

CASE REPORT

Occupational asthma due to zinc

J-L. Malo*, A. Cartier*, J. Dolovich**

Occupational asthma due to zinc. J-L. Malo, A. Cartier, J. Dolovich. ©ERS Journals Ltd 1993.

ABSTRACT: We describe a subject who developed asthma symptoms 2 yrs after being employed at a plant where metals were galvanized in heated zinc. The subject was not atopic. Baseline spirometry was normal three months after he left work but there was mild bronchial hyperresponsiveness to methacholine. Monitoring of forced expiratory volume in one second (FEV₁) during a day at work showed a maximum fall in FEV₁ of 24% at the end of the day and an increase in bronchial responsiveness on the following day. Environmental monitoring revealed that zinc and iron were present in the working environment at concentrations that were lower than the "threshold limit value - short term exposure level" (TLV-STEL) standards. Positive immediate skin tests to zinc sulphate at concentrations of 1 and 10 mg·ml⁻¹ were obtained, although no specific immunoglobulin E (IgE) antibodies to zinc could be found. Skin tests with copper, chromium and cobalt were negative. Specific inhalation challenges were performed, having the subject inhale a solution of zinc sulphate at a 10 mg·ml⁻¹ concentration for 6 min. An immediate reaction was elicited (maximum fall in FEV₁ of 23%). We conclude that zinc can cause occupational asthma.

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Low molecular weight agents are a common cause of occupational asthma and the physiopathological mechanism is often unknown [1, 2]. Metals such as platinum [3-5], nickel [6-8], chromium [9], and cobalt [10-13] are low molecular weight agents that can cause occupational asthma. WEIR *et al.* [14] described two subjects with occupational asthma, who used soft corrosive fluxes containing zinc chloride and ammonium chloride. The exact cause of the reaction was unknown. One of the workers was challenged with a zinc chloride solution and did not experience an asthmatic reaction.

In this article we describe a subject who developed occupational asthma after exposure to zinc, in whom there was evidence of: 1) a work-related fall in spirometry and changes in bronchial responsiveness after a day at the workplace, where environmental monitoring revealed the presence of zinc; and 2) immediate asthmatic reaction after inhaling nebulized zinc sulphate in the hospital laboratory.

Case report

A 47 yr old man was referred to us with the following history. After working for two and a half years at a company where metal was galvanized, he progressively noticed symptoms of shortness of breath, chest tightness and wheezing, which occurred in the middle of a working-day. He also suffered sneezing and burning eyes. His symptoms improved in the evening but woke him at night. He had no symptoms at weekends or during

vacations. His work consisted of processing metals, firstly in basins containing sulphuric acid and then in basins containing hot zinc. He left this workplace for seven months and found a similar job with a different employer. He became asymptomatic during the period that he was away from work. He started experiencing similar symptoms again when he was back at work and was forced to leave the job. He was seen three months after leaving work. He still had asthmatic symptoms on exercise and used an inhaled beta₂-adrenergic agent on an "as needed" (not a daily) basis. He had smoked between the ages of 15-27 yrs. He had no familial or personal atopic history.

Skin prick tests with a battery of 15 common inhalants were all negative, with a positive control reaction to histamine phosphate at a 1 mg·ml⁻¹ concentration. His forced expiratory volume in one second (FEV₁) / forced vital capacity (FVC) obtained using a Vitalograph spirometer (Vitalograph Ltd, Buckingham UK) according to the standards of the American Thoracic Society [15] was 2.51/3.46 l (72%) corresponding to an 81% predicted FEV₁ and an 89% predicted FEV₁/FVC [16]. The methacholine inhalation test was performed following a standardized methodology, using a Wright's nebulizer (output=0.14 ml·min⁻¹) at tidal volume breathing for 2 min, with methacholine instead of histamine; the provocative concentration causing a fall of 20% in FEV₁ (PC₂₀ methacholine) obtained from the dose-response curve drawn on a semilogarithmic scale was 4.0 mg·ml⁻¹ corresponding to mild airway hyperresponsiveness [17].

Specific inhalation challenges

Spirometry was monitored throughout a control day without exposure, spent in the hospital laboratory (Day 1 March 16, 1992). As can be seen (fig. 1), there were no significant changes in FEV₁. On the following day (Day 2, March 17, 1992) (fig. 1), the subject was sent to his usual workplace, where he underwent 7 h of serial FEV₁ monitoring under a technician's supervision. There was a progressive fall in FEV₁, reaching 24% at the end of the day. On the following morning with a baseline FEV₁ that was 3% less than the first methacholine test, PC₂₀ had dropped significantly from 4.0 (see above) to 0.88 mg·ml⁻¹ [18]. Environmental monitoring, performed in the workplace during a 4 h interval, detected 0.26 mg·m⁻³ of total zinc and 0.13 mg·m⁻³ of iron. The monitoring was repeated on another occasion and showed that the concentrations of total zinc and iron were 0.29 mg·m⁻³ and 0.03 mg·m⁻³ respectively, during an equivalent period of sampling. Five days after the exposure at work PC₂₀ was 2.7 mg·ml⁻¹ (not significantly different from the baseline value). Two days later (March 24, 1992), the subject was asked to perform soldering on black steel in the hospital shop. Monitoring of the air near the mouth showed that the concentrations of iron and zinc were 2.4 and 0.015 mg·m⁻³, respectively. There were no significant changes in FEV₁ (Day 3) (fig. 1).

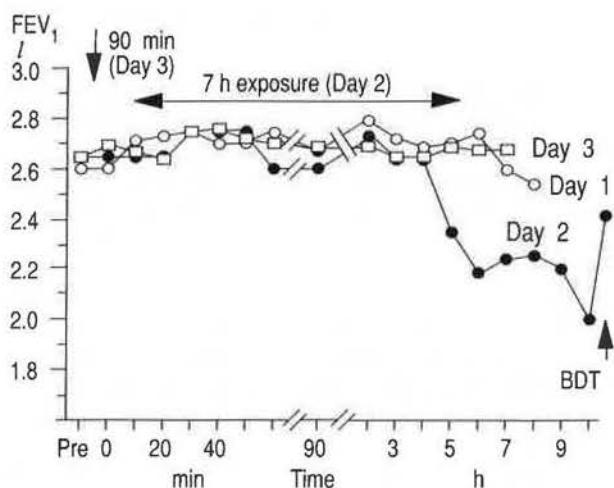


Fig. 1. — Results of specific inhalation challenges. No significant changes in FEV₁ were documented on the control day without exposure (Day 1). Performing usual work in the galvanization process for 7 h (horizontal arrow, top) resulted in a fall in FEV₁ that reached 24% at the end of the day (Day 2). Soldering on steel (Day 3) for 90 min (vertical arrow, top) did not cause significant changes in FEV₁. BDT: bronchodilator test with inhaled salbutamol (200 µg); FEV₁: forced expiratory volume in one second; ○: control no exposure day (Day 1); ●: day spent at work (galvanization) (Day 2); □: control day of soldering on steel (Day 3).

Skin prick tests were performed using zinc at 0.1, 1, and 10 mg·ml⁻¹ concentrations. The subject showed immediate reaction at concentrations of 1 mg·ml⁻¹ (weal = 3×3 mm) and 10 mg·ml⁻¹ (weal = 4.5×5 mm). The same tests carried out in a group of 25 asthmatic subjects seen in an out-patient clinic showed that only one had a 3×3

mm weal at a concentration of 1 mg·ml⁻¹, whereas eight had a 3×3 mm weal at a concentration of 10 mg·ml⁻¹. It was therefore decided to perform specific inhalation challenges with a Wright nebulizer (output = 0.14 ml·min⁻¹) (fig. 2). Nebulization of phosphate-buffered saline (PBS) did not result in any significant change in FEV₁ (Day 4, March 30, 1992). Nebulization of zinc sulphate at 0.1 and 1 mg·ml⁻¹ did not cause significant changes in spirometry (Day 5, March 31, 1992). However, when the subject inhaled zinc sulphate at a concentration of 10 mg·ml⁻¹ for a total assessment, PC₂₀ was 0.86 mg·ml⁻¹.

No significant changes in oral temperature or white blood counts were documented after each positive challenge day.

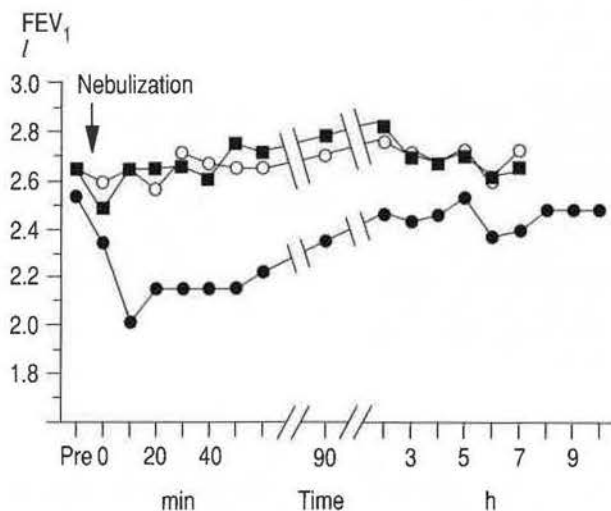


Fig. 2. — Results of specific inhalation challenges with PBS and zinc sulphate at three different concentrations. Exposure to zinc sulphate at a 10 mg·ml⁻¹ concentration in progressive intervals for a total of 6 min caused an immediate airway obstruction with progressive recovery in the first two hours. PBS: phosphate buffered saline; FEV₁: forced expiratory volume in one second; ○: PBS (15 min) (Day 4); ■: zinc sulphate, 0.1 (15 min) and 1 mg·ml⁻¹ (5 min) (Day 5); ●: zinc sulphate, 10 mg·ml⁻¹ (6 min) (Day 6).

Immunological tests

Specific immunoglobulin E (IgE) assessments were performed by the radio-allergosorbent test (RAST) method using zinc sulphate in the same way as for nickel [6]. Counts found in our subject were 316 by comparison with 284 to 419 in four high IgE controls and 245 and 285 in two non-allergic control subjects.

Discussion

To our knowledge, this is the first account of occupational asthma due to zinc. In a previous publication, we reported on two subjects who developed isolated late asthmatic reactions (accompanied by an alveolitis type of reaction in one case) after being exposed to galvanized metals. We did not identify the causative agent, although

monitoring the environment revealed that zinc was released into the air during the process [19]. More recently, WEIR *et al.* [14] reported on two solderers who were shown to have occupational asthma on exposure to fluxes containing zinc and ammonium chloride [14]. However, one of the two did not experience an asthmatic reaction after a laboratory challenge with zinc chloride.

It has been hypothesized that metal fume fever is related to exposure to zinc. This stems from the fact that metal fume fever is accompanied by increased blood serum levels of zinc [20]. In addition to potentially causing metal fume fever, exposure to zinc can cause an alveolitis type of reaction [21] with an accumulation of leucocytes, as shown by bronchoalveolar lavage [22]. Exposure to cobalt, which can also cause asthma and alveolitis, can induce the influx of leucocytes into the bronchoalveolar lavage [11].

Various metals can cause occupational asthma. An IgE-dependent mechanism has been elicited for platinum [3–5]. For other metals, evidence of an IgE-dependent mechanism has been seen in some instances [6, 8, 23], although not in all cases [7, 9]. Although specific IgE levels were within the ranges found in control subjects, our subject showed immediate skin reactivity to zinc sulphate at concentrations of 1 and 10 mg·ml⁻¹. Skin reactivity to zinc was shown in only one of 25 control asthmatic subjects at a concentration of 1 mg·ml⁻¹ but in eight subjects at a concentration of 10 mg·ml⁻¹. Therefore, evidence of an IgE-dependent mechanism is uncertain. Cross bronchial and immunological reactivity has been described between hard metals such as nickel and cobalt [13]. In our subject, no evidence of immunological reactivity could be shown as the subject had no evidence of IgE-dependent immunological sensitization to other metals such as nickel, chromium and cobalt.

There were significant changes in nonspecific bronchial responsiveness after a day spent at work which caused an asthmatic reaction at the end of the day. After specific bronchial challenges in the hospital laboratory, an isolated immediate bronchial response was demonstrated without changes in bronchial responsiveness. The cumulative dose of zinc inhaled during a 7 h workshift corresponds to approximately 0.6 mg (there was 0.26–0.29 mg·m⁻³ of zinc at work and the subject inhaled at least 2,100 l during this interval). By comparison, the dose of zinc inhaled during the laboratory challenge was 3.4 mg. These differences in concentration can explain why in the laboratory the reaction was immediate, whereas, it took more time to appear in the workplace. However, one should be cautious in interpreting these results, as in one instance zinc was inhaled as particles, whereas, in the other it was as a solution. The dose inhaled could therefore be different from the concentration that was nebulized. It is also not known whether the type and magnitude of asthmatic reactions is a function of duration of exposure and/or concentration, the total dose being constant.

Various functional and immunological methods of investigation were used in this study in a stepwise approach. Specific inhalation challenges in the workplace with environmental monitoring proved to be a valuable

means of assessment [24]. Once we had documented significant falls in FEV₁ at work and documented the presence of zinc in the air, we then decided to reproduce the working environment in the hospital laboratory. This was carried out in addition to the investigation of a possible IgE-mediated type of asthma. Specific inhalation challenges at the worksite in particular can be very useful. However, authorization should be obtained from the employer, which is not always the case.

As welding on galvanized metal is a frequent occupational hazard, it would be interesting to assess the prevalence of skin reactivity to zinc and other metals as well as of changes in airway calibre. It remains unknown if metal fume fever is accompanied by skin reactivity to metals and airway involvement.

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