

Allergic airway disease caused by methyl tetrahydrophthalic anhydride in epoxy resin

by Jörn Nielsen, MD, Hans Welinder, PhD, Staffan Skerfving, MD¹

NIELSEN J, WELINDER H, SKERFVING S. Allergic airway disease caused by methyl tetrahydrophthalic anhydride in epoxy resin. *Scand J Work Environ Health* 1989;15:154—5. Work-associated rhinitis and asthma occurred in a subject exposed to methyl tetrahydrophthalic anhydride (MTHPA) used as a curing agent in an epoxy resin system. He displayed bronchial hyperreactivity in provocation with methacholine, as well as skin prick test positivity and specific immunoglobulin E (IgE) serum antibodies, against a conjugate of MTHPA and human serum albumin. Thus, it seems likely that the disease was caused by an IgE-mediated allergy.

Key terms: bronchial hyperreactivity, epoxy resin system, occupational asthma, organic acid anhydride, rhinitis.

Organic acid anhydrides are being used in different ways in the resin industry, eg, as the curing agent in epoxy resin systems.

Among the organic acid anhydrides, phthalic anhydride (PA), tetrahydrophthalic anhydride, tetrachlorophthalic anhydride, hexahydrophthalic anhydride, trimellitic anhydride, himic anhydride, and maleic anhydride are all known sensitizing agents, causing symptoms of the eyes and airways (1—8). As these agents have, in addition, strong irritating properties, high frequencies of complaints have been reported in exposed worker populations (5, 9, 10).

In the present communication, we report a case of allergy to another organic acid anhydride, methyl tetrahydrophthalic anhydride (MTHPA).

Case history

The patient was a man 22 years of age who had never smoked. He had a heredity of rhinitis and had reacted since childhood with rhinitis while in close contact with cats.

After school he was employed as a nursing assistant and as a porter for one and a half years, until he, in August 1986, got his present job in a plastics-producing and plastics-manufacturing company. From August 1986 until February 1987, he was a mixer in a phenol-formaldehyde resin lamination department. During that period, he was only occasionally and slightly exposed to epoxy resin chemicals and had no work-related symptoms.

In February 1987 he was transferred to a department where barrels for grenade firearms were produced.

Rotating cylinders were prepared by hand swabbing, with a mixture of epoxy resin, MTHPA, and methylimidazole on glass fiber. Then the cylinders were wound automatically with glass-fiber cords, which had been running through a bath containing the epoxy resin mixture. The cylinders then passed a curing oven (temperature 90—120°C). After curing, the plastic barrels were processed mechanically.

The patient worked most of the time in the winding department. The time-weighted MTHPA exposure at this site was 0.1 mg/m³.

About four months after beginning his job in the winding department, he experienced symptoms of nasal secretion and congestion during work. The symptoms were especially grave when he had swabbed for a long time or when the ventilation system was less effective. Some time later he developed chest tightness and a continuous productive cough; sometimes he also had wheezing.

At the time of the first examination, in June 1988, he had no attacks of dyspnea. At the physical examination, expiratory rhonchi were heard over both lungs. In a skin prick test, with a standard panel of 14 common allergens (5), he was positive for cat and horse. The skin prick test was also positive to a conjugate of MTHPA and human serum albumin (HSA) (5) but negative to PA and HSA (PA-HSA). None of 34 unexposed reference workers in a nearby factory were positive to MTHPA-HSA.

The total immunoglobulin (Ig) E level was 235 kU/l. In the radioallergosorbent test (RAST), specific IgE antibodies to MTHPA-HSA were found (RAST ratio 7.5). In the enzyme-linked immunosorbent assay (ELISA), specific IgG antibodies were not present (optical density 0.32). Sera from 30 referents had a median total IgE of 11 (range 1—127) kU/l. When tested with MTHPA-HSA, the referents' RAST ratio for IgE was 1.1 (range 0.7—2.0), and their ELISA value for

¹ Department of Occupational and Environmental Medicine, University Hospital, Lund, Sweden.

Reprint requests to: Dr J Nielsen, Department of Occupational Medicine, University Hospital, S-221 85 Lund, Sweden.

specific IgG was 0.04 (range 0–0.4) in optical density.

From June 1988 until the middle of September, the patient had been on vacation or had worked as a consultant in another factory, where he had only occasional and slight exposure to MTHPA. During this period he had minor symptoms in connection with exposure periods.

From the middle of September on he worked at his ordinary workplace, with daily exposure to MTHPA. During this period his nasal symptoms increased in severity, and he experienced more serious chest tightness and productive cough. He also suffered from attacks of dyspnea, cough, and wheezing during physical exercise.

He was taken out of exposure in October, and the symptoms then gradually disappeared during the five next weeks. The day before a second examination, in November, he was once more exposed to MTHPA at his work site. After about 2 h of exposure, he suffered from nasal congestion and irritation.

At the examination, before work the next day, he displayed no symptoms or physical signs. He had a dynamic spirometry (vital capacity 5.9 l, forced expiratory volume in 1 s 5.5 l) above the lower reference limits (5.1 and 4.2 l, respectively). However, he had clear-cut bronchial hyperreactivity, as shown by a methacholine test ($PC_{85} = 0.3$ mg/ml; inhalation during 2 min). In the skin prick test, he was still positive to MTHPA-HSA and negative to PA-HSA.

Discussion

The symptoms of the patient were unequivocally related to the workplace, where an epoxy resin system was handled. Furthermore, there was a clear progression over time during the period of exposure, with increasingly severe symptoms of the upper airways, and finally engagement of the lower airways, with a history indicating a combination of fixed obstruction and asthma, and objective bronchial hyperreactivity. The convincing history, the positive skin prick test, and the presence of specific antibodies of type IgE against MTHPA-HSA strongly indicate an allergic reaction to MTHPA as the cause of the patient's complaints. To our knowledge, this is the first described case of sensitization to MTHPA.

In Sweden, no permissible exposure limit for MTHPA has been established. For PA, which is a similar compound, there is a standard of 6 mg/m³ (time-weighted average). The patient had been exposed to a level of less than one-tenth of this.

As several organic acid anhydrides used in the plastics industry have been shown to have a sensitization

effect, we think that it would be wise to suspect this group of agents as being potentially allergenic, even in cases in which no information about sensitization is available.

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