Is There a Relationship between Silicosis and Histoplasmosis?*

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In the older literature tuberculosis has been given as the cause of death in as much as 75 per cent of persons dying with silicosis. Recent studies by Sander and others have shown that this is no longer true. The incidence of tuberculosis among silicotics is only slightly higher than in the general population. Silicosis coexistent with tuberculosis does impair response to treatment and results in more serious disease. However, tuberculosis developing among workers with silicosis is infrequent and conditioned by contact with active tuberculous cases, as in the general population.

Due to the striking similarities of the clinical manifestations and x-ray appearances of pulmonary tuberculosis and pulmonary histoplasmosis, the question was raised as to whether there is a similar relationship between silicosis and histoplasmosis. Specifically, does silicosis have any effect on the clinical manifestations, prognosis, and response to treatment of pulmonary histoplasmosis? One reason for considering this relationship possible is the rather high incidence of active, chronic pulmonary histoplasmosis among the patients admitted to the Missouri State Sanatorium. A study was considered suitable because the Missouri State Sanatorium is located within a highly endemic area of histoplasmosis (Fig. 1) and the sanatorium population includes many patients from the tri-state area (Fig. 2) where hardrock mining is prevalent and exposure to silica is heavy.

Material

One hundred and fifty proved cases of histoplasmosis diagnosed at the Missouri State Sanatorium during the years of 1954 to 1960 were reviewed. The number was reduced to 80 cases of chronic pulmonary histoplasmosis in adult men by eliminating 70 cases in women and children, a group in which one would not expect to find exposure to silica. Most of the diagnoses were proved by positive sputum cultures for Histoplasma capsulatum, and some with positive blood or bone marrow cultures. The majority had far advanced disease.

Figure 2 shows the tri-state area where considerable lead and zinc mining is done and the exposure to silica is heavy. In Missouri this includes Newton and Jasper Counties.

Figure 3 demonstrates the relative numbers of patients with tuberculosis admitted to the sanatorium from each county of Missouri during the years of 1952 to 1958. The two Missouri counties represented in Fig. 2, Newton and Jasper, had two of the highest rates of admissions for tuberculosis to the sanatorium during this period.

Figure 4 illustrates that the rate of positive histoplasmin complement fixation among admissions from these two counties was significantly lower than it was from the other counties of the state. One-third of the patients admitted to the sanatorium with positive complement fixation tests

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§A complement fixation titer of 1:8 or more is considered positive.
eventually are proved to have progressive histoplasmosis.\(^1\)

**Results**

Only eight (10 per cent) of the 80 proved cases of chronic pulmonary histoplasmosis in men had a history of exposure to silica (Fig. 5). The length of exposure varied from five to 25 years, with an average length of exposure of approximately 16 years. Three had worked in coal mines, three in lead and zinc mines, one in a clay mine, and one had been a stone cutter for 20 years and had done welding for six years. Two of those who had worked in the coal mines did not have x-ray evidence of silicosis. Four of the remaining six had questionable x-ray evidence of silicosis. One of these had worked in a lead and zinc mine for five years. Another had worked in a soft coal mine for 16 years. These exposures were considered insignificant.

The remaining two cases with questionable x-ray evidences of silicosis had been exposed to silica for 27 and 25 years respectively. It is well to point out that the diagnosis of silicosis should not be based on chest x-ray findings alone.

One of these cases could not be adequately evaluated because he also had bronchogenic carcinoma and was discharged after a course of nitrogen mustard therapy, and there is no followup.

The other patient gave a history of 25 years of zinc mining. During his first hospitalization in 1958, he stayed for 196 days. Many sputa were positive for *Histoplasma capsulatum* on culture during this admission. He received amphotericin B according to our usual method.\(^1\) One month after admission, his sputum converted to negative and remained so until discharge seven months later. The cavitory lung lesions demonstrated by chest x-ray film remained essentially unchanged at the time of discharge. His physical condition, however, was improved.

He was readmitted ten days later because of increasing shortness of breath and poor home conditions. He stayed 44 days and was discharged as having received maximum hospital benefit. Two sputum tests were negative on culture for *Histoplasma capsulatum*. The yeast phase complement fixation titer was more than 1:256 as

![Image](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21371/)

**Figure 1:** (Courtesy of the American Public Health Association, Inc., published in the *American Journal of Public Health*, September, 1956.) Illustration showing that the Missouri State Sanatorium is within the highly endemic area for *Histoplasma capsulatum*. 

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previously. He did not receive antifungal therapy during his admission.

On February 3, 1960, he was readmitted for the third time because of cough with hemoptysis, loss of weight, and difficulty in swallowing. Three sputum tests were negative on culture for *Histoplasma capsulatum*. The bone marrow culture was also negative. He suffered extensive burns on the ninth hospital day while filling his lighter with fluid and expired one week later. A necropsy was not permitted. In our opinion, the probable silicosis had not influenced his clinical course.

The following two cases to be discussed in more detail present the strongest evidence in favor of definite silicotic involvement.

**CASE 1**

At the time of admission, C. J. was a 38-year-old white man with a history of mining clay for 18 years. His only complaint on admission was blood-streaked sputum. The diagnosis of chronic pulmonary histoplasmosis was confirmed by positive sputum cultures. The diagnosis of silicosis was later confirmed by the histopathology of resected lung tissue.

Figures 6, 7 and 8 show his chest x-ray films at various stages of his hospital course.

Amphotericin B was given intravenously according to our usual method. He remained afebrile, his chest x-ray films showed no change, and his sputum remained positive for *Histoplasma capsulatum*. Four months later, resection of the right upper lobe and superior segment of the right lower lobe was carried out.

One month after surgery, his sputum was still positive, showing an atypical *Histoplasma capsulatum*. Amphotericin B was continued until discharge two months after surgery. The chest roentgenogram on discharge was considerably improved and followup x-ray examination two years later, when we finally lost contact with him, showed no change.

**CASE 2**

On admission, O. L. was a 68-year-old white man with a 20-year history of underground exposure in a lead and zinc mine. After admission to the Missouri State Sanatorium, he was found to have chronic tamponade caused by pericardial effusion due to *Histoplasma capsulatum*. He was unable to take a full course of amphotericin B treatment because of untoward reaction to this drug; however, he recovered and has continued to improve following surgical creation of a pericardiopleural window. A detailed report of this unusual case is to be published.

**DISCUSSION**

Approximately 100 patients with chronic pulmonary histoplasmosis have been treated with amphotericin B at the Missouri State Sanatorium.
Figure 3: Newton and Jasper Counties which are the two counties included in the tri-state area (Fig. 2) where lead and zinc mining is abundant, are shown to have one of the highest incidence rates of tuberculosis, based on the number of admissions from those counties as compared to the rest of the state.

Figure 4: The same two counties (Newton and Jasper) are shown to have comparatively less serologically positive cases for Histoplasma capsulatum as compared to the other counties of the state.
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State Sanatorium and 50 per cent of these have shown moderate to marked roentgenographic improvement. In 97 per cent there has been conversion of the sputum to negative within the first month. In many, this conversion has apparently been permanent; but in others it was temporary, unless it had been feasible to do resectional surgery. We have not been able to distinguish between the response to treatment of patients with or without silicosis.

Definite conclusions should not be drawn from such a small series of cases as herein presented. The incidence of chronic pulmonary histoplasmosis in areas where silicosis is prevalent is not higher than in the general population (Figs. 2, 3 and 4). The evidence presented does not indicate that silicosis predisposes to histoplasmosis. Another problem is that the majority of persons who develop chronic pulmonary histoplasmosis are farmers and have not had significant exposure to silica.

With regard to the effect of silicosis on histoplasmosis once established, little can be deduced from the cases presented. One patient did have histologic findings characteristic of silicosis, and treatment with amphotericin B did not convert the sputum to negative. Right upper lobectomy was carried out and the patient made an uneventful recovery. He was able to return to work without relapse during two years of followup. It should be noted that one month after surgery the patient still had positive sputum cultures for Histoplasma capsulatum, the organism being classified as atypical. The surgical approach should be altered in histoplasmosis complicated by silicosis as is true with tuberculosis. Pulmonary silicosis usually contraindicates resectional surgery.

As may be seen from the map showing the percentage of the general population of Missouri positive on skin testing with histoplasmin, the two counties with the highest prevalence of silicosis have a lower rate of histoplasmin reactors. This apparently correlates better with the incidence of chronic pulmonary histoplasmosis among persons admitted to the sanatorium than does exposure to silica.

CONCLUSIONS

It is probable that there is infrequent coexistence of chronic pulmonary histoplasmosis and silicosis. Apparently, silicosis has little effect on benign histoplasmosis, since fewer patients with progressive histoplasmosis are admitted to the sanatorium from an area of high silicosis incidence than from other areas. It is true that this is also an area of a lesser rate of histoplasmin skin reactivity but the rate is still high (see map).

Further determination of the possible effect of silicosis on the progress of chronic pulmonary histoplasmosis will depend on a diligent search for and the accumulation of follow-up data on many more cases such as those presented here.

CONCLUSIONES

Es probable que no sea frecuente la coexistencia de histoplasmosis pulmonar-crónica y de silicosis. Aparentemente la silicosis tiene poco efecto sobre la histoplasmosis benigna, puesto que mas pocos enfermos con histoplasmosis progresiva se admiten al sanatorio de un área de elevada incidencia de silicosis que de otras áreas.

Es verdad que esa es también un área de menor incidencia de la reactividad a la histoplasmina, pero la proporción es aún elevada (vease el mapa).

Una determinación ulterior del posible efecto de la silicosis sobre el progreso de la histoplasmosis pulmonar crónica dependerá de la diligente búsqueda y de la acumulación de datos de seguimiento en mucho más casos como los aquí presentados.
Figure 6: Case No. 1, PA chest x-ray on admission. He has 18 years' history of clay mining and this x-ray is strongly suggestive of silicosis, as well as showing cavitary lesion in the right upper. Figure 7: Planigram of the same patient taken prior to surgery, showing dense and cavitary disease in right upper lobe. Figure 8: The same patient four months after surgery, showing no progression of disease.
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Résumé

Il est probable que la coexistence d'histoplas- 
smose pulmonaire chronique et de silicose soit 
peu fréquente. Apparemment, la silicose a peu 

de effet sur l'histoplasmosse bénigne, puisqu'il y a 

moins de malades atteints d'histoplasmosse pro-

gressive admis au sanatorium en provenance de 
zone de haute densité de silicose qu'en provenance 
de d'autres zones. Il est vrai que cette zone est 

aussi une zone de moindre taux de réactions 
cutanées à l'histoplasmine, bien que l'incidence 
de cette affection y soit élevée (voir dessin).

La détermination ultérieure de l'effet possible 
de la silicose sur l'évolution de l'histoplasmosse 
pulmonaire chronique dépendra d'une recherche 
attentive des cas et de l'accumulation des résul-
tats de l'étude de cas beaucoup plus nombreux 
que ceux présentés ici.

Zusammenfassung

Es ist wahrscheinlich, daß das gleichzeitige 
Vorkommen von chronischer pulmonaler Histo-
plasmosse und Silikose nicht häufig ist. Augen-
scheinlich hat die Silikose wenig Einfluß auf eine 
benigne Histoplasmosse, da weniger Patienten mit 
progredienter Histoplasmosse in das Sanatorium 
engewiesen werden aus einem Gebiet, in denen 
die Silikose häufiger vorkommt als in anderen 
Gebieten. Es ist wahr, daß in diesem Gebiet auch 
die Histoplasmosse Hauptreaktionsfähigkeit ge-
gringer ist, aber sie ist noch immer hoch (siehe 
die Zeichnung).

Weitere Ermittlung des möglichen Einflusses 
der Silikose, auch das Fortschreiten der chroni-
schen pulmonalen Histoplasmosse wird von einem 
sorgfältigen Suchen nach viel mehr Fällen dieser 
Art abhängen und von der Zusammenstellung 
von Verlaufbeobachtungen, als sie heir vorgelegt 
werden.

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FUNCTIONAL STATE OF EXTERNAL RESPIRATION OF THE LUNG IN PATIENTS WITH MITRAL STENOSIS

Results of inquiry into the functional status of 
external respiration in 329 mitral stenosis cases 
point to the presence in 84 per cent of the patients 
of respiratory insufficiency which manifests itself 
by excessive ventilation alone or by its association 
with oxygen deficiency in the organism. Derange-
ment of external respiration in patients with mitral 
stenosis is caused by congestion in the lesser circu-
lation and by functional and morphologic changes 
in the pulmonary tissue and vessels of the lesser 
circulation which had been affected by this conges-
tion.