CHRONIC PROGRESSIVE (CAVITARY) HISTOPLASmosis AS A PROBLEM IN TUBERCULOSIS SANATORIUMS 1, 2, 3

MICHAEL L. FURCOLOw AND CHARLES A. BRASHER

(Received for publication November 2, 1955)

INTRODUCTION

Chronic progressive histoplasmosis, in contrast to the acute progressive or disseminated form, occurs primarily among older persons and is localized to the lungs except in the terminal stages. Both forms of the disease, however, are eventually fatal. The early stage of the chronic form is characterized by apical or subapical pneumonia infiltrations which progress to multiple thick-walled, usually bilateral cavities. This type of disease was first described by Johnson and Batson (1) and by Bunnell and Furecolow (2) in 1948. Subsequent experience with the original and later cases has confirmed the progressive nature of the disease (3). Sutliff and associates (4) reviewed seven cases from the literature and described four additional cases in 1953, but classified the disease as "active chronic" and benign. Six additional cases have been reported (3, 5-7).

In order to avoid further confusion in terminology the descriptive term, chronic progressive (cavitary) histoplasmosis, is proposed to designate this type of disease.

The symptoms of this form of histoplasmosis are cough, moderate weight loss, usually a slight elevation of the erythrocyte sedimentation rate, occasional temperature, profuse sputum, sometimes hemoptysis. The disease is characterized by exacerbations; the patient usually seeks medical help after an acute bout of what is called "influenza," at which time pneumonic or cavitary disease is found. This bout may subside and the patient not be seen again until several years later, at which time he has a similar episode and further extension is discovered. Quite often the cavitation is only in one lung at the start and, later

2 Presented at the Fourteenth Veterans Administration-Army-Navy Conference on the Chemotherapy of Tuberculosis, Atlanta, Georgia, February 9, 1955.
3 Presented, in part, before the Medical Session, as part of Section 6B, at the annual meeting of the National Tuberculosis Association, Milwaukee, Wisconsin, May 25, 1955.
4 Chief, Kansas City Field Station, Communicable Disease Center, U. S. Public Health Service, University of Kansas Medical Center, Kansas City, Kansas.
on, following another bout of so-called "influenza," the disease spreads to the other lung. In the early stages large cystlike cavities may be seen, followed later by spread of the process.

The disease usually progresses to fatal termination and just before this occurs there is dissemination of the fungus throughout the body with enlargement of the liver and spleen. Frequently at post-mortem examination Histoplasma may be cultured from all organs of the body.

In this type of disease the sputum is usually loaded with Histoplasma capsulatum and positive cultures are readily obtained. Serologic tests are usually positive and serve as a good screening tool. Tubercle bacilli are occasionally found, but most of the cases are not complicated by tuberculosis.

Chronic progressive histoplasmosis closely resembles reinfection type of tuberculosis, and could be considered to be reinfection histoplasmosis. This classification is based on the finding in some cases of negative tuberculin tests, positive histoplasmin skin tests, positive serologic tests, positive cultures for the fungus, and the presence of chronic cavitary disease of the apices in association with calcified lesions in the hilar area. Autopsy on such patients fails to reveal evidence of tuberculosis and the criteria of "chronic reinfection histoplasmosis" appear to be fulfilled.

A total of only 16 cases of chronic progressive cavitary histoplasmosis has been previously reported. It is the purpose of the present paper to show that this type of disease occurs frequently among patients in a tuberculosis sanatorium.

**MATERIAL AND METHODS**

The studies to be reported have been conducted at the Missouri State Sanatorium at Mount Vernon, Missouri. This sanatorium has an average daily census of 550 patients, 85 per cent of whom are white and 15 per cent are Negro. Casual studies begun in 1952 revealed an occasional case of histoplasmosis. Between March and August, 1954, a systematic survey of the patients at the sanatorium was undertaken. During the survey, skin tests with tuberculin and histoplasmin were performed on all patients and serologic tests were made. The mycologic laboratory services were augmented and careful attempts were made to establish the diagnosis in all patients whose serologic tests were positive or whose diagnosis was in doubt in any way.

The tuberculin skin tests were performed with purified protein derivative (PPD-S), furnished by Dr. Florence Seibert of the Henry Phipps Institute, Philadelphia, Pennsylvania. A dose of 0.0001 mg. in 0.1 ml. was used. The histoplasmin used was 0.1 ml. of Lot HKC-5, diluted 2 parts to 1,000. This dose is equivalent to other standard histoplasmins. Readings of the skin tests were made at forty-eight hours, and any reaction showing an induration of 5 mm. or more was considered positive. The skin tests were administered and read by the ward physician in each case.

Serologic tests were performed by Dr. Samuel Salvin at Rocky Mountain Laboratory, U. S. Public Health Service, Hamilton, Montana, and by Dr. Joseph Schubert at the Communicable Disease Center Serological Laboratory, U. S. Public Health Service, Chamblee, Georgia. Dr. Salvin performed a complement-fixation test with yeast-phase Histoplasma organisms as antigen and a precipitin test with a purified histoplasmin antigen. Dr. Schubert performed a complement-fixation test with histoplasmin as antigen. A serologic test
was interpreted as positive if definite results were obtained in a serum dilution of 1:8 or higher.

Mycologic examinations were performed in the laboratory of the Missouri State Sanatorium and in the Kansas City Field Station. Specimens were shipped from Mt. Vernon to Kansas City in screw-capped vials with the addition of saline containing 10,000 units each of penicillin and streptomycin. Both cultures and mouse inoculation techniques were employed in the attempt to isolate the organism. Examinations for tuberculosis were performed in the laboratory in the Missouri State Sanatorium. Smears were usually employed although cultures were frequently done. Guinea pig injection was employed when the organisms were difficult to find or were atypical on culture.

Pathologic examinations were made by Dr. David Gorelick and Dr. Fred Coller of Springfield, Missouri.

In this paper a case was termed “mycologically proved” if organisms typical of *H. capsulatum* were isolated by culture from the patient or were seen in tissues removed surgically or at autopsy. A “serologically proved” case was one in which the serologic tests for histoplasmosis were positive (1:8 or higher) on either of the complement-fixation tests or the precipitin test. Adequate cultural studies on the “serologically proved” cases usually revealed the presence of the organism. However, in many of these cases the patient had left the hospital before mycologic studies could be completed, or the disease was of the milder type from which positive cultures could not be obtained because of passage of time since infection.

**RESULTS**

These essentially casual studies for the presence of histoplasmosis in a tuberculosis hospital have now yielded a total of 19 “mycologically proved” cases and 95 “serologically proved” cases. These cases have been observed over a three-year period. During the three-month survey, 14 “mycologically proved” cases and 29 “serologically proved” cases were found. Of the 600 patients in the survey, 14 (2.4 per cent) were proved to have histoplasmosis by actual demonstration of the organism. In an additional 20 (4.8 per cent), the diagnosis of histoplasmosis was established by serologic tests.

In table 1 are shown the detailed findings in the group of 19 “mycologically proved” cases. It may be noted that in most cases the patients were more than fifty years of age, that the males outnumbered the females, and that all but one of the patients were white. In a number of cases, the onset of illness had occurred a number of years prior to determination of the etiology. The chest roentgenographic findings in almost all cases showed bilateral cavitation. Skin tests were positive to tuberculin in 9 cases and to histoplasmin in 14 of the 18 tested. The serologic tests for histoplasmosis were positive in every patient. The organism was identified from every patient in most cases by culture from the sputum; occasionally, from cultures from the lung at operation or autopsy. The presence of the organism was demonstrated in tissue obtained at post-mortem examination in 2 cases in which fungal cultures were not done.

The patients have been observed from a minimum of several months to a maximum of seventy-six months. Three patients have died. It will be noted that progression of the disease occurred in 9 of the 19 cases. In the last column are indicated the numbers of microscopic and cultural examinations for tubercle bacilli which were made on each patient.
<table>
<thead>
<tr>
<th>Name</th>
<th>Age</th>
<th>Sex</th>
<th>Race</th>
<th>Onset Date</th>
<th>First Roentgenogram</th>
<th>Chest Roentgenographic Findings</th>
<th>Skin Tests</th>
<th>H. Serology</th>
<th>H. Culture</th>
<th>Lesions on Last Roentgenogram</th>
<th>Course</th>
<th>Tubercle Bacilli</th>
</tr>
</thead>
<tbody>
<tr>
<td>J.G.</td>
<td>62</td>
<td>M</td>
<td>W</td>
<td>11/49</td>
<td>12/50</td>
<td>Multiple cavities</td>
<td>+</td>
<td>+</td>
<td>+ S*</td>
<td>58 Alive</td>
<td>Progressive</td>
<td>10 3</td>
</tr>
<tr>
<td>S.D.</td>
<td>67</td>
<td>F</td>
<td>W</td>
<td>5/51</td>
<td>8/52</td>
<td>Bilateral cavities</td>
<td>-</td>
<td>+</td>
<td>+ S</td>
<td>7 Died, April, 1953</td>
<td>No change</td>
<td>13 5</td>
</tr>
<tr>
<td>S.R.</td>
<td>58</td>
<td>F</td>
<td>W</td>
<td>1/52</td>
<td>1/53</td>
<td>Multiple cavities</td>
<td>-</td>
<td>+</td>
<td>+ S</td>
<td>32 Neumonectomy, R. alive</td>
<td>Improved</td>
<td>19 2</td>
</tr>
<tr>
<td>F.S.</td>
<td>32</td>
<td>M</td>
<td>W</td>
<td>10/53</td>
<td>10/53</td>
<td>Bilateral cavities</td>
<td>+</td>
<td>+</td>
<td>+ S</td>
<td>24 Alive</td>
<td>No change</td>
<td>19 6</td>
</tr>
<tr>
<td>H.L.</td>
<td>60</td>
<td>M</td>
<td>W</td>
<td>11/49</td>
<td>1/50</td>
<td>Bilateral infiltration</td>
<td>-</td>
<td>+</td>
<td>+ S</td>
<td>59 Alive</td>
<td>Progressive</td>
<td>44 52</td>
</tr>
<tr>
<td>J.McC.</td>
<td>61</td>
<td>M</td>
<td>W</td>
<td>2/51</td>
<td>1/54</td>
<td>Multiple cavities</td>
<td>+</td>
<td>-</td>
<td>+ S</td>
<td>55 Alive</td>
<td>Progressive</td>
<td>16 16</td>
</tr>
<tr>
<td>H.G.</td>
<td>48</td>
<td>M</td>
<td>W</td>
<td>19511</td>
<td>12/53</td>
<td>Cavity R</td>
<td>-</td>
<td>+</td>
<td>+ S</td>
<td>20 Alive</td>
<td>Progressive</td>
<td>21 3</td>
</tr>
<tr>
<td>G.M.</td>
<td>46</td>
<td>M</td>
<td>W</td>
<td>11/53</td>
<td>12/53</td>
<td>Bilateral infiltration</td>
<td>+</td>
<td>-</td>
<td>Pathology, + L</td>
<td>6 Operated; died May, 1954</td>
<td>No change</td>
<td>24 7</td>
</tr>
<tr>
<td>E.M.</td>
<td>52</td>
<td>F</td>
<td>N</td>
<td>6/52</td>
<td>2/53</td>
<td>Bilateral infiltration</td>
<td>+</td>
<td>ND</td>
<td>ND Pathology, + L</td>
<td>24 Operated, October, 1953</td>
<td>Improved</td>
<td>6+ 40- 4+ 12-</td>
</tr>
<tr>
<td>D.B.</td>
<td>43</td>
<td>M</td>
<td>W</td>
<td>10/53</td>
<td>12/53</td>
<td>Bilateral cavities</td>
<td>+</td>
<td>+</td>
<td>+ L</td>
<td>23 Operated, June, 1954</td>
<td>No change</td>
<td>13 4</td>
</tr>
<tr>
<td>G.M.</td>
<td>62</td>
<td>M</td>
<td>W</td>
<td>19441</td>
<td>11/48</td>
<td>Bilateral cavities</td>
<td>+</td>
<td>+</td>
<td>+ S</td>
<td>76 Alive</td>
<td>Progressive</td>
<td>40 5</td>
</tr>
<tr>
<td>V.M.</td>
<td>44</td>
<td>M</td>
<td>W</td>
<td>8/54</td>
<td>10/54</td>
<td>Bilateral infiltration</td>
<td>+</td>
<td>+</td>
<td>+ S</td>
<td>11 Alive</td>
<td>No change</td>
<td>18 4</td>
</tr>
<tr>
<td>U.H.</td>
<td>58</td>
<td>M</td>
<td>W</td>
<td>2/55</td>
<td>2/55</td>
<td>Bilateral infiltration</td>
<td>-</td>
<td>+</td>
<td>+ S</td>
<td>7 Alive</td>
<td>No change</td>
<td>7 2</td>
</tr>
<tr>
<td>L.F.</td>
<td>71</td>
<td>M</td>
<td>W</td>
<td>12/54</td>
<td>1/55</td>
<td>Bilateral infiltration</td>
<td>-</td>
<td>+</td>
<td>+ S</td>
<td>8 Alive</td>
<td>No change</td>
<td>10 4</td>
</tr>
</tbody>
</table>

*S = Culture from sputum  
†L = Culture from lung
Detailed case descriptions and therapy trials will be discussed in separate papers. Hence, these subjects will not be discussed in detail in the present report. However, the reproductions of chest roentgenograms and brief clinical histories of 6 patients are shown in figures 1 to 9 at the end of this report. These serve to illustrate the type of lesion seen and its chronic character. The cavitary nature of the infection, the tendency to progress to bilateral involvement, and the usual presence of calcified lesions may all be seen from examination of the cases presented in the figures.

**DISCUSSION**

The finding that 7.2 per cent of the patients in a tuberculosis sanatorium have "serologically proved" histoplasmosis and that the actual presence of the microorganism was demonstrated in 33 per cent of the cases is indeed remarkable. It certainly calls for very serious consideration of the importance of histoplasmosis in tuberculosis sanatoriums. If it be assumed that a similar prevalence obtained throughout the general area of high histoplasmin sensitivity, quite startling figures would be obtained.

Calculations have been made of the number of tuberculosis sanatorium beds in the areas where histoplasmin sensitivity among adults exceeds 50 per cent. This area extends roughly from southern Ohio in a sweeping circle through central Indiana and Illinois, eastern Kansas and Oklahoma, northeast Texas, northern Louisiana, Mississippi and Alabama, and includes all of Tennessee, Arkansas, Missouri, and Kentucky. In this area it has been estimated that approximately 21 million people live. This region has approximately 16,500 sanatorium beds for tuberculosis. If one applies the figures arrived at in the Missouri State Sanatorium, it is estimated that approximately 400 "myologically proved" cases of histoplasmosis might be found in these sanatoriums.

In addition, 800 cases of "serologically proved" histoplasmosis might be found. In short, if the findings of the present study prove to be generally applicable to the histoplasmosis area, some 1,200 patients in tuberculosis hospitals would be found to have histoplasmosis. These 1,200 cases would obviously furnish an important reservoir for differential diagnosis as well as a complicating factor in any therapeutic trial of tuberculosis.

The accurate estimation of this problem is obviously of fundamental importance to all persons concerned with the care of the tuberculous. These patients not only occupy tuberculosis beds; they derive no benefit from antituberculosis therapy and, indeed, may contract the disease. Furthermore, the demonstration of more cases of histoplasmosis should furnish an adequate pool of cases for trials of therapeutic agents so urgently needed in this fungal infection. Moreover, the finding of histoplasmosis in the degree which might be encountered in this area might furnish an answer to the decreasing prevalence of tuberculosis and permit further usage to be found for beds in these sanatoriums. At present the general treatment of histoplasmosis is similar to that of tuberculosis before specific therapy was found.

That these suggestions are not too far out of line has already been confirmed by Sutliff and Campbell (8) who recently reported the finding of 7.3 per cent
positive serologic tests for histoplasmosis among 150 tuberculous patients in Memphis, Tennessee.

SUMMARY

The prevalence of histoplasmosis of the chronic progressive (cavitary) type in a tuberculosis sanatorium is presented. A clinical description of the disease is given and diagnostic suggestions are made.

Studies of the prevalence of both “mycologically proved” cases and “serologically proved” cases are presented. The frequency of “mycologically proved” cavitary cases was 2.4 per cent among the 600 patients in the hospital, and the frequency of the “serologically proved” cavitary cases was 4.8 per cent. The implications of these findings may be seen by applying them to the 16,500 tuberculosis beds in the area of high histoplasmmin sensitivity. If similar findings prevailed in the other sanatoriums, 1,200 cases of chronic progressive cavitary histoplasmosis might be expected to be found in these sanatoriums.

Suggestions are made for determining the prevalence of this disease among this group of patients. If the above predictions prove true, an adequate reservoir of patients for therapeutic trials would be available.

SUMARIO

La Histoplasmosis Evolutiva Crónica (Cavitaria) como Problema en los Sanatorios para Tuberculosos

Describese la frecuencia de la histoplasmosis de forma evolutiva crónica (cavitaria) en un sanatorio para tuberculosos. Se ofrece una descripción clínica de la dolencia y se presentan varias sugerencias para el diagnóstico.

Presentanse estudios de la frecuencia de los casos tanto “micológicamente comprobados” como “serológicamente comprobados.” La incidencia de casos cavitarios comprobados “micológicamente” fue de 2.4 por ciento entre los 600 enfermos del hospital y la de los comprobados “serológicamente” de 4.8 por ciento. Puede verse el alcance de estos hallazgos aplicándolos a los 16,500 lechos para tuberculosos en la zona de alta sensibilidad a la histoplasmina. Si fueren semejantes los hallazgos en los demás sanatorios, cabría esperar que hubiera en ellos 1,200 casos de histoplasmosis cavitaria evolutiva crónica.

Ofrecense sugerencias para determinar la frecuencia de esta dolencia en este grupo de enfermos. Si se cumplen las predicciones anteriores, habría a mano una reserva adecuada de enfermos para ensayos terapéuticos.

RESUME

Histoplasmosis chronique évolutive en qualité de problème des sanatoriums de la tuberculose

La fréquence de l’histoplasmosise sous la forme chronique évolutive (cavitaire), dans un sanatorium de la tuberculose, est exposée. Les auteurs fournissent une description clinique de l’affection et des suggestions quant au diagnostic.

Les études sur la fréquence des cas “mycologiquement” confirmés et de ceux “sérologiquement” confirmés sont présentées. La fréquence des cas cavitaires “mycologiquement” confirmés était de 2.4 % pour les 600 malades de l’hôpital et la fréquence des cas cavitaires “sérologiquement” confirmés s’élevait à 4.8 %. Les implications de ces résultats apparaissent lorsqu’ils sont appliqués aux 16,500 lits de la tuberculose dans les sanatoriums d’une région où l’allergie à l’histoplasmme est élevée. Si des résultats similaires étaient obtenus dans les autres sanatoriums, on pourrait s’attendre à découvrir 1,200 cas d’histoplasmosise dans ces sanatoriums.
Les auteurs indiquent les moyens qui permettraient de déterminer la fréquence de cette maladie parmi ce groupe de malades. Dans le cas où ces présomptions recevraient confirmation, on disposerait d'un réservoir adéquat de malades pour les essais thérapeutiques.

REFERENCES

(8) Sutliff, W. D., and Campbell, C.: Serologic screen tests for the systemic mycoses and suggestions for a cooperative study, Tr. Fourteenth Conference on Chemotherapy of Tuberculosis, Veterans Administration, Army, and Navy, 1955.

Fig. 1

Figs. 1 and 2. W. M., age 61, was admitted to the hospital in February, 1951, complaining of loss of weight, tiredness, and chest pain of fifteen months' duration. The roentgenogram (figure 1) revealed bilateral pulmonary infiltrations with calcifications in the left hilus. Ten sputum examinations were negative for acid-fast bacilli, and three cultures were negative. Tuberculin and histoplasmin skin tests were positive; coccidioidin and blastomyein tests were negative. Bronchial smears were negative for tubercle bacilli. Serologic tests for histoplasmosis were negative. Cultures for H. capsulatum were positive. The patient left the hospital against advice after two months. He refused to return, but recently he returned to his physician with a complaint that he was feeling ill and losing weight and appetite. A roentgenogram obtained in 1954 (figure 2) reveals considerable extension of the disease on the left with apparently some contraction on the right. There still appear to be cavities in the right lung by planigram. Recent serologic tests for histoplasmosis were doubtfully positive.
Fig. 3. W. F., age 58, was admitted to the sanatorium in February, 1953, with complaints of fatigue, loss of weight, and increasing productive cough following an attack of "viral" pneumonia thirteen months previously. She had considerable sputum, occasionally streaked with blood and often purulent. In January her symptoms increased, with nausea, vomiting, and pain in the left upper quadrant; she was referred to the sanatorium. A chest roentgenogram revealed pulmonary cavitation and infiltration in the right upper lobe. Calcification in the hilar areas was also evident. There is evidence of an old pleurisy at the right base. Nineteen sputum specimens were negative for acid-fast bacilli by microscopy and two by culture. Bronchial smear was also negative for tubercle bacilli. Skin tests were positive for histoplasmin, and negative for tuberculin, blastomycin, and coccidioidin. Following increase in the pulmonary disease, a right pneumonectomy was performed on September 25, 1953. Cultures of the excised lung were positive for H. capsulatum. Sputum was positive on several occasions for H. capsulatum. Complement-fixation tests for histoplasmosis were also positive. Following surgery the patient had a gradual weight increase of 15 pounds. Roentgenograms of the lungs have shown no evidence of spread of the disease. H. capsulatum was seen in the pathologic specimens. The patient has shown steady improvement since operation. Serologic tests for histoplasmosis continue positive.

(When the initials "W. M." and "W. F." appear in the legends of the figures, they indicate "white male" and "white female," respectively.)
Figs. 4, 5, and 6. W. M., age 50, was first seen in December, 1948, and was referred to the sanatorium because routine fluoroscopic study revealed pulmonary disease. A roentgenogram obtained at this time showed bilateral apical infiltration with calcification in several areas throughout the lung fields (figure 4). The patient had had progressive dyspnea since 1945. In 1952 he became considerably worse following the cutting of silage in an open field; had chills and fever, weakness, and weight loss with productive cough. Histoplasmin and tuberculin skin tests were positive; blastomyacin and coccidioidin were negative. A total of 24 smears was negative for acid-fast bacilli and 7 cultures were negative for tubercle bacilli. Complement-fixation tests for histoplasmosis were strongly positive and, in December, *H. capsulatum* was isolated from the sputum. Four sputum cultures on this patient were positive for *H. capsulatum*. A chest roentgenogram (figure 5) revealed extension of his disease on the left. Cavitation was later demonstrated and the disease progressed in some areas and contracted in others (figure 6). On August 13, 1954, a pneumonolysis of the left lung was done preparatory to lobectomy. However, this was not performed due to the extensive disease found. The patient was returned to the ward in poor condition and died three days later in postoperative shock. Autopsy revealed chronic granulomatous pneumonitis of the lung due to histoplasmosis and postoperative hemorrhagic enterocolitis. No evidence of tuberculosis was found at autopsy.
Fig. 7. W. M., age 59, was admitted to the hospital in October, 1953, because of chills and fever of approximately ten days' duration. The patient had lost about 30 pounds. The tuberculin skin test was negative; histoplasmmin was positive. Complement-fixation tests for histoplasmosis were positive. Roentgenograms revealed marked infiltration in the right upper lobe with cavitation. Cultures were positive for H. capsulatum in December, 1953, and in May, 1954, on at least three different occasions. Smears and cultures for tubercle bacilli were negative. Twenty-one months of observation have shown no significant change in pulmonary findings.

Fig. 8. W. M., age 31, whose illness began with chills, fever, productive cough, and weakness in October, 1953, had lost 22 pounds. A chest roentgenogram revealed pulmonary infiltration and he was sent to the tuberculosis sanatorium. Nineteen sputum specimens for acid-fast bacilli between November, 1953, and January, 1954, were negative. Six sputum cultures were negative for tubercle bacilli. Tuberculin and histoplasmmin skin tests were positive. Blastomyacin and coccidiodin were negative. Two gastric specimens were negative for M. tuberculosis on culture. Sputum was positive for H. capsulatum on a number of occasions; first on January 11, 1954. Complement-fixation test for histoplasmosis was positive in January, 1954, and subsequently. Roentgenographic examination shows bilateral pulmonary apical infiltration with bilateral cavitation. Observation for two years has not shown significant change.
Fig. 9. W. M., age 60, was admitted to the hospital in December, 1953, with a three-year history of weakness, easy fatigue, cough, and sputum. In December, 1953, he had a massive hemoptysis and was admitted to the sanatorium. A roentgenogram revealed infiltration in the first interspace on the right, and the entire upper part of the left lung was occupied by cavities. There was a large cystlike cavity occupying the apex. Skin test with histoplasmin was positive; with tuberculin, negative. Cultures were positive for *Histoplasmin* on at least two occasions. Serologic tests for histoplasmosis were positive. The patient's first admission to a hospital was in January, 1950. A roentgenogram at that time showed infiltration and cavitation which has shown some progression in the last several years. He has been observed for a total of sixty-nine months. A total of 12 sputum specimens has been negative for acid-fast bacilli on microscopy, and two cultures have been negative for tubercle bacilli.