Occupational asthma in a pharmaceutical worker exposed to penicillamine

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*From the Department of Chest Medicine, Hôpital du Sacré-Coeur, Montreal, and the Department of Pediatrics, McMaster University, Hamilton, Canada***ABSTRACT** A case of occupational asthma due to penicillamine is reported.

Many drugs have been reported as causing occupational asthma.^{1,2} Penicillamine ($C(CH_3)_2-SH-CHCOOH-NH_2$) is documented here as having caused occupational asthma in a pharmaceutical company worker.

Case report

A 32 year old man had worked for 14 years as an operator in a pharmaceutical company where he was exposed to different products, including penicillamine and guar gum. Seven years after starting work he noticed sneezing, dyspnoea, and wheezing on exposure to penicillamine and guar gum. These symptoms appeared immediately after exposure and persisted during the evening. The patient also reported symptoms of perennial rhinitis. Over the past 10 years exposure to cats had caused rhinitis symptoms and asthma. Occupational asthma due to guar gum had previously been confirmed in this patient and in other workers of a carpet company (personal observation). Skinprick tests showed a positive immediate reaction to cat dander and *Dermatophagoides farinae* extracts. Skinprick responses to penicillamine and to Penkit (benzylpenicilloyl polylysine and Minor Determinant Mixture, Stallergènes, Fresne, France), diluted in concentrations of 0.01, 0.1, and 1 mg/ml, were negative. Peak expiratory flow rates were measured for four weeks both at work and at weekends when he was away from work. Daily changes in peak flow of over 20% were documented on two occasions, once after exposure to guar gum and the other time after exposure to a cat. During this period, however, the patient was not exposed to penicillamine. Baseline results for FEV₁ and forced vital capacity (FVC) were 3.23 and 4.77 litres with a FEV₁/FVC ratio of 67% (percentages of predicted values 90, 114, and 81 respectively³).

Specific inhalation challenges were carried out four days after the patient had stopped work. On two consecutive days the patient tipped lactose or penicillamine powder from one tray to another in a cubicle.⁴ On the day the patient tipped lactose for 15 minutes there were no appreciable fluctuations in FEV₁ (< 6%) (figure). At the end of the day his bronchial responsiveness to histamine was assessed, a Wright nebuliser

with an output of 0.14 ml/mm being used.⁵ The provocative concentration causing a 20% fall in FEV₁ (PC₂₀) was 2.2 mg/ml (mild bronchial hyperresponsiveness). On the third day the patient tipped penicillamine for progressively increasing periods for a total of 30 minutes. He had an isolated late asthmatic reaction, seen as a fall in FEV₁ (figure). The subject also sneezed during this day. At the end of the day the PC₂₀ was 3.0 mg/ml. The penicillamine specific IgE value⁶ in our patient (225 cpm) was similar to the values found in four atopic controls (230 (SD 50.6) cpm) and four non-allergic control subjects (147 (12.1) cpm).

Discussion

This report shows that penicillamine can cause occupational asthma. In our patient the challenge test produced an isolated late asthmatic reaction. Skin test responses to penicillamine were negative and the specific IgE levels were normal. Thus the mechanism of the asthmatic reaction does not seem to be IgE mediated. Antibiotics causing occupational asthma^{1,2} are low molecular weight compounds and generally cause late asthmatic reactions. The mechanism responsible for the reaction is not yet understood but may be a pharmaco-

Change in FEV₁ in relation to inhalation challenges with lactose (duration 15 min) and penicillamine (duration 30 min).

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logically induced bronchoconstriction such as has been described with isocyanates.¹ No significant change in bronchial responsiveness to histamine was seen after this late reaction. Such a change might have been missed because the assessment was performed only once. These changes are not, however, always present after late asthmatic reactions.^{7,8}

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