

**Guidelines for the administration of Influenza vaccine
in Children with Egg allergy
BSACI-PAG Guideline 2008**

Final version

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1. Introduction

Influenza vaccine is usually contra-indicated in individuals with severe egg allergy because of the risk of adverse reaction. The vaccine is prepared in hens' eggs and contains varying amounts of egg protein. Influenza vaccine is currently recommended for high-risk groups, but wider use of influenza immunisation is likely to be recommended in the event of an avian influenza pandemic and the risk to benefit ratio for influenza vaccination is likely to change. Egg allergy is one of the commonest childhood food allergies and a significant number of children may be excluded from potentially beneficial vaccination. This guideline aims to provide guidance on influenza vaccination in children where egg allergy is suspected or confirmed.

2. Indications and contraindications for Influenza vaccination

In the UK influenza vaccination is currently recommended for all individuals >65 years and all individuals aged > 6 months in high risk groups (Table 1)¹. There is little evidence that influenza vaccination reduces asthma exacerbations in asthmatic individuals². A Cochrane review (2003) on influenza vaccination in individuals with asthma did not demonstrate significant benefit from influenza vaccination in preventing asthma exacerbations³. A subsequent large randomised double-blind placebo-controlled trial in children aged 6-18 years showed no significant reduction in the number, duration or severity of asthma exacerbations due to influenza type illness in children who received the influenza vaccine.⁴ A retrospective population cohort study in children aged 1-6 year indicated that this group had a reduction of asthma exacerbations over a 3 year period with influenza vaccination.⁵

Contra-indications for influenza vaccine are a confirmed history of anaphylaxis to a previous dose of the vaccine, confirmed anaphylaxis to any component of the vaccine, or confirmed anaphylaxis to hen's eggs¹. There is a paucity of published data on the risk of allergic reaction to influenza vaccine in egg allergic individuals. In a large population based study in the USA in 1976, there were 11 episodes of non fatal anaphylaxis in 48 million doses. None of the patients with anaphylaxis to the

influenza vaccine reported a prior history of egg allergy.⁶ A case of fatal anaphylaxis following influenza vaccine in an egg allergic child has been reported.⁷

There is insufficient evidence of benefit of influenza vaccine in asthmatic children to outweigh potential risk of adverse reaction in egg allergic asthmatic children. There is limited published evidence on the risks versus benefits of influenza vaccine in children in other groups of high risk patients such as chronic renal failure and decision to administer the influenza vaccine in egg allergic children should be made on an individual basis.

3. Possible dosage schedules for administration in egg allergic children

A few small studies^{8,9} and one larger multicentre study¹⁰ provide some evidence that influenza vaccine may be safely administered to egg allergic individuals when certain safety precautions are taken. Zeiger has published a proposed algorithm for administering influenza vaccination to patients with egg allergy.¹¹ It is important to note that these studies are too small to assess the risk of anaphylaxis for egg allergic individuals who receive the influenza vaccine.

The study by James et al was a prospective multicentre controlled clinical trial of 83 individuals with egg allergy confirmed by skin testing with egg and a convincing clinical history or oral food challenge. 27 of these patients had a convincing history of anaphylaxis to egg. Influenza vaccine was administered in 2 split doses 30 minutes apart; the first dose was 1/10th and the second dose 9/10th of the recommended dose. The 124 control subjects without egg allergy received a standard single dose of the vaccine. Skin prick tests to the vaccine were positive in 4 patients with egg allergy and 1 control subject. All patients with egg allergy tolerated the 2 dose vaccination protocol without any significant allergic reaction.¹⁰ It is important to note that the content of egg protein in the vaccines used was known and was less than 1.2µg/ml in all cases. Currently available influenza vaccines in the UK are now required to provide information on their maximum egg content. Some show a maximum egg protein content of 1µg per 0.5ml dose (2µg/ml) which is higher than the level in the study by James et al.

A graded multi-dose protocol has been proposed for administration of the influenza vaccine to individuals with severe egg allergy. Anolik et al used a graded multi-dose protocol in 8 egg allergic children with no adverse reaction.⁹ In a small study by Murphy and Strunk, a multi-dose protocol was successfully used in 6 children with egg allergy⁸. One child had mild wheezing which was treated with inhaled bronchodilators.

The American Academy of Paediatrics Red Book suggests a 5 step multi-dose protocol in a setting with full resuscitation facilities. Doses are administered intramuscularly 15-20 minutes apart:¹² This is time-consuming and unlikely to be

practical if the need arises for mass immunisation in the event of an outbreak of pandemic avian influenza.

Further study is needed to develop a safe protocol for the administration of influenza vaccine to children with severe egg allergy. Children who tolerate moderate amounts of egg in their current diet can receive the standard single dose of influenza vaccine regardless of past history of egg allergy or evidence of sensitisation to egg on skin testing or specific IgE.

Recommendation:

- Influenza vaccine is prepared on hen's eggs and may contain small amounts of egg protein. There is a risk of anaphylaxis for individuals with severe egg allergy.
- Individuals who tolerate foods containing moderate amounts of egg can receive the standard dose of influenza vaccine regardless of past history of egg allergy or evidence of sensitisation to egg on skin testing or specific IgE
- Only vaccines with a stated maximum egg content <1.2mcg/ml (0.6mcg per dose) should be used in egg allergic children.
- Individuals with severe egg allergy should only receive the influenza vaccine where careful assessment indicates that the benefits outweigh the risk of reaction. Consider referral to an allergy clinic.
- If influenza vaccine is administered to individuals with severe egg allergy, this should be done in a centre experienced in the management of anaphylaxis. Current evidence favours a split-dose regime of 1/10th the dose intramuscularly followed by a further intramuscular injection 30 minutes later.
- Note that the two doses of influenza vaccine 4-6 weeks apart are recommended in children between 6 months and 13 years old because of suboptimal responses to the vaccine, both should be provided in a centre experienced in the management of anaphylaxis.
- During the 2008/09 season BSACI-PAG are running a prospective audit of the safety of these guidelines. All immunisations under this schedule should be recorded, as should any adverse events.
- Serum for tryptase (5-10mL) should be taken if there is an adverse event, and the timing of the sample recorded in hospital notes. If serum tryptase is not available locally, measurement of tryptase and other mast cell mediators can be arranged through Dr Lajeunesse. Please arrange with your laboratory to spin and freeze a serum sample for later analysis.

References:

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- ¹ Department of Health guidelines August 2006. www.doh.gov.uk
- ² Carroll W, Burmiksher R. Is there any evidence for influenza vaccine in children with asthma? *Arch Dis Child* 2007 92(7):644-645
- ³ Cates CJ, Jefferson TO, Bara AI, Rowe BH. Vaccines for preventing influenza in people with asthma (Cochrane Review 2003).
- ⁴ Bueving HJ, Roos MDB, Van der Wouden JC et al. Influenza vaccination in children with asthma. *Am J Resp Crit Care Med* 2004 169: 488-493
- ⁵ Kramarz P, De Stefano F, Garguillo P et al. Does influenza vaccination reduce exacerbations in children? *J Pediatr* 2001 138:306-10
- ⁶ Retalliau HF, Curtis AC, Hartwick MA et al. Illness after influenza vaccination reported through a nationwide surveillance system 1976-1977. *Am J Epidemiol* 1980 111:270-278
- ⁷ Bierman CW, Shapiro GG, Fox JP et al. Safety of influenza vaccination in allergic children. *J Infect Dis* 1977 136:S652-655
- ⁸ Murphy KR, Strunk RC. Safe administration of influenza vaccine in asthmatic children hypersensitive to egg protein. *J Pediatr* 1985 106:931-933
- ⁹ Anolik R, Spiegel W, Posner M, Jakobovics E. Influenza vaccine testing in egg sensitive patients. *Ann Allergy* 1992; 68:69
- ¹⁰ James JM, Zeiger RS, Lestor MR, et al. Safe administration of influenza vaccine to patients with egg allergy. *J Pediatr* 1998;133:624-8.
- ¹¹ Zeiger RS. Current issues with influenza vaccination in egg allergy. *J Allergy Clin Immunol* 2002 110(6): 834-840
- ¹² Pickering LK (editor) 2006 Red Book: Report of the Committee of Infectious Diseases 27 edition. American Academy of Paediatrics

Table 1: Indications for influenza vaccine:

Clinical risk category	Some examples
Chronic respiratory disease including asthma	This includes chronic obstructive pulmonary disease, including disease (COPD) including chronic bronchitis and asthma emphysema, and such conditions as bronchiectasis, cystic fibrosis, interstitial lung fibrosis, pneumoconiosis and bronchopulmonary dysplasia (BPD). Asthma requiring continuous or repeated use of inhaled or systemic steroids or with previous exacerbations requiring hospital admission. Children who have previously been admitted to hospital for lower respiratory tract disease.
Chronic heart disease	This includes congenital heart disease, hypertension with cardiac complications, chronic heart failure and individuals requiring regular medication and/or follow-up for ischaemic heart disease
Chronic renal disease	Including nephritic syndrome, chronic renal failure, renal transplantation
Chronic liver disease	Including cirrhosis, biliary atresia, chronic hepatitis
Diabetes requiring insulin or oral hypoglycaemics	
Immunosuppression	Due to disease or treatment. Including asplenia or splenic dysfunction and HIV infection at all stages. Patients undergoing chemotherapy leading to immunosuppression. Individuals on or likely to be on systemic steroids for more than a month at a dose equivalent to prednisolone at 20mg or more per day (any age) or for children under 20kg a dose of 1mg or more per kg per day. <i>However, some immunocompromised patients may have a suboptimal immunological response to the vaccine.</i>