

Table 1. Results of study performed

	Patient 1	Patient 2	Patient 3
Tetrazepam 1% pet. ¹	++	+	+
Tetrazepam 5% pet. ¹	++	+	+
Tetrazepam oral challenge	Urticarial eruption (50 mg)	Micropapular rash (12.5 mg)	ND
Diazepam oral challenge (5 mg)	Negative	Negative	Negative
Bromazepam oral challenge (1.5 mg)	Negative	Negative	Negative

¹ Patch test reading at 96 h.

ND: not done.

urticarial eruption 3 h after ingestion of tetrazepam 50 mg. Patient 2 developed lesions similar to those previously described 10 h after ingestion of tetrazepam 12.5 mg. In patient 3, tests were not performed due to the severity of symptoms. All patients tolerated other benzodiazepines such as bromazepam 1.5 mg (Lexatin®, Roche) and diazepam 5 mg (Valium®, Roche) without ill effect.

Three patients with positive patch tests.

■ Clinical features in our patients as well as positive patch test and challenge test suggest a type IV hypersensitivity reaction to tetrazepam. The positive patch test to tetrazepam supports the use of patch testing in the diagnosis of adverse cutaneous reactions, to obviate oral challenge. There is only one case report in which oral challenges with other benzodiazepines were done (5). Our negative results of oral challenges with bromazepam and diazepam show that there is no cross-reactivity between these benzodiazepines.

Key words: angioedema; patch testing; tetrazepam; urticaria.

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Accepted for publication 26 June 1997

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ALLERGY 1997;52:1146–1147

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Asthma to latex and amoxicillin

IN recent years, natural rubber latex (NRL) has been increasingly recognized as a major cause of IgE-mediated allergic reactions among persons repeatedly exposed to NRL materials (1). The clinical manifestations of NRL allergy range from mild urticaria to life-threatening anaphylaxis after cutaneous, mucosal, or visceral exposure. Occupational asthma caused by airborne NRL allergens has been documented primarily in workers manufacturing NRL articles (2, 3) and in health-care providers wearing NRL gloves (4). We describe a pharmaceutical worker who developed occupational asthma from both NRL allergens and amoxicillin.

■ A 24-year-old woman began working in the production department of a pharmaceutical company processing amoxicillin in October 1991. After 6 months, she developed nasal stuffiness, sneezing, rhinorrhea, wheezing, cough, and chest tightness at work. These symptoms improved in the evening at home and on weekends, although she was awakened by nocturnal asthma on most workdays. Three months before the onset of respiratory symptoms, she noticed redness and itching of her hands while wearing NRL gloves. These cutaneous symptoms disappeared when she switched to vinyl gloves, although her coworkers continued to use NRL gloves.

In January 1993, an inhalation challenge with amoxicillin powder for 5 min produced a 23% fall in forced expiratory volume in 1 s (FEV₁) (data not shown). The subject was advised to avoid

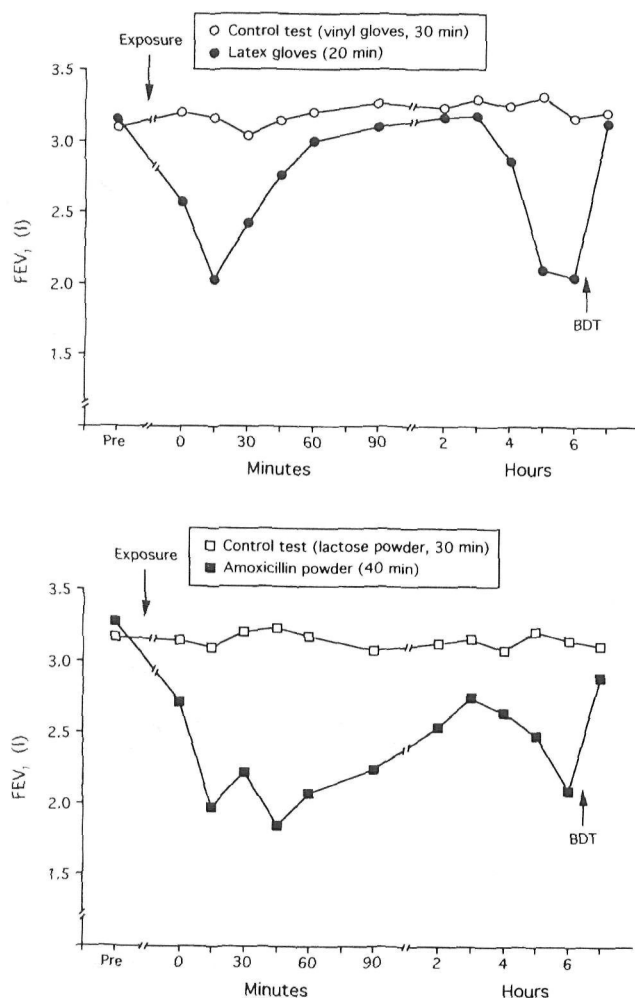


FIGURE 1 Results of inhalation challenges. Upper graph: exposure to vinyl gloves (open circles) and latex gloves (closed circles). Lower graph: exposure to lactose powder (open squares), and amoxicillin (closed squares). BDT: inhaled bronchodilator (salbutamol, 200 µg).

occupational exposure to penicillins, and she subsequently became symptom-free. She began to retrain to become an auxiliary nurse 9 months after removal from the workplace. On the second day of her practical training in hospital, she developed extensive urticaria while wearing NRL gloves. She also noticed rhinoconjunctivitis and asthma related to hospital exposure. Four months later, she had to discontinue training because her asthma had worsened despite treatment with inhaled beclomethasone dipropionate and terbutaline.

The subject was referred for investigation 2 weeks after the last hospital exposure. She had never smoked and reported no personal or familial history of atopy. She had never undergone surgical procedures. Skin prick tests with common inhalant allergens gave negative results. The prick test using

a commercial extract of NRL (Stallergènes SA, Brussels, Belgium) elicited an 8-mm wheal reaction. A high level of specific IgE against NRL was detected (>100 IU/ml, Pharmacia CAP System, Uppsala, Sweden). Baseline lung function tests showed a FEV₁ of 3.09 l (88% predicted value) and a FEV₁/forced vital capacity ratio of 72%.

Inhalation challenge tests with NRL gloves were carried out in the laboratory, as previously described (4). As a control challenge, the subject handled vinyl gloves for 30 min in a 5-m³ challenge room without eliciting significant changes in FEV₁.

At the end of the control day, the provocative concentration of histamine causing a 20% fall in FEV₁ (CP₂₀) was 0.07 mg/ml (5). On the next day, the subject handled NRL gloves while wearing vinyl gloves to prevent any direct contact of NRL with the skin. After 5 min of exposure, she experienced marked rhinoconjunctivitis. A cumulative exposure of 20 min resulted in a 36% fall in FEV₁, which recovered spontaneously over the next hour. The subject developed a late asthmatic reaction with a 35% fall in FEV₁ 6 h after the end of exposure. Three weeks later, inhalation challenge by pouring amoxicillin powder (diluted 1/10 in lactose powder) from one tray to another was performed after a control challenge with lactose for 30 min (Fig. 1). After exposure to amoxicillin for 40 min, the fall in FEV₁ reached a maximum of 43%, 45 min after challenge, followed by a progressive recovery and a later decline of 36% at 6 h.

Specific inhalation challenges provided convincing evidence that both NRL and amoxicillin were involved in the development of occupational asthma in our subject. These findings further emphasize that the agent(s) causing asthma should be precisely identified in order to implement appropriate avoidance procedures and professional retraining. Penicillin and derivative compounds are a well-documented cause of occupational asthma (6). In recent years, it has been shown that protein from NRL gloves can adsorb onto glove powder particles and become an airborne allergen (1). Inhalation of NRL allergens can also result from grinding NRL articles (3). Occupational asthma has been shown to occur in 6% of workers manufacturing NRL gloves (2) and in 2.5% of hospital employees (4). However, NRL gloves are used

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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Accepted for publication 30 June 1997

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ALLERGY 1997;52:1147–1149

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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.

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