

maximum after 9–12 h, and subsided after 24–36 h. We decided to resume low-dose oral prednisone (5 mg daily) together with cetirizine (10 mg daily). This treatment controlled symptoms, but after 1 month the patient stopped taking cetirizine, and urticaria returned. In the attempt to control the patient's symptoms, we prescribed a combined therapy of low-dose prednisone, cetirizine, and the leukotriene-receptor antagonist montelukast (Singulair®) – 10 mg daily. The patient did not present any further urticarial rash, and after 1 month cetirizine and prednisone were stopped. Montelukast is now the only drug taken by the patient, and she has not presented any symptom in over 2 months.

Recently, a few reports have shown that leukotriene antagonists (zafirlukast or montelukast) (4, 5) or leukotriene-synthesis inhibitors (zileuton) (6) may be effective in controlling CIU, particularly when associated with aspirin intolerance. Moreover, chronic autoreactive urticaria serum has been demonstrated to induce leukotriene production, in addition to histamine release, by basophils (7).

Our patient's urticaria was characterized by an immediate and prolonged response to intradermal autologous serum and therefore can be considered autoreactive. The favorable clinical response to montelukast provides an indirect demonstration that cysteinyl-leukotrienes play an important role in both early and late skin responses elicited by autologous serum. Leukotriene antagonists may have a role in the treatment of some patients with chronic autoreactive urticaria.

*Allergy and Immunopharmacology Unit
Third Division of Internal Medicine
IRCCS Ospedale Maggiore Policlinico
I-20122-Milan
Italy
Fax: 39 02 55192842
E-mail: albited@tin.it

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Anaphylaxis to starch

D. G. Ebo, A. Schuerwegh, W. J. Stevens*

Key words: basophil activation; CD63; flow cytometry; hydroxyethyl starch (Haes-Steril®); skin test.

● A 46-YEAR-OLD woman was investigated for a severe peroperative anaphylactic/anaphylactoid reaction. Induction of anesthesia with cisatracurium, propofol, and sufenta was uneventful. However, immediately after the beginning of infusion of the plasma expander Haes-Steril® (Fresenius Kabi), the patient developed hypotension (MAP <60 mmHg) associated with urticaria. The infusion was stopped, and she was successfully treated with epinephrine and dopamine. Personal history revealed an atopic background and several uneventful surgical interventions. Laboratory analyses, 4 months after the event, showed a normal blood count, normal complement profile, total IgE of 370 kU/l, and latex IgE of <0.35 kU/l (Immuno-CAP, Upjohn-Pharmacia, Belgium). Flow cytometric analysis (FACScan, Becton Dickinson) of activated basophils was performed with fluorescein isothiocyanate (FITC)-conjugated anti-CD63 and phycoerythrin (PE)-conjugated anti-IgE double labeling (Basotest®, Orpegen Pharma, Heidelberg, Germany) (Table 1). The stimulation with Haes-Steril was positive in the patient. In addition, donor basophil activation was assessed after prior incubation with serum of the patient. Upon challenge with Haes-Steril, passively sensitized basophils of the donor showed significant upregulation of CD63 expression. The patient did not allow skin testing.

A reaction to a plasma expander with basophil activation.

Hydroxyethyl starch (HES) compounds are synthetic polymers derived from amylopectin, and are classified by *in vitro* molecular weight (MW) into high, medium, and low MW preparations. However, HES is metabolized, and both the pharmacodynamic properties and adverse events of HES compounds depend on the *in vivo* MW. A low etherification index (0.4–0.5) and a low C2/C6 ratio (<8) lead to a rapid degradation, resulting in a small *in vivo* MW. In pentastarch, more than 90% of the amylopectin is etherified, and an average of four or five of the hydroxy groups in each 10-D-glucopyranose unit of the starch polymer is converted to OCH₂CH₂OH groups. Haes-Steril contains 6–10% pentastarch. To our knowledge, IgE-mediated hypersensitivity to a pentastarch solution has not been reported in the literature (1, 2). Generally, the diagnosis of IgE-mediated drug allergy is based upon history and the quantification of specific IgE and/or a positive skin test. In case of refusal/impossibility of skin testing and in the absence of the opportunity for a specific IgE determination, however, other methods are needed. IgE-sensitized basophils, on encounter with specific allergen, not only secrete and generate bioactive mediators (e.g., histamine), but also upregulate the expression of membrane markers (e.g., CD63). CD63 is anchored in the basophilic granule membrane and is weakly expressed on resting basophils. In contrast, as a result

of fusion between the granule and plasma membrane, CD63 is expressed with a high density on activated basophils, reflecting cell degranulation (3). This upregulation can be detected by flow cytometry, and calculation of the percentage of anti-IgE positive cells that coexpress CD63 allows assessment of basophil activation (4). CD63 upregulation can also be assessed with donor basophils that are incubated with serum of the patient.

Taken together, the results suggested the presence of pentastarch-specific IgE antibodies in the serum of this patient, sufficient to bind and activate the donor basophils. Given the temporal relationship, the clinical manifestations, and the positive activation test with basophils of the patient and passively sensitized basophils, an IgE-mediated reaction to Haes-Steril in this patient was established.

*Department of Immunology, Allergology and Rheumatology
University of Antwerp (UIA)
Universiteitsplein 1
B 2610 Antwerp
Belgium
Tel. 32-3-820.25.95
Fax: 32-3-820.26.55
E-mail: immuno@uia.ua.ac.be

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Are IVIG for chronic unremitting urticaria effective?

R. Asero

Key words: autoimmunity; intravenous immunoglobulins; urticaria.

● SOME patients with severe chronic idiopathic urticaria (CIU) do not respond to antihistamines alone and need high-dose, long-term corticosteroids for adequate control of the disease. For these patients, some alternative therapeutic approaches have been suggested, one of them being high-dose intravenous immunoglobulins (IVIG) (1). IVIG are extensively used to treat several autoimmune diseases. The rationale for their use in CIU stems from the observation that many patients show a wheal and flare reaction upon intradermal injection of autologous serum, and that

Table 1. Basophil activation tests

	Patient basophils	Donor basophils	Passively sensitized donor basophils
Negative control (without drug)	3	1	1
Positive control (fMLP)	58	38	n.d.
Haes-Steril [®] (30 g/500 ml)	77	0	18
Propofol (Diprivan [®]) 10 µg/ml	2	n.d.	n.d.
Cisatracurium (Nimbex [®]) 10 µg/ml	3	n.d.	n.d.
Sufenta (Sufentanyl [®]) 5 µg/ml	4	n.d.	n.d.

Results are expressed as percent CD63-positive basophils after activation. n.d.: not done.