

RESEARCH LETTER

Vaccines and atopic/allergic children: A survey among private paediatricians

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To the Editor,

The identification, assessment, and management of vaccine reactions, as well as vaccinations of atopic and allergic patients, particularly egg-allergic patients, have received several recent recommendations.^{1,2} However, these recommendations are likely to be read mostly by practitioners specialized in infectious diseases or allergy rather than by primary care general practitioners or paediatricians.

Our aim was to evaluate the vaccination practices of private non-specialized paediatricians concerning atopic and egg-allergic children and their attitude towards general vaccine reaction, by means of an online questionnaire. We proposed this survey to the 2300 paediatricians of the French Association of Private Pediatricians (AFPA) between October 2014 and March 2015. Twenty-five questions were asked on (i) demographic and epidemiological data of the responder (gender, age, length of practice, number of vaccines performed per week, number of vaccine reactions seen per year, epinephrine availability in office), (ii) preventive measures taken with an atopic child (ie child with past or ongoing atopic dermatitis), (iii) preventive measures taken for influenza and measles, mumps, and rubella (MMR) vaccines in egg-allergic children, and (iv) 2 clinical cases: a 12-month-old infant, preterm with chronic lung disease, with wheezing and hives 30 minutes after MMR and influenza vaccines, suggesting an anaphylactic reaction, and a second case of an 11-month-old infant developing a maculopapular rash 24 hours after his second pentavalent dose (DTCaPolioHib), evocative of a non-specific non-allergic reaction (suspected diagnosis; suspected culprit vaccine components; proposed laboratory investigations; and attitude regarding child revaccination).

Table 1 summarizes the main responses of the 350 paediatricians who took the survey (response rate 15.2%; 270 women, 77.4%; mean age 51.6 ± 12.3 years). Their mean length of practice was

18 ± 15.6 years. Virtually all respondents performed more than 5 vaccinations per week ($n = 336$, 96%), and half of them performed more than 30 per week ($n = 163$, 46.6%). A majority ($n = 207$, 59.1%) was confronted to vaccine reactions (once or twice a year, 87%). Before vaccinating an atopic child, 26 paediatricians (7.4%) took preventive measures such as sequential vaccination (5.25%), antihistamine intake prior to vaccination (2.75%), vaccine delay (0.9%), or no vaccine (0.3%). In egg-allergic children, respectively one-third and about two-thirds of the paediatricians did not recommend MMR and influenza vaccine, preferring in 51.7% for the latter vaccine to refer the child to an allergist.

In the first clinical case, 320 paediatricians (91.1%) identified the diagnosis of a post-MMR/influenza vaccines anaphylactic reaction. Possible culprits among vaccine components were poorly known, except for egg (Table 2). Blood tests were requested by a large majority of respondents (95.6%), consisting of egg IgE: $n = 170$, 47.6%; total IgE: $n = 39$, 11%; latex IgE: $n = 33$, 9.4%; tryptase: $n = 20$, 5.6%; Phadiatop[®]: $n = 20$, 5.6%; gelatin IgE: $n = 19$, 5.4%; and more surprisingly influenza IgE: $n = 12$, 3.4%; and measles IgE: $n = 12$, 3.4%. Most of them ($n = 292$, 83.4%) addressed the child to an allergist, particularly for delivering the second MMR dose in a hospital environment ($n = 308$, 88%). To note, 19 paediatricians (5.4%) intended to revaccinate the child themselves after premedication with antihistamines, 14 (4%) with no precaution, and 9 (2.6%) stopped the vaccination schedule. For this first case, 293 paediatricians (83.7%) achieved correct diagnosis and management.

In the second case of generalized delayed reaction to DTCaPolioHib vaccine, only 48 paediatricians (13.7%) falsely diagnosed an allergic reaction. Investigations were not proposed. Two paediatricians (0.6%) ceased immunization, 23 (6.6%) offered to revaccinate the child with an antihistamine premedication, 255 (72.9%) without

TABLE 1 Main responses of 350 French private paediatricians interviewed on their practices concerning vaccination in atopic/allergic children

Questions	Paediatricians responses and/or behaviours	Expected responses
Vaccination and atopy	Special precautions (n = 26, 7.4%)	No vaccine precaution
MMR/influenza vaccines and egg allergy	No MMR vaccination (n = 116, 33.1%); allergist referral (n = 107, 30.6%) No influenza vaccination (n = 224, 64%); allergist referral (n = 181, 51.7%)	MMR and influenza vaccines possible in any egg-allergic child
Anaphylaxis post-MMR and influenza vaccines	Correct diagnosis (n = 320, 91.1%); laboratory investigations (n = 335, 96%); allergist referral (n = 292, 83.4%); future dose injected by themselves (n = 33, 9.4%)	No investigation (tryptase?), to refer to allergist 4-6 weeks later, to revaccinate in hospital
Delayed non-specific reaction post-pentavalent vaccine	Correct diagnosis (n = 302, 86.3%); laboratory investigations (n = 0); allergist visit (n = 70, 20%); future dose injected by themselves (n = 278, 79.4%)	To revaccinate with no precaution, to refer to allergist when suspecting serum sickness (highly uncommon)
Epinephrine in medical office	Absence n = 14 (9.4%)	Mandatory for all vaccinators

TABLE 2 Vaccine components suspected by a panel of 350 French private paediatricians in case of anaphylactic reaction after MMR and influenza vaccinations in a 12-month infant

Paediatricians responses	Expected responses
Egg	n = 260, 74.3% Yes, exceptional
Preservatives	n = 91, 26% Yes, exceptional
Microbial antigens	n = 68, 19.4% Yes
Gelatin	n = 43, 12.2% Yes
Aminoglycosides	n = 37, 10.6% Yes, exceptional
Aluminium hydroxide	n = 27, 7.7% Never described
Latex	n = 22, 6.3% Yes
Don't know	n = 78, 22.3% -

any special precaution, and 70 (20%) after an allergist's evaluation. Proper diagnosis and management were chosen by 254 paediatricians (72.6%).

We regret that only 15% of the French paediatricians have responded to the survey. On the other hand, this sample was representative of the profession as a whole in terms of sex, age, and length of practice. We found that atopy and egg allergy could modify, in very few occasions for the former and frequently for the latter, paediatricians' attitude towards vaccination. However, an atopic child does not require any special precautions before vaccination.¹ The same holds true for an egg-allergic child regardless of severity, both for MMR and influenza vaccines, which contain only negligible amounts of egg protein.³ Most French paediatricians, despite a pro-vaccine attitude, were not aware of this. The results of our survey were similar to those of an Italian study interviewing 268 primary care paediatricians on the vaccination of egg-allergic children.⁴ Overall, paediatricians are not aware that the vaccination of egg-allergic children does not require referral to an allergist, with only two exceptions: vaccinations against Japanese encephalitis (except for the new formulation) and yellow fever. These are the only vaccines containing up to one milligram of egg protein.^{2,3}

Anaphylactic vaccine reaction is exceptional (estimated risk of 1.31 per million vaccine doses²), but this risk warrants keeping

epinephrine in the office. In our study, about 10% of the paediatricians did not. Vaccine components suspected by paediatricians to induce anaphylaxis were clearly unfamiliar. According to the literature, the main culprits are tetanus and diphtheria toxoids, gelatin (stabilizer) for MMR, chickenpox and Japanese encephalitis vaccines, pneumococcal antigens and latex present in the vaccine preparation equipment.⁴⁻⁶ Formaldehyde, pertussis antigens, and casein found in the DTaP vaccine; some antibiotics (neomycin, gentamicin, polymyxin B, streptomycin) present in MMR, DTaP, and influenza; and *Saccharomyces cerevisiae* from the hepatitis B and human papillomavirus vaccines are infrequent.⁷ Recently, influenza hemagglutinins contained in influenza vaccines⁸ and CRM-197, a non-toxic variant of tetanus toxoid contained in the 13-valent pneumococcal vaccine,⁹ have also been reported. Laboratory investigations requested by many paediatricians have little to no value during the acute phase, except maybe serum tryptase.¹⁰ Referral to an allergist is mandatory for skin testing and for the determination of specific IgE when available, but also of specific IgM/IgG when indicated. The allergist is also required for supervising the in-hospital administration of subsequent vaccine doses.¹ After a general delayed skin reaction attributable to a vaccine, management is more straightforward with most paediatricians offering to revaccinate the child themselves. However, they have to be informed of the exceptional serum sickness (combining delayed urticaria, arthralgia, lymphadenopathy, fever, and proteinuria, elevated levels of specific IgG to vaccine 2-3 weeks after reaction) which should delay further vaccine doses as long as the IgG levels are elevated.⁵

In conclusion, this study shows that paediatricians need more education on vaccines and allergy, with a particular focus on vaccine in egg-allergic children, on vaccine components susceptible to induce anaphylaxis, and on laboratory tests to propose (or not) in case of anaphylactic reaction.

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