

Histoplasmosis



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KEYWORDS

- Histoplasmosis • Histoplasma • Disseminated • Pulmonary
- Central nervous system • Serology • Antigen • Antibody

KEY POINTS

- Although histoplasmosis is highly endemic in certain regions of the Americas, disease may be seen globally and should not be overlooked in patients with unexplained pulmonary or systemic illnesses.
- Most patients exhibit pulmonary signs and symptoms, accompanied by radiographic abnormalities, which often are mistaken for community-acquired pneumonia caused by bacterial or viral agents.
- Once a diagnosis is considered, a panel of mycologic and non-culture-based assays is adequate to establish a diagnosis in a few days to a week in most patients.
- Once diagnosed, the treatment is highly effective even in immunocompromised patients.

INTRODUCTION

Histoplasmosis is the most common endemic mycosis in the United States and in certain areas of Mexico and Central and South America. In the United States, of the endemic mycoses, histoplasmosis was the most common cause for hospitalization and death.¹ Hammerman² cited Centers for Disease Control and Prevention surveillance records that estimated approximately 500,000 infections yearly. Analysis of skin test data suggests a higher infection rate. For example, 20% of recruits were positive for histoplasmin skin test reactivity in a landmark US Navy study.³ Assuming an average age of 20 years, the yearly infection rate is 1%, representing approximately 3 million infections per year based on the 2010 US census.

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EPIDEMIOLOGY

Histoplasmosis is most commonly understood as intensely endemic in the Ohio and Mississippi River Valleys in the United States and much of Latin America (Fig. 1),^{3,4} although it has been known for some time that other areas around the world saw cases as well.⁵ The HIV pandemic and the increasing use of other immunosuppressive medications, such as calcineurin and tumor necrosis factor inhibitors, has resulted in more cases of histoplasmosis and thus improved understanding of the distribution of this fungus.^{6–8} Factors accounting for the geographic distribution of histoplasmosis are poorly understood but include moderate temperature and bird or bat guano containing soil.

Histoplasma may be found in so-called microfoci inside and outside the endemic areas for histoplasmosis. The characteristic of these microfoci is contamination with bird/or bat guano. The activities that have been most commonly identified as sources for exposure to *Histoplasma capsulatum* include farming, exposure to chicken coops or caves, remodeling or demolition of old buildings, and cutting down trees or clearing brush from sites in which blackbirds have roosted.^{9–11}

These microfoci challenge the perception of where histoplasmosis might occur in the United States, as evidenced by recent reports from Idaho and Montana.¹² Outside the United States, histoplasmosis incidence is best understood and highest in parts of Mexico and South and Central America and is largely driven by the AIDS pandemic.^{13–18} In French Guiana, progressive disseminated histoplasmosis (PDH) is the most common AIDS-defining illness, where this condition was detected by 1 retrospective in approximately 41% of HIV-positive hospitalized patients with fever and a CD4⁺ count less than 200.^{13,14,16,19} In Columbia, more than 70% of patients with histoplasmosis included in a survey conducted from 1992 to 2008 had HIV/AIDS,²⁰ and in Brazil, histoplasmosis is highly endemic in several regions; histoplasmin positivity may be up to approximately 90% in some areas.⁴

Histoplasmosis also is endemic in parts of Asia, Southeast Asia, and India. In China, 75% of cases occur along the Yangtze River, most in association with AIDS,²¹ and histoplasmin skin test positivity ranges from 6% to 50%. More than 1200 cases of PDH have been reported in Thailand²² and recent cases have been reported in South Korea as well.²³ In India, cases have been recognized since the 1950s and histoplasmin sensitivity rates have been reported from 4.7% to 12.3%.^{24,25} Information is more limited in Africa, but cases have been reported in patients with AIDS in Zimbabwe, South Africa, Uganda, and Tanzania,^{9,26,27} and many cases were diagnosed in Europe after travel.^{25,28,29} Histoplasmosis in Europe without travel to endemic areas is rare but cases have been reported in Spain.³⁰ The newly recognized worldwide distribution clearly has an effect on histoplasmosis management.³¹

PATHOGENESIS

Infection with *H capsulatum* occurs by inhaling microconidia after disturbance of environmental sites containing the organism.³² Infection is usually asymptomatic in healthy individuals unless a large inoculum has been inhaled.²⁵ In the absence of immunocompromising conditions, acute infection resolves with the development of cell-mediated immunity.³³ As a consequence of production of T lymphocytes that recognize the organism, tumor necrosis factor α and interferon gamma are induced, activating macrophages to inhibit the growth of the organism and to provide protection against reinfection.^{32,33} Depletion of T cells resulting in lower levels of these cytokines results in increased mortality and fungal burden.³²

Although organisms persist in granulomas for life in most healthy individuals, the organisms are typically not viable and consequently latent infection, as seen in

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