furthermore, there is considerable variation in egg protein content between different brands of influenza vaccine and even between batches of the same vaccine [7]. Therefore, recommendations based on vaccine type that are applicable to the total egg-allergic population are not possible.

Current guidelines on influenza vaccination

So what are the current guidelines for administering influenza vaccine to subjects with egg allergy? The evidence suggests that vaccination is generally safe if the egg allergy is mild and therefore, the DoH recommends avoiding vaccination only in individuals with 'confirmed anaphylactic hypersensitivity to egg products (DoH green book)'. The American Academy of Pediatrics advises influenza vaccination in children with mild or local manifestation of allergy to egg, but not in subjects with a history of systemic anaphylactic symptoms, such as generalized urticaria, hypotension, or manifestations of upper or lower airway obstruction [8]. Hence, it is patients with severe egg allergy who have the potential to develop anaphylaxis after vaccination [9–12] with the risk of allergic reactions related to the ovalbumin content of the vaccine.

Swine flu vaccination

So what can be done for this group? One option is to avoid vaccinating individuals with significant egg allergy and allow herd immunity to act as a fire break. However, this is likely to prove unpopular and adequate herd immunity may

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not be achieved in time to protect non-vaccinated individuals against infection with the swine influenza virus. Therefore, strategies for vaccinating as many egg-allergic individuals as possible will have to be developed in order to limit the numbers to whom vaccination is denied. A further option is to use a vaccine with a low ovalbumin content. In patients with evidence of specific IgE and a history of severe egg hypersensitivity, vaccination with one-tenth dose followed at 30 min with the remaining nine-tenth dose was tolerated without any adverse reaction in 83 children. The vaccine used in the study contained no more than 0.6 µg egg protein per 0.5 mL dose. A single booster injection 1 month after the initial vaccination was tolerated by all 34 recipients who needed a second dose [13]. However, current influenza vaccines have a maximum ovalbumin content of 1 µg per 0.5 mL dose (2 µg/mL) that is higher than the level in above study.

Vaccine selection

The Standards of Care Committee of the BSACI has proposed that an influenza vaccine with an ovalbumin content of below 1.2 µg/mL (but preferably much lower) is used in all subjects with a history of egg allergy. Furthermore, the DoH should ensure that one or more manufacturers are encouraged to produce a swine flu vaccine with an ultra-low ovalbumin content that could be specifically reserved for individuals with severe egg allergy. This could be achieved using a new mammalian cell-based technique, which is both faster and more efficient than using eggs as a culture medium and unlikely to be contaminated with egg protein. Each batch should state the maximum ovalbumin content.

Patient selection

1. Patients with a relatively minor egg allergy who are able to tolerate foods containing moderate amounts of cooked egg or who only develop local symptoms after consuming a reasonable quantity of either lightly cooked or raw egg (such as a teaspoon of scrambled egg) should be vaccinated at the GP surgery with the usual precautions in place.
2. Patients with more severe egg allergy who have positive skin tests or RASTs to egg and with symptoms on exposure to small amounts of egg or a history of severe swelling or systemic features such as respiratory compromise or generalized urticaria should be referred to an allergy clinic for further assessment and vaccination if this is deemed appropriate.
3. Patients with poorly controlled asthma should also be referred to an allergy clinic regardless of the severity of the egg allergy.

Although skin testing with vaccine to predict hypersensitivity remains contentious, it is recommended that patients with severe egg allergy undergo skin testing with the

vaccine before administration. Vaccines resulting in a negative skin prick may be administered in two divided doses (1/10+9/10) 30-min apart with full resuscitation facilities available. If the skin test is positive, the risks should be explained and alternative options discussed with the patient including treatment with antiviral agents such as Oseltamivir (*Tamiflu*) and Zanamivir (*Relenza*). If influenza vaccination is the chosen option, then depending on the perceived risk the vaccine should be administered using either the two-dose protocol or a multiple graded-dose challenge/desensitization protocol [14, 15]. This procedure should only be undertaken by allergists experienced in treating anaphylaxis, following informed consent.

Conclusion

In summary, in all egg-allergic individuals, the risk of an allergic reaction to the influenza vaccine needs to be assessed against the risk of significant illness of infection with swine influenza. For the majority of egg-allergic individuals with mild egg allergy, the vaccine may be safely administered following routine vaccine precautions. For more severe egg allergy this may need to be done under observation in hospital, but no egg-allergic patient should be refused swine influenza vaccination without full assessment and discussion of the risks and benefits. The production of a low egg-content swine influenza vaccine is essential to ensure patient safety.

References

- 1 O'Brien TC, Malonet C, Tauraso MN. Quantitation of residual host protein in chicken-embryo-derived vaccines by radial immunodiffusion. *Appl Microbiol* 1971; 21:780-2.
- 2 Retailiau HF, Curtis AC, Storr G, Caesar G, Eddins DL, Hattwick MA. Illness after influenza vaccination reported through a nationwide surveillance system, 1976-1977. *Am J Epidemiol* 1980; 111:270-8.
- 3 Bierman CW, Shapiro GG, Pierson WE, Taylor JW, Foy HM, Fox JP. Safety of influenza vaccination in allergic children. *J Infect Dis* 1977; 136:S652-5.
- 4 Eggesbo M, Botten G, Halvorsen R, Magnis P. The prevalence of allergy to egg: a population-based study in young children. *Allergy* 2001; 56:403-11.
- 5 European Pharmacopoeia 01/2005:0158. Influenza vaccine (split virion, inactivated).
- 6 European Pharmacopoeia 01/2005:0869. Influenza vaccine (surface antigen, inactivated).
- 7 Chaloupka I, Schuler A, Marschall M, Meier-Ewert H. Comparative analysis of six European influenza vaccines. *Eur J Clin Microbiol Infect Dis* 1996; 15:121-7.
- 8 American Academy of Pediatrics. Influenza. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red book: 2006 report of the committee on infectious diseases*, 27th ed. Elk Grove Village, IL: American Academy of Pediatrics, 2006; 401-11.

- 9 Ratner B, Untracht S. Egg allergy in children; incidence and evaluation in relation to chick-embryo-propagated vaccines. *AMA Am J Dis Child* 1952; **83**:309–16.
- 10 Miller JR, Orgel HA, Meltzer EO. The safety of egg-containing vaccines for egg-allergic patients. *J Allergy Clin Immunol* 1983; **568**–73.
- 11 Murphy KR, Strunk RC. Safe administration of influenza vaccine in asthmatic children hypersensitive to egg proteins. *J Pediatr* 1985; **106**:931–3.
- 12 Anolik R, Spiegel W, Posner M, Jakobovics E. Influenza vaccine testing in egg sensitive patients. *Ann Allergy* 1992; **68**:9.
- 13 James JM, Zeiger RS, Lester MR *et al*. Safe administration of influenza vaccine to patients with egg allergy. *J Pediatr* 1998; **133**:624–8.
- 14 Zeiger RS. Current issues with influenza vaccination in egg allergy. *J Allergy Clin Immunol* 2002; **110**:834–40.
- 15 Madaan A, Maddox DE. Vaccine allergy: diagnosis and management. *Immunol Allergy Clin North Am* 2003; **23**:555–88.