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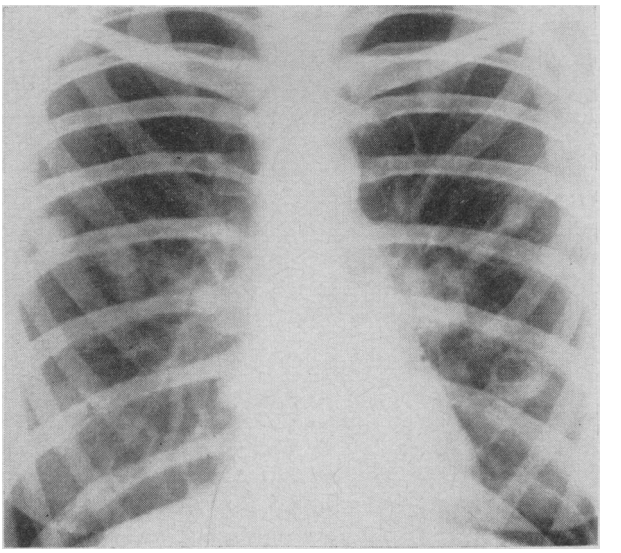

Fig. 1.—Chest roentgenogram taken May 25, 1951.

PULMONARY HISTOPLASMOSIS

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WITHIN THE LAST DECADE there have been several reports of histoplasmosis in Canada. These have included fatal cases in Ontario in the St. Thomas and Chatham area as reported by Haggar, Brown and Toplack,[1] as well as numerous benign cases.[2] In spite of the fact that histoplasmosis is apparently endemic in Southwestern Ontario, only three cases of active pulmonary histoplasmosis have been documented in Hamilton. One of these was a patient at the Mountain Sanatorium studied by Armstrong.[3] He was a 61-year-old man from Hamilton who died of coronary thrombosis in 1953. At autopsy, *Histoplasma capsulatum* was identified in consolidated areas and cavities in both lungs as well as in the hilar lymph nodes and bone marrow.

The second patient was a 57-year-old man who lived about 40 miles north of Hamilton. He had been under observation for many years because of suspected healed pulmonary tuberculosis. In November 1957, a nodular lesion appeared in the left lower lobe and was thought to be a carcinoma. It was removed at the Hamilton General Hospital on February 5, 1958, and proved to be a granulomatous lesion of histoplasmosis.

The third patient has been studied by us over a period of 11 years, and the case is reported below.

W.J.H. was first seen at the McGregor Clinic in 1948 at the age of 15 years. She gave a three-year history of recurring joint aches associated with fatigue. At no time had she had any pulmonary complaints. She had lived in Bolivia for the first three years of her life, during which time she had been well except for an attack of dysentery. From the age of three to 14 years she had lived in Southwestern Ontario, in London and Ridgetown. She then moved to Hamilton.

The results of physical examination, laboratory investigation and fluoroscopy of heart and lungs were normal on her first visit. During the following year her health improved but she fatigued easily.

In January 1951, while she was attending university, a routine chest radiograph was found to be abnormal. Throughout both lung fields there were scattered spherical lesions, most of which appeared to be solid and homogeneous although a few appeared cystic. A bronchoscopic examination was negative. A histoplasmin skin test (1:1000) was positive. Skin tests with coccidioidin, blastomycin, tuberculin, and hydatid cyst fluid were negative. The lesions slowly increased in size, as illustrated in Figs. 1 to 4. By 1953, the largest lesion was a cyst in the left lower lobe about 8 cm. in diameter. In spite of repeated negative Casoni skin tests, hydatid cyst disease was thought to be the most likely diagnosis.

On June 22, 1953, a left thoracotomy was performed at St. Joseph's Hospital by one of us (E.C.J.). About 12 localized caseous lesions were shelled out. No definite capsule was visible and the surrounding lung tissue appeared normal. The large cyst in the left lower lobe communicated with a bronchus. Microscopically, the lesions consisted essentially of caseous necrotic areas surrounded by a relatively thin rim of chronic granulomatous inflammation in which there was a

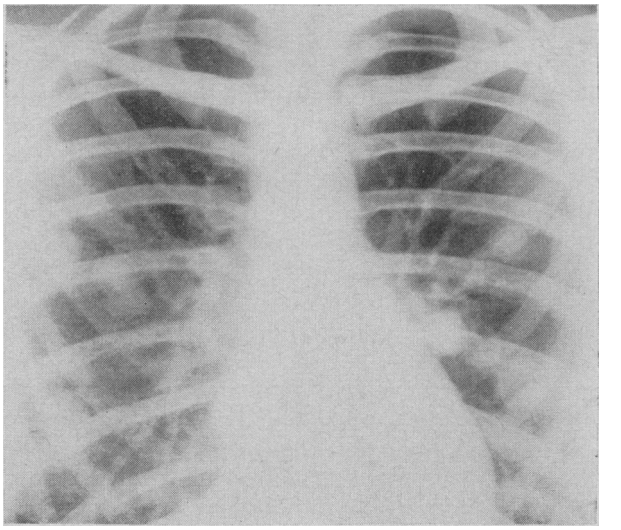

Fig. 2.—Chest roentgenogram taken May 21, 1952.

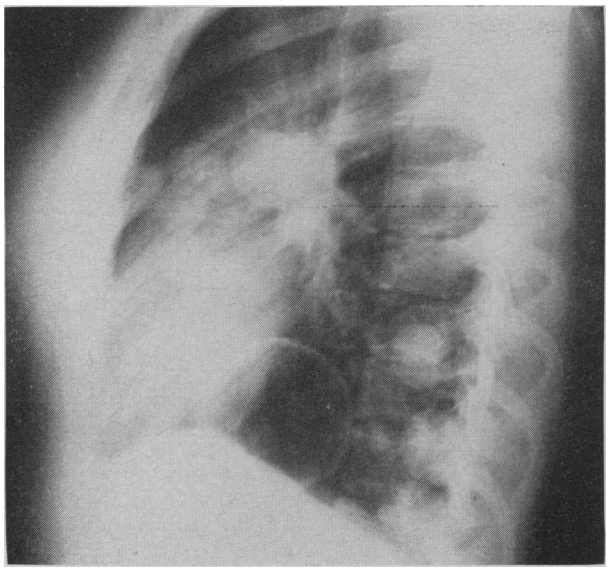

Fig. 3.—Chest roentgenogram (lateral view) taken March 23, 1953.

mixture of neutrophils, lymphocytes, epithelioid cells and occasional multinucleated giant cells. Fibrosis was minimal. Within the centre of these lesions there were small hyalinized rings which were thought to be artefacts. No bacteria or parasites could be identified, and smears and cultures for all types of organisms were uniformly negative. A diagnosis of granulomatous pulmonary lesions of unknown etiology was made.

About three months later, on September 10, 1953, a right thoracotomy was performed and eight similar lesions were removed from the right lung. The lesions were histologically similar to those previously removed. Representative sections were sent to various mycologists but no definite diagnosis could be made.

Since her operation, the patient has enjoyed good health. Laboratory studies have been normal except for a persistent elevation of the erythrocyte sedimentation rate which has remained around 40 mm. in one hour (Wintrobe). The white cell count has been about 12,000 with a normal differential. The urine has repeatedly shown a trace of albumin and one-plus red blood cells. Intravenous pyelograms in December 1955 and May 1958 were normal. Skin tests were

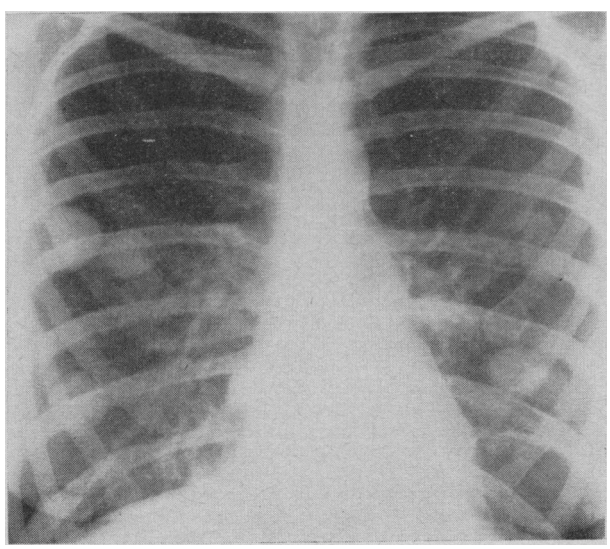

Fig. 4.—Chest roentgenogram taken May 21, 1953.

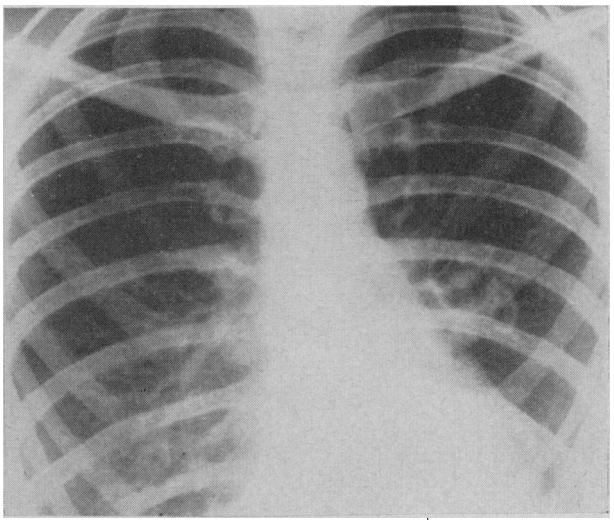

Fig. 5.—Chest roentgenogram taken April 29, 1954.

repeated and remained unchanged. A few lesions have reappeared (Figs. 5 and 6), but since 1956 there has been very little increase in their size.

In May 1958, the original pathological material was further investigated at St. Joseph's Hospital in Hamilton. By means of the Gridley fungus stain, small ring-like structures about three microns in diameter were identified which were morphologically identical with *Histoplasma capsulatum*. Since then, complement fixation tests for histoplasmosis have been carried out on five occasions. All have been positive in dilutions ranging from 1:16 to 1:64. Blood cultures for *Histoplasma capsulatum* were negative. No sputum has been available for study.

DISCUSSION

The diagnosis of chronic progressive pulmonary histoplasmosis was made on this patient on the basis of a positive histoplasmin skin test, positive complement fixation tests for histoplasmosis, and the presence of structures consistent with *Histoplasma capsulatum* in the lesions removed at operation. The diagnosis was not made for almost seven years after the first abnormal chest film. There were several reasons for this delay, the most important being failure to suspect the disease. Had the positive histoplasmin skin test found in 1951 been taken more seriously and followed through with complement fixation tests, the diagnosis of histoplasmosis would have been suspected earlier. However, the presence of cystic changes in some of the pulmonary lesions, and the fact that the patient once lived in Bolivia, made hydatid cyst disease seem most likely. Cystic changes in histoplasmosis must be extremely rare, although cavitation resembling that in tuberculosis is not unusual. Commonly, the lesions of histoplasmosis calcify, although it may take several years.[4] In our patient there had been no tendency to calcification. During the first two years of observation there was a marked increase in the size of the lesions. Even though the patient remained well, it was felt that dissemination of the disease was likely to occur unless some effort was made to halt the process.

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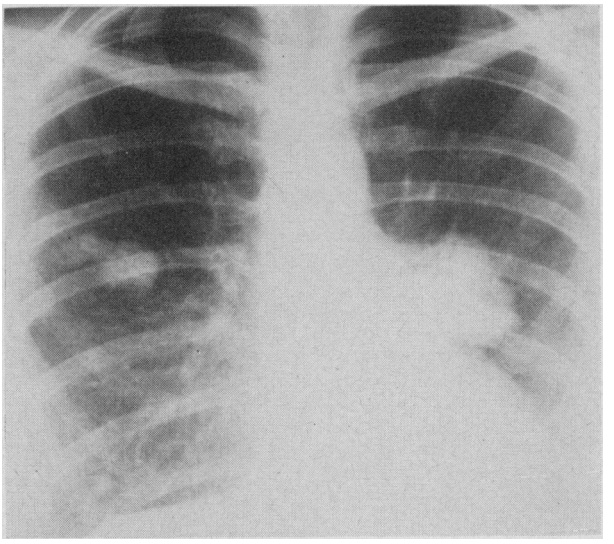

Fig. 6.—Chest roentgenogram taken February 21, 1959.

The decision to remove the lesions by surgery was made only after careful deliberation and consultation with others.

It is now appreciated that in benign, healed or slowly progressive disease, the organisms are very scarce or dead. Frequently, only the ghosts of the histoplasma remain, making identification difficult. Studies by Sweany[5] have also shown the difficulty in culturing the fungus in such lesions. In our patient, pathological diagnosis was made only after numerous sections had been taken and examined by various fungus stains.

The fact that the patient lived for 11 years in Southwestern Ontario, where the disease is probably endemic, may be significant. It is likely that she inhaled dust[6] containing the spores of *Histoplasma capsulatum* when she lived in this region. Failure to obtain a history of pulmonary symptoms, as in our patient, is not unusual, although the multiple lesions would suggest heavy exposure to the fungus.

Operation has been performed safely in pulmonary histoplasmosis,[7] but, as far as we know, not in such widespread disease as in this patient. Since her operations in 1953, lesions have reappeared in both lungs. These probably represent enlargement of nodules which were too small to be seen at the time of operation. The lesions near the left hilum could be a recurrence.

Although amphotericin B is now available and has been found useful[8, 9] in the treatment of histoplasmosis, we are inclined merely to observe the patient at the present time. She is well clinically, and during the past three years there has been very little tendency for the lesions to increase in size. We hope that the progress of the disease will become arrested and that the lesions will calcify.

SUMMARY

An unusual case of chronic progressive pulmonary histoplasmosis in a 26-year-old woman who once lived in Southwestern Ontario has been presented. The patient is well six years after the surgical removal of numerous histoplasmomas and cysts from both lungs.

The problems encountered in making the diagnosis are discussed.

ADDENDUM

After the preparation of this paper, Dr. M. L. Furcolow[10] reviewed the manuscript. He points out that, although the diagnosis on this patient is likely histoplasmosis, the progression of the lesions, the cystic cavitation and the apparent well-being of the patient are not entirely typical of this disease. He suggests that in the future some related fungus may be discovered which will give this picture. Dr. Furcolow and his colleagues also believe that the patient should be treated now for several reasons. She has not managed her disease well, results of complement fixation tests have remained elevated, the lesions are no smaller and, finally, she is getting older and her resistance may decrease.

We are indebted to Dr. Robert Haggar, Chief of Pathology at St. Joseph's Hospital, Hamilton, for his invaluable help in this case.

We also wish to acknowledge the assistance of Dr. Michael L. Furcolow, Medical Director of the Kansas City Field Station, Kansas City, Kansas, who reviewed the case, and offered helpful comments.

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THE USE AND ABUSE OF BLOOD TRANSFUSION IN OBSTETRICS

"The dramatic and gratifying decline in maternal mortality which has occurred during the lifetime of our older colleagues is due primarily to three innovations: (1) the replacement of blood loss; (2) the control of infection by antimicrobial drugs; (3) the improvement in indications for and technique of Cæsarean section. Each of these developments carries with it intrinsic dangers. The simplicity and safety of abdominal delivery has led to its abuse by those who see the obstetrician rather than the mother and her baby as the central figure in the obstetrical situation. The abuse of antimicrobial drugs has led in some instances to a tolerant attitude toward careless technique and also to the development of resistant strains of bacteria and the unrestrained growth of certain fungi. The abuse of blood transfusion has given rise to evils among which are: a false sense of security in the face of danger; a disregard for iron deficiency states; inadequate diagnosis and faulty treatment of anæmias; complications from blood transfusion itself, including immediate reactions due to incompatibility, delayed complications such as hepatitis and renal damage, and "occult" sensitization leading to hæmolytic disease in later pregnancies or reaction to subsequent transfusion."—S. C. Robinson, *Nova Scotia M. Bull.*, 38: 201, 1959.