

# Pulmonary eosinophilia caused by penicillamine

D DAVIES AND J K LLOYD JONES

From City Hospital, Nottingham and Harlow Wood Hospital, Mansfield, Nottingham

Penicillamine is used mainly in treating rheumatoid arthritis but it is also used in Wilson's disease and cystinuria. Its place in treating cryptogenic fibrosing alveolitis and histiocytosis X is being investigated. The common side-effects are nausea, vomiting, rashes, bone marrow depression, and albuminuria. A rare side-effect is Goodpasture's syndrome.<sup>1</sup>

One case of diffuse alveolitis has also been recorded in a patient with rheumatoid arthritis who had taken penicillamine for a year.<sup>2</sup> She became short of breath and had crackles at the lung bases, restrictive impairment of ventilation, reduced gas transfer, and patchy irregular basal shadowing on the chest radiograph. Improvement occurred fairly quickly after penicillamine was stopped. We report a case with similar features but with blood eosinophilia.

### Case report

A woman aged 64 years developed severe rheumatoid arthritis in 1963. Two years later extensor pollicis longus tendons in each hand ruptured and needed repair. Knee arthroplasties were done in 1970 and 1971 and the prosthesis on the right was replaced in 1976. Ruptured extensor tendons in the fingers were repaired in 1971. She was treated with ACTH from 1967 to 1972 and after this relied on non-steroid anti-inflammatory agents and analgesics. Severe arthritis continued and gold injections in 1974 produced little improvement. She became house-bound and needed help to dress and undress.

In May 1978 she developed abdominal pain and diarrhoea and was admitted to hospital. Examination showed pallor and active polyarthritis but no other abnormality. The haemoglobin was 9.7 g/dl with a low serum iron and normal iron binding capacity, the white blood count was  $9.4 \times 10^9/l$  ( $9400/mm^3$ ) with a normal differential count, the ESR was 130 mm in one hour (Westergren), and the alkaline phosphatase was 265 units/l. There was a slight reduction in serum albumin and an increase in alpha-2 and gamma globulins. The urea, electrolytes, and chest radiograph were normal.

The pain and diarrhoea settled and she was started on d-penicillamine 125 mg daily on 11 May. She was discharged on this together with flubriprofen, difunisal, Ferrograd C, and indomethacin suppositories. The dose of penicillamine was

increased by 125 mg every four weeks to 375 mg daily.

On 25 July she was readmitted to hospital for transfusion and after three units of blood the haemoglobin rose from 8.2 to 11.2 g/dl. By that time she was aware of increasing shortness of breath and it did not improve after transfusion. She was discharged on the same medicaments. The eosinophil count which had been normal rose to  $950/mm^3$  on 10 August and weekly readings thereafter were between 747 and  $1200/mm^3$  and the haemoglobin fell to 7.5 g/dl. Shortness of breath increased and became severe even with the slight activities she could manage. In mid-September there were widespread crackles over the mid and lower zones of the lungs but there was no clubbing of the fingers. The chest radiograph showed fairly extensive irregular and ill-defined coarse linear shadows in the lower halves of both lungs (figure). Lung function tests showed a moderately severe restrictive impairment of ventilation and a low transfer factor (table). Penicillamine was stopped on 12 October.

Dyspnoea improved over six weeks and this was matched by improvement in lung function and considerable radiographic clearing. By 23 November she was only slightly breathless. In the hope of avoiding residual lung damage she was treated with prednisolone for seven weeks, starting with 20 mg daily and reducing in steps after two weeks. During this time the radiograph became normal and the lung function tests were at their best. When prednisolone was stopped there was no clinical change but the breathing tests deteriorated slightly.

In the summer of 1979 she had no noticeable dyspnoea, the eosinophil count was normal, the chest radiograph was clear but she still had some restrictive impairment of ventilation (table).

Table Lung function tests before and after stopping penicillamine on 12.10.78

	PEFR l/min	FVC l	FEV <sub>1</sub> l	TLC l	RV l	Transfer factor mmol/min/kPa
Predicted normal	344	2.67	2.01	3.35	1.63	7.0
20.9.78	278	1.80	1.42	3.22	1.42	4.0
12.10.78		1.75	1.50			
25.10.78	300	2.00	1.65	3.59	1.59	4.7
22.11.78	315	2.25	1.70	3.68	1.43	5.3
20.12.78	320	2.35	1.85	4.04	1.69	6.8
10.1.79	315	2.20	1.80	3.74	1.54	5.5
25.7.79	325	2.20	1.75	3.85	1.65	5.5

Conversion: mmol/min/kPa  $\times$  2.98 = ml/min/mmHg

Address for reprint requests: Dr D Davies, Department of Thoracic Medicine, City Hospital, Hucknall Road, Nottingham NG5 1PB.

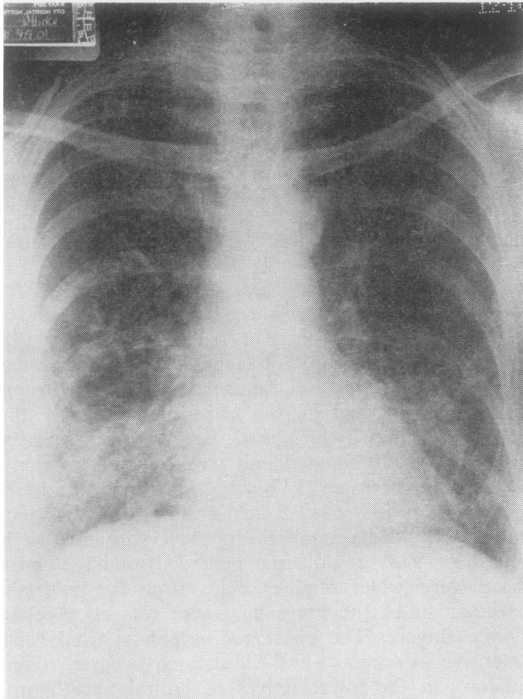


Figure Chest radiograph of patient, showing ill-defined irregular and linear shadows in the lower halves of both lungs.

### Discussion

It seems probable that the lung disease was caused by penicillamine. Fairly rapid improvement occurred when the drug was stopped and the other medicaments continued. There was nothing to suggest infection and the patient was not exposed to organic antigens. It is possible that equally good clearing would have occurred even without the later use of corticosteroids. She still has some restriction of ventilation but there were no readings before this episode. There is no clinical evidence of rheumatoid fibrosing alveolitis.

The other published case<sup>2</sup> was described as having diffuse alveolitis. Blood eosinophilia was not recorded and there was rapid improvement when penicillamine was stopped. At three months the lung function tests had returned to normal except for a reduced transfer factor. The reaction in our case was also at alveolar level and it is probably best classified as subacute pulmonary eosinophilia.

### References

- 1 Sternlieb I, Bennett B, Scheinberg IH. D-penicillamine induced Goodpasture's syndrome in Wilson's disease. *Ann Intern Med* 1975; **82**:673.
- 2 Eastmond CJ. Diffuse alveolitis as complication of penicillamine treatment of rheumatoid arthritis. *Br Med J* 1976; **1**:1506.