

treatment by corticosteroids probably has a considerable fibrosis and thus, predictably, is not likely to improve greatly. In the patients who improve, there appears to be a correlation between the duration of pulmonary symptoms and the amount of improvement. There does not appear to be any correlation between the length of time on nitrofurantoin therapy and the severity of the illness, or its reversibility.

Although pulmonary symptoms were present for only seven weeks in Case 3, the pulmonary infiltrate probably was present for a considerably longer time; the finding of fibrosis on biopsy of the lung usually implies that a process has been present for several months, but this is only conjecture. Also, because some of the measures of pulmonary function did not improve, this indicated that the process may have been going on for a long time.

The role of steroids in the improvement of the clinical condition in four of the patients is difficult to assess. These patients may have improved, although more slowly, without steroids and only by the withdrawal of the nitrofurantoin use, as is true in the acute onset variety. However, nitrofurantoin pulmonary reaction is a hypersensitivity reaction involving the interstitial tissue of the lung, for which prednisone therapy is probably indicated and may contribute to the prevention of irreversible pulmonary fibrosis. The exact nature of the apparent hypersensitivity phenomenon has not been established. Treatment should consist of terminating the use of the offending drug and of preventing irreversible fibrosis.

The diagnosis can be suspected from the history and physical examination when the roentgenogram of the chest gives evidence of diffuse interstitial infiltration. The only absolute way of establishing a diagnosis is by lung biopsy, as was carried out in our five patients.

Another method of diagnosing this condition is the provocative or rechallenge test (the first being to note improvement after withdrawal of the drug), but this was not done in any of the cases discussed here. It would be of interest to do this in the so-called chronic form of nitrofurantoin pulmonary reaction. However, the return of symptoms and abnormal pulmonary finding may be insidious and may produce further irreversible changes before they can be detected.

## REFERENCES

1. Wold, De W. E., and Zahn, D. W. Allergic (Löfller's) pneumonitis occurring during antituberculous chemotherapy: report of 3 cases. *Am. Rev. Resp. Dis.* 74: 445-453, 1956.
2. Petersen, A. G., Dodge, M., and Helwig, F. C. Pulmonary changes associated with hexamethonium therapy. *Arch. Int. Med.* 103: 285-288, 1959.
3. Hildean, T., Krogsgaard, A. R., and Vimtrup, B. Fatal pulmonary changes during medical treatment of malignant hypertension. *Lancet* 2: 830-832, 1958.
4. Rokseth, R., and Storstein, O. Pulmonary complications during mecamlamine therapy. *Acta med. Scandinav.* 167: 23-27, 1960.
5. Heard, B. E., and Cooke, R. A. Busulphan lung. *Thorax* 23: 187-193, 1968.
6. Steinberg, A. D. Pulmonary edema following ingestion of hydrochlorothiazide. *J.A.M.A.* 204: 825-827, 1968.
7. Graham, J. R., Suby, H. I., LeCompte, P. R., and Sadowsky, N. L. Fibrotic disorders associated with methysergide therapy for headache. *New Eng. J. Med.* 274: 359-368, 1966.
8. Fiegenberg, D. S., Weiss, H., and Kirshman, H. Migratory pneumonia with eosinophilia: associated with sulfonamide administration. *Arch. Int. Med.* 120: 85-89, 1967.
9. Israel, H. L., and Diamond, P. Recurrent pulmonary infiltration and pleural effusion due to nitrofurantoin sensitivity. *New Eng. J. Med.* 266: 1024-1026, 1962.
10. Murphy, K. J. Pulmonary reaction to nitrofurantoin ("Furadantin"). *M. J. Australia* 2: 607, 1966.
11. Strauss, W. G., and Griffin, L. M. Nitrofurantoin pneumonia. *J.A.M.A.* 199: 765, 1967.
12. Frankenfeld, R. H. Pulmonary edema caused by nitrofurantoin. *Ann. Int. Med.* 66: 1055, 1967.
13. DeMasi, C. J. Allergic pulmonary infiltrates probably due to nitrofurantoin. *Arch. Int. Med.* 120: 631-634, 1967.
14. Morris, A. J. Pulmonary and eosinophilic reaction to nitrofurantoin. *Delaware State M. J.* 39: 299-301, 1967.