

Asthma due to inhaled chemical agents—amprolium hydrochloride

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Summary

A man with no previous history of allergy or chest disease developed asthma after exposure to a heavy atmospheric concentration of amprolium hydrochloride which is a constituent of a poultry-food additive. Subsequent experimental exposure produced an immediate asthmatic reaction which was inhibited by sodium cromoglycate.

Introduction

Immediate or late asthmatic reactions have been reported following exposure to a wide variety of chemical agents (Hunter, Milton & Perry, 1945; McCullagh, 1968; Pepys *et al.*, 1972a; Pepys, Pickering & Hughes, 1972b; Pepys, Pickering & Loudon, 1972c; Chan-Yeung, 1973; Davies, Hendrick & Pepys, 1974; Davies & Pepys, 1975). We report an immediate asthmatic reaction to amprolium hydrochloride (B. Vet. C.) which is a constituent of a poultry-food additive.

Case report

The patient was a 68-year-old man who had worked in the chemical industry for many years. For five years he had been employed as a sampler and checker in the manufacture of a poultry-food additive ('Pancoxin'). For about a year before he presented he noticed some sneezing and nasal discharge after he had been in the room where solid amprolium (a constituent of Pancoxin) was milled to a powder, but he had had no symptoms referable to his chest prior to the day of admission. On that day he had been in the milling room when the atmospheric concentration of amprolium was very high. About 5 min after entering the room he developed tightness of the chest with severe breathlessness and wheezing and was taken to the Casualty Department of this hospital where 250 mg aminophylline i.v. completely relieved his symptoms within 20 min. He was admitted to hospital where he remained asymptomatic, and was discharged after 48 hr.

There was no personal or family history of allergy; he had smoked twenty ciga-

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rettes per day until 5 years previously, and the only drug he was taking was methyl dopa, 750 mg/day, for hypertension. Clinical examination was normal (BP 150/90).

Chest radiographs and blood count were normal, with only 2% eosinophils in a total white cell count of 7,500. There were no eosinophils in the sputum. Skin tests (prick) to twenty common allergens revealed mild positive reactions to cat fur and house dust. FEV_{1.0}, vital capacity and peak expiratory flow rate (PEFR) were all above 80% of predicted normal (predicted normal values being 2.9 and 3.81 BTPS and 590 l/min. respectively).

Experimental exposures

Exposure to amprolium was achieved in the following manner. The patient (and observer) were in a small room (10 × 6 × 10 feet) and the patient continuously poured powder from one jar to another in a rapid, vigorous and deliberately clumsy manner so as to produce a concentration of powder in the atmosphere. Measurements were made of FEV_{1.0} and PEFR using respectively a Vitalograph wedge spirometer and a Wright peak flow meter.

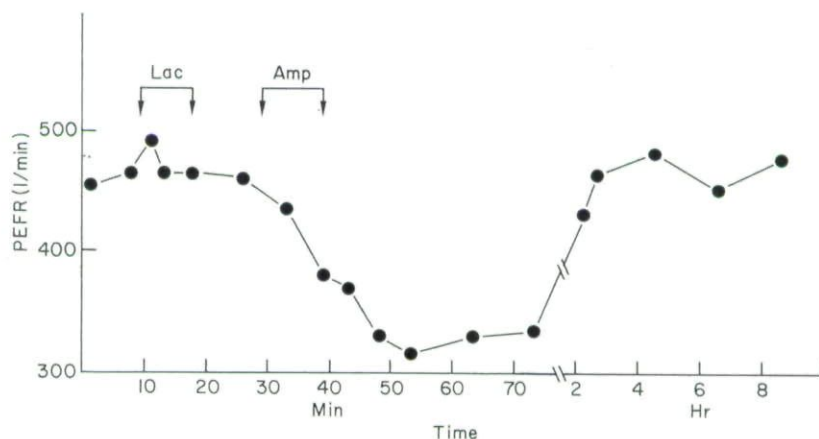


Fig. 1. Changes in peak expiratory flow rate after exposure to powdered lactose (Lac) and amprolium hydrochloride (Amp). FEV_{1.0} (not plotted) followed a similar course.

On the day after admission, following two sets of control measurements, the patient poured lactose for 10 min, and then after a 10 min interval, amprolium for a further 10 min. Measurements were made approximately every 5 min.

There was no response to lactose but amprolium produced a 36% fall in PEFR (Fig. 1) and a 20% fall in FEV_{1.0}. The bronchoconstriction began after a few minutes and lasted for approximately 30 min after the end of exposure. Further measurements at two hourly intervals for a further 7 hr did not reveal any evidence of a late reaction, and the patient remained asymptomatic during this period.

In the following week two further, similar, experiments were carried out, beginning at the same time on successive mornings. In each case, pouring of amprolium was preceded 10 min earlier by the inhalation from a 'Spinhaler' of the contents of two 'Spincaps'. On the first day these were a placebo, containing lactose, and on the second day each contained 20 mg of sodium cromoglycate (SCG). On both days the experi-

ment was terminated by the administration of 200 μ g of salbutamol by pressurized aerosol.

The results are shown graphically in Fig. 2. FEV_{1.0} fell by 27% and PEFR by 35% on the first day, but prior inhalation of SCG on the second day reduced the magnitude of the falls in FEV_{1.0} and PEFR to 11% and 12% respectively.

All three challenges with amprolium were accompanied by rhinitis, and by a feeling of tightness in the chest. The observer of these three exposures (S.F.) experienced no nasal or chest symptoms and showed no reduction in PEFR when the patient's values were at their lowest.

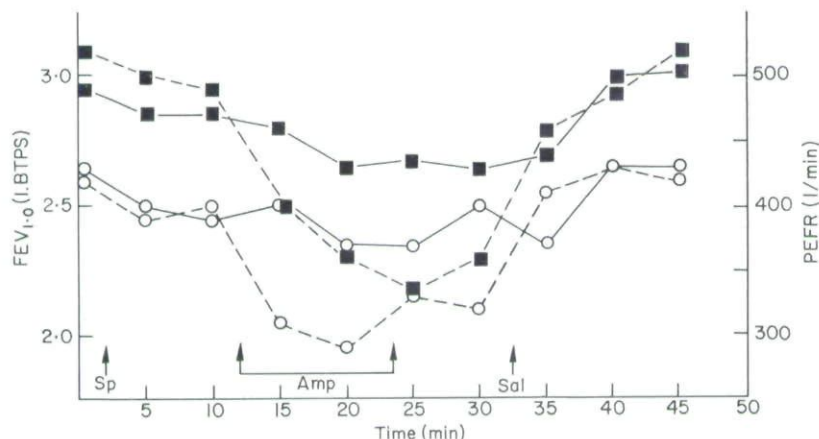


Fig. 2. Effect of exposure to powdered amprolium hydrochloride (Amp) on two successive days on FEV_{1.0}, (○) and peak expiratory flow rate, (■). On each day exposure to amprolium was preceded by inhalation of contents of two Spincaps (Sp) and followed by inhalation of 200 μ g salbutamol (Sal). On the first day (dotted line) the Spincaps contained lactose and on the second (solid lines) sodium cromoglycate (40 mg).

Discussion

The history and experimental challenges indicated that this patient had an immediate nasal and bronchial hypersensitivity to amprolium. He did not have a non-specific bronchial reaction to an inert dust (lactose) and the lack of any significant fall in ventilatory capacity after prior administration of SCG suggested that the reaction may have been allergic (Pepys *et al.*, 1968).

The absence of a late reaction is unusual for hypersensitivity to an inhaled chemical agent. It is possible that we missed a brief late reaction by only making measurements every 2 hr or by ceasing measurements at 7 hr, but the normality of the measurements and the complete absence of symptoms during the measurement period (which ended at 10.00 p.m.) and subsequently, overnight, makes this unlikely.

A feature of this patient's asthmatic reaction was the relatively greater fall in PEFR than in FEV_{1.0}, suggesting a possibly greater effect on upper airways (larynx and trachea) than on lower, intrapulmonary ones. However, the ratio of PEFR (% predicted)/FEV_{1.0} (% predicted) never exceeded 1.3 which is below the figure of 1.6 which Empey (1972) suggested was necessary to diagnose upper airway obstruction from tests of forced expiration.

The patient had no allergic history but prick testing did reveal evidence of skin

reactivity to two common allergens. Asthma due to inhaled chemical agents in non-atopic men is well recognized (Pepys *et al.*, 1972b) and the atopic state does not appear necessary for this type of hypersensitivity to occur.

Amprolium hydrochloride is a white, odourless substance, readily soluble in water. It is a thiamine antagonist and is used as an additive in poultry-feeds to prevent coccidiosis. It is present in the finished product ('Pancoxin'—Merck, Sharp and Dohme Ltd) in a concentration of 18% w/w together with sulphaquinoxaline (10.8%) and Ethopabate (0.9%) the remainder being made up of a cereal carrier. Pancoxin is fed to chicks, broilers and turkey chicks, but not to adult breeding birds or layers (except on veterinary prescription). When Pancoxin is used in the maximum recommended concentration of 40 oz/ton of feed, the resultant concentration of amprolium in the feed is about 200 parts/10⁶. Thus, while our patient required a relatively heavy atmospheric exposure to precipitate his asthma, it is possible that further cases of amprolium hypersensitivity will be found in people who handle poultry, and poultry-feeds.

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