giving an overall total of 29 families for analysis. Two possible modes of inheritance were suggested from this study – autosomal dominant (AD) with reduced penetrance in females and X-linked recessive (XLR) inheritance. Autosomal recessive inheritance was thought to be very unlikely.

The authors found differences between the AD and XLR forms with possible earlier onset in the XLR form and more frequent episodes in the AD form. The family described here clearly has autosomal dominant pneumothorax with no clinical features to suggest a co-existing connective tissue disorder. We were unable to find any specific physical differences between affected and unaffected family members. Even within this family the clinical expression is very variable with onset in the sister (III.6) at 17 years, in the index case (III.1) at 30 years, and recurrence in the other brother (III.5). The associated effects of smoking and other environmental factors cannot be accurately assessed.

The variability within this family is consistent with an autosomal dominant gene with variable

penetrance. We conclude that autosomal dominant pneumothorax is a definite entity and most of the cases reviewed by Abolnick *et al*² are inherited in an autosomal dominant mode with variable penetrance. In some families X-linked inheritance cannot be excluded. Further careful documentation of families with spontaneous pneumothorax may provide clarification in the future.

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Can reactive airways dysfunction syndrome (RADS) transform into occupational asthma due to “sensitisation” to isocyanates?

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Abstract

The case history is described of a worker who presented with a history suggestive of reactive airways dysfunction syndrome which occurred after an acute high level inhalation of diphenylmethane diisocyanate. Further exposure at work, at a time when concentrations of isocyanates were no longer “irritant”, suggested occupational asthma; this diagnosis was confirmed by a specific inhalation challenge test.

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Keywords: occupational asthma, reactive airways dysfunction syndrome, isocyanates.

Isocyanate exposure in the work place is the most frequent cause of occupational asthma.¹ By contrast, only few cases of reactive airways

dysfunction syndrome (RADS), a distinct type of occupational asthma without a latency period,² have been related to a brief high level exposure to isocyanates.^{3–7} We report a case of occupational asthma to diphenylmethane diisocyanate (MDI), documented by a specific bronchoprovocation challenge test, which might have been initiated by a history suggesting RADS. This observation suggests that “sensitisation” may develop as a result of an intense exposure, and demonstrates the need for objective testing before re-exposure to the offending agent in the case of concomitant chronic exposure at low levels.

Case report

A 54 year old man was hired to work in a foundry in 1993. He had a 30 pack year history of smoking and no personal history of asthma or atopy. His job consisted of making cores which involved frequent exposures to MDI. In March 1996 an accidental spill of a large volume of solvent containing MDI occurred in his work area. He was off duty during the spill and returned to work 48 hours later. There was a strong and irritant smell in the plant and within one hour he experienced headache, sore throat, cough, and chest tightness. Other workers in this area reported the same symptoms that were, however, transient. His chest symptoms increased gradually and a month later he consulted his physician. He then noticed that wheeze and chest tightness worsened at work and improved during weekends. He was put on sick leave and salbutamol was administered on an as needed basis without significant relief. In May 1996 a spirometric test revealed moderate airflow obstruction with a forced expiratory volume in one second (FEV₁) of 2.5 l

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Figure 1 Results of the specific bronchial provocation challenge to MDI.

(83% predicted) and a forced vital capacity (FVC) of 4.5 l (121% predicted). After 200 µg inhaled salbutamol FEV₁ increased to 2.8 l (an increase of 12%).

The patient was referred to us in September 1996. Persistent symptoms were reported despite current treatment with budesonide 400 µg twice daily. Baseline FEV₁/FVC was 2.8/4.3 and methacholine challenge confirmed the presence of mild hyperresponsiveness with a PC₂₀ of 3 mg/ml six months after the acute inhalation.

A bronchial provocation test was performed with isocyanates. On the first day, used as control, the patient was exposed to a resin (polyols) heated for a 30 minute cumulative exposure. No significant change in FEV₁ occurred within the next eight hours. Subsequently the patient was exposed to MDI (40% MDI, 60% polymethylene polyphenyl isocyanate) generated using a closed circuit isocyanate inhalation apparatus⁹ at concentrations close to 15 ppb. He was exposed to this in a progressive fashion for four, 30, and 60 minutes, respectively, on three consecutive days. On the 60 minute challenge day the patient developed an isolated late reaction with a 22% fall in FEV₁ seven hours after the end of exposure (fig 1). The PC₂₀ was 1.5 mg/ml at the end of this day.

Discussion

The initial exposure to presumably high concentrations of MDI followed immediately by symptoms was compatible with the diagnosis of RADS.¹⁰ However, on return to work, even when concentrations of isocyanates were no longer "irritant," our subject developed a history that suggested occupational asthma – that

is, asthmatic symptoms worsening while at work and improving at weekends. This prompted us to perform an occupational challenge test which demonstrated a late asthmatic response to low levels of MDI.

Although isocyanates may induce an occupational asthmatic state either as a specific agent – that is, acting as a "sensitiser" – or as a toxic irritant – that is, during an accidental inhalation at very high concentrations – few cases have been documented where both types of exposure have occurred. In a study of manufacturing workers Butcher and co-workers showed frequent excursions of toluene diisocyanate (TDI) concentrations above the threshold limiting value, and suggested that isocyanate-induced asthma might be initiated by exposure to high concentrations of isocyanates during spills.¹¹ This suggests that acute high level exposure may (as in our case) or may not lead to sensitisation. Other case reports of RADS caused by isocyanates, with³ or without^{6,7} evidence of "sensitisation", as demonstrated by specific inhalation challenges have previously been documented.

From a practical point of view our case report illustrates that, in a case of RADS due to an agent which can also cause occupational asthma, subjects may return to work if they can avoid high exposures and bronchial irritants above TLV. However, such subjects should be followed up and, if symptoms develop on exposure to low levels, specific inhalation challenges should be considered.

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