

Original Article

Canadian Allergists' and Nonallergists' Perception of Epinephrine Use and Vaccination of Persons with Egg Allergy

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What is already known about this topic? Despite published guidelines on epinephrine use and the safety of vaccination of persons with egg allergy, uncertainty persists among Canadian physicians about the management of anaphylaxis and measles, mumps, and rubella (MMR) and influenza vaccinations.

What does this article add to our knowledge? Allergists are more adherent to guidelines on intramuscular epinephrine use and the safety of MMR in persons with egg allergy. However, 25% of allergists and nonallergists would not administer epinephrine in cases of severe anaphylaxis.

How does this study impact current management guidelines? This survey identifies persistent knowledge gaps among physicians, confirming the need for more extensive education about epinephrine use and vaccination of persons with egg allergy.

BACKGROUND: Studies suggest knowledge gaps about epinephrine use and vaccination of persons with egg allergy.

OBJECTIVE: We compared the perception of Canadian allergists and nonallergists on issues related to epinephrine use and vaccination of persons with egg allergy.

METHODS: Canadian allergists, pediatricians, general practitioners/family physicians and emergency room physicians were recruited through medical associations and surveyed on these issues. Multivariate logistic regression models were used to identify determinants of specific responses.

RESULTS: One-hundred fourteen allergists and 613 nonallergists participated. For most issues with accepted best

practices, allergists were more likely to adhere to recommendations. Allergists versus nonallergists were more likely to recommend intramuscular epinephrine for anaphylaxis (odds ratio [OR] = 3.8; 95% CI, 1.43-10.11). Older physicians (OR = 0.98; 95% CI, 0.97-0.99), Canadian-Paediatric-Surveillance-Program participants (OR = 0.48; 95% CI, 0.24-0.96), family physicians (OR = 0.39; 95% CI, 0.16-0.96), and general practitioners (OR = 0.14; 95% CI, 0.04-0.52) were less likely to recommend intramuscular use. However, in severe anaphylaxis, >25% of both groups would not give epinephrine for patients presenting with breathing difficulties or hypotension. Use of epinephrine for severe anaphylaxis was less

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Supported by the Canadian Paediatric Surveillance Program, Canadian Society of Allergy & Clinical Immunology, Society of Rural Physicians of Canada, Canadian Association of Emergency Physicians, McGill University Health Centre, and Public Health Agency of Canada.

Conflicts of interest: M. Desjardins has received research support from the Public Health Agency of Canada and has received a travel grant from the American Academy of Allergy Asthma and Immunology. A. Clarke, R. Alizadehfar, H. Eisman, L. Joseph, G. Shand, and M. Ben-Shoshan have received research

support from the Public Health Agency of Canada. D. Grenier has received research support from the Public Health Agency of Canada; is the Medical Affairs Director; and is employed by the Canadian Paediatric Society. S. Carr has received consultancy fees from Merck and GlaxoSmithKline and has received lecture fees from Pfizer and Merck. T. K. Vander Leek has received research support from the Public Health Agency of Canada; has received consultancy fees from Graceway Pharmaceuticals, Pfizer Canada, and King Pharma; and has received lecture fees from Merck Canada, Mead Johnson Nutrition, and Pfizer Canada. L. Teperman and N. Higgins have received research support from the Public Health Agency of Canada and the Canadian Medical Protective Association.

Received for publication November 27, 2012; revised February 20, 2013; accepted for publication March 14, 2013.

Available online ■ ■ ■

Cite this article as: Desjardins M, Clarke A, Alizadehfar R, Grenier D, Eisman H, Carr S, et al. Canadian allergists' and nonallergists' perception of epinephrine use and vaccination of persons with egg allergy. *J Allergy Clin Immunol: In Practice*. <http://dx.doi.org/10.1016/j.jaip.2013.03.003>.

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2213-2198/\$36.00

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<http://dx.doi.org/10.1016/j.jaip.2013.03.006>

Abbreviations used

CAEP- Canadian Association of Emergency Physicians
 CPSP- Canadian Paediatric Surveillance Program
 CSACI- Canadian Society of Allergy and Clinical Immunology
d- Difference
 FP- Family physicians
 GP- General practitioners
 IM- Intramuscular
 MMR- Measles, mumps, and rubella
 SRPC- Society of Rural Physicians of Canada

likely in older physicians (OR = 0.97; 95% CI, 0.95-0.99), female physicians (OR = 0.60; 95% CI, 0.39-0.89), and those practicing in Ontario (OR = 0.56; 95% CI, 0.36-0.86), Manitoba (OR = 0.42; 95% CI, 0.19-0.90), or Nova-Scotia (OR = 0.31; 95% CI, 0.12-0.78). Allergists (OR = 6.22; 95% CI, 3.60-10.72) and physicians treating mainly children (OR = 3.41; 95% CI, 1.87-6.25), or practicing in Quebec (OR = 1.68; 95% CI, 1.12-2.55) were more likely to recommend measles-mumps-rubella vaccination in a community facility.

CONCLUSION: Knowledge gaps about mode and indications for epinephrine administration and vaccination policies need to be addressed in future education programs to ensure prompt epinephrine use and to avoid unnecessary restriction of vaccines. © 2013 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol: In Practice 2013;■:■-■)

Key words: Epinephrine use; Epinephrine autoinjectors; Egg allergy and vaccination; Knowledge gaps

Recent studies suggest an increased prevalence of food allergy and its most severe manifestation, anaphylaxis.¹⁻³ However, the number of allergists in training are insufficient to meet the current needs.⁴ Hence, other physicians, including pediatricians and general practitioners (GPs), are required to play a major role in the care of these patients.⁵ Yet, studies suggest that these physicians have substantial knowledge gaps.⁶ This led to the recent publication of Canadian consensus guidelines for anaphylaxis management in the primary care setting.⁷ This document discussed issues for which a consensus exists such as the necessity for immediate epinephrine delivery through the intramuscular (IM) route. However, it also acknowledged that certain aspects of anaphylaxis management remain controversial, such as whether moderate symptoms of an allergic reaction that may progress to anaphylaxis should prompt epinephrine administration and the age at which allergic children should start carrying their own epinephrine autoinjector. Similarly, for vaccination of persons with egg allergy, there are issues for which there is an accepted best practice and others which, until recently, remain disputed. It is now generally accepted that it is safe to administer the measles, mumps, and rubella (MMR) vaccine in community facilities in children with egg allergy, and the safety of the influenza vaccine in these children⁸ was only recently established.⁹ Given that some of the recommendations are relatively new and that certain issues remain unresolved, we aimed to characterize the perception of Canadian allergists and nonallergists toward the use of epinephrine and the vaccination of persons with egg allergy.

TABLE I. Demographic characteristics of 727 survey participants

	Allergists (n = 114)	Nonallergists (n = 613)
Age (y), median	45.0	49.0
Female (%)	51.3	56.6
English as preferred language of communication (%)	82.5	76.9
Medical associations		
CSACI (%)	73.7	-
CPSP (%)	21.9	82.9
SRPC (%)	-	6.4
CAEP (%)	-	10.6
Did not specify (%)	4.4	0.1
Medical specialty*		
Pediatrician (%)	-	81.2
GP/FP (%)	-	10.6
ERP (%)	-	10.8
Trained in Canada	88.5	83.3
Province		
British Columbia (%)	5.3	10.9
Alberta (%)	6.2	8.8
Saskatchewan (%)	2.6	2.3
Manitoba (%)	3.5	6.5
Ontario (%)	37.7	32.8
Quebec (%)	36.8	29.0
New Brunswick (%)	0.0	2.1
Nova Scotia (%)	4.4	3.5
Newfoundland (%)	3.5	2.2
Prince Edward Island (%)	0.0	0.5
Yukon (%)	0.0	0.7
Northwest Territories (%)	0.0	0.7
Patient age group		
Treat mainly children (%)	51.9	81.1
Treat mainly adults (%)	13.9	5.6
Both adults and children (%)	29.6	11.3
Does not treat patients with food allergies (%)	4.6	2.0
Type of clinical practice		
Hospital only (%)	37.6	37.2
Community only (%)	33.0	28.1
Both (%)	29.4	34.7

ERP, Emergency room physicians.

*Answers in this category are not mutually exclusive.

METHODS

A survey was distributed to Canadian allergists and nonallergists (pediatricians, family physicians [FPs], GPs, and emergency room physicians) through their respective medical associations, including the Canadian Society of Allergy and Clinical Immunology (CSACI), the Canadian Paediatric Surveillance Program (CPSP), the Society of Rural Physicians of Canada (SRPC), and the Canadian Association of Emergency Physicians (CAEP). Allergists were queried through both a hard copy of this survey distributed at the annual CSACI meeting (2010) and a Web-based questionnaire.

CPSP participants were queried through a 1-time mailed questionnaire (http://www.web.cps.ca/English/surveillance/CPSP/studies/food_allergy_survey.pdf), whereas SRPC and CAEP

members received only a Web questionnaire (all distributed between October 2010 and October 2011). Participants were queried on issues related to the use of epinephrine and vaccination of persons with egg allergy, including the route of administration of epinephrine during an allergic reaction, symptoms of an allergic reaction that should prompt epinephrine administration, and age at which allergic children should start carrying their own epinephrine autoinjector. Participants were also asked on their recommendations for MMR and influenza vaccinations of persons with egg allergy. We compared the answers between allergists and nonallergists with 95% CIs.

We examined determinants of the correct response to questions for which clinical guidelines existed at the time of the survey; that is, the preferred route of epinephrine is IM, epinephrine is absolutely indicated in severe allergic reactions that cause respiratory symptoms or hypotension, and MMR can be safely given in a community facility in persons with egg allergy. Given that no best practice for other issues is generally accepted, it was felt not to be informative to examine determinants of various responses to these issues. Multivariate logistic regression models were used to examine the association between a correct response and physician factors (age, sex, belonging to a certain medical association

TABLE II. Recommendations from Canadian allergists and nonallergists about epinephrine use and vaccination of persons with egg allergy

	Allergists (%)	Nonallergists (%)	Difference between the 2 groups (%)	95% CI
Epinephrine use				
What is the preferred route for epinephrine administration for a patient with an anaphylactic reaction to a food allergen?				
Subcutaneous	2.2	20.1	-17.9	-23.3 to -12.4
Intramuscular	93.3	70.5	22.8	15.7 to 30.3
Intravenous	3.3	7.9	-4.6	-9.6 to 0.6
Other	1.2	1.5	—	—
For a patient with a documented IgE-mediated food allergy, would you recommend the use of an epinephrine autoinjector? (Check all that apply)				
Immediately after exposure	21.0	30.1	-9.1	-18.5 to 0.3
Itchy or few hives	30.0	31.8	-1.8	-12.0 to 8.6
Swelling or generalized hives	68.0	61.7	6.3	-4.2 to 16.9
GI symptoms	64.0	52.1	11.9	1.1 to 22.7
Breathing difficulties, feels weak or faint	74.0	72.6	1.4	-8.6 to 11.3
Other	0.0	1.7	—	—
At what age would you recommend that a child (<18 y) start self-carrying an epinephrine autoinjector, rather than leaving the responsibility to someone else?				
School entry, 5-7 y	52.8	40.5	12.3	0.5 to 24.2
High school entry, 12-14 y	25.8	36.4	-10.6	-21.2 to 0.1
Leave the decision to parents	15.7	14.2	1.5	-7.2 to 10.3
Other	5.7	8.9	—	—
Vaccination of persons with egg allergy				
For a patient with a confirmed IgE-mediated egg allergy, would you recommend immunization for MMR?				
I would not recommend it	3.1	5.0	-1.9	-6.4 to 2.7
In community facilities/private office	51.0	20.9	30.1	18.9 to 41.4
Physician is present	34.4	39.2	-4.8	-15.9 to 6.2
Only in a hospital	4.2	12.0	-7.8	-13.3 to -2.2
Allergist is present	5.2	14.7	-9.5	-15.57 to -3.49
Other	2.1	8.2	—	—
For a patient with a confirmed IgE-mediated egg allergy, would you recommend immunization for influenza?				
I would not recommend it	8.2	27.6	-19.4	-26.6 to -12.1
In community facilities/private office	3.1	3.2	-0.1	-3.9 to 3.8
Physician is present	40.2	27.2	13.0	1.9 to 24.0
Only in a hospital	11.3	12.5	-1.2	-8.7 to 6.4
Allergist is present	37.1	21.8	15.3	4.4 to 26.1
Other	3.2	10.9	—	—

GI, Gastrointestinal.

TABLE III. Determinants of responses among participants for issues with available clinical guidelines at the time of the survey

	OR (95% CI)
What is the preferred route for epinephrine administration for a patient with an anaphylactic reaction to a food allergen?	
Intramuscular	
Allergist	3.80 (1.43,10.11)
Age	0.98 (0.97, 0.99)
CPSP member	0.48 (0.24, 0.96)
FP	0.39 (0.16, 0.96)
GP	0.14 (0.04-0.52)
What is the preferred route for epinephrine administration for a patient with an anaphylactic reaction to a food allergen?	
If patient has breathing difficulties, feels weak or faint	
Treats mainly children	2.12 (1.35-3.33)
Trained in Canada	1.77 (1.06-2.98)
Private clinic	1.64 (1.02-2.63)
Age	0.97 (0.95-0.99)
Female	0.60 (0.39-0.89)
Working in Ontario	0.56 (0.36-0.86)
Working in Manitoba	0.42 (0.19-0.90)
Working in Nova Scotia	0.31 (0.12-0.78)
Would you recommend MMR immunization in the presence of IgE-mediated egg allergy?	
In community facilities/private office	
Allergist	6.22 (3.60-10.72)
Treats mainly children	3.41 (1.87-6.25)
Quebec	1.68 (1.12-2.55)

OR, Odds ratio.

[CSACI, CPSP, SRPC, CAEP], physician subgroups [allergist, pediatrician, GP/FP, or emergency room physician], country of training, province of residence, the main population treated [children, adults, or both], and type of practice [private clinic, hospital or both]). By comparing univariate and multivariate results, we were able to assess possible confounding factors. All statistical analyses were performed with R version 2.12.0 (2010-10-15). The survey was approved by the McGill University Health Centre Ethics Review Board.

RESULTS

One hundred fourteen allergists and 613 nonallergists responded (Table I). Among allergists, the participation rate was 74.5%. The participation rates through the CPSP 1-time survey, the SRPC, and the CAEP were 20.7%, 5.2%, and 10.0%, respectively.

Epinephrine use

Ninety-three percent (93.3%) of allergists stated that the preferred route of epinephrine administration was IM compared with 70.5% of nonallergists (difference [d] = 22.8%; 95% CI, 15.7%-30.3%; Table II). Among allergists, 2.2% selected the subcutaneous route compared with 20.1% of nonallergists (d = -17.9%; 95% CI, -23.3% to -12.4%). Less than 10% of physicians in both groups would give intravenous epinephrine for anaphylaxis.

When managing a documented food allergic reaction, allergists were less likely to give epinephrine for isolated cutaneous

reactions (ie, "if the patient feels itchy or has a few hives" or "swelling or generalized hives"; d = -4.6%; 95% CI, -8.6% to -0.6%; Table II) and more likely to give epinephrine for gastrointestinal symptoms (d = 11.9%; 95% CI, 1.1%-22.7%). Even if both allergists and nonallergists were more likely to administer epinephrine to patients with allergic reactions that caused systemic symptoms, >25% in both groups would not give epinephrine even in cases of severe anaphylaxis (defined as difficulty breathing or symptoms consistent with hypotension in the context of a documented IgE-mediated food allergic reaction). Most physicians indicated that children with diagnosed food allergy should start to carry their own epinephrine at approximately 5 to 7 years of age. However, allergists were more likely to recommend self-carry at this age than were nonallergists (d = 12.3%; 95% CI, 0.5%-24.2%).

Vaccination of persons with egg allergy

A greater proportion of allergists indicated that patients with egg allergy could receive MMR vaccine safely in a community facility (d = 30.1%; 95% CI, 18.9%-41.4%; Table II) as long as the immunization provider had an emergency kit that contained epinephrine and was familiar with its use. However, 12.0% of nonallergists compared with 4.2% of allergists recommended that MMR be administered only in a hospital facility in children with egg allergy (d = -7.8; 95% CI, -13.3% to -2.2%).

Fewer allergists than nonallergists recommended complete avoidance of the influenza vaccine (d = -19.4%; 95% CI, -26.6% to -12.1%; Table II) in persons with egg allergy. The most common approach among allergists was to recommend administration of the vaccine as long as a physician is present."

Determinants of responses

Allergists were 3.80 times (95% CI, 1.43-10.11 times) more likely to recommend IM use of epinephrine (Table III), whereas older physicians, CPSP participants, FPs, and GPs were less likely to use the IM route. Physicians treating mainly children, physicians trained in Canada, and physicians working in private clinics were more likely to use epinephrine in cases of severe anaphylaxis, whereas older physicians, female physicians, and physicians practicing in Ontario, Manitoba, and Nova Scotia were less likely to use epinephrine in this clinical situation. Allergists, physicians treating mainly children, and physicians working in Quebec were more likely to allow MMR vaccination of children with egg allergy in a community facility/private office.

DISCUSSION

This survey shows substantial disparities between allergists and nonallergists on the use of epinephrine and the vaccination of persons with egg allergy. For most issues with accepted best clinical practices, allergists were more likely to adhere to guidelines. Numerous other physician factors were also associated with preferred approaches.

Epinephrine use

Guidelines for anaphylaxis management recommend IM administration of epinephrine as first-line medication, because more rapid absorption and higher plasma concentrations have been shown with IM than with subcutaneous delivery.¹⁰ Intravenous administration is not recommended, because it increases the risk of side effects, including hypertension, arrhythmia, and

myocardial ischemia.¹¹ Although most allergists and nonallergists preferred the IM route, 20.1% of nonallergists still recommended subcutaneous use. This is in line with a previous study suggesting that up to a third of nonallergists will use the subcutaneous route.¹² The findings that older physicians, CPSP participants, FPs, and GPs were less likely to adhere to current recommendations about IM use are consistent with other studies that suggest higher adherence to guidelines among younger physicians¹³⁻¹⁵ and among specialists compared with generalists.¹⁶

The survey shows a substantial percentage of both allergists and nonallergists who underuse epinephrine for severe anaphylaxis, a situation in which it is absolutely indicated. Failure to administer epinephrine even in severe anaphylaxis may be attributed to the lack of a uniformly accepted anaphylaxis definition and the absence of an objective marker to confirm anaphylaxis. However, because delay in therapy can contribute to fatalities, guidelines should promote early use of epinephrine when symptoms involve major organs/systems.¹⁷ Physicians who treat mainly children, who were trained in Canada, or who work in private clinics were more likely to recommend use of epinephrine for severe anaphylaxis. Given the higher rates of anaphylaxis in children¹⁸ and in the northern hemisphere,¹⁹ it is possible that physicians who treat mainly children and who trained in Canada have a higher exposure to anaphylaxis and are more aware of guidelines. It is also possible that physicians who treat children and who work in private settings tend to be more cautious and to treat allergic reactions more promptly. The consistent negative association between physician age and adherence to guidelines observed in this survey suggests that educational programs that target older physicians are crucial. In contrast to other studies that suggest higher adherence among female,^{15,20,21} our data documented that female physicians were less likely to give epinephrine for severe anaphylaxis.²² Differences between Canadian provinces in adherence to guidelines have been previously observed,²³ and other studies ascribe a major effect of the geographic practice site on adherence to guidelines.²⁴

The CSACI in collaboration with Canadian food allergy advocacy groups recommend that children old enough to understand the proper use of the autoinjector (usually by grade 1 to 2) should carry their own and that additional autoinjectors be kept in accessible locations in school.²⁵ However, these recommendations are not yet incorporated in official policy and are still open for interpretation. Although our survey indicates that almost 50% of allergists and 40% of nonallergists recommend self-carry at school entry, almost a third in both groups recommend self-carry only in high school. A US study has shown that most pediatric allergists believe that patients should begin to share responsibility for anaphylaxis recognition and management by 12 to 14 years of age.²⁶ Further, approximately 15% of physicians recommend that the decision be left to the parents. Broader dissemination of autoinjector policies is required.

Vaccination of persons with egg allergy

The National Advisory Committee on Immunization confirmed in 1996 that the MMR vaccine (Mo-Ru Viraten Berna) licensed in Canada can be used safely in patients with egg allergy.²⁷ In concordance with this literature, a greater proportion of allergists recommended the vaccine administration in community facilities and/or private offices. Physicians who treat mainly children were also more likely to recommend vaccination in their

office, and they were likely more aware of vaccine policies, given that these vaccines are used mainly in infants. However, up to 25% of nonallergists unnecessarily restrict MMR administration to a hospital setting or an allergy clinic.

Pandemic and seasonal flu vaccines contain a variable amount of egg antigenic proteins, and, until recently, their safety was questioned in persons with egg allergy.⁹ However, even in this at-risk population, anaphylaxis after administration of the vaccine is rare,²⁸ and the only absolute contraindication is a prior severe reaction to the vaccine itself. Since our survey, the Quebec Allergy Association and the Advisory Committee on Immunization Practices released a position statement that stipulates that patients with egg allergy can be safely vaccinated against influenza.^{9,29} Our survey (administered before the release of these guidelines) showed that 27.6% of nonallergists and 8.2% of allergists considered egg allergy a contraindication for flu vaccine.

This survey has potential limitations. The participation rate among members of the CPSP (20.7%), SRPC (5.2%), and CAEP (10.0%) is low, although consistent with rates reported in similar studies.³⁰⁻³² Interestingly, studies that analyzed low response rates among physicians in surveys suggest that selection bias is not a substantial problem.^{30,33,34} Further, even if an assumption is made that low participation rates result in selection bias, given that those who participate are reported to be more confident in their knowledge and aware of current guidelines, it is anticipated that the gaps identified in this survey may actually have been underestimated.^{35,36} Another potential limitation might have been the use of different recruitment methods for physicians, but these were mandated by the pertinent medical associations and could not be modified. Again, other studies have shown that the use of different strategies to distribute questionnaires among physicians does not lead to selection bias.³⁷ It is also possible that a subset of the 25% of allergists and nonallergists who would not have recommended epinephrine for respiratory symptoms and/or symptoms compatible with hypotension did not consider these symptoms in the context of an allergen exposure and considered these symptoms only in isolation. Hence, given that they did not necessarily attribute these symptoms to allergen exposure, they did not believe that there was sufficient indication to administer epinephrine. However, it was not possible to re-contact these participants, given that they completed the survey anonymously, and repeat survey of members was not permitted by their corresponding medical associations. In addition, a previous US study showed that a similar percentage of pediatricians (28% of participants) would not treat a clear food-induced anaphylaxis with epinephrine.³⁸

A greater proportion of allergists than nonallergists adheres to current guidelines/literature recommendations. Knowledge gaps were identified that need to be addressed in future educational programs to ensure prompt delivery of epinephrine, when there is a concern that the reaction is progressing to anaphylaxis and to avoid unnecessary restriction of MMR and influenza vaccines. Physicians who are less likely to adhere to current recommendations, including older, nonspecialist physicians, and physicians working in certain provinces, should be particularly targeted. These recommendations should be continuously updated to reflect advances in care.

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