

Diagnosis and "desensitization" in tetanus vaccine hypersensitivity

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A 5-year-old boy was evaluated for a history of an anaphylactic reaction to a DPT immunization at 18 months of age. Cutaneous tests and RAST disclosed high titers of IgE antibody to tetanus toxoid vaccine. Variable sensitivity to different vaccine commercial preparations was demonstrated. Immunization was achieved using a 9-step graded dosing schedule with the tetanus toxoid vaccine to which the patient was least sensitive.

INTRODUCTION

Anaphylactic reactions to tetanus toxoid have been observed since its large scale use began in 1938. Reactions were shown to be due to both tetanus toxoid protein and to various culture media proteins contaminating the vaccine.¹⁻³ Since the introduction of casein hydrolyzed peptone free media in the 1950s the number of reactions to tetanus immunization may have diminished but they continue to occur.

Although minor reactions such as local swelling are common, true IgE-mediated reactions are relatively rare. In one study of 784 DT immunizations and 15,752 DPT immunizations in children 0-6 years of age there were no reports of severe anaphylaxis or urticaria.⁴ Another study of vaccinations in 158,230 adult subjects found an incidence of anaphylactic responses to tetanus immunization to be 0.001%.⁵

We describe a patient who had an immediate allergic reaction to tetanus immunization and who successfully underwent immunization.

CASE REPORT

A 5-year-old boy presented with a history of a reaction to his fourth DPT immunization given at 18 months of age. Approximately 30 minutes after injection of the vaccine the patient had onset of large pruritic urticarial lesions over most of his body with some swelling of the lower lip. There was some lethargy but no other neurologic symptoms and no report of other symptoms such as respiratory compromise or gastrointestinal complaints.

The reaction was treated intramuscularly with 4-mg Decadron LA and Benadryl orally every four hours. The patient's urticaria resolved after 24 hours and there was no subsequent local reaction at the immunization site.

The patient's past medical history was remarkable for eczema after contact with nickel and stomachaches with diarrhea after ingesting chocolate. Prior immunizations with DPT, MMR, and oral polio myelitis vaccine had been received without adverse reaction. His mother had a history of seasonal rhinitis and eczema.

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RESULTS

Initial evaluation was with cutaneous tests by the prick and intradermal methods using Wyeth brand of vaccine. Positive (>4 mm) wheal/flare responses occurred at a 1:1,000 dilution of both diphtheria-tetanus and tetanus toxoid vaccines (Table 1). Two control subjects were negative.

On a return visit 6 months later, cutaneous tests were performed with three brands of vaccine, Wyeth, Connaught and Sclavo, which contain 5, 5, and 10 LFU (limit of flocculation units) respectively of tetanus toxoid per 0.5 mL immunizing dose (Table 2). A positive intradermal reaction occurred to Wyeth vaccine at a 1:1,000 dilution and to Connaught vaccine at a 1:100 dilution. There was some erythema only when tested with Sclavo vaccine. Intradermal testing with a Thimerosal control was negative. A third control subject similarly tested had negative responses.

A Prausnitz-Küstner test was performed, transferring the patient's serum to the mother and repeating the cutaneous tests with the three brands of vaccine. The only positive response was a 7-mm wheal with minimal erythema to Wyeth vaccine at a 1:100 dilution. When the serum was heated for 30 minutes at 56 °C, no reactions were observed.

Laboratory tests disclosed a total serum IgE of 170 U/mL. Individual

MATERIALS AND METHODS

Cutaneous tests were carried out using standard methods.⁶ All vaccines used were commercially prepared (Wyeth, Connaught, Sclavo) adsorbed toxoids with thimerosal as a preservative. Determination of serum antibody levels was performed by Advanced Allergy Man-

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Table 1. Initial Cutaneous Tests with Wyeth Diphtheria/Tetanus* and Tetanus Toxoids*

Antigen	Prick Wheal/Flare, mm	I.D. 1:1,000, 0.02 mL Wheal/Flare, mm
Dip/Tet	Negative	7/25
Tet	Negative	7/35
Saline	Negative	Negative
Histamine	5/20	not done

* Two control subjects negative.

Table 2. Repeat Cutaneous Tests with Three Brands of Tetanus Toxoid Six Months After Initial Visit*

Brand Tet Toxoid† (Lf units/0.5 mL)	Prick Wheal/Flare, mm	I.D. 1:1,000 Wheal/Flare, mm	I.D. 1:100 Wheal/Flare, mm
Wyeth (5 Lf)	Negative	9/30	not done
Connaught® (5 Lf)	Negative	Negative	6/25
Sclavo (10 Lf)	Negative	Negative	0/5
Histamine	6/25	not done	not done

* One control subject negative.

† Thimerosal 0.001% I.D. testing negative.

RASTs disclosed an antitetanus IgE of 2+ (positive, scale 0-4) and an antitetanus IgG of 1.4 U/mL (protective >0.1 U/mL).

The results of all tests were explained and discussed with the patient's mother. She understood that the current level of antitetanus IgG was protective and the medical recommendation was to delay repeat immunization until such time as the antitetanus IgG titer was below the protective level on a future measurement. Because of her lack of "peace of mind" due to her son's intense style of activity, she specifically requested that the 5-year tetanus immunization be given if at all possible. She understood the potential risks of immunization and gave

informed consent for the following procedure.

A graded challenge/desensitization was performed using the Sclavo brand of tetanus toxoid as outlined (Table 3). The patient had small wheal/flare reactions at the 1:100 dilution which was repeated once. The last four doses comprise a full strength 0.5-mL immunizing dose of vaccine. The procedure was tolerated well without any decrease in blood pressure or respiratory symptoms and there was no subsequent urticaria or large local reaction.

DISCUSSION

The use of cutaneous tests to assess hypersensitivity to tetanus vaccine is well documented. Usually indi-

viduals with a history of anaphylactic hypersensitivity to prior tetanus immunization have negative cutaneous tests up to a 1:100 dilution. In one of the more extensive studies by Jacobs only one of 95 adult patients with a history of anaphylactic symptoms had a positive cutaneous test.⁷

Our patient had a history of anaphylactic response to a DPT immunization that on further testing appeared to be due to the tetanus component of the vaccine. It is of interest that on cutaneous testing he demonstrated less sensitivity to that brand of vaccine that contained the greatest amount of tetanus toxoid implying that the patient's reaction may have been due to a nontoxoid component of the vaccine. It is conceivable that other proteins, possibly nontoxoid clostridial proteins occurring in the vaccine, were the antigen in this allergic reaction.

Several reports have been published detailing potential differences between lots or brands of vaccines that contain the same quantity of active immunizing agent. In 1989, Baraff described 9,920 subjects injected with 25 lots and four different brands of DPT vaccine with significant differences in delayed reactions between groups.⁸ In a 1987 study, Leen described the use of antibody affinity chromatography to reduce the nontoxoid protein content of commercially available tetanus toxoid vaccine.⁹ This study was also evaluating delayed reactions but supports the idea that a vaccine may contain antigenic components in addition to the toxoid itself.

Patients with a history of immediate hypersensitivity reactions to tetanus immunization may have demonstrable IgE antibodies to the vaccine. The degree of hypersensitivity may vary with different commercial preparations and lots of vaccine. This patient had protective levels of IgG antibody to tetanus protein that could have acted as "blocking antibody" reducing the risk of anaphylaxis during the

Table 3. Graded Challenge/Desensitization with Sclavo Tetanus Toxoid*

No.	Volume	Dilution	Route	Reaction
1	.02 ml	1:1,000	I.D.	none
2	.02 ml	1:100	I.D.	4/13 Wheal/Flare, mm
3	.02 ml	1:100	I.D.	1/18 Wheal/Flare, mm
4	.02 ml	1:10	S.Q.	none
5	.10 ml	1:10	S.Q.	none
6	.05 ml	full str.	S.Q.	none
7	.10 ml	full str.	S.Q.	none
8	.15 ml	full str.	S.Q.	none
9	.20 ml	full str.	S.Q.	none

* Injections given every 20 minutes.

course of desensitization. But, in view of the history and the IgE antibodies demonstrated on skin and RAST testing we felt it was necessary to proceed as if he were potentially at risk for anaphylaxis. We report a case of such an individual who was successfully immunized using a graded challenge protocol beginning below the patient's known level of sensitivity.

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IMPACT OF ASTHMA ON EMPLOYMENT IN YOUNG ADULTS

Data from the prospective study of a cohort of 17,319 births in the United Kingdom in 1958 permitted study of the relationships between employment and history of asthma or wheezing. Trained interviewers collected information about medical variables when the subjects were 7, 11, 16, and 23 years of age. Information about employment was obtained at 23 years of age from 12,534 subjects of whom 460 (4%) had current asthma or wheezing, 2758 (22%) had past asthma or wheezing, and 5161 (41%) had never had asthma or wheezing (others could not be classified). The risk of unemployment was higher in those with current asthma or wheezing (odds ratio 1.32, 95% CI 1.09-1.61) or past history of asthma or wheezing (odds ratio 1.54, 95% CI 1.27-1.85) than in those who had never had asthma or wheezing after adjustment for sex, region of birth, maximum educational qualification, and father's social class. Current or past asthma or wheezing was associated with a somewhat worse employment history including percentage of months employed since leaving school and mean number of months in current full time job.

These data indicate a small but significant adverse effect of asthma on employment in young adults. Adolescents and young adults with asthma should be counselled to seek employment that is not likely to aggravate asthma and should recognize that optimal management of asthma can minimize absence from work due to illness.

—RMS

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