

Enhanced Surveillance for Histoplasmosis

PARTICIPATING SITES

- Mycotic Diseases Branch (MDB), Centers for Disease Control and Prevention (CDC)
- Arkansas Department of Health
- Delaware Division of Public Health
- Indiana State Department of Health
- Kentucky Department for Public Health
- Louisiana Department of Health and Hospitals
- Michigan Department of Community Health
- Minnesota Department of Health
- Nebraska Department of Health & Human Services
- Pennsylvania Department of Health
- Wisconsin Division of Public Health

SUMMARY

Histoplasmosis likely causes tens of thousands of illnesses in the United States annually, but much remains unknown about the burden and sources of the disease. The project will consist of telephone interviews with patients with confirmed or probable histoplasmosis reported during one year in states where histoplasmosis is reportable. Information collected during the interviews will include demographics, underlying medical conditions, symptom type and duration, healthcare-seeking behaviors, exposures, diagnosis, treatment, and outcomes. This data will help guide and improve routine histoplasmosis surveillance.

BACKGROUND

Histoplasmosis is an infectious disease caused by inhalation of the environmental fungus *Histoplasma capsulatum* (1). Histoplasmosis can range from asymptomatic or mild illness to severe disseminated disease, and it is often described as the most common endemic mycosis in North America. Most epidemiologic data about histoplasmosis is derived from outbreak investigations, yet outbreak-associated illnesses represent a small proportion of overall cases. Therefore, much still remains unknown about the epidemiology and patient burden of histoplasmosis in the United States (2-4).

Histoplasmosis is currently reportable in 11 states but is not nationally notifiable. In June 2016, the Council of State and Territorial Epidemiologists (CSTE) passed a position statement to standardize the case definition for histoplasmosis, a first step towards more consistent surveillance methodology (5). Before this change, states used slightly different case definitions. A recent multistate analysis of histoplasmosis cases reported to public health during 2011–2014 also revealed variation in the data elements collected by each state, limiting inter-state comparability (6). In addition, data on possible exposures, underlying medical conditions, symptoms, and antifungal treatment was only collected in a few states. These types of data are often collected during outbreak investigations (4), and studies describing clinical features of histoplasmosis cases typically focus on specific high-risk groups such as patients with HIV/AIDS, patients taking TNF- α blocker therapy, transplant recipients, and older adults (7-11). Furthermore, no multistate data exists about histoplasmosis cases identified using the newly-created CSTE case definition.

Primary prevention strategies for histoplasmosis can be challenging to implement. Public health efforts aimed at promoting awareness of histoplasmosis among healthcare providers and the general public could potentially lead to earlier diagnoses and possibly better outcomes for patients. Improved surveillance data are essential for identifying such opportunities to promote awareness about this disease and for determining its true public health burden.

Therefore, more detailed data about histoplasmosis cases detected during routine surveillance in the general population are needed to better understand the features of persons at risk, characterize the effects of histoplasmosis on patients (e.g., delays in diagnosis, symptom duration, and decreased productivity), understand patient awareness of histoplasmosis, and determine its true public health burden. This information will not only help inform routine surveillance practices, but also guide awareness efforts and appropriate prevention strategies.

OBJECTIVES

- Describe patient burden, exposures, and laboratory diagnosis of cases in participating states
- Evaluate the new Council of State and Territorial Epidemiologists (CSTE) case definition and determine which data elements are most important to collect during routine histoplasmosis surveillance
- Identify opportunities for outreach efforts related to histoplasmosis awareness and education

METHODS

Case identification and interview process

The project is open to participation from state and local health departments in states where histoplasmosis is reportable. Cases will be identified through routine histoplasmosis surveillance; cases meeting the CSTE definition of a confirmed or probable case are eligible to be interviewed. Interviews will be conducted by state or local health department personnel. All cases reported in the year following the project start date will be contacted by telephone and invited to participate in the interview.

Ideally, cases should be contacted four to six weeks after they are reported to public health. A total of five attempts should be made for each valid phone number. At least one attempt should be made in the morning (8 am–12 pm) and one in the afternoon (12–5 pm) on weekdays. If there is no response after three attempts during the day, at least one attempt should be made on a weekday evening (5–8 pm).

A suggested script is available (see Appendix at the end of this document) for interviewers to inform patients of the purpose and the voluntary nature of the interview. A standardized case report form (CRF) will be used to collect information on demographics, underlying medical conditions, exposures, symptom type and duration, healthcare seeking behaviors, diagnosis, treatment, outcomes, and awareness of histoplasmosis. Each interview is estimated to take approximately 15 minutes. The last page of the CRF will not be used during the interview but will collect information about the laboratory method(s) used for histoplasmosis diagnosis based on available information in states' reportable disease databases. No personally identifying information will be recorded on the CRF. Each case will be assigned a unique identifier containing the state postal code followed by a hyphen and sequential numbering (e.g., AR-01, AR-02, etc.). A parent or guardian should be interviewed for cases in persons under 13 years old. For cases in persons aged 13–17 years old, the adolescent can be interviewed if permission from the parent or guardian is obtained. For cases in persons who are deceased or incapacitated, a proxy such as a family member or caregiver can be interviewed on the patient's behalf. Health departments should use their existing processes for gaining voluntary participation from patients/guardians with reportable conditions.

Estimated sample size and sampling strategy

Participation from AR, DE, IN, KY, LA, MI, MN, NE, PA, and WI would result in approximately 600 cases reported yearly and eligible to be interviewed. We estimate that approximately half of case-patients will be unable to be contacted, refuse participation, or will not be able to be interviewed for other reasons, resulting in an estimated 300 total interviewed patients. The range in cases reported by state might require different approaches to sampling to reduce the burden of interviews on health departments to which many histoplasmosis cases are routinely reported. For states in which <100 yearly cases are typically reported, attempting to interview every case is preferred. For states in which ≥ 100 yearly cases are typically reported, states could consider attempting

to interview every other reported case. However, each state may participate to the extent possible, and no minimum proportion of interviewed cases will be established.

Non-interviewed cases

For patients who health departments attempt to interview but are unable to do so (for any reason, such as missing or incorrect contact information, inability to identify an appropriate proxy if the patient is deceased or incapacitated, or patient refusal), health department personnel should complete only the “Case and interview information,” “Demographics,” and “Diagnosis of histoplasmosis” sections of the CRF using information available in their reportable disease databases. This will allow analysis of reasons why patients were not interviewed and basic comparisons between interviewed and non-interviewed patients.

Data transmission, storage, and analysis

Participating states can share completed CRFs with MDB via email (jsy8@cdc.gov) or fax (404-471-8529). This information will be stored electronically on secure CDC computers as password-protected files. MDB will enter the data into a password-protected Microsoft Access database and can provide a final copy of the completed database to each state containing only that state’s cases. MDB will merge data from all states and import the data to SAS v. 9.4 for analysis. Proposed analyses include but are not limited to:

- Overall description of case demographic features, clinical presentation, healthcare use, exposures, and treatment and outcomes
- Descriptive analysis of laboratory methods used for histoplasmosis diagnosis; analysis of positive test types stratified by clinical syndrome and/or other relevant variables
- Analysis of factors potentially associated with length of time from symptom onset to diagnosis
- Comparison of case characteristics by demographic groups (age, sex, race/ethnicity) and severity

Isolates

Sending *Histoplasma* isolates from reported cases to CDC is an optional component of this project. Isolates can be sent to the address below and should be accompanied by CDC form 50.34 (DASH form), available at: <http://www.cdc.gov/laboratory/specimen-submission/pdf/form-50-34.pdf>. If sending isolates, it is important to include the unique case identification number assigned for this project (state postal code and sequential numbering, as described above) on the DASH form or in an email to Kaitlin Benedict at jsy8@cdc.gov.

Dr. Shawn Lockhart
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Centers for Disease Control and Prevention
1600 Clifton Road NE
Re: Histoplasmosis surveillance
DASH Unit 40
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Request for non-research determination

As a project designed to characterize the scope and burden of histoplasmosis, and to gather feedback to assess current reporting practices, we request a determination of non-research. The proposed activities are not designed to develop or contribute to generalizable knowledge, but rather to apply existing knowledge about histoplasmosis to improve public health practice.

APPENDIX

Introductory script for histoplasmosis enhanced surveillance

“Hello, my name is (*name*). I work with (*name of your health department*). I’m calling because (*name of your health department*) and the CDC are doing a public health investigation about histoplasmosis to better understand how it affects the health of people in (*your state*). I’d like to talk to you because your healthcare

provider ordered a histoplasmosis test for you or because you might have histoplasmosis. As you might already know, histoplasmosis is a fungal infection that often affects the lungs and is not contagious. Your participation is voluntary, but I'm hoping you could complete a brief phone interview that will take about 15 minutes. May I ask you a few questions?"

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