

ally. Image analysis of the esophageal biopsy specimens was performed using a microscope (Eclipse E800M; Nikon Instruments Inc, Lewisville, Texas), a camera (model SPOT RT-SECCD; Diagnostics Instruments, Sterling Heights, Michigan), and software (IP lab 3.7; BD Biosciences, Rockville, Maryland). Briefly, the tissue was outlined on a photomicrograph, and an accurate calculation of the surface area was obtained. Image segmentation by hue was performed to quantify the proportion of tissue that stained blue with the Masson trichrome stain.

Pretreatment esophageal biopsy specimens showed 97 eosinophils per $\times 40$ HPF or 16 eosinophils per square millimeter of tissue in the most involved HPF (Fig 1A); 47.2% of the esophageal tissue stained positive with the Masson trichrome stain (Fig 1C).

Posttreatment esophageal biopsy specimens revealed resolution of eosinophilic infiltration, with 5 eosinophils per HPF or 0.5 eosinophils per square millimeter of tissue in the most involved HPF (Fig 1B), and a significant decrease in collagen deposition, with only 19.9% of the esophageal biopsy specimen staining positive with the Masson trichrome stain (Fig 1D). Subsequent spirometry at that time revealed a forced expiratory volume in 1 second of 106% predicted, with no significant reversibility after using the bronchodilator. Fourteen months after his second endoscopy, the boy remained symptom free while taking inhaled budesonide, 400 $\mu\text{g}/\text{d}$.

Further studies are needed to verify the effectiveness of a dry powder inhaler formulation of topical corticosteroid in the treatment of patients with EE and concomitant persistent asthma. We suggest that the use of image analysis for quantification of eosinophilic infiltration and submucosal collagen deposition would be optimal in the design of future studies investigating EE.

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THIMEROSAL IN INFLUENZA VACCINE: AN IMMEDIATE HYPERSENSITIVITY REACTION

Thimerosal is a mercury derivative used as a preservative and bacteriostatic agent. We report an immediate hypersensitivity reaction after skin testing with an adult influenza vaccine that seems to be due to thimerosal. The patient is a 31-year-old woman with seasonal allergic rhinitis and irritable bowel syndrome. She developed conjunctival erythema and local pain after using a thimerosal-containing contact lens solution 15 years before the evaluation. She then switched to and tolerated the same brand of contact lens solution without thimerosal. She received a booster dose of tetanus toxoid (0.05 μg of thimerosal per 0.5-mL dose) 2½ years before this evaluation without any difficulty. Because of her concerns regarding thimerosal, she received a thimerosal-free pediatric influenza vaccine 4 months earlier with no adverse events.

A skin prick test using the full-strength adult influenza vaccine (50 μg of thimerosal per 0.5-mL dose) generated a wheal consisting of a 3-mm induration with 25 mm of erythema with satellite lesions. Within 20 minutes, the patient developed generalized pruritus without hives, throat tightness, and a dry cough without wheezing on auscultation. Although her vital signs were stable, she was diffusely pruritic and short of breath. She was treated with 0.3 mL of epinephrine intramuscularly and 180 mg of fexofenadine orally. All symptoms resolved within 10 minutes. She returned to the clinic 2 months later for further skin testing (results of both sets of skin tests are given in the Table).

Allergic responses to thimerosal have been described, primarily as delayed-type local hypersensitivity reactions.¹ We found 1 case report² of a generalized reaction thought to be due to thimerosal in an influenza vaccine. However, the present patient is different from previous patients. First, the reaction was directly observed and there were no confounding ingestants. Second, we documented an immediate hypersensitivity reaction to the vaccine containing thimerosal and lack of a reaction to a similar vaccine without thimerosal.

Owing to the patient's history of contact sensitivity to thimerosal, the temporal relationship between skin testing with the adult vaccine and the clinically obvious reaction, and the otherwise similar constituents of the adult and pediatric vaccines, we postulate that this reaction was an IgE-mediated immediate hypersensitivity reaction to the thimerosal in the vaccine and that thimerosal probably acts

Authors have nothing to disclose.

Table 1. Selected Constituents of Relevant Vaccines^a

	Histamine control	Saline glycerol control	Adult influenza vaccine (thimerosal, ^b 25 µg/dose) ^c	Thimerosal-free pediatric influenza vaccine ^d		Egg	Tetanus toxoid (thimerosal, 0.05 µg/dose) ^e	Tetanus and diphtheria toxoids (thimerosal, ≤0.6 µg/dose) ^f
				1:10	Full strength			
Initial evaluation	5/25	1/1	3/25	ND	ND	ND	ND	ND
Follow-up evaluation	5/20	1/1	ND	1/1	1/2	1/1	1/2	1/2

Abbreviation: ND, not done.

^a Data are given as the size of the wheal/erythema in millimeters.

^b Thimerosal is approximately 50% mercury by weight.

^c Fluzone, Aventis Pasteur Inc, Swiftwater, Pennsylvania (thimerosal, 50 µg/dose).

^d A 0.5-mL prefilled syringe, 2005–2006 formula, Fluzone, Aventis Pasteur Inc (no preservative).

^e Tetanus Toxoid Adsorbed USP, Aventis Pasteur Inc (thimerosal, 0.05 µg/dose).

^f For adult use, DECAVAC, Aventis Pasteur Inc (thimerosal, ≤0.6 µg/dose).

as happen. However, this was not formally proved by in vitro IgE measurements, and, therefore, a non-IgE mechanism is possible. We believe that she tolerated earlier exposure to the tetanus vaccine and did not have skin test reactivity to the tetanus vaccine because the dose of thimerosal is much less than in the adult influenza vaccine (0.05 vs 25 µg).

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EVALUATION AND MANAGEMENT OF PEDIATRIC PATIENTS WITH ANAPHYLACTOID REACTIONS TO DEFEROXAMINE MESYLATE

Deferoxamine mesylate (Desferal; Novartis Pharmaceuticals Corp, East Hanover, New Jersey) is an iron-chelating agent indicated for the treatment of chronic iron overload.^{1,2} Anaphylactic reactions related to its use have been reported³; however, review of the literature reveals that the approach to the patient with an anaphylactic reaction to deferoxamine mesylate has been reported only by individual case reports and mainly in adult patients.^{4–8} Herein we describe 3 children with transfusion-dependent anemias for thalassemia major

(patients 1 and 2) and sickle cell disease (patient 3) who were evaluated for adverse reactions to deferoxamine mesylate.

Evaluation included prick (1/10 dilution) and intradermal (1/100, 1/1,000, 1/10,000, and 1/100,000 dilutions) skin tests. Five healthy patients were tested to establish a nonirritating dose. An advanced rapid desensitization protocol, as previously described,⁵ was used for patients 1 and 2. In short, a 7-step challenge was performed using 0.00375 mg in 10 mL of saline solution followed by 0.0375, 0.375, 3.75, and 37.5 mg in 10 mL of saline solution at 15-minute intervals and then 375 and 500 mg in 15 mL of saline solution at 70-minute intervals. If there were no adverse symptoms the day after desensitization, the patients continued with the next infusion of deferoxamine mesylate (35 mg/kg per day 5 days a week).

The 3 patients had started deferoxamine mesylate therapy at ages 6, 8, and 14 years. After exposure to deferoxamine mesylate they presented with anaphylactic-like symptoms, including breathing difficulties, wheezing, diffuse urticaria, and generalized itching in patient 1; diffuse hives in patient 2; and hypotension and severe abdominal pain in patient 3. The patients' conditions were diagnosed clinically, and tryptase or other measurements to ascertain whether the deferoxamine mesylate reactions were mast cell related were not performed. However, skin test results were positive in 2 patients (patients 2 and 3), including a pseudopod, which was evident in the 1/100 dilution (patient 3).

Patients 1 and 2 underwent successful desensitization procedures, and later the drug was used safely and effectively. Because at the time of the evaluation an alternative oral iron-chelating agent was available (deferisirox [Exjade; Novartis Pharmaceuticals Corp]), a desensitization procedure with Desferal was not indicated. The desensitization procedure is classically referred to as the process of immunologic tolerance to an antigen against which specific IgE antibodies are present.⁹ Detection of such antibodies against deferoxamine mesylate are usually not found even in the face of a true immediate-type reaction.^{4,6} We used an advanced protocol that is slightly different from what has previously been described.⁵ The protocol included the desensitization phase (infusing increasing concentrations of deferoxamine mesy-

Authors have nothing to disclose.