characterized by general malaise developed, but there was no fever and no worsening of the cough or dyspnea. Pneumonia was diagnosed by his physician on the basis of findings on a roentgenogram of the chest. The patient did not respond to routine antibiotic therapy. He was given a short course of corticosteroids, and his symptoms decreased in severity. He was seen again at our clinic in April, 1965, when a diffuse interstitial pulmonary process was noted. A previous roentgenogram of the chest taken at this clinic in April, 1964, had revealed no abnormality. During this time, he had continued to take nitrofurantoin.

Sputum cultures were negative for acid-fast bacilli and fungi. Tuberculin skin tests (5 and 250 tuberculin units) were negative. Results of routine laboratory tests were within normal limits.

The patient refused to undergo an open lung biopsy recommended for definitive diagnosis.

He returned on March 1, 1966, complaining of increased dyspnea and cough; in the interim he had continued to take nitrofurantoin because of intractable urinary symptoms. A roentgenogram (Fig. 1*A*) at this time revealed an increase in the diffuse pulmonary process, and pulmonary-function studies demonstrated a restrictive pattern, with impaired carbon monoxide diffusion. Subsequent transbronchoscopic lung biopsy showed moderate, chronic interstitial pneumonitis with slight fibrosis. Therapy with prednisone, 10 mg 4 times a day, was started, and the use of nitrofurantoin was discontinued.

A maintenance dose of 20 mg of prednisone a day was prescribed, and follow-up examination 6 weeks later revealed a dramatic improvement in the dyspnea. A roentgenogram of the chest (Fig. 1*B*) and pulmonary-function tests gave evidence of the improvement.

The patient died unexpectedly 4 weeks later; autopsy performed at another institution revealed findings of pulmonary fibrosis, mild bronchiectasis, bronchopneumonia of both lower lobes, cor pulmonale and atherosclerosis of the coronary arteries. A known sequel to pulmonary fibrosis is bronchiectasis, and we assume that this is the order of the cause-and-effect relation in this case; no abnormality had been noted on a roentgenogram taken 2 years before the onset of the present illness, and we assume that he did not have chronic bronchiectasis.

CASE 5. A 66-year-old housewife was seen at the Mayo Clinic on January 26, 1967, for evaluation of a 5-month history of progressive nonproductive cough, dyspnea on exertion and pain in the anterior part of the chest of gradual onset. There was no history of fever or chills. She had been receiving daily doses of nitrofurantoin for 15 months because of chronic recurrent urinary-tract infections. Examination revealed crackling rales at both lung bases and dyspnea on exertion. On x-ray examination there was evidence of a diffuse bilateral interstitial process (Fig. 2*A*) that had not been present on the last examination at our clinic in June, 1965.

Results of routine laboratory studies were normal. The lactic dehydrogenase level was 452 units per liter, and the L.E.-cell clot preparation revealed clumps of rosettes but no classic L.E. cells. The urine culture was positive for *Esch. coli*. Sputum studies did not disclose any acid-fast bacilli or fungi. Pulmonary-function studies showed abnormalities consistent with a restrictive pattern as well as an impairment of the carbon monoxide diffusion capacity. Transbronchoscopic lung biopsy indicated moderate chronic interstitial pneumonitis with fibrosis.

Therapy was started with prednisone, 10 mg 4 times a day, and the use of nitrofurantoin was discontinued. Follow-up evaluation 4 weeks later revealed definite improvement, with notable clearing of the diffuse process seen on the roentgenogram. The patient had been taking prednisone for 11 days at that time. Therapy was continued with smaller doses of prednisone for the next 7 months. When she returned to the Mayo Clinic 8 months after the initial examination, the roentgenogram of the chest showed no abnormality (Fig. 2*B*). The lactic dehydrogenase level had decreased from 452 initially to 163 units per liter, and the carbon monoxide diffusing capacity had increased from 9 to 14 ml per minute per millimeter of mercury.

DISCUSSION

Since Israel and Diamond (9) reported the first case of pulmonary nitrofurantoin reaction in 1962, all but two of the subsequent reports have dealt with the *acute* onset of pulmonary symptoms. Typically, in the acute onset, symptoms