MMR vaccination of children with egg allergy is safe

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ABSTRACT

INTRODUCTION: Measles, mumps and rubella (MMR) vaccination is part of the Danish Childhood Vaccination Programme. It is known that children may react with anaphylaxis to MMR vaccines containing traces of egg protein. In Denmark, national clinical guidelines recommend that children with egg allergy be referred to vaccination at a paediatric ward despite changed recommendations in other countries. The purpose of this study was to determine whether children with egg allergy presented with anaphylactic/allergic reactions to MMR vaccination and to discuss whether Danish recommendations should be upheld.

MATERIAL AND METHODS: Data collected through evaluation of the histories of children referred to the Paediatric Ward at Hillerød Hospital from 01.01.2008 to 28.02.2011 and coded according to the following action and/or supplementary diagnoses in the International Classification of Diseases 10 (ICD-10) for suspected (DZ03.8+) or confirmed food allergy (DK52.2, DK52.2A) and oedema angioneurotica (DT78.3) as well as the procedure code for oral food challenges (ZZ4392M, ZZ4392N).

RESULTS: The 32 patients had received a total of 41 doses of MMR vaccine. None of them had shown anaphylactic/allergic reactions to the MMR vaccines. 23% of the vaccines were given with considerable delay.

CONCLUSION: Based on our study, we conclude that the Priorix MMR vaccine may be administered just as safely to children diagnosed with egg allergy as to other children. We found no evidence in support of the current Danish recommendations. We therefore recommend that the Statens Serum Institut, the Danish Paediatric Society and/or the Danish Health and Medicines Authority reconsider these recommendations.

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skin prick test or positive to specific immunoglobulin E (IgE) to egg and had been MMR vaccinated. Patients for whom sufficient documentation was unavailable were excluded.

**Trial registration:** not relevant.

**RESULTS**
A total of 36 patients with egg allergy were indentified. Four patients with egg allergy were excluded for the following reasons: lack of information concerning MMR vaccination (two patients) and insufficient diagnostic criteria (two patients). The average age at the time of diagnosis was < 1 year. Of the 32 included patients, ten had showed sensitivity to egg both in a skin prick test and based on positive specific IgE to egg (IgE class > 2), 18 in skin prick test only, and four based on positive specific IgE only.

The diagnostic criteria are presented in **Table 1.** Oral challenge with egg was carried out 18 times in all on a total of 12 patients. Eleven were positive, one was inconclusive and six were negative in patients who had all shown definite allergic reactions to egg. Of the 12 patients, nine were positive. The three patients with negative oral challenges had all been challenged following the first MMR vaccination. At the time of vaccination, a definite positive anamnesis of reaction to egg existed for these three patients. Five patients presented with asthmatic symptoms when provoked with egg, three patients showed no asthmatic symptoms, and in four cases information was missing from the medical history.

A total of 15 patients had chronic asthma as comorbidity, 14 showed no symptoms of asthma and in three cases there was no information of existing asthma symptoms.

The 32 patients had been given a total of 41 doses of MMR vaccine. The distribution is presented in **Figure 1.**

![Figure 1](image)

**FIGURE 1**
MMR vaccination status.

The Priorix vaccine used in Denmark consists of living attenuated measles virus (Schwarz), living attenuated mumps virus (RIT 4385, derived by Jeryl Lynn) and living attenuated rubella virus (Wistar RA 27/3), and it may therefore contain egg protein [3]. It is thus recommended that patients who are allergic to egg be vaccinated at a paediatric ward [9]. Approximately two thirds of our patients had been vaccinated at a paediatric ward.

**DISCUSSION**
The Priorix vaccine used in Denmark consists of living attenuated measles virus (Schwarz), living attenuated mumps virus (RIT 4385, derived by Jeryl Lynn) and living attenuated rubella virus (Wistar RA 27/3), and it may therefore contain egg protein [3]. It is thus recommended that patients who are allergic to egg be vaccinated at a paediatric ward [9]. Approximately two thirds of our patients had been vaccinated at a paediatric ward.

All of the 32 patients had been vaccinated with MMR vaccine without developing anaphylactic or allergic reactions, regardless of the severity of their egg allergy, except for one patient who developed a small urticarial wheal at the site of injection and was treated with antihistamine. There were no reports of late reactions. Several of the patients presented with anaphylactic reactions including respiratory distress and Quincke’s
oedema when exposed to egg, and several showed symptoms of chronic asthma. Co-morbidity in the form of severe bronchial asthma is a risk factor that may lower the threshold of egg protein required to cause anaphylaxis [5]. Several of the patients suffered from severe chronic asthma, but none of them reacted to the vaccine.

Earlier reports have described anaphylactic reactions to MMR vaccination, but most of these relate to children who were not allergic to egg [2]. This suggests that other allergens than egg protein, such as gelatine, present at high concentration in the vaccine may cause the described anaphylactic reactions [5, 6].

Skin prick testing with MMR vaccine prior to vaccination has been used in an effort to predict hypersensitivity to the vaccine, but it has proven an invalid screening method to determine which patients are at risk [11].

A total of 23% of the MMR vaccines were given with delay. The number may be higher, since only the year and not the patients’ exact age at the time of vaccination were recorded due to the design of the study. One patient was not MMR-vaccinated until the year in which he turned 15 years old. Low vaccination coverage results in insufficient immunity of the population and increases the risk of new measles epidemics. It was mainly patients referred to a paediatric ward for vaccination who were vaccinated with delay.

Vaccines against influenza, influenza A, yellow fever and Central European encephalitis may also contain egg protein [12]. Whether influenza A vaccination of children with egg allergy can take place in general practice may be important in future epidemics, where referral to a paediatric ward is likely to delay potential vaccination and to cause parent concern, the result of which may be that their children are not vaccinated and remain at risk of infection. A prospective registration of all patients with verified egg allergy who fulfill all clinical criteria for vaccination with influenza A vaccine may be considered. In an American study, Chung EY et al demonstrated that persons allergic to egg may be safely vaccinated with influenza vaccine by giving the vaccine in two increasing doses [13] and, in a Canadian study, Gagnon R et al found that it was safe to give influenza A vaccine to persons allergic to egg [14], although these findings are, of course, subject to the specific type of vaccine and methods of production.

CONCLUSION

Based on our study, we cannot say anything about the relative risk that children with egg allergy may react with anaphylaxis to MMR vaccination, but our study supports the findings of foreign studies showing that the amount of egg protein in the MMR vaccine is not high enough to cause an IgE mediated allergic reaction in children with egg allergy [5]. In the present Danish material, which includes patients with a severe reaction to egg, no reaction to MMR vaccination was shown. However, it is necessary to bear in mind that different methods of production of different vaccines may lead to different amounts of egg protein in the final vaccine [4]. Prior life-threatening reaction to exposure to egg as well as co-morbidity with severe asthma bronchiale are risk factors that may lower the threshold value of egg protein required to cause anaphylaxis [5]. Several of the patients suffered from severe chronic asthma, but none of these patients reacted to the vaccine.

Based on our study, we conclude that the Priorix MMR vaccine may be administered just as safely to children diagnosed with egg allergy as to other children while observing standard vaccine safety precautions in general practice, but that an assessment based on the risk of anaphylaxis must be made based on the ana­

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CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk.

LITERATURE

1. www.ssi.dk/Vaccination/Boernevaccination/
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