Report of 193 Marrow Biopsy Specimens Cultured for Histoplasma Capsulatum

By Steven O. Schwartz, M.D. and Sidney Barsky, M.D.

With the technical assistance of Carrie Woolsey and Helen L. Gant

It is possible that histoplasmosis is extremely common and widespread.1 Recently it has been shown that it is not necessarily a fatal disease and that there are instances of localized, transient and even asymptomatic varieties of this infection.2 In the last few years, many studies have demonstrated the frequent association of pulmonary calcifications and sensitivity to histoplasmin,3,4 especially in residents of the middle western states. In the Mississippi River Basin, 38.6 per cent of 27,780 persons tested were histoplasmin positive; however, in only a few instances was the organism found in this group.5

Histoplasmosis is a disease of the reticulo-endothelial system in which the causative organism, the fungus Histoplasma capsulatum, is usually found in the macrophages of this system.6 Inasmuch as Histoplasma capsulatum was found in approximately 50 per cent of proved cases in which examination of the marrow was performed,6-9 it was felt that many more cases might be discovered if routine cultures of the marrow were made. Accordingly, such a study was undertaken in 193 cases observed in the medical and surgical wards of the Cook County Hospital.

Methods

Specimens of marrow were inoculated at the bedside into two kinds of mediums: Littman’s and Sheep’s brain broth. These were allowed to incubate at room temperature and at 37 C. respectively for six weeks before being discarded. Any suggestive growth was studied and transferred to Herrold’s egg agar medium for incubation at 37 C. Blood and marrow preparations of all patients were studied concurrently.

Results

Histoplasma capsulatum was cultured in only one case, and interestingly enough, in this case previous blood, marrow, and lymph node specimens had failed to reveal the organisms. In none of the other cases was the organism seen in blood, marrow, or tissue specimens.

Report of Typical Case

E. H., a Negro woman, aged 19, was admitted to the Cook County Hospital on May 7, 1950 because of severe weakness, cough and shortness of breath of eight days’ duration.
History
In the two months before admission, she had noted increasing weakness, fever and weight loss (approximately 20 pounds). About seven days before admission, she coughed up a small amount of blood (less than 1 teaspoon). At other times the cough was intermittent and nonproductive. The patient had spent most of her spare time as a baby sitter and denied recent exposure to any seriously ill or dying persons. She had never had any pet animals.

She had lived most of her life in Tennessee and came to Chicago about three months before admission. One month before admission, she was delivered normally of a 51 pound healthy girl. This was her only pregnancy and she had received no prenatal or postnatal care. She had a bloody vaginal discharge for three weeks following delivery but used only two boxes of Kotex during that time. Occasional hemoptysis began about three weeks before delivery; otherwise, there was nothing to suggest "toxemia of pregnancy." A roentgenogram of the chest taken three months before admission was said to have been negative for tuberculosis.

Examination
The patient was well developed though poorly nourished and appeared chronically ill and moderately flushed. The blood pressure was 125 systolic and 66 diastolic, the pulse rate 128, the temperature 101 F. and the respiration rate 24. Many of the teeth were carious and there was associated gingivitis. Moderately decreased resonance and decreased breath sounds were noted over both lung fields. The heart was normal except for tachycardia. The liver was slightly tender, smooth, firm-edged and could be palpated 11 cm. below the costal margin in the right midclavicular line. The spleen was not tender; it was firm, smooth, and extended 18 cm. below the costal margin in the left midclavicular line. The gynecologic consultant reported subinvolution of the uterus. There was nothing neurologically abnormal in the skin or mucous membranes. There was a moderate enlargement of the inguinal, axillary, cervical and right epitrochlear lymph nodes. The nodes were firm and discrete and were not tender.

Roentgenologic examinations revealed a normal heart, enlarged hilar nodes, and a diffuse mottled infiltration throughout both lung fields. There was, in addition, a ring-like increase in density in the fourth left anterior interspace just outside the heart border through which the lung markings could be seen (fig. 1).

Laboratory Reports
Laboratory studies showed 67 per cent hemoglobin (10.4 Gm.), 3.75 million red blood cells and 11,400 white blood cells with 43 per cent neutrophils, 9 per cent band cells, 25 per cent lymphocytes, 16 per cent monocytes, 1 per cent eosinophils, 2 per cent myelocytes, 4 per cent metamyelocytes. The urine had a specific gravity of 1.028, a 2 plus reaction for protein with no glucose or abnormal sediment. The nonprotein nitrogen was 41 mg. per cent, total protein 6.5 Gm. and gamma globulin, 2.39 Gm. per cent (method of Huerga). Inorganic phosphorus was 3.5 mg. per cent; alkaline phosphatase 1.5 Bodansky units; icterus index 6; cephalin flocculation 3 plus; thymol turbidity 15.2. The Kahn reaction was negative. Blood agglutination studies for Brucella, typhoid, and salmonella, as well as blood cultures for bacteria, were negative. Repeated smears and cultures of the sputum revealed nothing abnormal. Twenty-six days after admission the patient had 71 per cent hemoglobin, (11.0 Gm.) 4.38 million red blood cells and 5,300 white blood cells with 43 per cent neutrophils, 18 per cent band cells, 17 per cent lymphocytes, 13 per cent monocytes, 1 per cent eosinophils, 6 per cent metamyelocytes, 2 per cent myelocytes.

Mantoux test 1/100, coccidioidin 1/100, blastomycin 1/100, and histoplasmin 1/500 skin tests gave no reactions.

Biopsy
The biopsy specimen of an inguinal lymph node revealed nonspecific hyperplasia with severe proliferation of the sinusoidal endothelium. In one area there were focal aggregations of epithelioid cells suggestive of a hyperplastic type of tuberculosis.
Fig. 1.—Roentgenogram of chest. Heart normal; enlarged hilar nodes; diffuse mottled infiltration throughout both lung fields. Note ring-like increased density in fourth left anterior interspace outside heart border.

Fig. 2.—Macroscopic appearance of growth in sheep's brain broth.

Fig. 3.—Macroscopic appearance of growth on Littman's medium.
HISTOPLASMA CAPSULATUM IN MARROW BIOPSY SPECIMENS

The specimen of sternal marrow, obtained by aspiration, was hypercellular with increased numbers of megakaryocytes. The ratio of nucleated red blood cells to nucleated white blood cells was 1:2. There were rare pernicious anemia-like red cells. Granulopoiesis abnormal, showing a left shift, marked toxicity, and occasional giant band cells. Monocyte-like cells were present in increased numbers. This marrow was cultured and *Histoplasma capsulatum* was successfully grown on the mediums used. In spite of diligent search, no organisms were found in the marrow on re-examination after the results of the cultures became known.

![Image](image_url)

**FIG. 4.—** Macroscopic appearance of chlamydomes of *Histoplasma capsulatum*.

<table>
<thead>
<tr>
<th><strong>Table 1.</strong> Types and Numbers of Cases Studied</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pernicious Anemia and Suspected Cases...........</td>
</tr>
<tr>
<td>Blood Dyscrasias..................................</td>
</tr>
<tr>
<td>Lymphoblastoma and suspected cases...............</td>
</tr>
<tr>
<td>Fevers of Undetermined Origin....................</td>
</tr>
<tr>
<td>Cirrhosis of the Liver............................</td>
</tr>
<tr>
<td>Hypochromic Anemia of Undetermined Origin.......</td>
</tr>
<tr>
<td>Pulmonary Tuberculosis............................</td>
</tr>
<tr>
<td>Subacute Bacterial Endocarditis..................</td>
</tr>
<tr>
<td>Miscellaneous, including Addison's disease, collagen disease, etc.</td>
</tr>
<tr>
<td>Histoplasmosis....................................</td>
</tr>
<tr>
<td><strong>Total</strong>...........................................</td>
</tr>
</tbody>
</table>

**Therapy**

The patient received courses of penicillin, streptomycin, neomycin, and neomecin with fradacin with no apparent benefit. About ten days before she signed her release from the hospital she was given ACTH, 20 mg. every 8 hours for three days, then 10 mg. every 8 hours for seven days.
Course

During this period she experienced subjective improvement with euphoria and for a few days, some lowering of the high fever. There was, however, a gradual return of the fever, 103 F., and a resumption of the downhill course. Contact with the patient was lost following her discharge from the hospital, but it was learned from a relative that she died about one month after discharge.

Comment

The cases studied were those in which marrow examination was indicated for a variety of conditions (table 1). By coincidence this group includes cases that present at least one and in some instances all the classical clinical conditions of systemic histoplasmosis: splenomegaly, hepatomegaly, anemia, leukopenia, irregular elevations in temperature, pulmonary disease and generalized lymphadenopathy; hence, *Histoplasma capsulatum* would be most likely to be found in this group. The lymphoblastoma and “blood dyscrasia” groups formed a special part of this study because of their possible association with histoplasmosis.

Summary and Conclusions

One hundred ninety-three cultures of marrows were studied for the presence of fungi.

Many of the cases studied had one or more of the classical conditions of histoplasmosis, such as anemia, leukopenia, splenomegaly, hepatomegaly, irregular elevations in temperature, pulmonary disease, and generalized lymphadenopathy.

*Histoplasma capsulatum* was found in only one case.

Considering the high incidence of histoplasmin reactors in this locality, it appears that routine cultures of the marrow for *Histoplasma capsulatum* have little value in histoplasmosis case findings.

References

Report of 193 Marrow Biopsy Specimens Cultured for Histoplasma Capsulatum

STEVEN O. SCHWARTZ, SIDNEY BARSKY, CARRIE WOOLSEY and HELEN L. GANT