

## SHORT REPORT

## Occupational asthma due to porcine pancreatic amylase

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### Abstract

**A case of occupational asthma in a 41 year old histopathology laboratory technician attributable to a powder preparation of the porcine pancreatic enzyme amylase is reported. The diagnosis was confirmed by a double blind, placebo controlled, inhalation challenge study which showed immediate and late asthmatic reactions associated with a significant increase in airway responsiveness to methacholine.**

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The SWORD project has collated reports of newly diagnosed cases of occupational lung disease in Britain since 1989.<sup>1</sup> It has shown that occupational asthma is the single most common work related respiratory disease, with 941 cases reported in 1994 (29% of all reports).<sup>2</sup> Enzymes accounted for only 2% of these cases. Powdered pancreatic extracts are known to cause asthma in pharmaceutical workers and in parents and health workers caring for children with cystic fibrosis.<sup>3-5</sup> However, occupational asthma specifically due to amylase has only been described previously in bakers.<sup>6</sup>

### Case report

#### THE PATIENT

A 41 year old ex-smoker had worked as a laboratory technician in a histopathology department for 22 years. He had no previous history of respiratory illness, no history of atopic disorders, and no family history of either. He was taking no medication and was generally well. One year before investigation he started using an anhydrous powder preparation of the enzyme amylase. This was derived from pig pancreas and was used in the staining of slide mounted tissue samples. The powder replaced the former practice of using his own salivary amylase. He would tap about 2 mg of the dry powder into a slide container from a height of 5-10 cm once a day, on most days of the week. The tapping action released a fine powder plume into the immediate atmosphere. His face would only be 20 cm from the slide container and he took no precautions against exposure. He had no symptoms for the first four to six months but then he started to feel

breathless and wheezy within a few minutes of exposure and often remained like this until late evening. He initially experienced no symptoms on working days when he was not exposed to the powder and no symptoms at weekends or on holiday. His symptoms continued for six weeks before he consulted a physician and was given salbutamol and beclomethasone metered dose inhalers (200 µg as required and 200 µg twice daily, respectively). These largely abolished his symptoms despite continued exposure to the powder. He was subsequently referred to a respiratory physician who suspected that the amylase had caused occupational asthma.

#### INVESTIGATION

For four weeks before investigation he was asked to discontinue all medication and to avoid any possible exposure to the amylase. He had few further symptoms. After this period, spirometry showed a forced expiratory volume in one second (FEV<sub>1</sub>) of 4.22 l (106% predicted) and a forced vital capacity (FVC) of 5.1 l (105% predicted). Two standardised methacholine tests within a week produced PC<sub>20</sub> values (provoking concentration responsible for a 20% decrement in FEV<sub>1</sub>) of 73 µg (baseline FEV<sub>1</sub>=4.15 l) and 77 µg (baseline FEV<sub>1</sub>=4.22 l). Values of PC<sub>20</sub> <200 µg are usually associated with active asthma.<sup>7</sup>

Laboratory based inhalation provocation tests were designed to reproduce the circumstances of the occupational exposure as closely as possible. Analar lactose is similar in appearance to the amylase powder and was used as the carrier for it. The lactose was dried in an oven at 105°C overnight before use because of its hygroscopic nature. The amylase was then added to form mixtures containing 1%, 3.2%, 10%, or 32% by weight of amylase for sequential inhalation challenges on separate days. The challenge tests were conducted in a double blind, placebo controlled fashion. Lactose alone was used for placebo, neither the patient nor the supervising physician knowing whether placebo or a sequential challenge with amylase was being used each day. The challenges were given over five minutes at 10 00 am each day. The patient sat at a table and three times tipped 10 g of the lactose or lactose mixture back and forward between two aluminium containers in a fashion which simulated his exposure at

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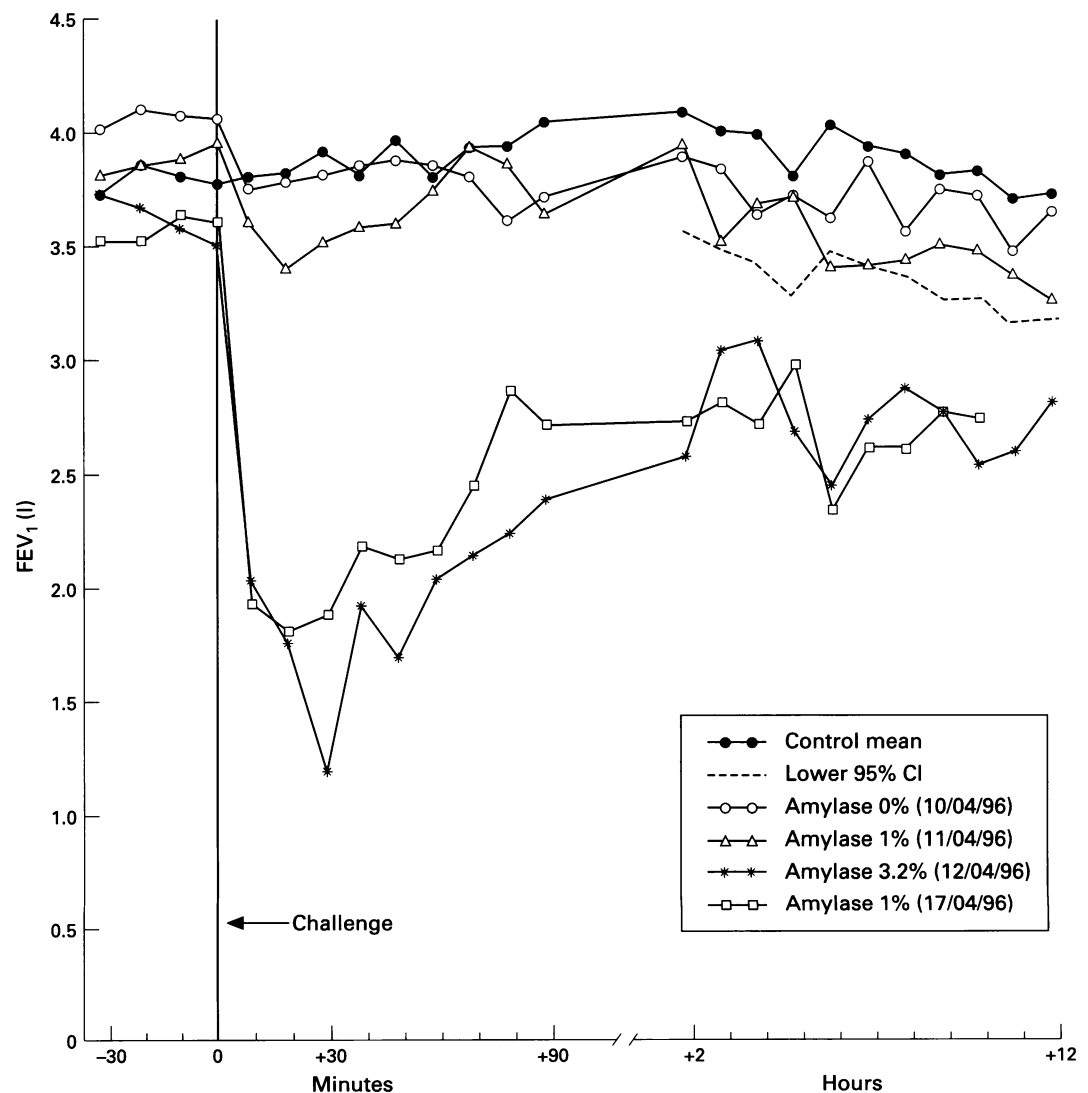
work. He wore a nose clip to disguise the odour of the amylase powder and remained seated for a period of five minutes, after which time there was no further exposure.

The FEV<sub>1</sub> was monitored at 10 minute intervals for 30 minutes before and 90 minutes after the start of challenge at 10 00 am. It was then recorded hourly by the subject at home for the period two to 12 hours after the start of challenge according to our usual protocol. The FEV<sub>1</sub> was recorded similarly for three days before the challenge tests to produce control data. From these, the mean FEV<sub>1</sub> at each time point was calculated together with a pooled lower 95% confidence interval.<sup>8</sup> A significant late asthmatic reaction during the two to 12 hour period after the start of challenge would be indicated by at least two consecutive hourly FEV<sub>1</sub> recordings below this limit. Airway responsiveness to methacholine was measured before the challenge series and as soon after as was practical. The patient had access to the supervising physician by telephone at all times.

### Results

The first challenge, with placebo, was not followed by symptoms nor any significant change in FEV<sub>1</sub> (figure). The second challenge,

using the 1% amylase mixture, failed to produce symptoms and was not accompanied by a late asthmatic reaction. However, there was a hint of an immediate asthmatic reaction in the first hour after challenge, with a 15% decrement in FEV<sub>1</sub>. The third challenge, with the 3.2% mixture, produced a dramatic immediate asthmatic reaction with a decrement in FEV<sub>1</sub> of the order of 75%. This closely reproduced the symptoms and level of discomfort he had experienced at work, and he remained surprisingly undistressed despite this pronounced fall in FEV<sub>1</sub>. Monitoring was therefore continued without bronchodilator intervention. He remained symptomatic but the FEV<sub>1</sub> improved steadily. However, it remained significantly decreased throughout the two to 12 hour surveillance period after challenge. This indicates that the immediate reaction was succeeded by a late reaction. It resolved within 24–48 hours and so a further methacholine test was carried out 24 hours later—that is, 72 hours after the 3.2% challenge. The PC<sub>20</sub> proved to be 19 µg (baseline FEV<sub>1</sub>=3.64 l), 25% of the value initially. A decrement to 1/3 or less of the prechallenge value indicates a significant increase in airway responsiveness.<sup>7</sup>



FEV<sub>1</sub> measurements during challenge days with placebo, 1%, and 3.2% amylase mixtures. Duration of each challenge exposure was five minutes.

It is our custom when investigating novel causes of occupational asthma to show that a positive response to challenge testing is repeatable. Therefore, a second series of challenges was carried out. A second placebo challenge (16 April 1996) produced no symptoms and no asthmatic reaction. However, a second challenge with the 1% amylase mixture (17 April 1996), unlike the first, produced an asthmatic reaction of similar magnitude and characteristics to that produced by the 3.2% amylase mixture in the first challenge series (figure). The  $PC_{20}$  measured the day after this challenge had decreased further, to 15  $\mu\text{g}$  (baseline  $FEV_1=3.41$  l), although this was not a significant decrease in airway responsiveness compared with the previous result of 19  $\mu\text{g}$ .

### Discussion

The combination of asthmatic symptoms, late asthmatic reactions, and a significant increase in airway responsiveness after a specific inhalation provocation test confirms a diagnosis of occupational asthma attributable to the amylase enzyme. The asthmatic response proved to be repeatable and the test protocol was conducted under double blind, placebo controlled conditions, making it particularly robust.

Late asthmatic reactions were provoked by the 3.2% amylase mixture in the first challenge series and the 1% mixture in the second challenge series. We think that the lowered threshold was a consequence of the increase in airway responsiveness (decrease in  $PC_{20}$  from 73–77  $\mu\text{g}$  to 19  $\mu\text{g}$ ) which resulted from the first challenge series. Such an induction of airway hyperresponsiveness provides valuable evidence that the challenge agent is a cause of occupational asthma and not merely a non-specific trigger of irritant asthmatic reactions. It is characteristic of challenge tests which provoke late asthmatic reactions (whether or not these are associated with immediate reactions), but not of tests which provoke immediate reactions only.

Enzymes are well recognised and potent causes of occupational asthma, but to our knowledge, occupational asthma involving amylase has not been previously described in this context. The practice of using amylase in histopathology laboratories is widespread and the risk associated with its use in powdered (and hence respirable) form should be appreciated. In practice, many laboratories use amylase in aqueous suspension, which is satisfactory provided nebulisation is avoided. The suspension should be prepared in an extractor controlled and exhaust filtered biohazard cupboard.

After these investigations, our patient avoided any further exposure to the powdered amylase. His asthma remained mildly active, and he continued to use inhaled steroid and bronchodilator medication. Further methacholine tests after three months and 15 months gave  $PC_{20}$  values of 64  $\mu\text{g}$  (baseline  $FEV_1=4.29$  l) and 213  $\mu\text{g}$  (baseline  $FEV_1=3.64$  l) respectively. This indicates that there was an appreciable improvement since his presentation, but it confirms that a clinically meaningful level of airway responsiveness persisted.

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