Safe administration of yellow fever vaccine in patients with suspected egg allergy

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Background: The evidence available in the literature on the administration and safety of the yellow fever vaccine in patients with egg allergy is limited.

Objective: We sought to describe the administration of yellow fever vaccine in children with suspected egg allergy using a simplified protocol.

Methods: Children referred to the service from February 2018 to January 2020 with a history of possible egg allergy were classified as probably egg-allergic or not on the basis of history and specific IgE testing. A vaccine prick test was performed only in those with a history of an anaphylactic reaction to egg ingestion and if the result was positive the vaccine was administered in a 2-step protocol (2 equal doses of 0.25 mL with an interval of 30 minutes between the 2 applications). All other children received the vaccine as a single dose.

Results: A total of 435 children were evaluated; 48.27% were probably not allergic, and 51.72% were probably allergic to egg, of which 32.88% were considered anaphylactic. A total of 414 (95.2%) children had no vaccine reactions. Of the 21 (4.8%) children who had some reaction, 10 experienced a local reaction, 9 a mild skin reaction distant from the vaccine site, 1 presented local cutaneous reaction distant to the vaccination site, and 1 patient developed possible anaphylaxis. The vaccine prick test did not predict a vaccine reaction (odds ratio, 1.29; 95% CI, 0.25-6.72; $P = .67$).

Conclusions: Yellow fever vaccine can be safely administered as a single dose in children with a confirmed or suspected egg allergy. (J Allergy Clin Immunol Global 2023;2:100089.)

Key words: *Child, infant, yellow fever, vaccination, food allergy, infectious disease, safety*

Abbreviation used:
YF: Yellow fever

Yellow fever (YF), an acute febrile infectious disease transmitted by arthropod vectors, is caused by a virus of the *Flavivirus* genus belonging to the *Flaviviridae* family.[1] More than 900 million people in tropical Africa and South America, as well as unvaccinated travelers entering endemic areas, are at risk of developing the disease, which is an acute hemorrhagic fever transmitted by mosquitoes (genus *Aedes*). Each year, 200,000 new cases of the disease occur worldwide, with a reported mortality rate of 20% to 50%. Approximately 50% of the patients who develop hemorrhagic complications end up dying, and there is no specific treatment for the disease.[2]

Vaccination against YF was introduced in 1937, representing to this day the most effective and important measure against the disease.[1] The are 2 types of vaccines available in Brazil, one is produced by Biomanguinhos-Fiocruz, which supplies YF vaccine to several parts of the world and is available through the Brazilian public network. The other vaccine is available in private clinics. Both are composed of live attenuated virus strain 17D-204, which has greater than 95% immunogenicity.[1] These vaccines are cultivated in chicken eggs and may contain in their formulation residual egg protein and sucrose, glutamate, sorbitol, bovine gelatin, erythromycin, kanamycin, L-histidine hydrochloride, L-alanine, and sodium chloride. During vaccine manufacture, the embryos were homogenized and centrifuged. Residual amounts of egg protein may be present in the YF vaccine because it does not undergo a heating process during its production. Varying levels of ovalbumin, between 0.067 μg/0.5 mL and 2.21 μg/0.5 mL, were documented in different batches of vaccines produced by manufacturers in the United States and the United Kingdom.[3] Despite the World Health Organization recommendation of only a single dose of YF vaccine for travelers, the Ministry of Health recommends for Brazilian children the vaccination schedule of 0.5 mL subcutaneous in 2 doses for children 9 months and older, with a booster at age 4 years.[4] This recommendation has been in effect since December 2019 and is based on 2 Brazilian studies that demonstrated an early drop in neutralizing antibody titers, cellular immunity, and immune memory among children vaccinated between age 9 months and 24 months. After 4 years of vaccination, less than 60% of the children had neutralizing antibody titers above the value considered protective.[5,6]

The ovalbumin as well other components of the YF vaccine may cause hypersensitivity and anaphylactic reactions in children.[7] The rate of anaphylaxis is 0.42/100,000 doses of the vaccine alone and 0.8/100,000 when administered with other vaccines.[8] The YF vaccine may be contraindicated in individuals with a history of

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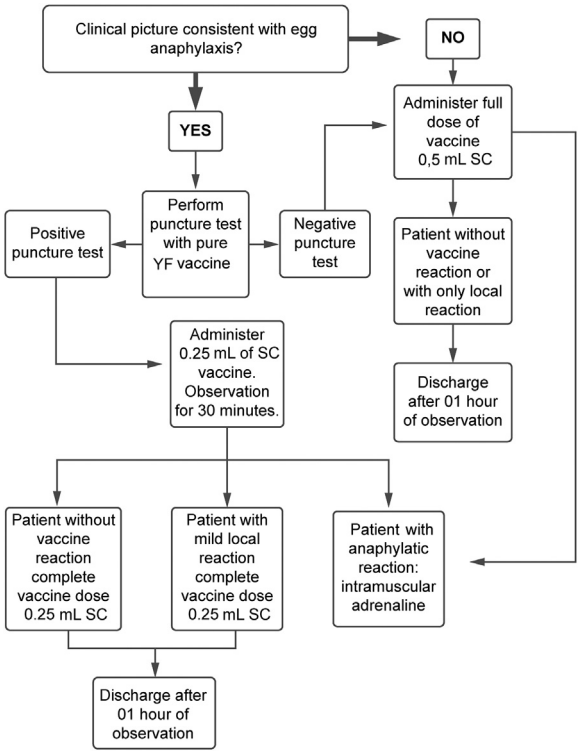

FIG 1. Vaccine protocol for the YF vaccine in egg-allergic children. *SC,* Subcutaneous.

anaphylaxis to previous doses or an allergy to the vaccine components.[9] The evidence available in the literature on the administration of the YF vaccine in egg-allergic patients is limited, with no randomized studies on the safety of the vaccine in this group of patients. Current recommendations indicate that individuals with mild nonanaphylactic reactions to egg protein can receive the vaccine under medical supervision in a medical facility equipped to treat anaphylactic reactions.[8] Patients with severe reactions to egg should be evaluated by a specialist to define the risk/benefit of the vaccine and the need for skin tests and desensitization protocols.[10,11]

Between 2017 and 2018, Brazil experienced one of the largest YF epidemics ever recorded. Because of the outbreak, the Ministry of Health conducted vaccination campaigns to control the disease and prevent the urbanization of the virus. The recommendation for vaccination was a single dose for the entire national territory.[12,13] We aimed to develop a vaccination protocol in partnership with the Minas Gerais State Health Department for the pediatric population that had not received the YF vaccine due to a suspected or confirmed egg allergy.

This study aimed to describe the use of the YF vaccine in children with a confirmed or suspected allergy to egg protein in the absence of complex screening and desensitization protocols and to determine whether the skin prick test with the vaccine may be used as a predictor of the vaccine reaction.

METHODS

This study was cross-sectional, analytical, and quantitative. The study was conducted at the João Paulo II Children's Hospital in Belo Horizonte, Brazil. The hospital is the reference center for infectious and rare diseases in the state of Minas Gerais and the municipalities that make up the microregion and the metropolitan region of the city of Belo Horizonte, offering free treatment linked to the Brazilian Unified Health System.The study was approved by the Ethical Committees of João Paulo II Children's Hospital and the Federal University of Minas Gerais (CAAE: 93598518.7.0000.5119 and CAAE: 93598518.7.3001.5149). Written informed consent was obtained from the legal guardians of the children.

The children were referred to the food allergy clinic of our institution from February 2018 to January 2020 for the YF vaccination. The children included in the study had a history or suspicion of egg allergy and may or may not have a true allergy. The sample of this study was nonprobabilistic because all the children that were referred to the clinic during the study period were considered for inclusion in this study. After obtaining detailed medical histories, the children were classified as "probably nonallergic" and "probably allergic" to egg. Those without a confirmed medical history of immediate reaction, an absence of a sensitization to egg protein (confirmed using a serum IgE level <0.35 kU_A/L for egg and its fractions performed up to 6 months before vaccination), and those who consumed egg or egg products without experiencing symptoms were considered to be "probably nonallergic" to egg. In contrast, those children with a medical history of immediate reaction and evidence of sensitization to egg protein (serum IgE level >0.35 kU_A/L for egg and its fractions) were classified as "probably allergic" to the egg. All the children included in the "probably allergic" group had a serum IgE test for egg or 1 of its fractions (>0.35 kU_A/L) performed in the last 6 months. The individuals in the "probably allergic" group were divided subsequently into the anaphylactic and nonanaphylactic reaction groups. Egg protein anaphylaxis was defined according to Sampson et al.[14]

A simplified protocol was developed for the administration of a YF vaccine in children with a suspected egg allergy (Fig 1). To avoid losing the window of opportunity to vaccinate as many egg-allergic children as possible during the YF pandemic, food oral challenge and serum IgE testing for egg allergy were not performed at the time of vaccination. Instead, the serum IgE test results for egg and its fractions performed in the last 6 months before vaccination were recorded. The children classified as "probably allergic" with no history of anaphylactic reactions received the full subcutaneous dose of the YF vaccine (0.5 mL). Those classified as "probably allergic" with a history of anaphylactic reactions were subjected to a prick test with the undiluted vaccine. The prick test was performed according to the Pepys technique, which defined a positive result as a wheal diameter (that was) at least 3 mm more than that of the negative control when read at 15 minutes.[15,16] The children with a positive test result received the vaccine divided into 2 equal doses (0.25 mL with an interval of 30 minutes between the 2 applications). The vaccine reactions were classified as local reactions, diffuse reactions limited to the skin (rash or urticaria and/or angioedema), and vaccine anaphylaxis.

Statistics

Data collected from medical records and interviews were transcribed and coded using the Excel 10.0 program. The database was later exported to Epi Info, statistical software developed by the Centers for Disease Control and Prevention. Initially, a descriptive analysis was performed, using calculations of the frequencies and percentages for the categorical variables and means and medians, with SDs or amplitudes for the continuous variables. Subsequently, to compare the quantitative variables with the categorical ones, the Kruskal-Wallis tests were used for asymmetric distributions and the ANOVA for symmetrical distributions. In the bivariate analysis of categorical variables, Pearson chi-square and Fisher exact tests were used. The magnitude of risk was assessed using the odds ratio, and the CIs of 95% were presented when both variables were dichotomous. The level of statistical significance was set at P less than .05.

RESULTS

During the study period, 435 children were referred to our food allergy clinic for YF vaccination with the diagnosis of an egg allergy. All 435 patients were included in the analysis, because there was no refusal to participate in the supervised vaccination

TABLE I. Clinical and immunologic characteristic of the study population

Characteristic	n	%
Sex		
Female	219	50.34
Male	215	49.66
Probably allergic to egg		
No	210	48.3
Yes	225	51.7
History of anaphylaxis	74	32.8
Prick test result with YF vaccine (n = 114)		
Positive	21	18.4
Negative	93	81.5
Vaccine reaction		
No	414	95.2
Yes	21	4.8
Nature of the reaction		
Local reaction	10	47.6
Mild skin reaction	10	47.6
Anaphylactic reaction	1	4.7

	Mean	SD	Median	Min-Max
Age (mo)	23.33	28.38	12	9-204
IgE whole egg (>0.35 kU_A/L) (n = 124)	7.76	14.20	2.50	0.1-100
IgE egg white (>0.35 kU_A/L) (n = 118)	8.12	15.65	2.2	0.1-100
IgE ovoalbumin (>0.35 kU_A/L) (n = 50)	5.08	7.73	1.91	0.1-4.82
IgE ovomucoid (>0.35 kU_A/L) (n = 45)	4.02	8.05	1.05	0.1-48.2

against YF. The descriptive analysis of the children in this study is presented in Table I. Two hundred sixteen (49.6%) individuals were male. The median age was 12 months, and 51% of the children were 12 months or younger.

Two hundred twenty-five children (51.7%) were classified as "probably allergic" to eggs. Of these, 32.8% (74 of 225) had a history of anaphylaxis to egg ingestion and underwent a skin prick test with the undiluted YF vaccine. Forty vaccine tests were performed on children who did not meet the study criteria for probable egg allergy, therefore belonging to the group of those probably not allergic to egg. Of these 40 vaccine test results, 6 were positive, of which 3 children had a local vaccine reaction. All of the 435 children were vaccinated successfully. Most of the participants (95.2%) experienced no vaccine reactions. Only 21 individuals (4.8%) reacted to the vaccine, of which 10 experienced a local reaction, 10 a mild skin reaction distant from the vaccine site (erythema, urticaria, and/or angioedema), and only 1 child developed an anaphylactic reaction that required an epinephrine injection. Among the children who reacted to the vaccine, only 2 had a positive skin test result, 7 had a negative vaccine prick test result, and 12 were not subjected to the skin test because there was no history of anaphylactic reactions. Ten children with vaccine reactions were classified as "probably not allergic" to egg, of which 4 had a skin reaction distant from the vaccine and the other local reactions restricted to the vaccination site. The average time for a vaccine reaction was 26 minutes, with the earliest reaction occurring 10 minutes and the latest 60 minutes after vaccine injection. The average age of children who had a vaccine reaction was 26 months, with a minimum age of 9 months and a maximum of 204 months. The characteristics of the children who had a vaccine reaction are presented in Table II.

The only possible anaphylactic reaction to the YF vaccine occurred in a 11-month-old female with mild atopic dermatitis, history of anaphylaxis to egg ingestion, and egg IgE level 13.5 ku/L, but with a negative skin prick test result for the undiluted YF vaccine. Twenty minutes after the administration of a single, subcutaneous 0.5-mL dose of the YF vaccine, she developed diffuse urticaria, vomiting, tachycardia, and irritability. Intramuscular epinephrine and oral antihistamines were administered with complete symptom resolution. The infant was discharged home asymptomatic after an observation period of 2 hours. Fig 2 shows the distribution of the vaccine protocol based on the result of the vaccine prick test.

Table III presents the comparison of the categorical and numerical variables between the children with and without a vaccine reaction. Table IV presents the comparison of the quantitative values of IgE according to the presence or absence of vaccine reaction. There were no statistically significant differences in vaccine reaction outcomes in relation to age, sex, and history of egg allergy. Furthermore, contrary to what was clinically expected, children with positive egg IgE values had fewer reactions than children with negative IgE values (odds ratio, 0.06; 95% CI, 0.01-0.27; $P < .01$), indicating a statistical association without clinical significance. The skin prick test with undiluted YF vaccine could not predict a reaction (odds ratio, 1.29; 95% CI, 0.25-6.72; $P = .67$).

DISCUSSION

The YF vaccine is highly efficacious, with an immunogenicity greater than 95%.[15] Most vaccine reactions are mild and include local pain, headache, malaise, and low-grade fever, occurring in approximately 1% of vaccinated individuals. The data provided

TABLE II. Characteristics of children with vaccine reaction

Age (mo)	Sex	Allergy classification	IgE value (kU_A/L)	Vaccine prick test	Vaccine reaction	Time (min)	Approach
13	F	Probably not allergic	Egg white <0.1	—	Fleeting rash	30	Antihistamine
12	F	Probably not allergic	Egg and ovomucoid <0.1	Negative	Local hives and rash	30	Antihistamine
10	M	Probable anaphylaxis	Egg 7.9	Negative	Hives	26	Antihistamine
12	F	Probably allergic	Egg 4.69 Egg white IgE 6.35	—	Erythema on the face	30	Antihistamine
11	M	Probably allergic	Egg white 3.95	—	Itchy rash in cubital fossa	30	Antihistamine
13	F	Probably not allergic	Egg IgE and its fractions negative	—	Hives on trunk and limbs	30	Observation
9	F	Probably not allergic	—	Negative	Local papules	21	Observation
10	M	Probably allergic	Egg 23	—	Local papules	18	Observation
9	M	Probably not allergic	—	—	Diffuse papules on trunk and limbs	20	Antihistamine
9	M	Probably not allergic	—	Negative	Local papules	15	Observation
10	F	Probably allergic	Egg white 100 Albumin 1.4 Ovomucoid 6.6	—	Local erythema	15	Observation
11	F	Possible anaphylaxis	Egg 13.5	Negative	AD history, rash, papules on trunk, face, and limbs followed by vomiting and irritability	20	Adrenaline IM single dose
12	F	Probably not allergic	Egg and fractions <0.1	—	Papules on neck and trunk	20	Antihistamine
204	F	Probably not allergic	Ovomucoid 10.3	Positive	Local urticaria	10	Antihistamine
19	M	Probable anaphylaxis	Egg 3.8	Positive	Erythema in abdomen	30	Observation
11	M	Probably not allergic	—	Negative	Local erythema	32	Antihistamine
37	F	Probably allergic	Egg 100 Albumin 13.5	—	Local papule	10	Antihistamine
83	M	Probably allergic	Egg 8.5	—	Hives	30	Antihistamine
11	F	Probably not allergic	—	—	Local papule	33	Antihistamine
24	F	Probable anaphylaxis	Egg 1.1 Ovomucoid 0.8	Negative	Papules on lower limbs	10	Antihistamine
15	M	Probably not allergic	—	—	Diffuse papules	40	Antihistamine

AD, Atopic dermatitis; *F*, female; *IM*, intramuscular; *M*, male.

by the Vaccine Adverse Event Reporting System have reinforced the safety of the YF vaccine, with more than 90% of adverse reactions being nonserious events with an anaphylaxis rate of 0.42/100,000 doses for the vaccine alone and 0.8/100,000 when administered with other vaccines.[8] The YF vaccine may also be related to 2 rare complications, the acute viscerotropic disease and neurotropic reactions, which are contraindications for subsequent doses.[1]

Other vaccines containing live attenuated viruses have egg proteins in their composition. The measles, mumps, and rubella (MMR) vaccine is manufactured in chicken embryo fibroblasts containing negligible amounts of egg protein, which is insufficient to cause hypersensitivity reactions. Therefore, all children with egg allergies, even those with an anaphylactic reaction, should receive the MMR vaccine.[17,18] Although the influenza vaccine is cultivated in allantoid fluid from embryonated chicken eggs, it has low concentrations of ovalbumin (<0.12 μg/mL). There is robust evidence that it can be safely administered to patients allergic to egg, even in those with a history of severe reactions.[19,20] The amount of ovalbumin in the YF vaccines is extremely variable, being reported by manufacturers in the United Kingdom to be between 0.13 and 0.61 μg/mL and in the United States from 2.43 to 4.42 μg/mL.[3] The Fiocruz/Biomanguinhos laboratory responsible for the production of Brazilian YF vaccine has indicated that although the amount of ovalbumin varies from batch to batch, it is always less than or equal to 5 μg/dose (Fiocruz/Biomanguinhos, personal communication, March 3, 2021).

Protocols for vaccinating patients allergic to any vaccine component are usually not validated. Skin testing with a vaccine is recommended frequently. However, data on the sensitivity and

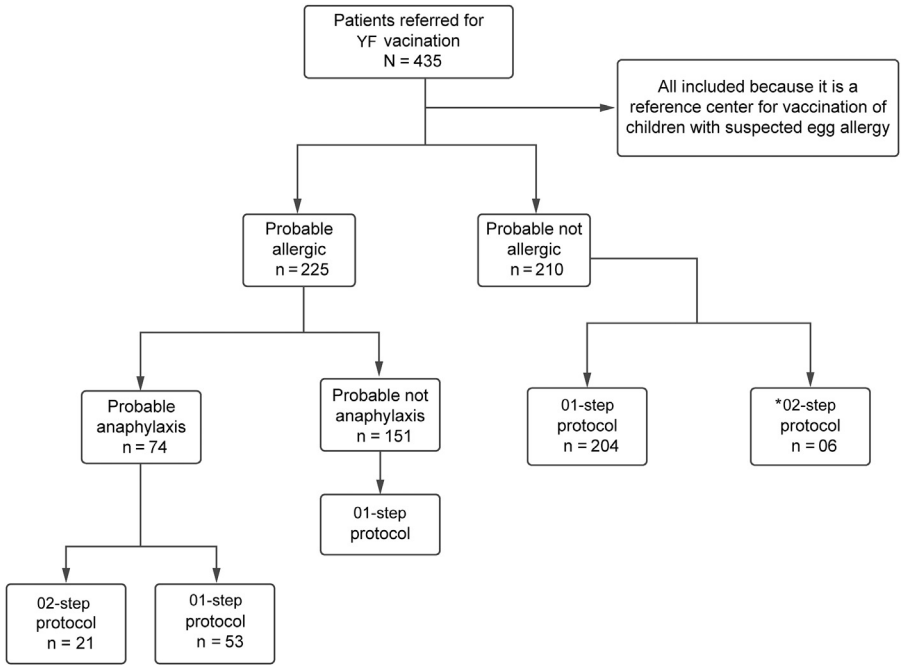

FIG 2. Distribution of the vaccine protocol based on the result of the vaccine prick test. *Six positive vaccine prick test results in patients who did not meet the study criteria for probable egg allergy.

TABLE III. Vaccine reaction and studied variables

Variable	Vaccine reaction		OR	95% CI	*P* value
	Yes	No			
Sex			1.33	0.55-3.23	.66(3)
Female	12 (5.5)	207 (94.5)			
Male	9 (4.2)	207 (95.8)			
Probably allergic to egg			1.41	0.41-4.92	.78(3)
Yes	18 (5.1)	335 (94.9)			
No	3 (3.7)	79 (96.3)			
Egg anaphylaxis			2.20	0.90-5.38	.12(3)
Yes	9 (7.9)	105 (92.1)			
No	12 (3.7)	309 (96.3)			
Vaccine prick test result (mm)			1.29	0.25-6.73	.67(3)
Positive	2 (9.5)	19 (90.5)			
Negative	7 (7.5)	86 (92.5)			
IgE/Egg (>0.35 kU_A/L) (N = 145)			0.06	0.01-0.27	<.001(3)
Positive	3 (2.4)	121 (97.6)			
Negative	6 (28.6)	15 (71.4)			
IgE/Albumin (>0.35 kU_A/L) (N = 59)			0.33	0.03-4.12	.39(3)
Positive	2 (4.0)	48 (96.0)			
Negative	1 (11.11)	8 (88.8)			
IgE/Ovomucoid (>0.35 kU_A/L) (N = 73)			0.92	0.14-5.93	1.0(3)
Positive	3 (6.7)	42 (93.3)			
Negative	2 (7.1)	26 (92.9)			
IgE/Egg white (>0.35 kU_A/L) (N = 133)			0.41	0.08-2.18	.27(3)
Positive	7 (5.93)	111 (94.06)			
Negative	2 (13.33)	13 (86.66)			

The number (3) refers to the Fisher exact test.

specificity of the vaccine skin test at different concentrations are scarce, which makes it unreliable in predicting or excluding vaccine reactions.[11,21] The most widely used protocol was proposed by Pickering et al, where the vaccine is administered in 5 progressive stages with intervals of 15 to 30 minutes until the total dose is achived.[9,15]

McCallum et al,[22] in a retrospective study, described their experience after evaluating 38 patients who were referred because

TABLE IV. Quantitative values of IgE and vaccine reaction

IgE value	n	Average	Dp	Median	ANOVA	Kruskal-Wallis
IgE/Egg white						
No reaction	110	8.9	16.4	12.5	0.67	0.09
Reaction	7	11.6	15.2	3.6		
Negative result	13					
IgE/Egg						
No reaction	121	9.6	15.3	18.7	0.55	0.67
Reaction	3	4.2	3.6	4.7		
Negative result						
IgE/Ovomucoid						
No reaction	42	6.4	9.8	3.5	0.92	0.65
Reaction	3	17.7	4.8	6.6		
Negative result	26					
IgE/Albumin						
No reaction	414	23.2	27.6	12.0	0.78	0.93
Reaction	21	25.1	42.3	12.0		
Negative result	0					

of the potential risk of a vaccine reaction. Twelve patients were vaccinated for YF uneventfully in this study, 9 of whom had been referred with an egg allergy.

Rutkowski et al[8] described 2 desensitization protocols for administering the YF vaccine to 6 egg-allergic patients referred to the Department of Allergy of the University of Cambridge Hospital Foundation between 2006 and 2012. The patients were 3 British Air Force military personnel aged 22 to 35 years and 3 children aged 2 to 8 years. All 6 patients had a positive prick test result for eggs, and 4 had a positive skin test result for the vaccine. All 6 individuals were vaccinated successfully without any reactions.[8] Gerhardt et al[23] demonstrated the safety of the YF vaccine in 43 patients known to be allergic to eggs. The vaccination protocol included a skin test with the YF vaccine and for egg white, ovalbumin, and ovomucoid. All the patients included in this study had a negative skin prick test result for the vaccine. Only 6 patients with a positive intradermal test result were submitted to the desensitization protocol, of which 3 had mild skin rash.[23]

Sharma et al[24] reported the experience of 2 tertiary pediatric hospitals in Australia over an-8-year period with the vaccination of 11 egg-allergic patients (age 11 months to 13 years), 2 of whom had egg anaphylaxis. Patients were considered allergic in the presence of a compatible clinical history associated with a positive prick test result. The decision to perform the vaccine skin test and the fractionation of vaccine doses was at the discretion of the attending physician. Of the 11 children vaccinated, 7 were submitted to the vaccine test with a negative result, and only 1 patient underwent the intradermal test, the result for which was also negative. These patients were vaccinated with a 2-step protocol (10% of the dose followed by the remaining 90% after a 30- to 60-minute observation period). The remaining 4 patients were vaccinated without a skin test, 3 in a 2-step protocol and 1 with a single dose of vaccine. There were no severe reactions, 2 patients had mild reactions, a 2-year-old with a history of egg anaphylaxis had a reaction at the vaccine site 20 minutes after the second dose (vaccine test not performed), and a 19-month-old girl with a negative vaccine prick test result had a fleeting erythematous rash on the neck and face 20 minutes after the second dose of YF vaccine.[24]

Bédard et al[25] in a retrospective study reported the experience with YF vaccination in 24 patients with confirmed egg allergy or sensitization (6 patients never had introduced eggs in their diet but had a positive confirmation test result). The number of steps for vaccination was at the physician's discretion. Most physicians used either 1-step (100% of the vaccine) or 5-step protocol (1%, 10%, 20%, 30%, and 40% of the total dose) with injections every 20 minutes. Although 83% of vaccine intradermal test results were positive, no allergic reactions were reported in the study. Two patients with an egg white IgE level greater than 100 kU_A/L and 1 with egg anaphylaxis tolerated the single-dose vaccine.[25]

To our knowledge, there have been no large-scale studies on the safety of the YF vaccine in egg-allergic patients. The present study included 435 children, with 225 (51.72%) classified as probably allergic to egg protein. Adverse reactions to the YF vaccine are rare, even in patients with a history of anaphylactic reactions. With the urgency to vaccinate as many children with egg allergy as possible during the YF epidemic, we proposed a simplified protocol to screen and vaccinate children with a suspected or confirmed egg allergy (Fig 1). Of the 435 vaccinated children, 95.2% experienced no vaccine reaction. Most of the vaccine reactors presented with mild skin rash and were managed with clinical observation, or with a single dose of an oral antihistamine. The skin test did not predict a vaccine reaction. Only 1 child, with a negative skin test result, experienced a severe vaccine reaction (possible anaphylaxis). Of the 21 children with a vaccine reaction, only 2 had a positive vaccine skin test result, 7 had a negative skin test result, and 12 children did not undergo a skin test because there was no history of anaphylactic reactions or because they were classified as probably not allergic. Age, sex, egg allergy, and history of anaphylaxis did not predict a vaccine reaction.

The main limitation of our study was that the diagnosis of egg allergy was made using a medical interview with a trained physician. The oral provocation test is still considered the criterion standard method for diagnosing food allergies. However, it has disadvantages related to the time required for its execution, a properly trained specialized team, and the costs involved, being generally available only in large centers or at teaching hospitals. In the protocol used in our service, because of the need to vaccinate a large number of children susceptible to YF, we decided for the clinical diagnosis of egg allergy, respecting the criteria of clinical reproducibility and evidence of sensitization to the egg protein (serum IgE level for egg and its fractions >0.35 kU_A/L performed

up to 6 months before vaccination). Although unlikely, there is also the possibility that children in the "probably allergic" group were not truly allergic or had already developed a tolerance to egg, which could be one of the contributing factors to explain the fact that patients considered probably allergic did not have higher rates of vaccine reaction than nonallergic children. However, children in the probably not allergic group may have had an egg allergy. We did not perform an intradermal skin test with the undiluted vaccine in children with a negative prick test result; therefore, its role as a screening test to predict vaccine reaction could not be evaluated. Likewise, a desensitization protocol was not carried out in those with a positive skin test result to the undiluted vaccine; therefore, it was not possible to assess its role in reducing adverse reactions.

However, the vaccine protocol proved unnecessary before the vaccination of children with suspected egg allergy. This finding makes YF vaccine more accessible and safer, ensuring universal immunization against a dangerous pathogen, especially in a population that needs prevention in an epidemiological context of risk. Further studies are needed to determine the degree of sensitivity and specificity of vaccine skin tests, as well as to demonstrate whether successful desensitization will confer long-term tolerance.

In conclusion, YF vaccine can be safely administered as a single dose in children with a confirmed or suspected egg allergy without prior vaccine skin testing and in the absence of complex protocols. The skin prick test with the undiluted vaccine did not predict a vaccine reaction. However, as with all vaccines, it is important that the YF vaccine be administered in an appropriate facility and in the presence of a professional trained to recognize and treat exceedingly rare adverse vaccine reactions. Children with a history of anaphylactic reactions to eggs should be observed for at least 60 minutes after injection.

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Key messages

- **Skin test and desensitization protocols with undiluted YF vaccine are not necessary before vaccination of egg-allergic children. The prick test with undiluted vaccine was not a predictor of vaccine reaction.**
- **The YF vaccine can be safely administered as a single dose to egg-allergic children without prior vaccine skin testing, and (like all other vaccines) should be administered in a setting prepared to recognize and treat rare anaphylactic reactions.**

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