

increasingly in various nonmedical environments, including those leading to contact with irritant chemicals, foods, and plants (7, 8). This report suggests that the possibility of occupational asthma due to NRL should be suspected and properly investigated in all workers with work-related asthma, even when they are exposed to other agents known to cause asthma. NRL-induced asthma may remain undiagnosed for a long time because exposure to airborne NRL allergens can be indirect, resulting from coworkers using gloves. Further epidemiologic investigations are needed to assess the prevalence of occupational asthma caused by NRL gloves in industrial environments.

Key words: asthma; bronchial provocation tests; latex; occupational diseases; penicillin.

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REFERENCES

1. Turjanmaa K, Alenius H, Mäkinen-Kiljunen S, Reunala S, Palosuo T. Natural rubber allergy. *Allergy* 1996;51:593-602.
2. Tarlo SM, Wong L, Roos J, Booth N. Occupational asthma caused by latex in a surgical glove manufacturing plant. *J Allergy Clin Immunol* 1990;85:626-31.
3. Orfan NA, Reed R, Dykewicz MS, Ganz M, Kolski GB. Occupational asthma in a latex doll manufacturing plant. *J Allergy Clin Immunol* 1994;94:826-30.
4. Vandenplas O, Delwiche JP, Evrard G, et al. Prevalence of occupational asthma due to latex among hospital personnel. *Am J Respir Crit Care Med* 1995;151:54-60.
5. Cockcroft DW, Killian DN, Mellon JJA, Hargreave FE. Bronchial reactivity to inhaled histamine: a method and clinical survey. *Clin Allergy* 1977;7:235-43.
6. Davies RJ, Hendrick DJ, Pepys J. Asthma due to inhaled chemical agents: ampicillin, benzylpenicillin, 6-aminopenicillanic acid and related substances. *Clin Allergy* 1974;4:227-47.
7. van der Walle H, Brunsveld V. Latex allergy among hairdressers. *Contact Dermatitis* 1995;32:177.
8. Carillo T, Blanco C, Quirarte J, Castillo R, Cuevas M, Rodriguez de Castro F. Prevalence of latex allergy among greenhouse workers. *J Allergy Clin Immunol* 1995;96:699-701.

Possible role of IgE in acute-phase response

VARIOUS injuries, such as infection or trauma, induce the systemic acute-phase response, expressed by release of several hormones; activation of clotting, complement, and kinin-forming pathways; and drastic increase in certain plasma proteins (1).

We have recently described a characteristic response of IgE to tissue injury. It was observed in patients undergoing coronary artery bypass surgery who did or did not develop perioperative myocardial infarction, in patients undergoing various thoracic surgical operations, and in those who underwent abdominal surgery, such as cholecystectomy or repair of inguinal hernia (2). In all the groups of patients studied, as opposed to controls, serum IgE began to rise shortly after surgical operations, continued to increase over the following days, reached a peak by day 5, and then gradually declined. This was accompanied by a rise in serum levels of IgG4 and interleukin (IL)-6.

When we first observed the surprising behavior of serum IgE after myocardial infarction (3), we were inclined to think that it represents a specific immunologic response to antigens released from the necrotic heart muscle. However, the data obtained by us recently in the large prospective study (2) indicate that this may be a more general reaction, precipitated by tissue injury, leading to inflammation. Our results may clarify several reports which indicated the unexplained phenomenon of a transient IgE rise in various pathologic situations; i.e., after severe burns (4), splenectomy after trauma (5), sepsis after traumatic injury (6), pulmonary thromboembolism (7), and coronary artery bypass grafting (8).

Corticosteroids may be among the factors responsible for the immune response discussed. Their plasma concentration rises after stress and trauma. Unlike those of other serum immunoglobulins, IgE levels increase after initiation of corticotherapy (9). Glucocorticoids in low concentrations markedly enhance biosynthesis of IgE by IL-4. IL-6, which increases dramatically in patients undergoing major surgery (10), is critical to induce IgE synthesis. In 1993, Jabara et al. (11) described sequential switching from mu to epsilon via gamma 4 in human B cells stimulated with IL-4 and hydrocortisone. Newly synthesized IgE is not specific to allergens; isotype switching in human B cells leads to increased polyclonal IgE production.

Mast cells are considered to play a pivotal role in the inflammatory reaction, and eosinophils, mac-

The behavior of human serum IgE seems to bear much resemblance to that of acute-phase proteins; IgE might modulate the participation of many cells in the inflammatory reaction.

rophages, platelets, and B cells are also involved in this process. Transient, increased production of IgE could activate these cells; IgE may be part of the mechanism of the acute-phase response. This would corroborate recent results pointing to higher serum IgE levels during exacerbation of rheumatoid arthritis (12) and chronic obstructive pulmonary disease (13).

The discovery of IgE gave an insight into the fundamental mechanism of allergy. Atopy, one of the most common genetically determined traits, characterized by overproduction of IgE, became well defined. The observations here briefly discussed point to still another role of IgE, a role in the acute-phase response, which should be carefully examined.

Key words: acute-phase proteins; IgE; surgical stress.

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REFERENCES

1. Koj A. Initiation of acute phase response and synthesis of cytokines. *Biochim Biophys Acta* 1996;1317:84-94.
2. Szczeklik A, Jawień J. Immunoglobulin E in acute phase response to surgical stress. *Clin Exp Allergy* 1996;26:303-7.
3. Szczeklik A, Sladek K, Szczerba A, Dropinski J. Serum immunoglobulin E response to myocardial infarction. *Circulation* 1988;77:1245-9.
4. Polacek V, Jira M, Fara M, Strejcek J, Konigova R. Immunoglobulin E (IgE) in patients with severe burns. *Burns Incl Therm Injury* 1987;13:458-61.
5. Chelazzi G, Pinotti G, Nicora C, Rossi D, Senaldi G. Increased total serum IgE concentration in patients who have undergone splenectomy after trauma. *J Clin Pathol* 1995;38:1309-10.
6. DiPiro JT, Howdieshell TR, Hamilton RG, Adkinson NF, Mansberger AR. Increased plasma IgE levels in patients with sepsis after traumatic injury. *J Allergy Clin Immunol* 1996;97:135-6.
7. Takekawa H, Miyamoto K, Yamaguchi E, Munakata M, Unger F. Acute rise in serum immunoglobulin E concentration in pulmonary thromboembolism. *Chest* 1993;104:61-4.
8. Ghosh PK, Pohla-Gubo G, Pohla H, Antretter H, Unger F. Perioperative immunoglobulin E response to coronary artery bypass grafting. *J Cardiovasc Surg (Torino)* 1992;33:28-32.
9. Hiratsuka S, Yoshida A, Ishioka C, Kimata H. Enhancement of *in vitro* spontaneous IgE production by topical steroids in patients with atopic dermatitis. *J Allergy Clin Immunol* 1996;98:107-13.
10. Szczeklik A, Jawień J, Stadler BM, Radwan J, Piwowarska W, Dziatkowiak A. Possible relationship between interleukin-6 and response of immunoglobulin E to surgical trauma. *Ann N Y Acad Sci* 1995;762:477-9.
11. Jabara HH, Loh R, Ramesh N, Vercelli D, Geha RS. Sequential switching from mu to epsilon via gamma 4 in human B cells stimulated with IL-4 and hydrocortisone. *J Immunol* 1993;151:4528-33.
12. Kutsyk RV, Neiko IM. The level of total immunoglobulin E in the blood serum of rheumatism patients. *Vrach Delo* 1992;10:35-7.
13. Sherill DL, Lebowitz MD, Halonen M, Barbee RA, Burrows B. Longitudinal evaluation of the association between pulmonary function and total serum IgE. *Am J Respir Crit Care Med* 1995;152:98-102.

Anaphylactic reaction to methotrexate

METHOTREXATE is an antimetabolite of folic acid which acts as an antineoplastic agent and also has immunosuppressant properties; both effects are due to its inhibition of the dihydrofolate reductase enzyme. We report a case of anaphylactic reaction due to methotrexate in which clinical data and positive skin tests suggested an IgE-mediated hypersensitivity mechanism.

A 49-year-old woman with breast cancer was admitted to our hospital to receive her first chemotherapy cycle. Cyclophosphamide, 5-fluorouracil, adriamycine, vincristine, and prednisone were administered for 4 days with no adverse reaction. On day 5, while cyclophosphamide was being infused, the first dose of methotrexate was administered. After a few minutes, the patient developed urticarial rash, breathlessness, hypotension, and loss of consciousness; she was then treated with fluidotherapy and corticosteroids, with remission.

There was no family or personal atopy background. Total IgE was within normal values, and specific IgE to common inhalants and food allergens were negative.

As the reaction might have been caused by either of the two drugs – methotrexate or cyclophosphamide – both were studied. Skin prick tests with methotrexate and cyclophosphamide were performed at concentrations of 25 and 20 mg/ml, respectively. Intradermal tests were carried out at a dilution of 1/100 of the concentrations previously described. The positive and negative skin test

A patient with a positive skin prick test to methotrexate.

controls were histamine and saline solution, respectively. The same tests were carried out in 10 healthy patients in order to rule out irritant responses. To investigate the possible IgE-mediated mechanism, we attempted to detect specific IgE *in vitro* by

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