

treated with steroids and methylxanthine derivatives plus β_2 -adrenergic agonists. As shown in Table 1, the patients from group I, followed up for 7 years of treatment, had not increased significantly the doses of steroids taken (0.8 and 0.5 mg; $P < 0.01$). Nor were steroid doses increased by patients in group IV, who were taking, apart from steroids, also methylxanthines plus drugs from the group of β_2 -adrenergic receptor agonists or atropine derivatives (0.4 and 0.6 mg; $P < 0.01$). Significant increase of the doses of steroids taken was observed in the group of two patients taking, apart from steroids, also drugs from the group of β_2 -adrenergic receptor agonists (from 0.6 to 4.1 mg daily; $P < 0.01$). A similar increase was observed in the doses of steroids taken in the group of three patients treated with atropine derivatives (from 0.7 to 3.9 mg daily; $P < 0.01$). Table 1 shows that sudden deaths were observed only in the group of patients chronically taking steroids plus drugs from the group of β_2 -adrenergic receptor agonists (six deaths) and in the group of patients treated with steroids plus atropine derivatives (three deaths).

Our observations show that drugs from the group of β_2 -adrenergic receptor agonists, administered systematically and for long time periods, can impair the clinical condition of patients with asthma and can increase the requirement for steroids. They can cause sudden death in patients in whom no accompanying diseases, apart from asthma, were previously diagnosed. Nine sudden deaths occurred in patients taking relatively high doses of drugs from the group of β_2 -adrenergic receptor agonists, and three deaths were observed in patients taking atropine derivatives. All deaths were sudden, occurring at railway stations, or in trains or buses. None of the dying patients had reported previously any complaints which could indicate heart disease or other accompanying pathologic conditions. Periodical medical examinations found no circulatory system diseases. Postmortem examinations performed in six cases suggested that sudden deaths occurred through the mechanism of cardiac

arrhythmia. In all autopsies, acute myocardial ischemia was diagnosed.

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Genetic studies on atopy and helminthiasis

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Key words: atopy; genetic studies; helminth infections.

● STUDIES carried out so far have shown that deciphering the genetics of atopy is a very complex task. Atopy may be defined as the presence of either a positive skin prick test to one or several common allergens, or a positive *in vitro* test for allergen-specific IgE, associated with a serum total IgE level higher than normal. However, in some studies, subjects have been diagnosed as atopic on the basis of a single increase of their serum total IgE titer (1, 2).

Besides atopy, helminth infections are the other common cause of elevated total IgE level. Why helminthiasis elicits such a laboratory abnormality remains unclear. The first observation was published in 1968 by Johansson et al. (3), who worked on Ethiopian preschoolchildren with ascariasis. High serum total IgE concentrations were then reported from patients with cystic echinococcosis, filariasis, schistosomiasis, strongyloidiasis, or toxocariasis. Ascariasis and echinococcosis are rather uncommon in most Western countries, and the next two diseases are quite exotic. Strongyloidiasis exists both in tropical and temperate (e.g., northern Italy or Spain) areas. In the USA, it is endemic in the Appalachian region, in the southern states, and along the Mississippi river (4), where a genetic survey was carried out by Khurana-Hershey (2). Toxocariasis is a worldwide zoonosis, and seroprevalence rates of 23-37% have been reported from rural areas in Austria, the Swiss Jura region, and southwestern France (5). In the northeastern, southern, and western USA, the seroprevalence rate is around 7% (6).

We found a mean serum total IgE level as high as 982 ± 222 IU ml^{-1} in 21 French strongyloidiasis outpatients (unpublished results). *In vitro*, we also assessed in 84 French toxocariasis outpatients the presence of specific IgE for 14 common inhalant allergens (Matrix Aero[®], Abbott Laboratories, Chicago, IL, USA). In 41 patients exhibiting a negative Matrix Aero test, the mean serum total IgE concentration was 1752 ± 674 IU ml^{-1} . In the other 43 subjects, who were probably atopic since they displayed a titer of >0.49 IU ml^{-1} for any allergen from the panel, the mean value was 1747 ± 469 IU ml^{-1} . The difference was not significant (Mann-Whitney U test).

Epidemiologic data on strongyloidiasis and toxocariasis associated with these results suggest that these helminthiasis could act as a confounder in genetic studies. Since parasite infection clusters within families, pairs of siblings recruited for high total IgE levels may be concordant because of this environmental

We should exclude helminthiasis among subjects in a genetic survey of atopy.

factor rather than genetics. However, their sharing of genes will not be increased above that expected (based on their relatedness) unless there is an association between gene and phenotype. It is possible that one might detect genes for susceptibility to helminthiasis (e.g., *Toxocara canis* or *Strongyloides stercoralis*) (7) rather than atopy, but it is more likely that the study's power to detect atopy genes would be decreased.

In view of these findings, if we were carrying out a genetic study of total serum IgE level, we would consider it prudent to test all subjects with high levels for the presence of helminth infections, even in families recruited in Western countries. These data would be included in the genetic analysis, and could also be used, along with genotype information, to examine the vexed question of the relationship between helminth infections and atopy (8).

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Glutaraldehyde-induced asthma

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Key words: glutaraldehyde; nonspecific bronchial hyperresponsiveness; occupational asthma; specific bronchial challenge test.

● GLUTARALDEHYDE is a low-molecular-weight aliphatic dialdehyde widely used as a 2% aqueous solution in the cold sterilization of medical equipment and as a hardener in the development of radiographs. Exposure to this disinfecting agent has been

shown to cause symptoms of irritation of the upper respiratory tract, dermatitis (1, 2), and occupational asthma of uncertain mechanism (3-6).

We describe a 61-year-old nurse, an ex-smoker, who began working in a renal dialysis unit in 1976. Ten years later, she experienced sporadic and mild episodes of chest tightness and shortness of breath related to exposure to formalin, which was used to sterilize artificial kidney machines. In 1994, formalin was replaced with 2% glutaraldehyde (Cidex[®], Johnson & Johnson Medical, Skipton, UK), which she handled daily in an open environment. She was symptomless until February 1998, when she developed symptoms of irritation of the eyes and upper respiratory tract, dyspnea on exertion, dry cough, and episodic attacks of wheezing, which she associated with glutaraldehyde exposure. Her symptoms were progressively severe, and she had an acute asthma attack requiring hospital admission. She then took sick leave, during which she slowly recovered. When initially evaluated in our clinic, she had been away from work for 3 months, had been

Glutaraldehyde disinfectant caused occupational asthma in a nurse.

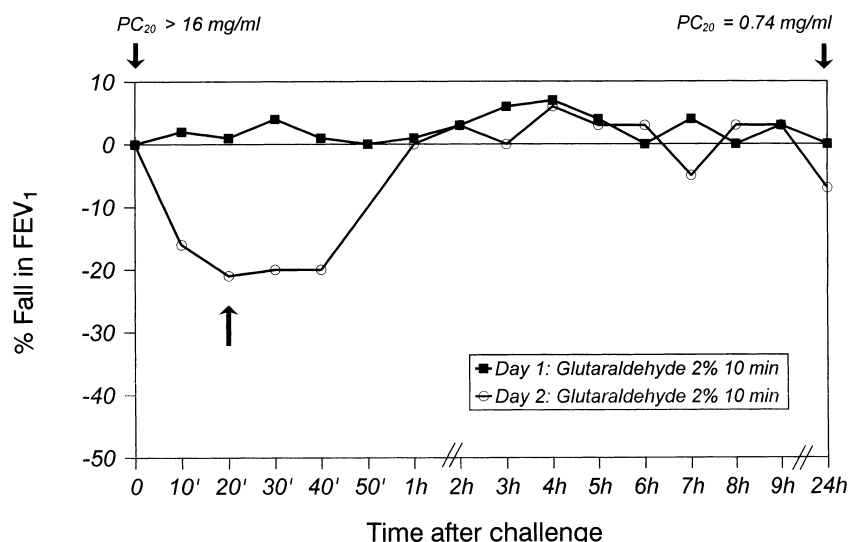


Figure 1. Exposure to 2% glutaraldehyde aqueous solution for 10 min on test day 1 did not induce significant changes in FEV₁, but methacholine inhalation test became positive (PC₂₀ 0.74 mg/ml). Re-exposure to 2% glutaraldehyde for 10 min on test day 2 elicited immediate asthmatic response. Arrow: salbutamol 200 µg.