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Delayed occupational asthma from epoxy Exposure

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Background A delayed asthma reaction occurring several hours after exposure is difficult to diagnose.

Aims To confirm a delayed asthma reaction in five workers following epoxy exposure.

Case report Working conditions with exposure to epoxy encountered at the workplace were reproduced in a challenge chamber. Specific inhalation challenge (SIC) with epoxy was compared to a control challenge. All five cases had delayed an asthma response 6–15 h after epoxy exposure.

Conclusions Our study confirms that SIC is a useful tool in diagnosing delayed asthma response.

Key words Delayed asthma; epoxy; occupational asthma; specific inhalation challenge.

Introduction Occupational asthma is one of the most prevalent lung diseases and is estimated to represent one in six cases of adult asthma [1, 2]. Making an accurate diagnosis of occupational asthma is important not only because of the health consequences but also due to the socio-economic impact on workers, employers and the community [3].

Epoxies are low molecular weight (LMW) agents used in resin-hardener systems in paints, fibre-reinforced plastic materials, and in flooring and protective coatings. Occupational exposures to epoxy resins may cause serious side-effects [4–6]. They are a common cause of allergic contact dermatitis and, more rarely, give rise to asthma. Diagnosing occupational asthma may be difficult as sensitization cannot be demonstrated with blood tests or skin prick tests (SPT). A specific inhalation challenge (SIC) is usually required. A further difficulty is that occupational asthma due to epoxies may manifest through a delayed reaction with symptom onset up to 12 h after exposure potentially masking the relationship with work. We present five cases of occupational asthma due to airborne epoxy exposure where a SIC was used to confirm the diagnosis and a delayed response was demonstrated.

Case report

Five epoxy workers were referred to our specialist clinics. All patients were male with an age range of 41–57 years.

Three were windmill wing builders (cases 1, 2 and 4), one was a floor layer (case 3) and one was a worker in the automotive industry (case 5). SPT to a range of common aeroallergens showed that case 1 was sensitized to Phleum pratense, Dermatophagoides farinae and Alternaria alternate. Case 2 was sensitized to just Dermatophagoides farinae, and cases 3, 4 and 5 were non-atopic. We undertook SIC in each case using the epoxies from the patients’ places of work:

Case 1: Hardener (CAS nos. 2855-13-2; 68479-98-1) and Resin (CAS nos. 28768-32-3; 285513-2)
Case 2: Hardener (CAS nos. 589-37-7; 2855-13-2) and Resin (CAS nos. 25068-38-6, BADGE (bisphenol-A-dicycldylyether polymer); 28064-14-4; 16096-31-4)
Case 3: Hardener (CAS nos. 934-98-5; 1761-71-3) and Resin (CAS nos. 25068-38-6, BADGE (bisphenol-A-dicycldylyether polymer); 100-51-6; 68609-97-2; 26761-45-)
Case 4: Hardener (CAS nos. 28768-32-3; 2425-79-8) REN HY 5212 and Resin (CAS no. 68479-98-1)
RENAGL SW5200
Case 5: Hardener and Resin HysolR EA 9394C-2, full content not available (CAS no. 429-90-5)
None of the relevant material safety data sheets listed these epoxies as respiratory sensitizers and none had significant asthma hazard indices [7].

Pre-SIC monitoring with serial measurement of peak expiratory flow (PF) was either not possible or not diagnostic. Active and control SIC were performed on different days in an exposure chamber. For safety reasons it was not possible to blind the patients. The standard protocol included an active challenge with 200–300 ml of resin and hardener which were mixed and brushed on to paper. Control challenges were performed with a similar volume and method of water-based paint (cases 1–4) or N-propyl bromide (case 5) for the same duration as the active challenge (up to 30 min). The five different epoxies from the patients’ workplaces were used. Responses were measured by forced expiratory volume in 1 s (FEV1) or PF prior to and up to 16 h after each exposure. Transportable spirometers were not available for patients 1 and 5 where peak flow meter was used. Histamine release (HR) tests, which are an in vitro method to detect allergen-induced histamine release from basophil leukocytes, were carried out on cases 1–4. FENO and non-specific bronchial hyperreactivity were not consistently measured. All SICs had a positive response defined by a fall in FEV1 ≥ 15% or PF ≥ 20% from baseline and demonstrated delayed asthmatic reactions 6–15 h after the active challenge [7]. Cases 1 and 5 had PF falls of 29% and 24%, respectively (Figure 1). Case 3 had an acute attack with a FEV1 fall of 31% at 15 h (Figure 2). Cases 2–5 were hospitalized on the pulmonary ward during SIC. The SIC results correlated well with the symptoms developed, often at night, following exposure at work during daytime. The HR test was positive for case 2 (hardener component only) but negative for IPA (Isophorondiamine, CAS no. 2855-13-2) and negative for cases 1, 3 and 4. Because of the diagnosis of occupational asthma, four of the patients changed careers; a fifth remained in the workplace with tighter controls on his exposure which prevented further symptoms of asthma.

![Figure 1. Result of SIC to resin and hardener, cases 1 and 5.](image-url)
Discussion
Occupational asthma due to LMW agents can be difficult to diagnose due to the lack of available immunological tests and often a delayed onset of asthma symptoms arising several hours after exposure. This means that workers and healthcare professionals do not always make the connection with workplace exposures. A SIC is considered the gold standard for the diagnosis of occupational asthma and is often required to diagnose the condition and ensure proper subsequent management. In line with European guidelines a SIC should include a control challenge to rule out a non-specific irritant reaction [8]. As seen in this short case series, severe asthma attacks which are potentially life threatening may occur and therefore admission to hospital is recommended for observation after active challenges, particularly where the agent is known to cause a delayed response. The results from these SICs did not identify what component of the epoxy-hardener system was responsible for triggering the asthmatic reaction. However, confirmation of diagnosis is very valuable for the patients’ chances to stay in the labour market by avoiding further exposure. SIC is an important tool in diagnosing delayed asthma and guiding the patient in treatment and future work. Whilst SIC is generally considered to be the reference standard, the technique is complex, specialized and practiced only in a limited number of centres. This is probably one of the reasons why only few cases of epoxy-related asthma have been previously described [8–10].

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None.

Competing interests
None declared.

References

Figure 2. Result of SIC to resin and hardener, cases 2, 3 and 4.

**KEY LEARNING POINT**

**What is already known about this subject?**
- Occupational asthma due to low molecular weight agents can be challenging to diagnose in the absence of available immunological testing
- Occupational asthma due to epoxy resins often causes an isolated late response and so it can be difficult to correlate symptoms with work
- Specific inhalation challenge is the gold standard for diagnosing occupational asthma, but this is a highly specialized technique and only performed at a few centres

**What this study adds:**
- We demonstrated a characteristic isolated late response to epoxy resins in five patients with a positive specific Inhalation challenge
- Epoxy resin exposure in those with occupational asthma may cause a significant fall in lung function
- Safety data sheets may not identify that chemicals are respiratory-sensitizing agents

**What impact this may have on practice or policy:**
- An increased awareness of the late or delayed fall in lung function up to 12 h after exposure with a less clear work-related pattern in symptoms
- Patients may have an isolated late fall in lung function after specific inhalation challenge and this should be considered when assessing the appropriate safe environment for monitoring

**Published:**