

Occupational asthma caused by ethanolamines

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Amino alcohols are used in various industries, often as minor constituents of compounds to modify the properties of the compound. Generally, they are considered to be safe, but they have been known to cause local skin irritation at higher concentrations in solutions. We report on three cases of occupational asthma caused by ethanolamines: two metal workers exposed to a cutting fluid containing triethanolamine, and one cleaner exposed to a detergent containing monoethanolamine. The diagnosis was based on work-related symptoms and on a chamber challenge with the suspected agent. Persistence of the symptoms after exposure ended was a common feature of the three cases.

Amino alcohols are extensively used in the chemical and pharmaceutical industries today, as plasticizers, lubricant additives, emulsifiers, corrosion inhibitors, textile-finishing agents, and intermediates in the production of soaps and detergents, and in cosmetic formulations (4). Ethanolamines are amino alcohols in which one to three (e.g., mono-, di-, and triethanolamine) ethanol groups are attached to an amino group (NH_3).

Generally, amino alcohols are considered to have low toxicity, but they may have a local irritant effect in concentrated solutions (4, 10). In view of their low vapor pressure, significant exposure by inhalation is improbable under normal circumstances (15). Triethanolamine is a mild skin irritant (10) which has caused some cases of allergic contact dermatitis (3, 7). Except for one case report on asthma and one on rhinitis (11, 14), no other adverse health effects caused by pure amino alcohols (e.g., mono-, di-, and triethanolamine) have thus far been reported. However, other amines, especially the ethylene amines, e.g., ethylenediamine (EDA), diethylenetriamine (DETA), and triethylenetetramine (TETA), are well-known contact sensitizers. Occasional reports of occupational asthma or respiratory symptoms caused by EDA (8, 11, 12, 19, 21), aminoethyl ethanolamine (25, 27), dimethyl ethanolamine (29), and other amines (5) have also been published.

We report on two cases of occupational asthma caused by triethanolamine. We also present one case

of occupational asthma caused by an ethanolamine-containing detergent.

Methods

Skin prick tests

All patients were tested for immediate allergy. Prick tests were done with 15–20 common environmental allergens, according to a standard procedure (1).

Lung function and provocation tests

Nonspecific bronchial reactivity was tested according to a modified protocol of Laitinen (18). In all cases, the specific asthma diagnosis was based on a provocation test in an inhalation challenge chamber with the suspected agent, and it was followed up with peak expiratory flow (PEF) measures for 24 h, as described by Newman Taylor & Venables (22). These measurements were supplemented with forced expiratory volume in 1 s measurements (FEV_1). All measurements were controlled by a nurse. Placebo challenges were performed with unheated polyol. One patient (no. 3) was exposed also to metal dust from his workplace. The challenges with cutting fluids and detergents were made with the examinee stirring 200 ml of the suspected agent cold, heated to 100°C , or both in a shallow dish in the chamber for 30 min. The test was considered to be positive if there was a fall of over 20% in the PEF values within

1 h after the challenge (immediate reaction) or later within 24 h (delayed reaction), as compared with both the values of the morning before the challenge and the concurrent values of the negative control test. Two control asthmatic patients, one with mild and the other with moderate hyperreactivity of the airways, were exposed to heated triethanolamine and to triethanolamine aerosol, but neither of them got respiratory symptoms or showed prominent PEF drops. The PEF surveillance at home and at work was done as described by Burge (6). Recordings were made every 2 h; the best of three readings was accepted. The daily maximum and minimum of these best readings were plotted.

Case reports and Results

The main characteristics of the three patients are summarized in Table 1. The heredity of the subject was considered to be atopic if there was a history of asthma, allergic rhinitis, or atopic eczema in the subject's parents or siblings. None of the patients had a family history of atopy, but patient no. 1 himself had a history of allergic rhinitis.

Patient no. 1

The patient had been working in his present workplace since 1967. His work consisted of various metal-tooling, turning, and cutting tasks. He was exposed to metal dust and oil fumes from his own tasks, but also from the neighboring work benches. The cutting fluid he had been using contained 85% triethanolamine. He began to experience shortness of breath and cough during working days; these symptoms worsened at the end of the week. On vacations, he was symptomless. Later he noticed

that oil fumes provoked his symptoms. His spirometric values were normal, but he had bronchial hyperreactivity. Challenges were performed with polyol, with cutting fluid A (no triethanolamine), with cold cutting fluid B, and with heated cutting fluid B. Cold cutting fluid B caused an immediate, long-lasting PEF drop of 18%; heated (100°C) it caused an immediate, long-lasting reaction with PEF drops of 21% and a decrease of 13% in FEV₁ (Fig. 1).

After the diagnosis, the patient left his job, and his exposure to triethanolamine thus ended. Half a year later, he still had asthmatic symptoms and needed regular medication.

Patient no. 2

The patient had worked as a turner for 34 years. In his work, he was exposed to smoke from grease heating when the lathe was turning, and to fumes from turning and cooling fluids. He had experienced some chest tightness in the early 1980s, at which time he stopped smoking, and his symptoms were subsequently relieved. Some years later, the symptoms returned, i.e., cough, dyspnea, chest tightness, rhinitis, and eye irritation at work. Soon afterwards, he also began to suffer from nocturnal cough and wheezing. Initially, the symptoms subsided during vacations and sick leaves, but recurred when he returned to work. Later the symptoms did not improve during the weekends. PEF surveillance for 2 weeks showed values typical of occupational asthma (Fig. 2). His spirometric values were normal and he had no bronchial hyperreactivity. A chamber challenge with heated turning fluid (100°C) containing 14% triethanolamine caused an immediate PEF drop of 17% and wheezing, and a challenge with cold pure triethanolamine caused an immediate PEF drop of 21%.

Table 1. Characteristics of three patients suffering from asthma probably caused by ethanolamines

	Patient 1	Patient 2	Patient 3
Personal			
Age (years)	43	52	52
Sex	M	M	F
Work	Metalworker	Turner	Cleaner
Smoker	No	Former	Yes
Atopy own/family	Yes/no	No/no	No/no
Prick-positivity (standard series)	Yes	No	No
IgE (kU/l)	180	53	100
Agent			
Chemical	Triethanolamine	Triethanolamine	Ethanolamine
Time from first exposure to onset of symptoms (months)	Over 120	97	Over 120
Max. PEF drop	21%	21%	24%

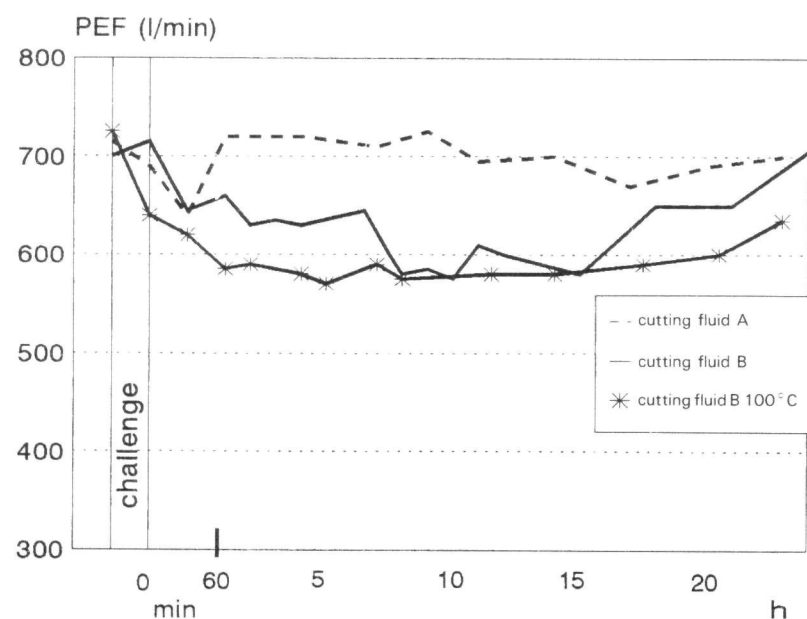


Fig. 1. Response to cold cutting fluid A (no triethanolamine), cold cutting fluid B, and heated cutting fluid B in chamber challenge test in patient no. 1, showing maximal PEF drop of 21%.

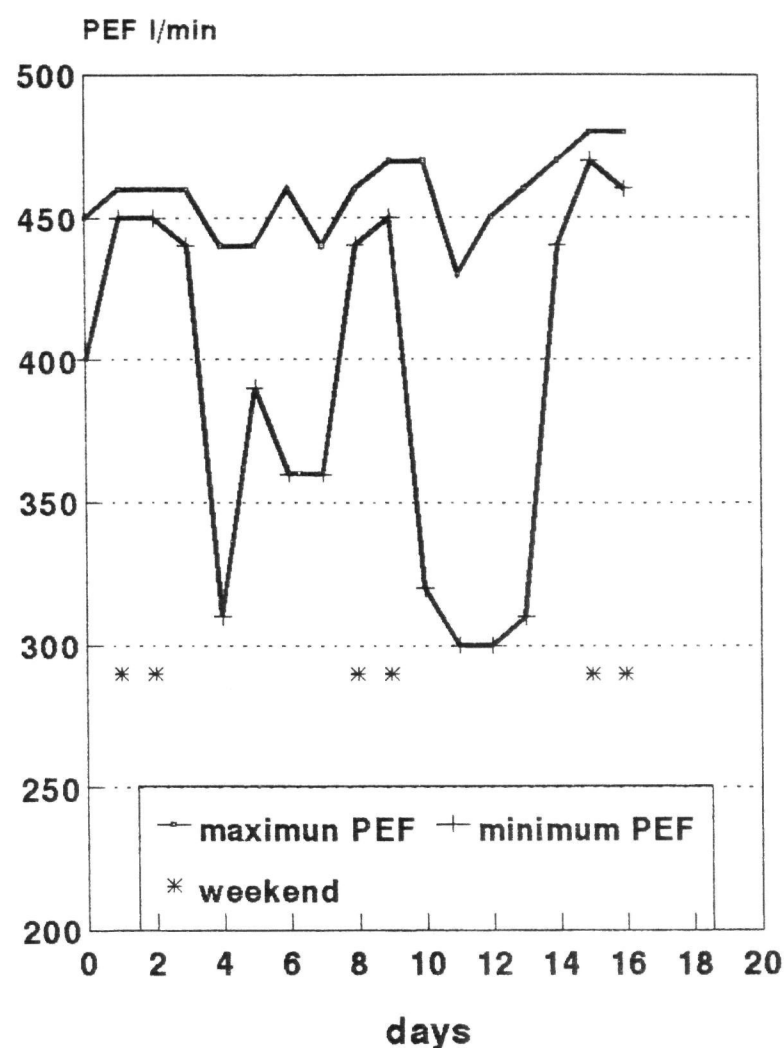


Fig. 2. PEF workplace surveillance of patient no. 2 for 2 weeks, showing typical pattern of occupational asthma.

After the diagnosis, the patient was granted a disability pension. Half a year later, he still had symptoms and needed medication.

Patient no. 3

The patient had been working for 18 years at the same firm, cleaning mostly floors. She was exposed to various cleaning chemicals, soaps, detergents, and waxes. She began to feel weakness at work, and had cough, chest tightness, rhinorrhea, and sometimes also fever. Initially, she had fewer symptoms at the weekends, and during vacations she was symptomless. She developed strong symptoms of rhinorrhea, wheezing, and irritating cough when using a detergent for removing wax, containing 8% ethanolamine and 9% sodium metasilicate. She used this detergent in hot water. Her spirometric values were normal and she had no bronchial hyperreactivity. PEF surveillance for 2 weeks showed a pattern typical of occupational asthma. Because of the fever, her diffusion capacity was also followed up in the challenge tests. The placebo test with polyol was negative. The test with a detergent containing ethanolamine (no. 2, Fig. 3) in hot water induced an immediate but long-lasting asthmatic reaction, and 7 h after the test a fever of 38.0°C but no changes in diffusion capacity.



Fig. 3. Response to detergent 1, detergent 2, and workplace metal dust in chamber challenge test in patient no. 3, showing maximal PEF drop of 24%.

The decrease in FEV_1 was 27%. A challenge with another detergent (no. 1, Fig. 3) containing 9% triethanolamine, 4.5% potassium hydroxide, 15% butylenic glycol, and 9% isopropanol was negative, as was a test with metal dust from her workplace.

After the diagnosis, she tried to continue her former work, but could not totally avoid being exposed to this detergent. The asthmatic symptoms did not abate, and she was later granted a disability pension.

Discussion

Altogether, 598 cases of occupational asthma were diagnosed at our institute in 1983–90. By far, the most common low-molecular-weight chemicals (LMWC) causing occupational asthma were isocyanates (142 cases) (17), followed by formaldehyde (31 cases) (23), epoxy resin and epoxy resin hardeners (30 cases) (16), and cyanoacrylates (10 cases) (26). Ethanolamines seem to be a new group of LMWCs capable of causing occupational asthma.

The reported cases share one common feature; all the patients had been exposed to the ethanolamines at temperatures higher than that of the ambient air. This agrees with the former conception (e.g., Beard & Noe (4) and Järholm (15)) that significant exposure by inhalation to ethanol amines does not happen during normal use of these compounds, but only

when they are heated or vaporized. Once a person is sensitized to these compounds, exposure even at an ambient temperature may provoke symptoms, as shown by the chamber challenges of patients 1 and 2.

Monoethanolamine is a normal product of the metabolic pathway of the degradation of amino acids and is a normal constituent of mammalian urine (20). However, LWMCs are not true allergens, but probably combine in the respiratory tract with a protein, e.g., human serum albumin, and the hapten-protein conjugate is the complete antigen (30).

The asthma caused by LWMCs may resemble that caused by formaldehyde (13, 23), which also is an intermediate in a metabolic pathway of the human body.

IgE-mediated allergic reactions have so far been reported from several LMWCs, such as a number of reactive dyes, acids in wood dust, ethylene oxide, chloramine T, isocyanates, acid anhydrides, piperazine, metal salts, and epoxy resin (2, 9, 16, 24, 28, 30, 31). A possible IgE-mediated reaction caused by triethanolamine is suggested in one case reported by Herman (14), on the basis of a positive skin prick test. We did not conduct tests on our patients to prove an IgE-mediated reaction, but the immediate asthmatic reactions of the patients at challenge might also support the existence of this type of reaction. We have recently prepared amine-protein (human serum albumin) conjugates for prick testing, but we do not yet know whether these conjugates have diagnostic significance. The hapten-protein conjugates are prepared mostly by trial and error (30) in which the pH and temperature of the reaction and the concentration of the chemicals influence the final product.

The mechanism could also be irritant, but, according to our experience, ethanolamines are not very irritant. Two hyperreactive control patients did not develop significant PEF falls at challenge.

We have no data on the level of exposure to ethanolamines in these cases. The exposure had usually been regular during the working days. In all cases, the exposure time before the onset of symptoms was several years.

The symptoms of patient no. 3 were different from those of patients 1 and 2, and she developed a fever concomitant with the exposure to ethanolamine. The fever reaction indicates some alveolitic/pneumonitic reaction, which, however, could not be verified by lung function tests. The patient also developed fever at work when exposed to this detergent. Fever has also been reported in asthmatic reactions provoked by aminoethyl ethanolamine (25).

The challenges were performed with the patient's detergent, which also contained a possibly irritating alkaline compound, sodium metasilicate. For safety

reasons, we could not perform a challenge with pure ethanolamine despite the urgent need for one, because of the low concentration (8%) of ethanolamine in the detergent. The possibility of some other type of reaction than an allergic one, and also of some other cause of the reaction than monoethanolamine, cannot be excluded in this case. Monoethanolamine as a cause of occupational asthma has previously been described in one case report (11). We are hoping to be able to measure the concentration of ethanolamines during challenge tests, a measurement which we could not make when these patients were investigated.

The significance of this case is doubtful; nevertheless, there is still a need to report also on possible occupational hazards, especially in occupations usually considered to be safe.

A common feature of the cases reported here was the persistence of the symptoms after ending the exposure to the causative agent. In this respect, these cases differ from the other amine-induced asthma cases in which the recovery usually was fast or the symptoms subsided after ending exposure (8, 21, 25, 29). One reason for this difference could be the relatively long exposure time to the causative agent in these cases, even though the symptoms were not especially long-lasting; another reason might be a low exposure through common home chemicals.

In summary, ethanolamines, despite their vast use in various industries today, seem to be safe as regards their sensitizing capacity. However, the possibility of allergic respiratory symptoms caused by ethanolamines must be borne in mind. Ethanolamines are often minor constituents of chemical compounds, but, especially if they are heated, substantial exposure to their vapors may induce asthma.

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