Published in final edited form as:

Ann Allergy Asthma Immunol. 2009 October ; 103(4): 337–341. doi:10.1016/S1081-1206(10)60534-0.

Do Dose and Frequency of Antigen Injection Influence IgE Development in Young Children: A Comparison of Fire Ant Stings and Tetanus Immunizations

Dennis R. Ownby, M.D.^a, Megan E. Partridge, M.D.^b, Ganesa R. Wegienka, Ph.D.^c, Kimberley J. Woodcroft, Ph.D., MPH^c, Edward L. Peterson, Ph.D.^c, Christine L. M. Joseph, Ph.D., MPH^c, L. Keoki Williams, M.D., MPH^c, and Christine C. Johnson, Ph.D., MPH.^c

^aMedical College of Georgia, Department of Allergy and Immunology, 1120 15th Street BG 1019, Augusta, GA 30912

^bThe Allergy, Asthma & Sinus Center, 5045 Old Hickory Blvd, Suite 201, Hermitage, TN 37076

^cDepartment of Biostatistics and Research Epidemiology, Henry Ford Hospital, 1 Ford Place, Detroit, MI 48202, USA

^dDepartment of Pediatrics, Henry Ford Hospital, 1 Ford Place, Detroit, MI 48202, USA

Introduction

We have previously reported that over 50% of preschool children residing in a fire ant endemic area of the United States have IgE antibodies to fire ant venom.⁽¹⁾ This high prevalence of sensitization to imported fire ant venom (IFAV) was surprising. However, children and adults living in areas where fire ants are endemic are stung frequently. One study reported a sting rate of 51% among 137 medical students during 3 weeks of training in Texas.⁽²⁾ This is similar to reports of stings in 39% of 176 children during the previous

Corresponding Author: Dennis R. Ownby, M.D., Betty B. Wray Professor of Pediatrics and Professor of Medicine, Medical College of Georgia, 1120 15th Street, BG 1019, Augusta, GA 30912-3790, Phone: 706-721-3531, Fax: 706-721-2527, downby@mcg.edu.

Contributions of each author to the study:

1. Dennis R. Ownby M.D. was involved in the design and conduct of both the study of fire ant sensitivity and WHEALS cohort. He supervised and obtained funding for all anti-tetanus IgE measurements presented and was the principal author of the manuscript.
2. Megan E. Partridge M.D. designed and conducted the study of fire ant sensitivity, reviewed and revised the current manuscript.
3. Ganesa R. Wegienka Ph.D. was involved in the design and conduct of the WHEALS study, supervises WHEALS data collection, reviewed and revised the current manuscript.
4. Kimberley J. Woodcroft Ph.D., MPH was involved in the design and conduct of the WHEALS study especially the laboratory processing of all biologic samples and who reviewed and revised the current manuscript.
5. Edward L. Peterson Ph.D. is a senior biostatistician who performed or checked all data analyses and who reviewed and revised the current manuscript.
6. Christine L. M. Joseph Ph.D., MPH is an epidemiologist involved in all aspects of the design and conduct of the WHEALS study and who reviewed and revised the current manuscript.
7. L. Keoki Williams M.D., MPH was involved in the design and conduct of the WHEALS study and whose grant provides funding for the 1-year and 2-year follow up visits during which the blood samples used in this manuscript were obtained, who reviewed and revised the current manuscript.
8. Christine C. Johnson Ph.D., MPH is the senior epidemiologist who conceived and obtained funding for the WHEALS study and who reviewed and revised the current manuscript.

month.⁽¹⁾ This high exposure rate could result in IgE antibody formation in several ways. IFAV could have unique properties strongly promoting IgE production such as substances with strong adjuvant properties. IgE production to IFAV could also be promoted by intracutaneous delivery of small doses of venom by accidental stings at the relatively frequent intervals previously reported.

Several studies have suggested that IgE production is more likely to occur if an antigen is encountered frequently at low doses rather than infrequently at high doses.^(3;4) This is an important question since there is a growing debate about the value of trying to reduce allergen exposure in early life intending to prevent sensitization versus increasing allergen exposure intending to induce tolerance.⁽⁵⁾ The concept of shifting a Th2 response from IgE to IgG₄ with high dose allergen exposure as a means of reducing allergic disease has also been introduced.⁽⁶⁾

Vaccines are normally thought of as a method of inducing IgG antibodies for protection against infectious diseases by administering sufficiently large amounts of immunogen as infrequently as possible. Thus, vaccines are examples of relatively high doses of antigen encountered infrequently in early childhood.⁽⁷⁾ The currently recommended schedule for primary immunization with diphtheria, tetanus and acellular pertussis (DTaP) vaccines in the United States calls for injections at 2, 4, 6 and 15–18 months of age. The question of how frequently vaccines induce the production of vaccine-antigen specific IgE antibodies has received little attention.^(8–12) However, previous investigations have shown that tetanus and pertussis vaccines induce IgE specific antibodies in >90% of 4 to 10 year-old children receiving booster immunizations.^(11;13) Vaccines contain well controlled doses of antigens to be delivered by injection on prescribed schedules. Most children receive DTaP vaccines at intervals close to those prescribed.

Our primary hypothesis was that sporadic exposure to the relatively small amounts of IFAV through natural accidental stings in young children would produce a significantly higher prevalence of detectable IFAV-IgE than would be found in similar age children undergoing routine immunizations with tetanus toxoid. Each imported fire ant (*Solenopsis invicta*) sting transfers 10 to 100 ng of protein, and presumably these stings become more common after children begin to crawl and walk between 6 and 24 months of age.^(14;15) In contrast each dose of tetanus toxoid for primary immunization of children contains at least 5 to 10 Lf units (15 – 30 µg of protein).^(16;17)

As part of a birth cohort study of factors related to the risk of allergic disease, anti-tetanus IgE (anti-T IgE) was measured in children at 6, 12 and 24 months of age. Our primary analysis compared the previously reported prevalence of IFAV-IgE to that of anti-T IgE determined in our birth cohort. Secondarily, we analyzed the prevalence of anti-T IgE at 6, 12 and 24 months of age with stratification by sex or race.

Methods

This study uses previously published data on the prevalence of IgE antibodies to IFAV⁽¹⁾ among children living in an imported fire ant endemic area of Georgia and data collected as part of the Wayne County Health, Environment, Allergy, and Asthma Longitudinal Study (WHEALS) in Michigan, where there are no imported fire ants. The institutional research board of the Medical College of Georgia approved the study of IgE to fire ant venom. The WHEALS study was approved by the institutional research boards of the Henry Ford Hospital and the Medical College of Georgia as appropriate.

Serum samples for measurement of anti-IFAV IgE were obtained as residual serum from samples submitted to an immunology laboratory for clinical assay in a fire ant endemic area of Georgia. No information was available concerning the children from whom these samples were taken beyond their age and gender.⁽¹⁾ For the WHEALS cohort, pregnant women were recruited after giving informed consent if they resided in an area of western Detroit and adjacent suburbs defined by contiguous ZIP codes. Recruitment began in August, 2003 and was completed in December, 2007. To be eligible, pregnant women in their 2nd or 3rd trimester had to be at least 21 years of age; live in the defined recruitment area; and attend 1 of 5 selected Henry Ford Hospital clinics for their prenatal care. Women were required to speak English well enough to provide written informed consent. Mothers were asked to identify their race and the race of their child using the categories of the 2000 US Census surveys. All children were expected to receive routine health care including all immunizations as recommended by the American Academy of Pediatrics. The recommended schedule includes diphtheria, tetanus and acellular pertussis (DTaP) immunizations at 2, 4 and 6 months of age with a booster immunization at 15–18 months of age. The majority of children in our cohort received Pediarix® vaccine within the Henry Ford Hospital system. We did not obtain the brand names of vaccines given to children from other health care sources but all brands are considered interchangeable for purposes of immunizing children in the United States.⁽¹⁷⁾ Blood samples were obtained during home visits when the children were approximately 6 and 12 months of age and during a clinical examination at approximately 24 months of age.

Both anti-IFAV and anti-T IgE antibodies were assayed using the Pharmacia UniCAP assay (Phadia AB, Portage, MI). As previously reported, the solid phase for anti-IFAV IgE was prepared from IFAV which differs from the standard UniCAP reagent which uses a whole-body extract. For anti-T IgE the Pharmacia CAP Rc208 was used which is a research only reagent. The ranges of the assays are from 0.1 to 100 kU/L of IgE. Samples with values of 0.1 kU/L were considered positive although the results for IgE 0.35 kU/L are given for comparison with other studies. Repeat assay of samples consistently demonstrated coefficients of variation between assays of less than 6%.

To test the linearity and analytic sensitivity of a value of 0.1 IU/ml in the anti-tetanus IgE assay, we selected 4 plasma samples with sufficient volumes and values of 0.56 to 1.20 IU/ml and measured anti-T IgE after performing five, serial two-fold, dilutions of each sample. The calculated IgE concentration of each dilution was compared to the actual measured concentration. The measured concentrations of the dilutions declined as expected to less than 0.1 IU/ml and the Pearson correlation between calculated and measured values was $r=0.992$, $p<0.001$.

Statistical Analysis

Data were described using routine descriptive statistical techniques. The IgE values were log transformed to reduce the influence of outliers on the estimated mean; the means reported are geometric means. Prevalences were compared using chi square tests. P-values less than 0.05 were considered significant. All statistical analysis was performed using SAS version 9.1 (SAS Institute, Raleigh, NC).

Results

Our previous report of IgE to IFAV involved a sample 183 children of whom 42 were 2 to 5 years-of-age.⁽¹⁾ Of these 42, 22 (52%) were female and 20 (48%) were male. Information on race was not obtained for these children. Information on anti-T IgE was obtained for 395 children from the WHEALS cohort. Four hundred four infants had completed a 6-month

follow up in our birth cohort and were potentially eligible; however, after excluding one child in each set of twins and those ineligible for other reasons such as area of residence, 395 children remained. Of these children, 193 (48.9%) were female, 225 (57.0%) were Black, 116 (29.4%) were White and 54 (13.7%) were from other racial groups. Results from fewer children were available at 12 and 24 months of age because they had not yet reached these ages or because they had not yet been evaluated.

As shown in Table 1 the 52.9% prevalence of detectable anti-T IgE at 24 months of age using 0.1 kUa/L is not statistically significantly different from the 57.1% prevalence of anti-IFAV IgE in children 2–5 years of age. There were 14 children who were 24 months old among those studied for anti-IFAV IgE and 6 (42.9%) of these had detectable anti-IFAV IgE.

Detectable anti-T IgE increased with age from 15.2% at 6 months to 52.9% at 24 months as seen in Table 2. If an anti-T IgE antibody level of 0.35 kUa/L is used as the cutoff, the prevalence increases from 6.6% to 42.7% between 6 and 24 months of age, respectively. The prevalence reported at each age reflects all children with valid values at that age regardless of whether they had samples from other ages resulting in variation in the numbers of children. At 6 months, boys were significantly more likely to have detectable anti-T IgE than girls and this difference was nearly significant at 12 months but had disappeared by 24 months of age. The differences in the prevalence of anti-T IgE did not differ by reported race at any of the three ages.

Some children developed relatively high levels of anti-tetanus IgE as shown in Table 3. By 24 months of age nearly 29% of children had serum anti-T concentrations greater than 1 kUa/L and almost 5% had concentrations greater than 5 kUa/L.

We next examined the prevalence of anti-T IgE at 6 months of age in relationship to the number of DTaP immunizations reported for each child. As shown in table 4, none of the 31 children who had only received one immunization had detectable anti-T IgE but there was no significant difference in either the prevalence or mean anti-T IgE levels among children who had received two or three immunizations.

Discussion

Our findings do not support the hypothesis that the prevalence of anti-IFAV IgE antibodies would be significantly higher than the prevalence of anti-T IgE antibodies in young children because of differences in the antigen doses and patterns of exposure.^(3;4) The amount of tetanus toxoid protein delivered per injection (15,000 to 30,000 ng) is approximately 150–3,000 times larger than the total amount of protein delivered by a fire ant sting (10–100 ng). The difference in dose between tetanus and IFAV would be reduced if large numbers of fire ant stings were experienced at one time. It is not known whether the non-protein components IFAV act as adjuvants for IgE production but tetanus toxoid is adsorbed onto alum to enhance immunogenicity.⁽¹⁷⁾ While exposure to both antigens is by injection, tetanus toxoid is delivered intramuscularly while fire ant stings only penetrate into the epidermis.

Few studies have directly examined the relationship between antigen dose and probability of IgE production in humans with neo-antigens.⁽⁴⁾ Riedl et al. used the neo-antigen, keyhole limpet hemocyanin, at doses of 0.1-, 10-, 1,000-, and 100,000- μ g with diesel exhaust particles as adjuvant delivered intranasally to study IgE sensitization in 51 atopic adults. The 10 μ g dose produced sensitization in 100% of the subjects while the 100,000 μ g dose produced sensitization in only 11%, supporting the hypothesis that high doses of an antigen are less likely to produce IgE than are lower doses⁽³⁾

Our findings concerning the production of anti-T IgE in young children confirm and extend those of others. Dannemann et al. found that approximately 50% of 538 children had developed detectable anti-T IgE at 24 months of age and Gruber et al reported a prevalence of 53.6% compared to our finding of 52.9%.^(8;10) These numbers are remarkably consistent considering that the other studies used a different technology, the radioallergosorbent test (RAST), to detect anti-T IgE. The populations they studied were drawn from several European countries and all participants were likely of European ancestry. Levels of anti-T IgE are thought to decline in most, if not all children, until their next DTaP booster as was observed in a study of children boosted at 10 years of age and followed for two years.⁽¹⁸⁾

Strengths of our study include the ability to compare the prevalence of specific IgE to two different antigens in young children using the same IgE assay system. The use of the same IgE assay system reduces the risk that a difference in prevalence would be caused by differences in assay sensitivity. Both antigens studied are delivered by injection, although, at different depths. The anti-T IgE portion of the study used samples from a large, geographically-based, multiracial, birth cohort allowing assessment of anti-T IgE at three ages during early childhood. The assay used for measuring anti-T IgE is commercially available.

The principle weakness of our study is that anti-IFAV was measured on a random sample of children at various times and not on a birth cohort from an endemic area so we could not compare IgE development between the two populations and have no assurances that the IFAV sample was representative of the general population. We chose to compare specific IgE at 2 years of age because our previous work with anti-IFAV IgE suggested that antigen-specific IgE developed rapidly from birth to 2 years of age and increased more slowly after 2 years. The rate of increase in the prevalence of anti-IFAV IgE was modest between 2–5 years of age to 6–10 yrs, increasing from 57.1% to 64.4%⁽¹⁾ suggesting that most sensitization occurred during the preschool years. While the number of children studied at 2 years for anti-IFAV was small the prevalence of IgE in these 2 year old children was only slightly lower than the prevalence for the entire age group. Additional weaknesses of our study include possible variations in the number and timing of each DTaP immunization for participating children which we did not adjust for, and the fact that some children did not provide blood at all time points. As with all prospective studies there are some children who are lost to follow up or for whom samples are missed, but there is no reason to suspect that loss from the study is related to anti-T IgE formation. We did not question parents in detail about adverse reactions to immunizations so we can not determine whether the presence of anti-T IgE was associated with more frequent adverse reactions. However, Edelman et al. did not find an association between local reactions following booster immunization in 71 two-year-old children and the presence of detectable anti-pertussis toxin IgE antibodies.⁽¹⁹⁾

All DTaP vaccines currently used in the United States contain acellular pertussis antigens. The 52.9% prevalence of anti-T IgE we found is very similar to the 53.6% prevalence at 24 months for children who had received tetanus and diphtheria toxoids but not whole-cell pertussis antigens during primary immunizations as reported by Gruber et al.⁽¹⁰⁾ However when Gruber et al. co-administered whole-cell pertussis toxin with tetanus and diphtheria toxoids the prevalence of anti-T IgE antibodies was only 12.7% in contrast to the 53.6% prevalence found in children not given whole-cell pertussis. This suggests that acellular pertussis vaccines do not shift antibody responses away from IgE production to the same extent that whole-cell pertussis vaccines do as shown by Ausiello et al.⁽²⁰⁾ Whether this has an affect on the risk of later allergic disease in children has not been studied.

In summary, we found that by 24 months of age 52.9% of unselected children receiving a primary series of two or three DTaP immunizations formed anti-T IgE antibodies and that

this prevalence was not statistically significantly different from the 57.1% prevalence of anti-IFAV IgE antibodies we have previously reported. Knowledge of the high prevalence of IgE to both of these potential allergens is important to physicians called upon to evaluate children who have had apparent allergic reactions because positive tests are found in the majority of children who have not had any symptoms of an allergic reaction when exposed to these antigens.^(21–23) Available information suggests that the risk of allergic reactions to tetanus immunizations is approximately 1:1,000,000.⁽²⁴⁾

Acknowledgments

Funding Sources include NIH grants: AI59415, AI50681, AI61774 and the Fund for Henry Ford Hospital.

References

1. Partridge ME, Blackwood W, Hamilton RG, Ford J, Young P, Ownby DR. Prevalence of allergic sensitization to imported fire ants in children living in an endemic region of the southeastern United States. *Ann Allergy Asthma Immunol.* 2008; 100:54–8. [PubMed: 18254483]
2. Tracy JM, Demain JG, Quinn JM, Hoffman DR, Goetz DW, Freeman TM. The natural history of exposure to the imported fire ant (*Solenopsis invicta*). *J Allergy Clin Immunol.* 1995; 95:824–8. [PubMed: 7722162]
3. Riedl MA, Landaw EM, Saxon A, Diaz-Sanchez D. Initial high-dose nasal allergen exposure prevents allergic sensitization to a neoantigen. *J Immunology.* 2005; 174:7440–5. [PubMed: 15905593]
4. Arts JHE, Mommers C, de Heer C. Dose-response relationships and threshold levels in skin and respiratory allergy. *Critical Reviews in Toxicology.* 2006; 36:219–51. [PubMed: 16686423]
5. Holt PG, Thomas WR. Sensitization to airborne environmental allergens: unresolved issues. *Nature Immunology.* 2005; 6:957–60. [PubMed: 16177798]
6. Platts-Mills T, Vaughan J, Squillace S, Woodfolk J, Sporik R. Sensitization, asthma, and a modified Th2 response in children exposed to cat allergen: a population-based cross-sectional study. *Lancet.* 2001; 357:752–6. [PubMed: 11253969]
7. Ada G. Vaccines and Vaccination. *N Engl J Med.* 2001; 345(14):1042–53. [PubMed: 11586958]
8. Dannemann A, van Ree R, Kulig M, Bergmann RL, Bauer P, Forster J, et al. Specific IgE and IgG4 immune responses to tetanus and diphtheria toxoid in atopic and nonatopic children during the first two years of life. *Int Arch Allergy Immunol.* 1996; 111:262–7. [PubMed: 8917121]
9. Businco BB, Paganelli R, Bruno G, Grossi O, DiRienzo A, Businco L. Allergy to tetanus toxoid vaccine. *Allergy.* 2001; 56:701–2. [PubMed: 11421933]
10. Gruber C, Lau S, Dannemann A, Sommerfeld C, Wahn U, Aalberse RC. Down-regulation of IgE and IgG4 antibodies to tetanus toxoid and diphtheria toxoid by covaccination with cellular *Bordetella pertussis* vaccine. *J Immunol.* 2001; 167:2411–7. [PubMed: 11490032]
11. Mark A, Bjorksten B, Granstrom M. Immunoglobulin E responses to diphtheria and tetanus toxoids after booster with aluminium-adsorbed and fluid DT-vaccines. *Vaccine.* 1995; 13(7):669–73. [PubMed: 7668036]
12. Wahren E, Bengtsson C, Bjorksten B, Mark A, Granstrom M. Capture EIA for determination of IgE to diphtheria and tetanus toxins in comparison to RIA. *Vaccine.* 1998; 16:873–6. [PubMed: 9682330]
13. Ryan EJ, Nilsson L, Kjellman NIM, Gothefors L, Mills KHG. Booster immunization of children with an acellular pertussis vaccine enhances Th2 cytokine production and serum IgE responses against pertussis toxin but not against common allergens. *Clin Exp Immunol.* 2000; 121:193–200. [PubMed: 10931131]
14. Kemp SF, DeShazo RD, Moffitt JE, Williams DF, Buhner WAI. Expanding habitat of the imported fire ant (*Solenopsis invicta*): A public health concern. *J Allergy Clin Immunol.* 2000; 105:683–91. [PubMed: 10756216]
15. Deslippe RJ, Guo Y-J. Venom alkaloids of fire ants in relation to worker size and age. *Toxicon.* 2000; 38:223–32. [PubMed: 10665803]

16. Johansen P, Men Y, Audran R, Corradin G, Merkle HP, Bander B. Improving stability and release kinetics of microencapsulated tetanus oxide by co-encapsulation of additives. *Pharmaceutical Research*. 1998; 15:1103–10. [PubMed: 9688067]
17. Advisory Committee on Immunization Practices. Use of diphtheria toxoid-tetanus toxoid-acellular pertussis vaccine as a five-dose series. *MMWR*. 2000; 49(RR13):1–8.
18. Mark A, Bjorksten B, Granstrom M. Immunoglobulin E and G antibodies two years after a booster dose of an aluminum-adsorbed or a fluid DT vaccine in relation to atopy. *Pediatric Allergy and Immunology*. 1997; 8:83–7. [PubMed: 9617777]
19. Edelman K, Malmstrom K, He Q, Savolainen J, Terho EO, Mertsola J. Local reactions and IgE antibodies to pertussis toxin after acellular diphtheria-tetanus-pertussis immunization. *Eur J Pediatr*. 1999; 158:989–94. [PubMed: 10592076]
20. Ausiello CM, Urbani F, LaScala A, Lande R, Cassone A. Vaccine- and Antigen-Dependent Type 1 and Type 2 cytokine induction after primary vaccination of infants with whole-cell or acellular pertussis vaccines. *Infect Immun*. 1997; 65(6):2168–74. [PubMed: 9169747]
21. Sakaguchi M, Nakayama T, Inouye S. Cases of systemic immediate-type urticaria associated with acellular diphtheria-tetanus-pertussis vaccination. *Vaccine*. 1998; 16:1138–40. [PubMed: 9682371]
22. Martin-Muñoz MF, Pereira MJ, Posadas S, Sánchez-Sabaté E, Blanca M, Álvarez J. Anaphylactic reaction to diphtheria-tetanus vaccine in a child: specific IgE/IgG determinations and cross-reactivity studies. *Vaccine*. 2002; 20:3409–12. [PubMed: 12213411]
23. Mayorga C, Torres MJ, Corzo JL, Alvarez J, García JAC, Rodriguez CA, et al. Immediate allergy to tetanus toxoid vaccine: determination of immunoglobulin E and immunoglobulin G antibodies to allergenic proteins. *Ann Allergy Asthma Immunol*. 2003; 90:238–43. [PubMed: 12602673]
24. Bohlke K, Davis RL, Marcy SM, Braun MM, Destefano F, Black SB, et al. Risk of anaphylaxis after vaccination of children and adolescents. *Pediatr*. 2003; 112:815–20.

Table 1

Comparison of the Prevalence of Prevalence of Tetanus Toxoid Specific IgE Among Children 2 Years of Age to the Prevalence of Imported Fire Ant Venom (IFAV) Specific IgE Among Children 2–5 Years of Age

	Anti-Tetanus IgE 0.1 kUa/L, n (%)	IFAV* IgE 0.1 kUa/L, n (%)
Positive	109 (52.9)	24 (57.1)
Negative	97 (47.1)	18 (42.9)
Total	206 (100)	42 (100)

$$\chi^2 = 0.25 \text{ p}=0.616$$

*
IFAV = imported fire ant venom

Table 2

Prevalence of Anti-Tetanus IgE 0.1 IU/ml by Sex and Race

Child's Age in Months	All children * % (positive/n)	Males * % (positive/n)	Females * % (positive/n)	P-value ^{**}	Whites * (37/75)	Blacks * (51/100)	P-value ^{**}
6	15.2 (60/395)	19.3 (39/202)	10.9 (21/193)	0.02	16.4 (19/116)	13.8 (31/225)	0.52
12	35.9 (113/315)	40.7 (63/155)	31.1 (50/160)	0.08	40.9 (45/110)	33.1 (58/175)	0.18
24	52.9 (109/206)	53.4 (55/103)	52.4 (54/103)	0.89	49.3 (37/75)	51.0 (51/100)	0.83

* Prevalence of detectable anti-tetanus IgE antibodies at cutoff values of 0.1 kUa/L. The numbers of Whites and Blacks do not equal the total number of children because children of other racial groups are included in the category of all children.

** The p values are related to the difference in the prevalence of anti-T IgE between males and females and between Whites and Blacks at each age studied using a Wilcoxon rank sum test.

Table 3

Distributions of Anti-Tetanus IgE Concentrations at 6, 12 and 24 Months of Age and Anti-Imported Fire Ant Venom IgE at 12 to 36 Months of Age

IgE Concentrations IU/ml	Anti-Tetanus IgE			Anti-Fire Ant Venom IgE
	6 Months of Age n (%)	12 Months of Age n (%)	24 Months of Age n (%)	0 to 36 Months of Age n (%)
<0.1	335 (84.8)	202 (64.1)	97 (47.1)	18 (58.1)
0.1 – 0.99	52 (13.2)	71 (22.5)	62 (30.1)	3 (9.7)
1.0	8 (2.0)	42 (13.3)	47 (22.8)	10 (32.2)

Table 4

Relationship between the Number of DTaP Injections Received and the Prevalence and Average Concentrations of Anti-Tetanus IgE Antibodies at approximately 6 Months of Age

Number of Injections Prior to 6 Months	n	Prevalence* % (positive/n)	Geometric Means of Positive Samples		
			Geo-Mean**	Ln IgE Mean†	Ln-IgE SD‡
0	20	0 (0/20)			
1	31	0 (0/31)			
2	235	15.7 (37/235)	0.46	-0.78	1.08
3	106	21.7 (23/106)	0.30	-1.22	0.63
4	3	0 (0/3)			
Total	395	15.2 (60/395)	0.39	-0.94	0.95

* Prevalence of detectable anti-tetanus IgE antibodies at 0.1 kU/L as percent followed by number of positive and total number of samples tested.

** Geometric mean concentration of anti-tetanus IgE antibodies for all samples.