An Epidemic of Histoplasmosis in a Family*

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Histoplasmosis is caused by the fungus Histoplasma capsulatum, which enters the body through the lungs is disseminated via the blood stream and involves chiefly the lungs and the reticuloendothelial system. It is usually a benign subclinical process, detectable only by the conversion of the skin test. In a moderate number of persons the primary infection is followed by dissemination which is manifested by a mild illness lasting several weeks. In this intermediate group the complement fixation test is usually positive, and the organisms can sometimes be identified microscopically in tissue, blood or sputum or by culture on appropriate media. The pulmonary lesion is in the form of a coarsely nodular infiltration which later calcifies. Other rarer manifestations of the disease are: a chronic disseminated process, tertiary cavitary lesions of lung resembling chronic pulmonary tuberculosis and a fulminating and highly fatal dissemination.

In central United States the organism is a common saprophyte in soil, especially in the soil from an environment where chickens or other fowl have lived. Human primary infection in this area, as reflected by positive skin test, varies from 27 to 73 per cent or more of the population. When several persons are heavily exposed at the same time and become ill, a so-called epidemic results. The authors wish to report an epidemic which occurred in the six members of a family residing somewhat outside the endemic region of the Mississippi Valley from which most epidemics have previously been reported.

A family of migrant workers consisting of father, mother and four children ranging in age from five to 11 years had moved from Maryland to Virginia within the preceding year and were living in a country farm house on the north branch of the Shenandoah River in Warren County, Virginia. On a hot dry Sunday, believed to have been May 13th, 1956, they decided to clean their chicken house. The father shoveled most of the guano from the floor while the children assisted him or simply entered and left the shack several times. The mother walked into the chicken house briefly on a single occasion. During this activity, the atmosphere was so filled with dust that they coughed frequently and on several occasions had to emerge for fresh air. On about May 23rd, 1956, the father became ill with fever and prostration. He was sufficiently ill to see a physician, who thought he had pneumonia. After 10 days at home he gradually improved. He continued to have weakness, however, pleuritic pain in the chest, a non-productive cough and low grade fever. On June 8, 1956, he was admitted to the Veterans’ Administration Hospital at Martinsburg, West Virginia, where he remained a month. This hospital has been good enough to make their findings available, as follows.

Physical examination revealed a man in his mid thirties who was well developed, but quite thin, with a languid and chronically ill appearance. The liver edge could be felt on deep inspiration. Questionably enlarged, non-tender, discrete, and movable cervical and inguinal lymph nodes were palpated.

The urinalysis was normal. The white blood cell count was 7000 with a normal differential count. The sedimentation rate was 47 mm./hour. A roentgenogram of the chest made several years earlier at the same institution had shown nothing abnormal (Fig. 1A). The roentgenogram made on his admission in June, 1956, however, revealed extensive granular infiltration, widely and uniformly distributed throughout both lungs. (Fig. 1B). The skin test with histoplasmin was reported as 4+ within 72 hours. The complement-fixation test was positive in a titer of 1:128. The blastomycin titer was 1:16, but the coccidioidin was negative. The patient continued to have an irritative cough, mild pleuritic pain and low-grade fever. After exactly one month he went home on leave and did not return.

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<table>
<thead>
<tr>
<th>Case No.</th>
<th>Patient</th>
<th>July 20, '56</th>
<th>Dec. 10, '56</th>
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<tr>
<td>1.</td>
<td>E. H.</td>
<td>1:128</td>
<td></td>
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<td>2.</td>
<td>T. H.</td>
<td>1:32</td>
<td>1:8</td>
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<tr>
<td>3.</td>
<td>C. H.</td>
<td>1:256</td>
<td>1:16</td>
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<td>4.</td>
<td>J. H.</td>
<td>1:64</td>
<td>1:32</td>
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<td>5.</td>
<td>E. W. H.</td>
<td>anti-complementary</td>
<td>1:8</td>
</tr>
<tr>
<td>6.</td>
<td>N. H.</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
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**FIGURE 1A**

**FIGURE 1B**

**FIGURE 2**

**FIGURE 3**
A day or so after onset of symptoms in the father, the children became feverish and irritable, with anorexia, nausea, malaise, frontal headache, and non-productive cough. Since the father had been hospitalized with a pulmonary infection of unknown etiology, roentgenograms of the four children were made by the local health department. All films showed pulmonary changes varying from spotty infiltration to multiple heavy nodules with miliary distribution (Fig. 2-5). It was possible to bring the children and the mother to the Pediatric Clinic of the University of Virginia Hospital for two visits, the first on July 20th, 1956, and the second on August second, 1956.

On examination the children were malnourished but alert. They all had minimal to moderate adenopathy in the cervical and inguinal regions, but neither spleen nor liver could be palpated. There were no other localizing signs and none had fever at this time.
Urinalyses on the four children showed no abnormality. The white blood cell count and differential count on each child were within normal limits, as were the values for hemoglobin and the hematocrit. Intradermal histoplasmin tests on each child were interpreted by a physician between 48 and 72 hours after performance as representing 3+ reactions. In the same period a Mantoux test (Old Tuberculin 1:1000) was negative. The complement fixation data are summarized in Table 1. Additional roentgenograms of the chest showed coarse, irregular, nodular to patchy soft densities scattered symmetrically through both lung fields with mild to moderate hilar adenopathy in all.

Approximately two weeks later the children returned to the Pediatric Clinic for a follow-up visit. Marrow was obtained from the iliac crest from each child and cultured on various appropriate media, but no growth was present at the end of eight weeks.

The mother was examined on each of the two visits to the Clinic. For several weeks prior to her first visit she had experienced malaise, anorexia, vague and fleeting chest pains, weakness, feverishness, cough productive of mucoid sputum and exertional dyspnea. Despite these manifestations of illness she had been able to care for the children while her husband was hospitalized. On physical examination she proved to be a 31-year-old white woman, an epileptic of moderate severity, whose attacks were controlled with sedatives and anti-convulsive medications. She was well developed and well nourished and presented no significant abnormal findings. The urinalysis and blood studies were within normal limits. A histoplasmin skin test, read at 72 hours, showed an area of erythema and induration approximately 3 cm. in diameter with vesiculation at its center, a result interpreted as 4+. The tuberculin (1:1000 O.T.) skin test was negative. The complement fixation test was negative. Roentgenograms of the chest revealed several localized areas of infiltration, the most prominent of which was located beneath the anterior end of the left first rib and measured about 1.5 cm. in diameter. (Fig. 6). Cultures of the bone marrow were sterile.

On Saturday, July 26th, the authors visited this farm where specimens were obtained from the floor of the chicken house and Petri dishes were exposed to the air near the floor. All cultures for pathogenic fungi in the Clinical Laboratories at the University of Virginia were negative. A residuum of the specimen was sent to the Communicable Disease Center of the United States Public Health Service in Kansas City, Kansas.*

Since the second visit to the Pediatric Clinic on August 2, 1956, none of the members of this family has been seen at the University of Virginia Hospital. The public health physician collected a second specimen of blood for complement fixation tests about December 10th at which time the patients had moved into a neighboring district. Later the family migrated into an adjoining part of West Virginia and are said to be alive and well.

Discussion

At least 30 epidemics of a respiratory illness, which altogether involved more than 370 persons, are known to have followed the inhalation of dust in silos, chicken houses, belfries, caves, cellars, and even in the open air. Some of the “epidemics” have been proved to be due to Histoplasma capsulatum, while in others the final cultural link in the evidence has not been possible to obtain. The cases reported in this communication are examples of a dust-borne infection manifested by moderately severe systemic symptoms and evidence of generalized pulmonary involvement. Organisms could not be cultured from the patients at the times they were seen but were recovered from the point source. The diagnosis was made from the familiar pattern of exposure to contaminated dust, subsequent mild to moderate illness, positive skin test, positive and changing complement-fixation tests and characteristics roentgenographic changes.

SUMMARY

An “epidemic” of histoplasmosis results when several persons become ill from generalization of a pulmonary infection incurred by simultaneous inhalation of dust containing the organism Histoplasma capsulatum. A number of such epidemics have been reported, involving almost 400 persons. For the most part these have occurred in the endemic area of central United States. The authors report an epidemic in a family from northern Virginia consisting of young parents and four children, five to 11 years of age, who were exposed at the same time to the dust raised during the cleaning of a

*Culture reported positive for Histoplasma capsulatum.
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chicken house. In 10 to 12 days they became variably ill with fever, malaise, non-productive cough, irritability, weakness, nausea, anorexia, and headache. Roentgenograms of the chest showed pathology in all proportional to the degree of exposure and comparable to the severity of the symptoms. The only significant physical abnormalities were mild generalized adenopathy in the children and palpable liver in the father. The skin tests and complement fixation tests were positive in all six members of the family. Cultures of blood and marrow in the mother and children were negative for H. capsulatum, but this organism was ultimately recovered on culture from a specimen of the guano from the floor of the chicken house. The illness lasted about six weeks. The roentgenograms showed a tendency to improvement, but the family, who are migrants, have not been heard from for some months.

RESUMEN

Una epidemia de histoplasmosis resultó cuando varias personas enfermaron de una afeción pulmonar generalizada después de la simultanea inhalación de polvos que contenian el organismo Histoplasma capsulatum. Se han relatado cierto número de epidemias que han incluido casi 400 personas. La mayoría han ocurrido en el área central de los Estados Unidos. Los autores relatan una epidemia en una familia del norte de Virginia, la que consistía en padre y madre jóvenes y cuatro hijos de 5 a 11 años de edad que se expusieron al mismo tiempo a polvo levantado al asear un gallinero. En un término de 10 a 12 días cayeron enfermos en forma variable, con fiebre, malestar, tos no productiva, irritabilidad, debilidad, náusea, anorexia y cefalalgia. Las radiografías del tórax mostraron cambios patológicos en todos, en proporción al grado de exposición y comparable a la gravedad de los síntomas. Las únicas anormalidades físicas fueron moderada adenopatía generalizada en los niños e hígado palpable en el padre. Las reacciones cutáneas y las de fijación del complemento fueron todas positivas en los seis miembros de la familia. Los cultivos de la sangre y de la médula ósea de la madre y de los niños, fueron negativas para el H. capsulatum pero este organismo fue encontrado en cultivo de una muestra de guano del piso del gallinero.

La enfermedad duró como seis semanas. La radiografía mostró tendencia a la mejoría pero la familia que es de inmigrantes se ha perdió de vista por varios meses.

RESUME

Une "épidémie" d'histoplasmosis survient lorsque plusieurs personnes deviennent malades après généralisation d'une contamination pulmonaire survenue à la suite d'une inhalation simultanée de poussières contenant l'histoplasma capsulatum. Un certain nombre d'épidémies ont été rapportées, atteignant non loin de 400 personnes. Elles sont survenues pour la plupart dans la zone endémique du centre des Etats-Unis. Les auteurs rapportent une épidémie dans une famille originaire du nord de la Virginie, ayant atteint de jeunes parents et quatre enfants, âgés de 5 à 11 ans, qui furent exposés en même temps à la poussière soulevée pendant la désinfection d'un poulailler. En dix à douze jours, ils furent atteints à des degrés divers de fièvres, malaise, toux non productive, irritabilité, faiblesse, nausées, anorexe et maux de tête. Des radiographies de la poitrine mon-
trèrent une atteinte proportionnelle au degré d'exposition et en rapport avec la sévérité des symptômes. Les seules anomalies significatives à l'examen physique furent une légère atteinte ganglionnaire généralisée chez les enfants, et un foie palpable chez le père. Les tests cutanés, et les tests de complément de fixation furent positifs chez les six membres de la famille. Les cultures sur le sang et la moelle chez la mère et les enfants furent négatives pour l'histoplasma capsulatum, mais ce germe fut finalement retrouvé en culture dans un échantillon du fumier recueilli sur le sol du poulailler. La maladie dura environ six semaines. Les radiographies montrèrent une tendance à l'amélioration, mais le famille n'a pas donné de ses nouvelles depuis quelques mois.

ZUSAMMENFASSUNG

Eine "Epidemie" von Histoplasmosis kommt zustande, wenn mehrere Personen erkranken infolge einer Generalisation einer pulmonalen Infektion, die sie sich zugezogen haben durch gleichzeitige Inhalation von der Erreger Histoplasma capsulatum) enthaltenden Staub.


REFERENCES