

Allergic Disease at the Age of 7 Years After Pertussis Vaccination in Infancy

Results From the Follow-up of a Randomized Controlled Trial of 3 Vaccines

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Objective: To prospectively assess sensitization rates and the development of allergic diseases in a follow-up of a randomized controlled pertussis vaccine trial.

Setting: Two-month-old infants were the subject of this double-blind study in 1992 in a collaboration between the Pediatric Clinic and the Primary Care Centers in Linköping.

Patients and Intervention: Allergic diseases were evaluated in 667 children, who were randomized to 1 of 4 vaccine groups: a 2-component, a 5-component, or a whole cell pertussis vaccine (all of which were administered with the diphtheria and tetanus toxoids vaccine) and the diphtheria and tetanus toxoids vaccine alone. Allergy development was assessed by questionnaires (n=667) and skin prick tests (n=538) at the age of 7 years.

Main Outcome Measures: Allergic diseases and skin prick test results at the age of 7 years.

Results: The cumulative incidence of allergic diseases was 34.9%, and was similar in the 4 groups (33.3%-

37.3%, $P=.89$), even after adjusting for family history, sex, pets, dampness, environmental smoking at home, and other living conditions. Positive skin prick test results were more prevalent, however, after vaccination with the 2-component acellular vaccine (19.4%) than in the other 3 groups (11.1%-13.5%, adjusted for confounding factors, $P=.01$). Furthermore, allergic rhinoconjunctivitis was more common in children who were initially immunized with the 2-component pertussis vaccine and received a booster dose with an acellular vaccine compared with those who received no booster vaccination (relative risk, 3.6; 95% confidence interval, 1.1-12.0).

Conclusion: Pertussis vaccination in infancy with any of these vaccines was not associated with allergic manifestations at the age of 7 years, apart from a higher prevalence of positive skin prick test results after an experimental 2-component vaccine, which is no longer in use.

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ASTHMA AND allergy originate from an interaction between genetic and environmental factors, particularly factors encountered early in life.^{1,2} Besides a family history of allergy, changes in the microbial intestinal flora, birthplace, and immunizations have been suggested as risk factors. Odent et al³ found a 5-fold increase in bronchial asthma in children who had been vaccinated with pertussis in infancy. Furthermore, other studies^{4,5} have found pertussis immunization to be associated with subsequent atopic disease.

Low levels of circulating IgE antibodies to pertussis toxin (PT) have been found in infants after primary immunization with whole cell (WC) and acellular pertussis vaccines and after pertussis infection.⁶ The induction of a high level and frequency of IgE response to PT is particularly shown after a pertussis booster vaccination if the child has received an acellular pertussis vaccine

in infancy.⁷ Immunoglobulin E antibodies to PT are also more common in atopic children compared with healthy children.⁸

One reason for the possible allergy-inducing effect of pertussis immunization could be that PT increases sensitization to coadministered antigens.^{9,10} As the immune response to acellular pertussis antigen in infancy is T helper (Th) 2 cell polarized,¹¹ or associated with the secretion of Th1 and Th2 cytokines,^{12,13} and the subsequent Th cell memory generation is largely restricted to the Th2 cell component,¹⁴ early vaccination could, in theory, facilitate the development of asthma and allergy. On the other hand, WC vaccine inhibits IgE response to diphtheria and tetanus toxoids (DT).¹⁵ Aluminum hydroxide and aluminum phosphate, which are used as adjuvants in the vaccines, are also Th2 cell stimulants.¹⁶

In a previously published prospective trial of pertussis vaccinations in infancy, the prevalence of allergic diseases was similar

at the age of 30 months in subjects who had received WC, 2-component pertussis (Pa2) or 5-component pertussis acellular (Pa5) vaccines, or placebo in infancy.^{17,18} In another prospective study,¹⁹ the incidence of asthma was similar in pertussis-immunized and nonimmunized children at the age of 42 months.

In the present study, we report the prevalence of allergic symptoms and positive skin prick test (SPT) results at the age of 7 years in the previously described cohort^{17,18} who received in infancy 1 of 3 pertussis vaccines with the DT vaccine or the DT vaccine only. The follow-up was indicated by the fact that respiratory allergies are usually not manifest during the first years of life.

METHODS

STUDY GROUPS

In a Swedish pertussis vaccine trial, 9829 children in 14 study centers were randomized to a double-blind comparison of the protection against whooping cough and the prevalence of adverse effects. The vaccines were a Pa2 (SmithKline Beecham, Rixensart, Belgium) and a Pa5 (Connaught Ltd, Toronto, Ontario) vaccine, a WC pertussis vaccine (Connaught Laboratory Inc, Swiftwater, Pa), and a DT vaccine (Swedish National Bacteriological Laboratory, Stockholm) used as placebo.²⁰ The randomization process was described in the efficacy study.²⁰ In addition to the efficacy evaluation, all 788 infants recruited in Linköping were asked to participate in a study focusing on the development of bronchial asthma and allergy in relation to vaccination (**Figure 1**). This cohort was described in more detail in a previous publication.¹⁸

The children received the first of 3 vaccine doses at the age of 2 months (56-92 days) in 1992, and were examined at the ages of 7 months (1 month after the third dose) and 2½ years (mean, 2 years 5 months; range, 2 years 3 months–2 years 8 months).

PROCEDURES

The 3 pertussis vaccines contained pertussis antigens and aluminum gels as described in the efficacy study.²⁰

The children who were primarily vaccinated with the Pa2 vaccine were offered a booster injection with a 3-component acellular pertussis vaccine (containing PT, 25 µg; pertactin, 8 µg; filamentous hemagglutinin, 25 µg; and aluminum hydroxide, 0.5 µg, as adjuvant). Of the 173 families, 111 (64.2%) accepted, and the booster was given at a mean (and median) age of 3 years 7 months (range, 36-51 months; SD, 4 months). Children who received the WC vaccine as their primary immunization were offered the Pa5 vaccine at a mean age of 3 years 5 months (median, 3 years 6 months; range, 35-49 months; SD, 3 months); 78 (59.1%) of the 132 families accepted. Of the 182 children primarily immunized with the Pa5 vaccine, 72 (39.6%) had a booster with the same Pa5 vaccine between the ages of 4 and 6 years. The group receiving only the DT vaccination (n=75) was given 2 or 3 doses of an acellular pertussis vaccine at the age of 3 to 4 years, while the remaining 102 children in this group received no pertussis vaccination.

At follow-up, 667 of the 788 children were still living in the area. Of these children, 538 (80.7%) agreed to participate in the follow-up, including SPTs and responding to a questionnaire read by a research nurse. One of the parents of the remaining 129 children was contacted by telephone and responded to the questionnaire read by the same research nurse.

Skin prick tests were performed at the age of 7 years in duplicate on the volar aspect of the forearm with allergens (10

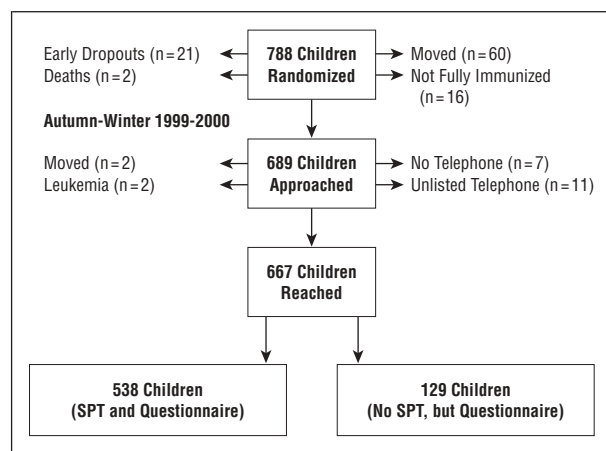


Figure 1. Flowchart of the follow-up study of 667 children at the age of 7 years. The children were given 1 of 3 pertussis vaccines with a diphtheria and tetanus toxoids (DT) vaccine or the DT vaccine alone. SPT indicates skin prick test.

histamine equivalent pricks) (Allergologisk Laboratorium A/S, Hørsholm, Denmark). The SPTs were for cat dander, timothy and birch pollens, and house dust mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*). The tests were performed according to the recommendations of the European Academy of Allergology and Clinical Immunology.²¹ Tests were regarded as positive if skin wheals had a mean diameter of at least 3 mm after 15 minutes. Histamine dihydrochloride, 10 µg/mL, was included as a positive control. No antihistamines were used 3 days before the SPT.

DIAGNOSTIC CRITERIA

The diagnoses were based on a questionnaire from the International Study of Asthma and Allergies in Childhood,²² clinical findings, and information in medical records as described in detail previously.¹⁸

Pertussis (whooping cough) was diagnosed according to criteria established by the World Health Organization.²³ The families were contacted by telephone every 6 weeks up to the age of 2½ years. Blood samples for serological analyses and nasopharyngeal cultures for *Bordetella pertussis* were obtained after 7 days of coughing. A case of pertussis was defined as the presence of paroxysmal cough for at least 21 consecutive days plus one of the criteria listed by the World Health Organization. Between 1992 and June 30, 1995, there were 48 children diagnosed as having whooping cough. Between July 1, 1995, and February 14, 2000, children with culture results positive for whooping cough and symptoms of whooping cough were defined as cases of pertussis (n=12). The sampling was conducted via the Primary Care Centers.

The investigation was blinded with respect to vaccine type until the diagnoses were established in all the children in 1995 at the age of 2½ years.¹⁸ For ethical reasons, the double-blinded design was not subsequently maintained. At the follow-up at the age of 7 years, however, the families were aware of which vaccine the child had received.

STATISTICAL ANALYSIS

Statistical comparisons were made using χ^2 tests or Fisher exact tests when appropriate. Adjustments for differences in family history of atopic disease were made in the main comparisons of study groups using a logistic regression model with SAS statistical software (StatView, version 5.0.1; SAS Institute Inc, Cary, NC). For relative risks and 95% confidence intervals, another software pro-

Table 1. Demographic Data of 667 Children Immunized in Infancy With 3 Injections of 1 of 3 Pertussis Vaccines or the DT Vaccine*

Variable	Type of Vaccine				P Value†
	Pa2 (n = 174)	Pa5 (n = 182)	WC Pertussis (n = 134)	DT (n = 177)	
Heredity‡					
None	42.5	41.2	46.2	39.8	.71
Single	46.0	47.8	45.5	49.4	.89
Double	11.5	11.0	8.3	10.8	.83
Asthma					
Mother	8.7	7.1	11.4	8.0	.60
Father	8.7	6.6	7.7	8.0	.91
Pets at home	44.3	36.3	34.3	32.8	.13
Male sex	55.7	49.5	51.5	53.1	.68
Indoor environment§					
Damp	8.1	8.8	9.7	8.5	.97
Smoke	4.6	3.8	4.5	7.3	.45
Dry	13.9	13.2	10.4	22.6	.01

Abbreviations: DT, diphtheria and tetanus toxoids; Pa2, 2-component pertussis; Pa5, 5-component pertussis; WC, whole cell.

*Data are given as percentage of each group unless otherwise indicated.

†Using the χ^2 test.

‡Refers to 0, 1, or 2 parents with allergic disease ever (bronchial asthma, atopic dermatitis, or allergic rhinoconjunctivitis ever).

§See the "Statistical Analysis" subsection of the "Methods" section for a description of these variables.

gram (Epi Info 2000, version 1.0) was used. Power analysis was made for 669 children in the earlier examination at the age of 2½ years.¹⁸ The variables in the multiple logistic regression analyses were single heredity vs no heredity; double heredity vs no heredity depending on 0, 1, or 2 parents with allergic disease (bronchial asthma, atopic dermatitis, or allergic rhinoconjunctivitis); furred pets in the home or not; dampness according to a question if the parents had found dampness in the home (leaking pipes or condensation at the inside of the windows when the temperature is <0°); smoking indoors where the child lives; and dryness if the parents had considered the air in the home to be dry.

ETHICAL CONSIDERATIONS

The parents of all participating children gave their informed consent. The study was approved by the Human Research Ethics Committee of the Medical Faculty of Linköping University.

RESULTS

Allergic disease during the first 7 years was verified in 34.9% (n = 233) and during the last year in 26.1% (n = 174) of the children. The cumulative incidence of bronchial asthma was 11.1% (n = 74) and the prevalence was 7.2% (n = 48), whereas cumulative atopic dermatitis was found in 23.7% (n = 158) of the children, with 15.4% (n = 103) having atopic dermatitis during the last year. Children who were examined at the ages of 2½ and 7 years (n = 599) had a similar prevalence of allergic diseases at the age of 7 years as those examined at the age of 7 years only (212/599 vs 21/68; $P = .55$). At least one positive SPT result was recorded in 14.1% (76/538) of the children at the age of 7 years, ie, to cat in 7.2% (n = 39), to timothy in 5.9% (n = 32), to birch in 5.8% (n = 31), and to house dust mites in 0.6% (n = 3) of the children.

The 4 vaccine groups did not differ significantly with respect to confounders (family history of allergy, pets in the home, sex, environmental tobacco smoke, and other environmental risk factors), except that a dry climate at home was more common in the DT vaccine group (**Table 1**).

A family history of allergy was associated with bronchial asthma, allergic rhinoconjunctivitis, and a positive SPT result for no, single, and double family history of allergy, while an association with atopic dermatitis was not significant (**Table 2**).

The cumulative incidence and the prevalence of allergic diseases were similar in the 3 pertussis vaccine groups and the DT-only vaccine group (**Table 3**). This was also the case for positive SPT results, except against birch, which was more common among children immunized with the Pa2 vaccine than those immunized with the other vaccines. Compared with the other 3 vaccines, the Pa2 vaccine was associated with a higher prevalence of a positive SPT result when adjusted for heredity for allergy, pets at home, moisture and dryness at home, and environmental smoking. The Pa2 vaccine was also adjusted for pertussis infections, and the significance ($P = .045$) for a positive SPT result remained. The SPT results were similar in the 4 groups at the ages of 7 months and 2½ years (**Figure 2**).

There were no significant differences for any allergic disease in any of the vaccine groups, as assessed in a multiple logistic regression model with adjustment for heredity, pets, sex, dampness or dryness indoors, and smoke (Table 2). However, there was a positive association between allergic diseases and heredity and a negative association between pet keeping and allergic diseases (Table 2). Allergic rhinoconjunctivitis and positive SPT results were more common in boys, whereas eczema was more common in girls (Table 2).

The prevalence of allergic rhinoconjunctivitis (crude relative risk, 3.6; 95% confidence interval, 1.1-12.0) (**Table 4**) was increased in children who were primarily immunized with the Pa2 vaccine in infancy and subsequently received a booster dose with an acellular pertussis vaccine vs children who did not receive a booster injection; this was found also after adjustment for the confounders described in the "Statistical Analysis" subsection of the "Methods" section. Allergic rhinoconjunctivitis was not increased for children immunized with the Pa5 or the WC pertussis vaccine, or for those in the DT vaccine group who were immunized with an acellular pertussis vaccine at the age of 3 to 4 years (Table 4).

COMMENT

The prevalence of allergic diseases was similar in the 3 pertussis vaccine groups and the placebo group, confirming and extending the previous follow-up of this study group at the age of 2½ years. Multiple regression analyses did not show any significant differences between children who were vaccinated with pertussis and those given placebo (the DT vaccine) at the age of either 2½ or 7 years. The most important confounding factor, family history of allergy, was evenly distributed between the pertussis vaccine groups and the DT vaccine group. These clinical follow-up results are in line with the results in the prospective study by Henderson et al,¹⁹ which com-

Table 2. Prevalence of Allergy and Sensitization After Pertussis Immunization in a Regression Analysis*

Variable	Bronchial Asthma	Allergic Rhinoconjunctivitis	Atopic Dermatitis	Any Allergic Disease	Positive Skin Prick Test Result
Type of vaccine					
Pa2	1.08 (0.4-2.5)	1.12 (0.5-2.2)	0.90 (0.4-1.7)	0.97 (0.6-1.6)	2.44 (1.2-5.0)
Pa5	1.09 (0.4-2.5)	0.78 (0.3-1.6)	0.94 (0.5-1.8)	0.95 (0.6-1.5)	1.33 (0.6-2.8)
WC pertussis	0.77 (0.2-2.1)	1.02 (0.4-2.1)	1.48 (0.8-2.8)	1.17 (0.7-1.9)	1.42 (0.6-3.2)
Heredity					
Single	2.33 (1.0-5.0)	3.76 (2.0-7.1)	1.14 (0.7-1.9)	1.91 (1.3-2.8)	2.60 (1.4-4.8)
Double	6.23 (2.5-16.0)	3.95 (1.7-9.2)	1.56 (0.7-3.2)	3.28 (1.8-5.7)	4.60 (2.0-11.0)
Pets at home	0.53 (0.2-1.1)	0.61 (0.3-1.1)	0.64 (0.4-1.1)	0.64 (0.4-1.0)	0.66 (0.3-1.2)
Male sex	1.77 (0.9-3.4)	1.93 (1.1-3.4)	0.51 (0.3-0.9)	0.91 (0.6-1.3)	2.30 (1.3-4.0)
Indoor environment					
Damp	0.78 (0.2-2.7)	0.44 (0.1-1.5)	0.84 (0.3-1.9)	1.15 (0.6-2.1)	0.95 (0.3-2.4)
Smoke	1.41 (0.4-5.0)	1.08 (0.3-3.3)	0.92 (0.3-2.6)	0.91 (0.4-2.0)	0.93 (0.2-3.3)
Dry	1.58 (0.7-3.4)	1.35 (0.7-2.6)	1.53 (0.8-2.7)	1.19 (0.7-1.9)	1.10 (0.5-2.2)

Abbreviations: Abbreviations are explained in the first footnote to Table 1.

*Data are given as the adjusted odds ratio (95% confidence interval). The prevalence of allergic diseases (in the children primarily immunized with the Pa2, Pa5, WC pertussis, or DT vaccine) and positive skin prick test results at the age of 7 years are dependent variables and possible risk factors are independent variables in the multiple logistic regression model. The analyses are adjusted for heredity for allergy, pets in the home, sex, and indoor environment.

Table 3. Prevalence of Allergic Disease and Sensitization in Relation to Vaccination*

Variable	Type of Vaccine				P Value†
	Pa2 (n = 174)	Pa5 (n = 182)	WC Pertussis (n = 134)	DT (n = 177)	
Allergic disease					
Any					
Prevalence	23.0 (0.80 [0.5-1.2])	25.3 (0.88 [0.6-1.3])	27.6 (0.96 [0.6-1.4])	28.8	.62
Cumulative incidence	33.3 (0.94 [0.7-1.3])	34.1 (0.96 [0.7-1.3])	37.3 (1.05 [0.7-1.5])	35.6	.89
Bronchial asthma					
Prevalence	7.5 (0.94 [0.4-2.0])	7.7 (0.97 [0.4-2.0])	5.2 (0.66 [0.2-1.6])	7.9	.80
Cumulative incidence	13.2 (1.23 [0.7-2.2])	11.5 (1.07 [0.6-2.0])	9.7 (0.90 [0.4-1.8])	10.7	.79
Atopic dermatitis					
Prevalence	13.2 (0.87 [0.5-1.5])	14.3 (0.94 [0.5-1.6])	20.1 (1.32 [0.8-2.2])	15.3	.37
Cumulative incidence	21.3 (0.90 [0.6-1.4])	22.5 (0.95 [0.6-1.4])	28.4 (1.20 [0.8-1.8])	23.7	.51
Allergic rhinoconjunctivitis	12.6 (0.97 [0.5-1.7])	9.3 (0.72 [0.4-1.3])	11.2 (0.86 [0.4-1.6])	13.0	.69
Positive SPT result	(n = 144)	(n = 146)	(n = 104)	(n = 144)	
Any	19.4 (1.8 [0.99-3.1])	12.3 (1.1 [0.5-2.1])	13.5 (1.2 [0.6-2.4])	11.1	.18
Birch	10.4 (5.0 [1.4-16.9])	4.8 (2.3 [0.6-8.8])	5.8 (2.8 [0.7-10.9])	2.1	.02
Cat	11.1 (1.8 [0.8-3.9])	5.5 (0.9 [0.3-2.3])	5.8 (0.9 [0.3-2.6])	6.3	.22
Timothy	6.9 (1.1 [0.4-2.7])	6.2 (1.0 [0.4-2.5])	3.8 (0.6 [0.1-2.0])	6.3	.77
<i>Dermatophagoides pteronyssinus</i>	0	0.7	1.0	0.7	NA

Abbreviations: NA, data not applicable. Other abbreviations are explained in the first footnote to Table 1.

*Data are given as percentage of patients in each group positive for the specific disease or allergen (crude relative risk [95% confidence interval]).

†Using the χ^2_3 test.

pared wheezing at the age of 42 months in children who were or were not immunized with the WC pertussis vaccine. A recent large cohort study²⁴ found a relative risk of asthma of 0.92 (95% confidence interval, 0.83-1.02) for children immunized with the DT and WC pertussis vaccine. However, in that study,²⁴ the median age at the last follow-up was only 28 months (an age when respiratory allergies are seldom manifest).

Three observational studies have suggested an increased risk of allergy after pertussis vaccination. A 5-fold increased risk of asthma has been claimed for WC pertussis-vaccinated children compared with nonvaccinated children at the age of 8 years.³ In another study,⁴

23% of 1011 children vaccinated with the WC pertussis and the DT vaccines had asthma symptoms, compared with no asthma cases in a nonvaccinated group of 23 children. In the third study,³ the odds ratio was 1.8 for atopic manifestations among WC pertussis-vaccinated children compared with nonvaccinated children. Because the studies were observational, the study groups were more likely to differ with regard to socioeconomic and educational factors, smoking habits, and family history. A review²⁵ from the Institute of Medicine concluded that the evidence is inadequate to accept or reject a causal relationship between multiple immunizations and an increased risk of allergic disease, particularly asthma. The present prospec-

tive study, with a follow-up at the age of 7 years, clearly indicates that none of the pertussis vaccines given in infancy were associated with an increased risk for allergy.

In our study children who were primed with the Pa2 vaccine, allergic rhinoconjunctivitis was more common in those who received a booster dose with an acellular pertussis vaccine than in those who did not. The difference could be coincidental because of the few children in the subgroups. Furthermore, we cannot exclude a selection bias because the children were not randomized to a booster dose. Similarly, the higher prevalence of a positive SPT result in the children primarily vaccinated with the Pa2 vaccine could be a chance observation. On the other hand, it has been reported that children who receive a booster dose

with an acellular pertussis vaccine express increased levels of interleukin (IL) 4 and IL-5.²⁶

Children not available for follow-up at the age of 7 years (n=121) (Figure 1) were not likely contributing to selection bias. Children who underwent the SPT were evenly originating from the 4 initial vaccine groups, and they did not differ significantly in family history from those not tested at the age of 7 years.

Previous studies^{13,27} have shown that peripheral blood mononuclear cells from children immunized with acellular vaccines exhibit a Th2 or a mixed Th1/Th2 type cytokine profile, as indicated by the production of IL-4, IL-5, and interferon γ . This was not the case after WC pertussis vaccination nor after pertussis infection.

Pertussis toxin-specific IgE antibodies can be detected in atopic and nonatopic children, but only at low levels and in a few of the children after 3 primary shots in infancy. After a booster, 14 of 15 children had detectable PT-IgE—most at high levels.²⁶ Children who were vaccinated with the WC pertussis vaccine, combined with the DT vaccine, suppressed IgE and IgG4 to the toxoids.¹⁵ The effect of down-regulated IgE formation in response to the WC pertussis vaccine could be related to lipopolysaccharides in the WC vaccine because the lipopolysaccharides are known to enhance Th1 cell-like responses.

The increased prevalence of a positive SPT result in children immunized with the Pa2 vaccine could be because of the higher level of PT in the Pa2 vaccine (25 μ g) than in the Pa5 vaccine (10 μ g) and because of fewer cell wall components with Th1 cell-like effects, such as lipopolysaccharides, than in the WC pertussis vaccine. Immunization with purified bacterial antigens adsorbed to aluminum and devoid of endotoxin and other residually additive toxins that stimulate IL-12 favors the induction of Th2 cells.²⁸

Theoretically, it is also possible that the aluminum gels in the vaccines could influence the Th1/Th2 cell regulation.¹⁶ Although all 4 vaccines had aluminum as an adjuvant, only the experimental Pa2 vaccine had aluminum hydroxide, whereas the Pa5, the WC pertussis, and the DT vaccines all had aluminum phosphate as an adjuvant.²⁹ The physiological properties of aluminum salts differ (eg, the

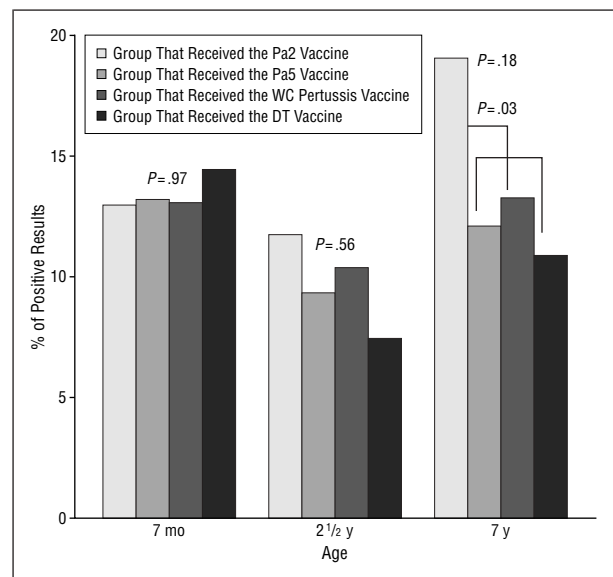


Figure 2. Positive skin prick test results to common allergens at the ages of 7 months (n=711) (egg, milk, and cat), 2½ years (n=676) (egg, birch, timothy, cat, dog, and house dust mites [*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*]), and 7 years (n=538) (birch, cat, timothy, and house dust mites [*D pteronyssinus* and *D farinae*]). A difference is shown only at the age of 7 years, when the 2-component pertussis acellular (Pa2) vaccine was compared with the 3 other vaccines. Pa5 indicates 5-component pertussis acellular; WC, whole cell; and DT, diphtheria and tetanus toxoids.

Table 4. Allergy and Sensitization in 7-Year-Old Children in Relation to a Booster Vaccination*

Variable	Pa2 Booster			Pa5 Booster			WC Pertussis Booster			DT Immunization		
			Crude RR (95% CI)			Crude RR (95% CI)			Crude RR (95% CI)			Crude RR (95% CI)
	Yes	No		Yes	No		Yes	No		Yes†	No	
	(n = 111)	(n = 63)		(n = 72)	(n = 110)		(n = 80)	(n = 54)		(n = 75)	(n = 102)	
Allergic disease												
Any	25.2	19.0	1.32 (0.7-2.5)	26.4	24.5	1.08 (0.6-1.8)	30.0	24.1	1.25 (0.7-2.3)	29.3	28.4	1.03 (0.6-1.7)
Bronchial asthma	9.1	4.8	1.89 (0.5-6.7)	6.9	8.2	0.85 (0.3-2.5)	5.0	5.6	0.90 (0.2-3.9)	10.7	5.9	1.81 (0.6-5.1)
Allergic rhinoconjunctivitis	17.1	4.8	3.60 (1.1-12.0)	11.1	8.2	1.36 (0.5-3.4)	12.5	9.3	1.35 (0.4-3.8)	16.0	10.8	1.48 (0.6-3.2)
Atopic dermatitis	14.4	11.1	1.30 (0.5-3.0)	13.9	14.5	0.95 (0.4-2.0)	20.0	20.4	0.98 (0.4-2.0)	16.0	14.7	1.09 (0.5-2.2)
Positive SPT result	(n = 97)	(n = 47)		(n = 57)	(n = 89)		(n = 68)	(n = 36)		(n = 62)	(n = 82)	
	18.6	21.3	0.87 (0.4-1.8)	12.3	12.4	0.99 (0.4-2.5)	16.2	8.3	1.94 (0.5-6.6)	12.9	9.8	1.32 (0.5-3.4)

Abbreviations: CI, confidence interval; RR, relative risk. Other abbreviations are explained in the first footnote to Table 1.

*Data are given as percentage of patients in each group positive for the specific disease or with a positive test result. Data in parentheses and brackets are crude RRs and 95% CIs, are used in the comparisons between the groups. The booster dose was given after the age of 4 years.

†This group was primarily immunized at the age of 4 years with a 3-component acellular pertussis vaccine.

What This Study Adds

Vaccination is a cornerstone of the preventive health system; however, it is periodically questioned. Some observational studies have shown an increased risk of development of allergy after pertussis vaccination in infancy. We found that children vaccinated with pertussis in infancy had no more allergies during the first 7 years of life than children not vaccinated with pertussis in infancy. Positive skin prick test results were more prevalent after the administration of one of the acellular pertussis vaccines; however, this vaccine is no longer manufactured. We recommend continued pertussis vaccination in early infancy.

resorption of antigen into the tissues seems to be easier from aluminum phosphate-adsorbed vaccines than from aluminum hydroxide-adsorbed vaccines).³⁰

Vaccination is a cornerstone of the preventive health system; however, it is periodically questioned. Some observational studies have shown an increased risk of development of allergy after pertussis vaccination in infancy. Compared with the DT vaccine, none of the 3 pertussis vaccines given in infancy was a risk factor for the development of allergy during the first 7 years of life. However, the Pa2 experimental vaccine was associated with an increased incidence of allergic symptoms after a booster vaccination. Positive SPT results were also more frequent for the Pa2 vaccine. This vaccine is no longer manufactured.

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