A LARGE OUTBREAK OF HISTOPLASMOSIS AMONG AMERICAN TRAVELERS ASSOCIATED WITH A HOTEL IN ACAPULCO, MEXICO, SPRING 2001


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Abstract. During spring 2001, college students from Pennsylvania reported an acute febrile respiratory illness after returning from spring break vacation in Acapulco, Mexico. Acute pulmonary histoplasmosis was presumptively diagnosed and the cluster of illness was reported to the Centers of Disease Control and Prevention. A large investigation then ensued, which included finding student-travelers for interviews and requesting sera for histoplasmosis testing. We defined a clinical case by fever and at least one of the following: cough, shortness of breath, chest pain, or headache, in an Acapulco traveler during March–May 2001. A laboratory-confirmed case had positive serology. An initial study determined that the likely site of histoplasmosis exposure was Hotel H; we therefore performed a large cohort study among travelers who stayed at Hotel H. Of 757 contacted, 262 (36%) met the clinical case definition. Of 273 serum specimens tested, 148 (54%) were positive. Frequent use of Hotel H’s stairwells, where construction was ongoing, was associated with increased risk of illness (relative risk = 10.9, 95% confidence interval = 3.7–30.5; P < 0.001). This is the first histoplasmosis outbreak associated with a hotel undergoing construction. Hotels in endemic areas should consider construction precaution measures to prevent histoplasmosis among their guests.

INTRODUCTION

Outbreaks of acute histoplasmosis, an infection caused by the dimorphic fungus Histoplasma capsulatum, have often been reported. These outbreaks have usually been associated with disturbances of accumulations of bird or bat droppings.1–3 The exposures to droppings have typically occurred while visiting caves or following cleaning and construction activities at infested sites in endemic areas in the United States and Central and South America.

We report here the results of an investigation of a large outbreak of acute pulmonary histoplasmosis among American travelers, mostly college students, who were vacationing in Acapulco, Mexico from March to May 2001 (spring break). Persons affected during this outbreak did not participate in any activities typically associated with histoplasmosis outbreaks.

BACKGROUND

On March 30, 2001, the Pennsylvania Department of Health was notified by alert clinicians of a cluster of acute febrile respiratory illness among student-travelers from two colleges; the Department of Health in turn notified the Centers for Disease Control and Prevention (CDC). Within two weeks of their return, 21 students had presented to various health care providers with an acute illness characterized by fever, chills, dry cough, chest pain, and headache; two students were hospitalized. Chest radiographs of some ill students showed diffuse infiltrates and hilar lymphadenopathy, suggestive of acute histoplasmosis. These findings prompted CDC notification. Simultaneously, the CDC received reports from colleges in other states of a febrile respiratory illness among students returning from Acapulco. A transbronchial lung biopsy specimen from a student hospitalized in Missouri was obtained in early April; histopathologic examination showed a round budding yeast compatible with H. capsulatum.

To identify additional ill spring-break student-travelers, CDC notified state health departments and other agencies of the possibility of an outbreak of histoplasmosis. On April 6, CDC issued a travel advisory alerting Acapulco-bound travelers about this outbreak and recommending that students who had traveled to Acapulco since March 1, 2001 seek medical care if they developed a febrile respiratory illness.

We conducted an initial cohort study to identify the site of histoplasmosis exposure. This initial study was conducted among a randomly selected group of student-travelers who had traveled in the first two weeks of March 2001 to Acapulco. These student-travelers were identified from lists provided by the two largest travel agencies that had managed college spring-break travel to Acapulco in 2001. Among the 109 student-travelers contacted and interviewed with a standardized questionnaire, 26 (84%) who had stayed at Hotel H versus 6 (8%) who had stayed at other hotels, developed an acute febrile respiratory illness (relative risk = 10.9, 95% confidence interval = 5.2–23.9, P < 0.01). Since no other site or activity was associated with illness, the site of exposure was considered to be Hotel H.
We subsequently conducted a larger cohort study, the main cohort study, among travelers who stayed at Hotel H, to identify risk factors associated with the acquisition of histoplasmosis and specific sources of infection. In addition, in collaboration with the Mexico Ministry of Health (MMoH), we conducted an environmental assessment of Hotel H and surroundings.

MATERIALS AND METHODS

Case finding and telephone survey. To identify ill Acapulco spring-break student-travelers, CDC notified and requested assistance from all state health departments, the American College Health Association (ACHA), and travel agencies that service colleges in the United States for Acapulco spring-break related travel. State health departments and the ACHA contacted colleges to inquire if enrolled groups of students had traveled to Acapulco during the spring-break vacation period in 2001. Information on the outbreak was also reported in the mass media and through the Epidemic Information Exchange (EPI-X), and published in the Morbidity and Mortality Weekly Report (MMWR) on April 13 and May 11, 2001 to notify public health officials and health care providers.4,5 In addition, a telephone hotline at CDC was made available for the public to report cases.

A list of travelers’ names and contact information was compiled; a standardized survey interview was developed regarding college attendance and location of college, contact information, and the presence of various symptoms. Travelers were contacted, and the survey was completed by telephone. In addition, patients with symptoms were encouraged to see a health care provider and have sera drawn and sent to CDC for histoplasmosis testing to confirm infection.

Case definitions. During the case-finding phase and initial cohort study, and prior to confirmation of histoplasmosis as the cause of illness among travelers to Acapulco, a clinical case definition for febrile respiratory illness was developed. A case of febrile respiratory illness was defined as the presence of fever and one or more of the following symptoms: cough, shortness of breath, chest pain, or headache in an American traveler to Acapulco from March 1 until May 31, 2001. Non-ill travelers were those American travelers to Acapulco from March 1 until May 31, 2001 who had none of these symptoms.

Subsequently, we defined a laboratory-confirmed case of histoplasmosis as the presence of any of the following: H or M band on an immunodiffusion (ID) test, or a titer ≥ 1:32 on complement fixation (CF) test on either an acute- or convalescent-phase serum specimen, or a four-fold increase in titer between acute- and convalescent-phase sera in an American traveler to Acapulco from March 1 until May 31, 2001. A laboratory-negative case was defined as no serologic evidence of histoplasmosis, in either a single or paired sera sample, and no fever, cough, shortness of breath, chest pain, or headache in an American traveler to Acapulco from March 1 until May 31, 2001.

Main cohort study. This study was conducted to determine risk factors for the acquisition of histoplasmosis among American travelers who stayed at Hotel H and potential sources of infection within Hotel H. To confirm infection, serum specimens were requested, after obtaining informed consent, from all study participants and sent by state health departments to CDC. Whenever possible, acute- and convalescent-phase serum specimens were obtained.

The main cohort study was initiated in May 2001 by contacting American travelers to Acapulco who had stayed at Hotel H from March 1 until May 31, 2001. The study included ill and non-ill student-travelers identified during the case finding phase and those identified after CDC visited two colleges in the United States to recruit more study participants, and after obtaining informed consent, collect sera. These colleges were known to have large numbers of Acapulco student-travelers. In addition, a limited list of non-college-student travelers with contact information available (~40) who had stayed in Hotel H between March and May 2001 was obtained from the hotel. These travelers were contacted by telephone to invite them to participate in the cohort study.

A detailed questionnaire was distributed by mail or by electronic mail to the colleges and self-administered by the students; non-students were interviewed by telephone. The questionnaire included demographic information, prior medical conditions, activities in and near Hotel H, floor where hotel room was located, amount of time spent in different areas of the hotel, amount of alcohol and or recreational drugs consumed, exposure to soil and hotel construction activities, and the presence of symptoms.

Observational and environmental studies. With assistance from the MMoH, information on construction and maintenance work in and around Hotel H since the beginning of February 2001 was obtained by interviewing employees, as was information about recent renovations and products used for landscaping and maintenance of plants inside and outside the hotel.

Inspection of Hotel H and its surroundings was performed by personnel from the MMoH and CDC from April 20 to April 23 and from May 15 to May 16, 2001. Areas inspected included rooms where some ill persons had stayed, the air conditioning system, various hotel floors, stairwells, roof, restaurants, pools, and surrounding areas. Sites near Hotel H were visited and assessed, including abandoned buildings, parking lots, vendor huts, the beach, and a large rocky prominence in the bay facing the hotel.

Environmental samples were collected from the hotel utility shaft, large planters containing potted plants inside the hotel, return air grills in guest rooms, and abandoned buildings adjacent to the hotel.

Laboratory studies. All submitted serum specimens were tested for antibodies to H. capsulatum by standard ID and CF methods at CDC.6 Environmental samples collected from various sites were tested for the presence of H. capsulatum by intraperitoneal mouse inoculation method.7

Statistical analysis. Data were analyzed using Epi-Info version 6.04b (CDC, Atlanta, GA) and SAS version 8 (SAS Institute, Cary, NC). Categorical variables were compared using Fisher’s exact test, while continuous variables were compared using the Wilcoxon two-sample test. Univariate analysis was used to determine risk factors for histoplasmosis, and relative risks (RRs) and 95% confidence intervals (CIs) were calculated using Cochran-Mantel-Haenszel methods. Multivariable analysis was performed using unconditional logistic regression with backward elimination (SAS version 8). The multivariable model included variables found to be significant in univariate analysis at P < 0.1. Since the frequency
of stairwell use showed an incremental increase in risk of illness, it was included in the multivariable analysis as an ordinal variable. Odds ratios (ORs) and 95% CIs were calculated.

Latent class analysis (LCA) is a procedure used to correct the misclassification bias of imperfect assays that are used to determine disease status.15 When no definitive gold standard is available for the determination of true infection, as was the case for this outbreak investigation, LCA provides a framework for the analysis of misclassified categorical data. It uses the maximum likelihood method for combinations of symptoms to predict a case of illness. During this investigation, LCA analysis indicated that the febrile respiratory illness case definition used early in the study was very predictive of histoplasmosis. Therefore, for the univariate and the multivariable analyses in the cohort study, we conducted analysis using the laboratory-confirmed and the febrile respiratory illness case definitions.

RESULTS

Case finding and telephone survey. We identified 964 residents of the United States who traveled to Acapulco between March 1 and May 31, 2001; among these travelers were students from 51 colleges in the United States. Of these travelers, 757 (79%) were contacted. Of those who responded, 666 (88%) were college students and 241 (32%) were male. The median age was 21 years (range = 15–61 years). A total of 262 travelers met the febrile respiratory illness case definition used for case finding; 245 (32%) were student-travelers from 44 colleges in 23 states (Arizona, Connecticut, Delaware, Florida, Illinois, Iowa, Maryland, Massachusetts, Michigan, Minnesota, Missouri, New Hampshire, New Jersey, New York, North Carolina, North Dakota, Ohio, Oklahoma, Pennsylvania, Rhode Island, South Dakota, Texas, and Wisconsin) and the District of Columbia, and 17 non-student travelers.

Clinical characteristics. The distribution of symptoms among laboratory-confirmed histoplasmosis cases, and those who met the febrile respiratory illness case definition is shown in Table 1. Headache was the most common symptom, followed by fever (for the laboratory-confirmed cases; the clinical cases all had fever by definition) and myalgias, cough, and chest pain; ~11% were hospitalized, and 25% received antifungal treatment (itraconazole, fluconazole, or ketoconazole).

LCA showed that the presence of fever and any of the following symptoms: cough, or shortness of breath, or chest pain, or headache (case definition for febrile respiratory illness used during the telephone survey), had a high probability (P = 99.9%) of predicting acute histoplasmosis. The distribution of illness by dates of onset of fever (epidemic curve) among febrile respiratory illness cases (n = 159), and laboratory-confirmed cases (n = 97) who responded to the query regarding the presence of fever is shown in Figure 1. Ill travelers who met the clinical case definition but either had negative serologic test results (n = 36) and those who never had serologic analysis performed (n = 123) are included.

Main cohort study. A total of 388 student-travelers from 11 states (Delaware, Illinois, Maryland, Massachusetts, Missouri, New Jersey, North Carolina, Pennsylvania, Rhode Island, Texas, and Washington) and 114 non-college student guests who stayed at Hotel H were identified to participate in this study: 191 (38%) completed questionnaires. Of these, 86 (45%) were male and 148 (77%) were college students; the median age was 21 years (range = 15–63 years). A total of 122 individuals (64%) had a febrile respiratory illness that met the case definition used for the telephone survey.

Of the 191 subjects who completed questionnaires, 112 provided specimens for serologic testing: 75 (67%) met the definition of laboratory-confirmed histoplasmosis. Symptomatic laboratory-confirmed cases started developing manifestations of disease 1–3 weeks (range = 4–23 days) after arriving at Hotel H, with a mean incubation period of 14 days. The median time from the date of arrival at Hotel H to the first blood draw for histoplasmosis testing was 37 days (range = 20–60 days), and to the second blood draw was 53 days (range = 38–63 days). Among the clinical cases who had a febrile illness but negative laboratory results, the mean time between

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>LCC with characteristic/LCC who responded (%)</th>
<th>FRI cases with characteristic/FRI cases who responded (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td></td>
<td></td>
</tr>
<tr>
<td>College student</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age between 18 and 25 years</td>
<td>58/142 (41)</td>
<td>106/260 (41)</td>
</tr>
<tr>
<td>Headache</td>
<td>136/145 (94)</td>
<td>243/260 (93)</td>
</tr>
<tr>
<td>Fever</td>
<td>125/133 (94)</td>
<td>246/257 (96)</td>
</tr>
<tr>
<td>Myalgias</td>
<td>115/132 (87)</td>
<td>233/250 (90)</td>
</tr>
<tr>
<td>Cough</td>
<td>9/130 (75)</td>
<td>262/262 (100)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>97/130 (75)</td>
<td>188/242 (78)</td>
</tr>
<tr>
<td>Shortness of breath</td>
<td>93/131 (71)</td>
<td>203/259 (78)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>129/130 (55)</td>
<td>150/222 (66)</td>
</tr>
<tr>
<td>Rash</td>
<td>10/124 (8)</td>
<td>134/226 (59)</td>
</tr>
<tr>
<td>Hospitalized for acute illness</td>
<td>35/94 (37)</td>
<td>76/210 (36)</td>
</tr>
<tr>
<td>Received medication for acute illness</td>
<td>10/124 (8)</td>
<td>25/237 (11)</td>
</tr>
<tr>
<td>Received antifungal treatment for acute illness</td>
<td>13/130 (10)</td>
<td>62/111 (56)</td>
</tr>
</tbody>
</table>

* A laboratory-confirmed case of histoplasmosis has an H or M band on an immunodiffusion test, or a titer ≥ 1:32 on a complement fixation test on either an acute- or convalescent-phase serum sample, or a four-fold increase in titer between acute- and convalescent-phase sera, in an American traveler to Acapulco from March 1 until May 31, 2001.
† By definition, all FRI cases had fever.
‡ The presence of fever and one or more of the following symptoms: cough, shortness of breath, chest pain, or headache in an American traveler to Acapulco from March 1 until May 31, 2001.
§ Antifungal treatment includes itraconazole, fluconazole, or ketoconazole.
date of arrival at hotel H and blood draw was 34 days (range = 21–56 days).

Univariate analysis using the febrile respiratory illness case definition (ill travelers) showed that the following activities were found to be associated with disease: ever using Hotel H’s central stairwells, witnessing construction and/or construction workers in the stairwell, and other activities (Table 2). The frequency of stairwell use revealed an incremental dose-response risk for illness: taking as a reference the travelers who did not use the stairwells (12 [10%] of 114 ill travelers and 14 [51%] of 27 non-ill travelers), those who used the stairwells 1–3 times a day (76 [67%] of 114 ill travelers and 14 [48%] of 27 non-ill travelers) were at an increased risk of illness (RR = 1.8, 95% CI = 1.2–2.7) and those who used the stairwells more than three times a day (26 [23%] of 114 ill travelers and 0 non-ill travelers) were at even higher risk (RR = 2.1, 95% CI = 1.4–3.1). Demographic and behavioral factors (sex, occupation, tobacco or drug use) were not significantly associated with risk of disease. Multivariable analysis showed that only the frequency of stairwell use remained independently associated with increased risk of illness.

Subsequent analysis using the laboratory-confirmed case definition found no variables to be significantly associated with confirmed infection by either univariate or multivariable analysis.

Observational and environmental study. A fire had occurred in the basement of Hotel H in January 2001, and this had necessitated renovation of the affected areas. No signs of ongoing fire-related repair work were evident during March and April when spring break travelers were present, or at the time of the inspections conducted by MMoH and CDC. However, maintenance work was taking place in the utility shaft adjacent to the central stairwell of Hotel H during March and April 2001. During this time, hotel staff reported

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**TABLE 2**

Risk factors for febrile respiratory illness* (FRI) among travelers staying at Hotel H during March–May 2001, by univariate and multivariate analysis†

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>FRI among exposed</th>
<th>FRI among non-exposed</th>
<th>RR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Univariate analysis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Used the stairwells ever</td>
<td>107/122 (88)</td>
<td>12/25 (48)</td>
<td>1.8 (1.2–2.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Saw construction or construction workers</td>
<td>53/60 (88)</td>
<td>66/87 (76)</td>
<td>1.2 (1.0–1.4)</td>
<td>0.06</td>
</tr>
<tr>
<td>Contact with soil from broken planter</td>
<td>26/29 (90)</td>
<td>61/84 (73)</td>
<td>1.2 (1.0–1.5)</td>
<td>0.06</td>
</tr>
<tr>
<td>Attended beach “happy-hour”</td>
<td>84/95 (88)</td>
<td>34/51 (67)</td>
<td>1.3 (1.1–1.6)</td>
<td>0.002</td>
</tr>
<tr>
<td>Had any alcoholic beverage</td>
<td>108/129 (84)</td>
<td>13/22 (59)</td>
<td>1.4 (1.0–2.0)</td>
<td>0.03</td>
</tr>
<tr>
<td>Spent time in parking lot</td>
<td>21/22 (95)</td>
<td>89/116 (77)</td>
<td>1.2 (1.1–1.4)</td>
<td>0.05</td>
</tr>
<tr>
<td><strong>Multivariable analysis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency of stairwell use‡</td>
<td>OR (95% CI)</td>
<td>P</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10.5 (3.7–30.5)</td>
<td>&lt;0.001</td>
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</tbody>
</table>

* The presence of fever and one or more of the following symptoms: cough, shortness of breath, chest pain, or headache in an American traveler to Acapulco from March 1 until May 31, 2001.
† RR = relative risk; CI = confidence interval; OR = odds ratio.
‡ Defined as the incremental use of stairwells from none, one to three times a day, and greater than three times a day.
posting signs indicating that the stairwells were not to be used by guests. However, these instructions were not strictly enforced and guests continued to use the stairwells frequently (88% reported using the stairwells, Table 2). Under normal conditions, when all stairwell doors were closed, the stairwell was under positive pressure. A new access to the utility shaft had been opened from the stairwell located in the hotel lobby and had remained uncovered, and access portals from the stairwells into the utility shaft were opened to allow entry for workers to the utility shaft. Also, during the maintenance work the utility shaft’s roof vent was opened. These factors resulted in a pressure differential that allowed significant airflow from the utility shaft into the stairwell when the stairwell doors were opened, demonstrated by flutter strips taped to the utility shaft access portals. Inspection indicated that a moderate amount of debris, including soil and organic material, was present in the utility shaft.

No obvious large accumulations of bird or bat droppings, consistent with a source of histoplasmosis, were identified or reported by hotel staff, or in or around the hotel. However, it was noted that birds and bats roosted in palm trees near the hotel. Student-travelers reported an incident in which a planter containing large potted plants, located on the eighth floor of the hotel adjacent to the elevators, was broken during the second week of March. Soil from the broken planter was dispersed throughout the eighth floor. The soil used for the planters was reported to have come from a local chicken farm near Acapulco. The fertilizers for the potted plants throughout the hotel were reported to be chemical.

Inspection of the air conditioning system indicated that it was a closed chilled-water system, and that each room had independent ventilation. Natural ventilation occurred when hotel guests opened doors to the balconies.

Laboratory studies. Two hundred seventy-three travelers submitted serum specimens for histoplasmosis testing; 66 (24%) provided acute- and convalescent-phase samples and 52 (79%) of these paired samples gave positive results. A total of 47 samples were positive by both ID and CF tests; 8 were positive by CF, but negative by ID. Of 207 persons who provided only one sample, 96 (46%) had laboratory-confirmed histoplasmosis; 54 were positive by both ID and CF tests, 36 were positive by the CF test, but negative by the ID test, and five were positive by the ID test, but negative by the CF test.

The correlation between the laboratory-confirmed cases and LCA was excellent: among 63 laboratory-confirmed cases with available information on symptoms from the second cohort study, LCA analysis predicted 62 (98.4%) of them. The laboratory-confirmed traveler who was not predicted by LCA was asymptomatic.

Using the intraperitoneal mouse injection method, we recovered H. capsulatum from the soil sample taken from the planter adjacent to the eighth floor elevators. Specimens of dirt obtained from the stairwells did not yield a positive culture of H. capsulatum using this method.

DISCUSSION

We have described the investigation of the largest outbreak of histoplasmosis known to have occurred among American travelers. This outbreak is unique not only in its magnitude, but also because none of the travelers had exposures typically associated with the acquisition of histoplasmosis. Our findings suggest that the site of exposure was a large hotel, where minor construction activities were taking place indoors. This has important implications for travelers visiting areas endemic for histoplasmosis, in that typical exposures to accumulated bird or bat droppings may not be necessary for infection.

The results of our cohort and observational studies lead us to conclude that H. capsulatum spores spread from Hotel H’s utility shaft into the central stairwell. We hypothesize that the maintenance work in the utility shaft led to the aerosolization of dust contaminated with H. capsulatum spores into the stairwell. Many travelers frequently used the stairwell thereby exposing themselves to the contaminated environment. We found that the more travelers used the stairwell, the greater the risk of developing a febrile respiratory illness, which supports our hypothesis. Additionally, the epidemic curve (Figure 1) suggests a continuous source of exposure, which correlates with the duration of the maintenance work and of the outbreak. It is not clear how the utility shaft became contaminated with H. capsulatum. However, it is possible that birds roosting in the area had access to the utility shaft through the open roof vent while maintenance work was taking place. Although H. capsulatum was not isolated from the implicated utility shaft, similar outbreak investigations of other endemic mycoses have documented exposure to dust to be associated with increased risk of diseases in the absence of positive environmental cultures. Exposure to the dispersed soil from the broken planter on the eighth floor was also associated with illness; however, it accounted for only a small proportion of cases and could not explain the continuous occurrence of cases throughout the duration of the outbreak. Isolation of H. capsulatum from the soil used in some of the planters in the hotel may only be a reflection of the endemic nature of this fungus in the state of Guerrero, where Acapulco is located and where the soil was obtained.

Health care providers evaluating travelers returning from a histoplasmosis-endemic area need to consider this disease in the differential diagnosis of an acute febrile respiratory illness, regardless of the exposure history. Health care providers may not suspect acute pulmonary histoplasmosis due to the non-specific signs and symptoms. In addition, physicians may not always obtain a detailed travel history from these patients. As a result, many patients with acute histoplasmosis may be misdiagnosed and prescribed inappropriate therapy; only 25% of the symptomatic laboratory-confirmed cases in this outbreak received antifungal treatment; 56% received other antimicrobials. It is unclear whether antifungal treatment is of benefit in this situation.

The limitations of histoplasmosis diagnostic testing can also contribute to the misdiagnosis of the disease. It is rare to obtain tissue samples from patients with acute disease for histopathologic examination and culture. Therefore, the diagnosis of acute pulmonary disease in the non-immuno-compromised host is usually dependent on serologic tests. However, because two serum samples (acute- and convalescent-phase) are required for unequivocal confirmation of acute disease, these tests are not ideal for making a diagnosis in the early stages of acute illness. This investigation further confirmed the importance of obtaining acute and convalescent serology because the yield of serologic testing im-
proved significantly when a convalescent specimen was obtained (from 46% with a single serum specimen to 79% with acute and convalescent samples). Although travelers with more severe illness may have been more inclined to submit paired serum specimens and not just one specimen, most of the travelers who submitted even one specimen were symptomatic.

Our efforts to determine the source of *H. capsulatum* in this outbreak were hampered by a number of factors. First, travelers were interviewed several weeks after returning from Acapulco, thus affecting the recall of activities. Second, the statistical power of the main cohort study using the laboratory-confirmed case definition was limited. This was due to the lower number of observations among the controls in the analysis (36 laboratory-confirmed cases and 7 laboratory-negative cases), due to the high attack rate among Hotel H visitors. Third, our attempts to recover *H. capsulatum* from environmental samples collected in and near Hotel H were subject to the limitations of environmental isolation methods of *H. capsulatum.*

This investigation posed major challenges, many of which are common to outbreak investigations among travelers returning with an acute infection. For example, obtaining the identities and contact information for a large group of Acapulco travelers, and for persons who stayed at Hotel H, was difficult. In addition, once a list of contact information had been obtained, coordination with state and local health departments in 24 states was required to directly contact individuals. Obtaining and arranging for the shipment of serum specimens from all over the United States was another major challenge: of the 757 travelers contacted during this outbreak investigation, 207 submitted one sample and only 66 submitted two samples for testing. Moreover, the response to requests for interviews and especially for serum specimens among travelers who were asymptomatic was very low. These important logistic issues need to be overcome so that effective multi-state outbreak investigations among travelers can be undertaken.

Our findings suggest that travelers to histoplasmosis-endemic areas may be exposed to environmental sources of the disease regardless of their activities while in these areas. The hotel industry in these endemic areas should consider implementing and enforcing standard environmental protective measures when hotel construction, even if seemingly minor in nature, is to take place. Recommendations by the MMoH and CDC to Hotel H included enforcing restricted access to the stairwells, and using temporary barriers to seal off construction-generated dust. As in the event of construction activities in hospitals, guidelines for prevention of exposure to fungi among tourists, while construction is ongoing in hotels, may be appropriate.
REFERENCES