the clinical syndrome of acute, febrile, noncardiac pulmonary edema caused by the drug.

We have seen five patients at our institution who received nitrofurantoin for periods from six months to six years before pulmonary symptoms developed. The purpose of this report is to present the observations on these five patients and to record what we believe represents chronic nitrofurantoin pulmonary reaction. Lung-biopsy specimens taken from the five patients showed a nonspecific pattern of diffuse interstitial pneumonitis and fibrosis.

We have no proof that nitrofurantoin caused the pulmonary changes presented in the five cases reported herein. Nevertheless, since nitrofurantoin has been strongly implicated in the genesis of interstitial pneumonitis on an acute basis, the five cases indicate the possibility of a spectrum of nitrofurantoin-induced pulmonary disease on a chronic basis. Because nitrofurantoin is used extensively today and because of the dire consequences of interstitial pneumonitis, it seems justifiable to call attention to another possible untoward effect of the drug.

CASE REPORTS

CASE 1. A 68-year-old woman came to the Mayo Clinic in January, 1968, for a general examination. In 1960, she had received nitrofurantoin (Furadantin) for chronic recurring urinary-tract infections, and for 6 or 7 years before examination she had been taking 50 mg a day. In 1962, 2 years after the nitrofurantoin therapy was begun, cough and dyspnea on exertion developed. The onset of symptoms was gradual, and there were no febrile episodes associated with the early manifestations of the pulmonary disease. Several months after the onset of pulmonary symptoms, examination at another institution resulted in the diagnosis of Hamman-Rich syndrome on the basis of the histologic appearance of an open lung-biopsy specimen. (Our pathologist reviewed the tissue and reported "marked chronic interstitial pneumonitis and fibrosis compatible with Hamman-Rich syndrome.") After the biopsy, the patient was given dexamethasone, 0.75 mg twice each day. During the interval from the time of biopsy until she came to the Mayo Clinic, she was seen by her family physician for the urinary-tract complaints but had no follow-up examination for the pulmonary problem.

On examination at the Mayo Clinic, she complained of minimal cough but definite dyspnea with any exertion. Physical examination revealed inspiratory rales at the bases and anteriorly. The hemoglobin was 11.3 gm per 100 ml, and the white-cell count 7000, with a normal differential. Rheumatoid-factor and L.E.-cell clot tests were negative. An electrocardiogram showed an abnormal ventricular depolarization, with a questionable old anteroseptal infarction. The urine was normal, and 2 urine cultures were negative. A roentgenogram of the chest gave evidence of a bilateral diffuse process, most severe at the bases.

Complete pulmonary-function studies demonstrated a significant amount of restrictive disease.

The use of nitrofurantoin was stopped, but the dexamethasone therapy was continued. A follow-up letter 6 weeks later revealed that the patient's condition was improved and that she had less dyspnea with exertion. She has not returned for a follow-up roentgenogram or evaluation of pulmonary function.

CASE 2. A 62-year-old man was admitted to the hospital on June 28, 1967, with a history of febrile episodes 3 or 4 times each year during the past 4 years. The episodes became more frequent and were attributed to recurring urinary-tract infections, for which he was treated intermittently with nitrofurantoin. During the last year, the treatment with nitrofurantoin was on a continuous basis (averaging 100 to 200 mg per day) to prevent attacks. The patient had noticed increased shortness of breath during the past 6 months. One year before, a roentgenogram of the chest taken at another institution had shown no abnormality.

Results of physical examination were normal, except for decreased chest expansion and leathery crackling rales at both bases posteriorly.

Abnormal results of laboratory tests included an elevated sedimentation rate of 60 mm in 1 hour (Westergren method), pyuria of Grade 3 and a urine culture growing *Escherichia coli* and *Aerobacter aerogenes*. The gamma-globulin fraction