Increased Neutrophil Leukocyte Chemotaxis Induced by Release of a Serum Factor in Toluene-Diisocyanate (TDI) Asthma

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Abstract. The activation of blood neutrophil leukocytes has been proven in subjects with IgE-mediated and non-IgE-mediated asthma. This event appears to be modulated by the release of humoral factors. We submitted 12 toluene-diisocyanate (TDI) asthmatic workers to TDI provocation. During the late asthmatic reaction there was release of a serum chemoattracting factor for normal neutrophil leukocytes and activation of asthmatic neutrophil leukocytes. This appears to be the first demonstration of neutrophil chemotactic activity liberated during the late TDI reaction in humans. The results are explained by an acute inflammatory process occurring during the late asthmatic reaction induced by TDI.

Key words: Asthma—Neutrophil leukocytes—Chemotaxis.

Introduction

Occupational exposure to toluene diisocyanate (TDI) frequently causes asthma, but the pathogenesis is not clear [4, 6, 17]. A chemoattractive factor for normal neutrophil leukocytes has been found in the serum of subjects with IgE-mediated asthma [3, 5], as well as those with aspirin- [15] or exercise-induced [18] asthma. Moreover it has been shown that there is an activation of polymorphonuclear leukocytes after the induction of bronchial obstruction in these subjects [5, 22].

A group of TDI asthmatic subjects was studied with nonspecific and specific bronchial provocative tests in order to determine whether, after the induction of bronchial obstruction, there were (1) a release of a serum chemoattrac-
tive factor for normal neutrophil leukocytes and (2) an activation of the asthmatic neutrophil leukocytes.

Methods

Selection of Subjects

TDI-exposed workers were identified by selecting all persons who had sprayed polyurethane varnishes for at least one year in 2 furniture plants. We selected 12 (9 men, 3 women) TDI asthmatic subjects, age 34.4 ± 9.7 yr, and 12 (9 men, 3 women) nonasthmatic subjects, age 35.1 ± 8.9 yr. The asthmatic subjects had developed nasal symptoms, chest tightness, and wheezing after TDI exposure. These symptoms occurred during the active work week and improved appreciably or disappeared during 2-day-off periods. In all cases symptoms had cleared completely during longer vacation periods. In all asthmatic cases bronchial provocation with polyurethane varnish had shown a significant reduction of FEV1.

None of the TDI workers was a smoker. Allergic prick tests with a panel of 14 common inhalants and pollen allergens (Lofarma Series, Lofarma, Milan, Italy) were negative in each subject. Serum total IgE level and specific anti-isocyanate IgE were determined by radioimmunoassay techniques (Phadebas PRIST and RAST Kits, Pharmacia Diagnostics, Uppsala, Sweden). IgE were normal, and specific anti-isocyanate IgE were always negative.

At the time of the study all the asthmatic subjects were free of symptoms and signs of asthma and had refrained from taking any medication for 7 days. The time interval between the last exposure to isocyanate and the study ranged from 30 to 60 days. All the subjects gave informed consent.

Study Design

Each subject was submitted to nonspecific bronchial provocation test with methacholine. Immediately before the test and after the maximum fall of FEV1, samples of serum and neutrophil leukocytes were taken. After at least 24 hr, each subject was also submitted to a TDI provocation bronchial test. In TDI asthmatic workers immediately before and after the maximum fall of FEV1, which occurred between the second and fourth hour following TDI inhalation, samples of serum and neutrophil leukocytes were taken. Similarly, in nonasthmatic workers samples of serum and neutrophil leukocytes were taken immediately before the test and after 3 hr.

For each subject, serum was tested against neutrophil cells obtained from normal health laboratory personnel, while neutrophil leukocytes were tested against a standard chemoattractive stimulus. The nonspecific bronchial provocative test with methacholine was performed according to Sherwood Burger [25], and the dose of methacholine provoking a 20% decline in FEV1 (PD20) was calculated.

The specific bronchial provocative test with TDI was performed according to Zedda et al. [27] with some modifications. One hundred ml of a 2-pot polyurethane varnish with TDI in the activator was painted on the surface of wood laminas with a brush in a cabin of 15 m³. TDI concentration in the air, which increased during the time, was measured by the Marcali method [21] during the first 5 min and before the end of the test (Table 1). Each subject remained in the cabin until the varnishing was finished or for at least 10 min. Four male subjects (CE, PA, CD, ER) who did not complete the varnishing in 10 min remained in the cabin 11, 12, 13, and 15 min, respectively. Before and 5, 15, 30, and 60 min after varnishing the FEV1 was recorded and the measurement was repeated each hour up to 8 hr. A fall in FEV1 greater than 15% was considered a positive response. The responses were classified as positive-immediate if the fall was found within the first hour after the exposure test, and positive-late if it was found after one hour. Control tests were performed with varnish contain-