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OUTBREAK OF HISTOPLASMOSIS AMONG CAVERS ATTENDING THE NATIONAL SPELEOLOGICAL SOCIETY ANNUAL CONVENTION, TEXAS, 1994

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Abstract. In June 1994, 18 people developed serologically confirmed histoplasmosis following cave exploration associated with the annual National Speleological Society Convention in Brackettville, Texas. Six others had an undiagnosed illness suspected to be histoplasmosis. Two persons were hospitalized. We conducted a survey of convention attendees and a nested case-control study of those entering caves. We also conducted a histoplasmin skin test survey of a subgroup of the society, the Texas Cavers Association, who were attending a reunion in October 1994. Among the national convention attendees, exposure to two caves was identified as responsible for 22 (92%) of the 24 cases; 12 (75%) of 16 people exploring one cave (Cave A) and 10 (77%) of 13 exploring a separate cave (Cave B) developed acute histoplasmosis. Additional risk-factors included fewer years of caving experience, longer time spent in the caves, and entering a confined crawl space in Cave A. Of 113 participants in the separate skin test survey, 68 (60%) were found to be skin test positive, indicating previous exposure to *Histoplasma capsulatum*. A positive skin test was significantly associated with male sex and more years of caving experience. Those less experienced in caving associations should be taught about histoplasmosis, and health care providers should pursue histories of cave exposure for patients with bronchitis or pneumonia that does not respond to initial antibiotic therapy.

Histoplasmosis is caused by *Histoplasma capsulatum*, a dimorphic fungus that grows in soil. In the United States, the Mississippi and Ohio River Valleys are considered areas where *H. capsulatum* is endemic. In 1981, before the epidemic of acquired immunodeficiency syndrome (AIDS), it was estimated that 50,000–200,000 cases occur annually in the United States and of those, 500 were severe disseminated infections.¹ However, most infections go undiagnosed, since patients usually recover without medical attention.¹

The infection results primarily from inhalation of aerosolized spores from soil. Histoplasmosis (once referred to as cave disease) can be acquired by occupational or recreational exposure to environmental sources, usually in areas with endemic histoplasmosis. Caves represent one of the foci that favor the propagation of the fungus,^{2,3} and bat-inhabited caves may harbor *H. capsulatum* even in areas where histoplasmosis is of low endemicity.⁴

The significance of bird and bat droppings in the ecology of histoplasmosis, through enhancing conditions for *H. capsulatum* growth, has been described.^{5–12} In addition to improving soil conditions with guano, bats contribute to propagation of *H. capsulatum* by transmitting the organism to new sites.^{10,11,13} This is because the gastrointestinal tracts of bats can be colonized with *H. capsulatum*.¹³ Unlike bats and other mammals, avian species do not harbor the fungus, possibly because their core temperatures are too high.

Although caving has been shown to be associated with exposure to *H. capsulatum*, review of the literature suggests that cave-associated epidemics are uncommon or not recognized,⁴ and little is known about infection rates associated with this activity. There are an estimated 50,000 cavers in the United States (Luckins R, President, National Speleological Society, unpublished data).

From June 19 to 26, 1994 approximately 620 members of the National Speleological Society attended their annual convention in Brackettville, Texas. Convention participants camped out-of-doors and were involved in workshops and

daily excursions for cave exploration. During the convention, excursions were organized for 19 different caves. During the last two weeks of July, four convention attendees developed headache, fever, cough, myalgia, severe fatigue, and chest pain. Two persons were hospitalized for more than one week; they were suspected to have acute pulmonary histoplasmosis and they responded to antifungal therapy. Serum specimens from the four patients were tested by the complement fixation (CF) and immunodiffusion (ID) assays at CDC and found positive for antibodies to *H. capsulatum*.¹⁴ Biopsy specimens were not available for analysis.

The objectives of our investigation were to determine the rates of clinically apparent infection among convention attendees, assess the extent of associated morbidity, determine which caves were associated with infection, define risk factors associated with infection (including caves visited, activities in caves, environmental exposure, age, sex, race, occupation, and predisposing medical conditions) among those entering suspect caves, and estimate the prevalence of *H. capsulatum* infection in a subgroup of cavers.

To determine the size of the outbreak and to identify risk factors for infection, we conducted a case-finding survey of National Speleological Society members, a case-control study of convention participants, and a cohort study of cavers entering high-risk caves. In addition, because little is known about the prevalence of infection among what is considered to be a high-risk group, we conducted a separate study to estimate the prevalence of histoplasmosis among cavers attending a reunion of the Texas Cavers' Association, a subpopulation of the society.

METHODS

Case definition. For the purposes of this investigation, a confirmed case of acute histoplasmosis was defined as onset of illness between June 28 and July 30, 1994 and a positive serology for *H. capsulatum* infection (CF titer greater than

1:32 or the presence of M bands in ID test) in a caver who attended the convention. When sera were not available, a suspected case was defined as a caver who attended the convention and had onset of illness between June 28 and July 30, 1994, and fever, chills, headache, cough, and two of the following symptoms: fatigue, sweats, myalgias, or chest pain.

Case finding. By distributing the questionnaire in the society's monthly news publication, we conducted a survey of convention attendees to identify additional cases of histoplasmosis. The questionnaire included questions regarding attendance of the convention in Brackettville, demographic variables, caves entered during the convention, time spent caving, symptoms, treatment, underlying illness, current therapies, and outcome. Serum was obtained from persons who were suspected cases. Each participant, or a physician he/she designated, was notified of serologic results and was provided information about symptoms and management of histoplasmosis. Informed consent was obtained from participants in this study, and the guidelines for human experimentation of the U.S. Department of Health and Human Services were followed.

Case-control study. To determine which of 19 caves visited during the convention were associated with infection, we conducted a nested case-control study using responses to the survey of convention participants. Two controls per case-patient were chosen randomly from 221 respondents who attended the convention, entered caves, but did not develop illness. Patients and controls were compared regarding which caves were visited during the convention.

Cohort study. Twenty-nine convention participants who entered the two caves (Cave A or Cave B) associated with infection were evaluated for risk factors for histoplasmosis, including age, years of caving experience, pre-existing illness, and specific activities in the caves (e.g., rappelling [sliding down a rope]).

Histoplasmin skin test survey. In a separate study, we conducted a survey at the annual reunion of the Texas Caver's Association that was held October 21–23, 1994. After obtaining informed consent, we administered a questionnaire to 113 participants and applied a histoplasmin skin test. Histoplasmin (Parke-Davis Laboratories, Detroit, MI) and spherulin (ALK Laboratories, Berkeley, CA) as a control, were applied intradermally to all meeting attendees who agreed to be tested and were read 30–48 hr later by the same observer. A blood specimen was also obtained from all consenting participants. A skin test was considered positive if induration ≥ 5 mm was present.

Laboratory assays. Blood samples were allowed to clot for 2–6 hr, and serum was separated, frozen, and shipped to CDC for testing. Serum specimens were tested for antibodies to *H. capsulatum* by both CF tests with histoplasmin and yeast-form antigens and by ID with histoplasmin. Complement fixation titers $\geq 1:32$ and the detection of M or both M and H bands with the ID assay were considered presumptive evidence of acute infection with *H. capsulatum*.¹⁴ In the ID assay, the presence of M or H precipitation bands indicates the presence of specific antibodies to *H. capsulatum* in case-patient sera.

Statistical methods. To evaluate differences in the potential risk factors, univariate analysis was done using chi-

FIGURE 1. Epidemic curve of acute histoplasmosis cases following the National Speleological Society Convention in Brackettville, Texas, June 18–26, 1994.

square. To identify independent associations, multivariate analysis was done using logistic regression including those variables that were significant in the univariate analysis and potential confounding variables.

RESULTS

Case finding. Two hundred twenty-one (36%) of the 620 convention participants responded to the mailed survey. In addition to the initial four cases, 14 confirmed and six suspect cases were detected resulting in 18 of 24 suspect cases being confirmed by serology. A histogram of the outbreak is shown in Figure 1. Twenty-two (92%) of the 24 case-patients had explored one of two caves, referred to as Caves A and B. None of those people entering Cave A entered Cave B and vice-versa. Each of the groups entering Cave A and Cave B had a team leader. From these team leaders and team participants, complete lists of those who entered Cave A or Cave B were generated. Sixteen people entered Cave A and 13 people entered Cave B. Twelve of 16 attendees entering Cave A and 10 of 13 exploring Cave B developed histoplasmosis, giving cave-specific attack-rates of 75% and 71%, respectively. The range of incubation periods, from cave exposure to onset of symptoms, was 10–14 days for symptomatic participants. All case patients were previously healthy, and reported not having entered other caves in the one month before the National Speleological Society convention. All patients exhibited fever, chills, headache, and cough of at least two-weeks duration. Cough and fatigue persisted for 12 weeks in three patients. Eighteen of the 24 case-patients sought medical attention as a result of their illness; of these, the mean time to diagnosis after first seeking medical attention was three weeks. Bacterial bronchitis or pneumonia was the most common initial diagnosis. Sixteen (89%) of the 18 patients who sought medical attention were treated with antibacterial therapy.

Case-control study. Of 19 caves entered during convention activities, two caves were significantly associated with acute histoplasmosis: Cave A (odds ratio [OR] = 13.3, 95% confidence interval [CI] = 3.2–60.2) and Cave B (OR = 12.9, 95% CI = 2.7–69.2).

Cohort study. Table 1 shows the analysis of risk factors among those cavers entering Cave A or Cave B. Among the cohort of those people entering the high risk-caves, younger

TABLE 1
Risk factors* associated with histoplasmosis among cavers who entered Cave A or Cave B by univariate analysis†

Variable	Cases (n = 22)	Non-cases (n = 8)	RR	95% CI	P
Male sex (%)	15 (68)	5 (63)	0.9	0.3–2.5	NS
Mean age (range)	29 (18–43)	44 (32–62)	NA	NA	≤0.05
Smoke (%)	3 (14)	1 (13)	0.8	0.1–6.5	NS
Years caving, mean (range)	10 (2–29)	22 (2–26)	NA	NA	≤0.05
History of histoplasmosis (%)	2 (9)	0	Undefined	Undefined	NS
Hours in cave, mean (range)	5.16 (2–7)	2.16 (0.5–3)	NA	NA	≤0.05
Rapped in cave (%)	13 (59)	4 (50)	1.1	0.7–1.7	NS
Saw bats (%)	21 (95)	6 (75)	2.3	0.5–11.7	NS
Touched guano (%)	21 (95)	7 (86)	1.5	0.4–6.1	NS
In Cave A only (12 cases, 4 non-cases) entered long tunnel‡ (%)	11 (92)	1 (25)	3.3	1.1–20.2	≤0.05

* No cave explorers entering Cave A or Cave B used masks or reported immunocompromising conditions (including HIV/AIDS).

† RR = risk ratio; CI = confidence interval; NS = not significant; NA = not applicable. Risk ratios were not calculated for comparison of means.

‡ See schematic of Cave A (Figure 2).

age, fewer years of caving experience, and more hours spent in the cave were all associated with acquiring acute histoplasmosis ($p \leq 0.05$). In Cave A, disease was associated with crawling into or beyond a narrow tunnel (Figure 2). No cave explorers reported using masks during the convention. None of those cavers entering Caves A and B reported having a pre-existing illness or condition (diabetes, cancer, human immunodeficiency virus/AIDS or other immunocompromising condition) or receiving steroid therapy, which might predispose them to acute histoplasmosis. The sex of the caver was not found to be a risk factor for disease.

Skin test survey. Of the 228 Texas Caver's Association reunion participants, 113 (50%) participated in the separate skin test survey. Of those, 68 (60%) were skin test positive (induration > 5 mm). Five (4%) of the 113 participants had serologic evidence of recent infection with *H. capsulatum* and symptoms consistent with acute histoplasmosis. Results of a multivariate analysis of risk factors for infection are shown in Table 2. Skin test reactivity was significantly associated with males (OR = 1.5, 95% CI = 1.1–2.5) and with more years of caving experience (OR = 1.8 per 10-year increment, 95% CI = 1.2–2.6). Of respondents, 68 (63%) reported never having used a mask in their caving experience.

FIGURE 2. Schematic of Cave A showing the narrow tunnel associated with development of histoplasmosis among participants at the National Speleological Society Convention. This is a lateral view.

DISCUSSION

As we have shown, exposure to *H. capsulatum* during caving may be associated with significant morbidity. A lack of awareness of histoplasmosis among cavers may increase the risk of infection and delay them seeking medical attention if symptoms develop. The continued reporting of cave-associated outbreaks suggests that current practice among cavers continues to place them at risk for this potentially serious infection. The data from our investigation suggest that during the National Speleological Society Convention in Brackettville, Texas, acute histoplasmosis was associated with exposure to two caves. Findings from our cohort study suggest that younger age and fewer years of caving experience may be risk factors for the development of acute histoplasmosis among cavers. These two variables are correlated, and only fewer years of caving experience remained independently associated with infection in multivariate analysis among the skin test survey participants. Multivariate analysis was not performed in the cohort study of those entering Caves A and B. Also, in the cohort study, we found that longer time spent in the caves was significantly associated with acquiring this infection. While this suggests a dose response, it has been previously noted that histoplasmosis has developed in individuals whose sole exposure was merely standing at the entrance to caves.⁴

As in other studies,^{1,6,15} diagnosis was delayed among those convention attendees who developed illness. In addition, health care providers may fail to consider the diagnosis. Although histoplasmosis is often a mild disease, delay in diagnosis of severe cases may increase the likelihood of hospitalization and severe complications.¹ This outbreak was detected by an astute clinician who noticed the correlation with caving among a few of his patients. The fact that cave-associated epidemics are infrequently reported⁴ may be due to a lack of recognition by physicians and a tendency toward mild illness. However, because of increasing numbers of cavers, histoplasmosis may become more common as a recreational disease. In addition, severity of symptomatic illness may be related to intensity of exposure, and in this case, both Caves A and B were heavily infested with bats. Entering a narrow tunnel in Cave A, which was approximately a meter in diameter, was associated with acquiring histoplas-

TABLE 2

Multivariate analysis of a risk factors for infection among participants in the skin-test survey, Texas Caver's Association reunion*

Variable	Cases (n = 71)	Controls (n = 42)	OR	95% CI	P
Male sex (%)	52 (73)	22 (52)	1.5	1.1–2.5	≤0.05
Mean age (range)	40 (18–57)	35 (18–44)	0.9	0.8–1.1	NS
Smoke (%)	13 (18)	7 (17)	1.2	0.4–3.4	NS
Years caving, mean (range)	15 (0.1–38)	9 (0.1–30)	1.8	1.2–2.6	≤0.05
Hours caving previous year, mean (range)	179 (0–2,000)	64 (0–400)	3.1	0.5–8.9	NS
History of histoplasmosis (%)	6 (8)	1 (2)	1.4	0.4–1.9	NS
Live in endemic disease state†	15	6	1.4	0.5–5.2	NS

* OR = odds ratio; CI = confidence interval; NS = not significant.

† States along the Mississippi and Ohio River Valleys in the United States.

mosis. The tunnel was reported to be dry and dusty at the time of the convention.

For histoplasmosis, certain risk factors predispose individuals to develop more serious disease. The likelihood of requiring hospitalization or of dying increases for a patient with a pre-existing immunocompromising condition or therapy.^{16,17} Such risk factors are increasing among the United States population in general because of an increase in the use of immunocompromising medications and the spread of the HIV epidemic. Although youth and inexperience were found to be risk factors in our study, the numbers of cavers reporting pre-existing conditions were insufficient to assess differences in the occurrence of these conditions between patients and controls. However, because this is a generally healthy and active population, the high rate of disease found in this outbreak is more likely to be due to intense exposure in the caves.

The finding of 60% skin test positivity in the Texas Caving Association survey suggests that histoplasmosis is more prevalent among cavers than the 31% rate previously reported in a national histoplasmin skin test survey of naval recruits who gave their state of origin as Texas.¹⁸ Johnson and others found a histoplasmin skin test sensitivity of 4.3% for rural residents who lived near caves in Florida but a skin test sensitivity of 64% among cavers from the same area.¹⁹ In South Africa, Murray and others reported a skin test positivity rate of 94.5% for cavers.²⁰ Also, older cavers may be more likely to have positive skin test reactions, reflecting past exposure to *H. capsulatum*, and it is known that infection with *H. capsulatum* provides partial immunity to reinfection.¹⁵

Only 63% of cavers surveyed reported having ever used a mask, and of all the cavers entering the high risk caves, none used a mask. Although no studies have shown that masks would prevent exposure during caving, the dust-mist respirators now recommended for use in hospitals for tuberculosis control have the capacity to filter particles of 1–2 microns, which is the size of *H. capsulatum* spores.²¹ Preventive measures should be investigated to decrease the risk of histoplasmosis among cave explorers, in particular, education of cavers and use of appropriate masks in caves. Specific control measures instituted following our investigation included publishing a report of the caves involved in the monthly newsletter of the National Speleological Association and posting warning signs at the caves. Routine culture of soil samples from caves is not recommended because *H. capsulatum* may be found in soil without an association with disease. Decontamination of caves is not feasible or desir-

able because bat populations may be affected. To our knowledge, the effectiveness of chemoprophylaxis for cavers entering high-risk caves has not been studied. However, cavers and their associations should expand their surveillance and reporting systems, notify members about high-risk caves, and educate young and recent members about the risks of histoplasmosis associated with caving. Health care providers should include questions regarding environmental exposure to bird or bat guano, including caving, when interviewing patients with symptoms of acute bronchitis or pneumonia that may be compatible with histoplasmosis.

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