Modified abstract as of June 6, 1957

Albert B. Sabin, M. D.
Professor of Research Pediatrics
University of Cincinnati College of Medicine
The Children's Hospital Research Foundation
Cincinnati, Ohio

Abstract for Meeting of National Tuberculosis Association

May 18, 1951 — Cincinnati, Ohio

Miliary Granulomatous Pneumonitis in a Group of Men Exposed to Pigeon Excreta

The epidemiological, clinical, roentgenological and pathological data on an outbreak, which occurred in Cincinnati in 1947 and was previously reported by Feldman and Sabin in abstract form (J. Clin. Invest., 1948, 27, 533), will be presented and information received from others on similar cases observed since then will be discussed. The 1947 Cincinnati outbreak involved 12 men who were either actively engaged in cleaning an old water tower full of wet pigeon manure or visited there while the work was in progress. All developed similar illnesses of varying severity within 5 to 14 days. There were no secondary cases in the homes or other contacts of these patients. Three were only slightly ill with low-grade fever for 2 to 5 days, while 9 were severely affected with fever for 8 to 21 days, generalized malaise, headache, chills, non-productive cough and marked weakness. The leukocytes were within normal limits quantitatively and qualitatively. "Cold agglutinins" were not demonstrable. Penicillin in large doses, given because ornithosis was suspected, had no effect. Loss of weight, ranging from 13 to 56 pounds, occurred during the acute phase but was regained within 2 months after onset.
Although no significant signs were elicited on physical examination, all of the 12 men exhibited extensive, diffuse, miliary-like infiltrates in both lung fields, giving rise to the most striking feature of this disease, the "snowstorm" roentgenogram. These X-ray changes persisted with varying diminution of intensity for 2 months, or longer, despite clinical recovery. By the end of 6 months, the lungs appeared normal in 4 patients, while in 4 others resolution was still incomplete at 18 months. Dr. Benjamin Felson, who has followed these patients roentgenologically, believes that 4 of them still exhibited minor infiltrative changes at 4 years, but none of 7 examined at 4 years had developed calcification.

One of the men, who, like all the others, had recovered from this illness, met sudden death 5 months later as a result of an acute myocardial infarction in an arteriosclerotic heart. Although the X-ray of his lungs was practically clear 2 months prior to his death, multiple microscopic granulomatous lesions, 1 to 2 mm. in diameter, were found in the lungs and peribronchial lymph nodes. The lesions were in various stages of organization, but, in both the lungs and lymph nodes, there were many with central caseous necrosis and "Langhans-type" giant cells unassociated with acid-fast bacilli. Inoculation of mice or embryonated eggs with blood from 11 of the 12 men and sputum from 2 men obtained during the acute stage yielded no infectious agent. Complement fixation, neutralization or skin tests were carried out to determine the possible role of ornithosis, Q fever, blastomycosis, coccidioidomycosis, histoplasmosis, toxoplasmosis or avian tuberculosis, but there was no evidence that any of these agents were etiologically related to this disease.
In 1948, Dr. Grant Taylor of Duke University informed us of a similar outbreak in Warrenton, N. C., which affected 7 men who removed about one-half ton of pigeon manure from an old church belfry. The incubation period, clinical manifestations, X-ray findings in the lungs, and the absence of secondary cases in associates were in accord with the findings in the Cincinnati outbreak.

Through the cooperation of Dr. Joseph H. Schubert of the Communicable Disease Center in Chamblee, Georgia, a number of serum specimens obtained from our patients in 1947 at various times after onset and stored in the frozen state were tested for complement-fixing antibodies with histoplasmin antigen. Nine of 11 patients, whose sera were tested at 3 to 4 weeks after onset, had complement-fixing antibodies for histoplasmin in titers varying from undiluted to 1:64 (undil., 1:2, 1:4, 1:8, 1:16, 1:32, 1:64, 1:64). In 2 of these 9 patients the titers changed from negative in undiluted serum 7 and 9 days after onset to 1:8 and 1:16 four weeks after onset. By 6 months after onset the patients who had titers of 1:32 to 1:64 at 4 weeks were positive only in the undiluted serum or in the 1:2 dilution. Sera obtained from 9 family associates 1 to 4 weeks after onset of illness in the patient all yielded negative results in the undiluted serum. In view of the negative skin tests with histoplasmin (1:1,000) in all our patients at 5 months after onset, and the rapidly dropping complement-fixing titers with histoplasmin, it is possible that a fungus related to, but not identical with, histoplasma may have been responsible for this disease. However, since all of our patients received large doses of penicillin, this conclusion is valid only if penicillin and histoplasmin do not share a common antigen.