

Histoplasmosis is a disease caused by infection with the fungal microorganism *Histoplasma capsulatum*. *H. capsulatum* lives in the soils of temperate climates and especially in association with bird and bat guano. Human infection occurs most commonly by inhalation of infectious particles when soils are disturbed and aerosolized by wind or by human activities including agriculture, excavation, and construction. Histoplasmosis cases have been reported worldwide. In the U.S., histoplasmosis is most commonly seen in the southern Great Plains and especially in the Mississippi and Ohio river valleys eastward to the Chesapeake Bay region.

Clinical manifestations of histoplasmosis are highly variable. The lungs are the typical site of primary infection, resulting in an interstitial pneumonitis with hilar and mediastinal lymphadenopathy. The great majority (>90%) of primary infections in otherwise healthy individuals are either asymptomatic or clinically non-specific, mild, and self-limited such that these cases are either not recognized by health care providers or the affected individual never seeks medical attention. Clinically recognized acute pulmonary histoplasmosis syndrome includes fevers, chills, headaches, non-productive cough, and non-pleuritic chest pain. Immunologic phenomena (arthralgias, erythema nodosum, erythema multiforme) may sometimes accompany the primary symptoms. Serious illness occurs in only a small minority of infected individuals and is most commonly seen in association with identifiable immune dysfunction such as the immunoimmaturity of young children, the immunosenescence of the elderly, iatrogenic immunosuppression, congenital immunodeficiency, and AIDS. Manifestations of serious illness may include chronic cavitary pulmonary disease, chronic mediastinal adenopathy and fibrosis, and acute, subacute, or chronic progressive disseminated histoplasmosis with involvement of multiple organ systems. Regardless of initial clinical manifestations and possibly even of antifungal treatment, *H. capsulatum* establishes persistent infection in which viable yeasts persist in body tissues for many years and possibly for life. These dormant organisms may later reactivate and cause serious illness, especially in individuals who receive iatrogenic immunosuppression or develop AIDS. Previously infected and clinically resolved individuals may also later become reinfected with *H. capsulatum*, with clinical manifestations again ranging from mild pulmonary to severe disseminated disease.

A suspected diagnosis of histoplasmosis is confirmed by fungal culture and/or immunohistochemical staining that identifies *H. capsulatum* in collected body fluids or tissue specimens. Serologic testing of blood or urine specimens to identify antigens from or antibodies to *H. capsulatum* may support the diagnosis, but interpretation may be complicated by issues of sensitivity (e.g., false negatives with antigen detection) and specificity (e.g., antibodies representing previous versus active infection).

Mild cases of acute pulmonary histoplasmosis syndrome in otherwise healthy individuals are self-limiting and generally do not require antifungal treatment. Other disease manifestations can be treated with oral itraconazole, and severe disease in individuals with immune dysfunction is typically treated with intravenous amphotericin B. Adjunctive corticosteroid therapy may be used in certain situations.

#### References:

1. Wheat LJ, Kauffman CA. Histoplasmosis. *Infect Dis Clin North Am* 2003; 17: 1-19.
2. Cano MVC, Hajjeh RA. The epidemiology of histoplasmosis: a review. *Semin Respir Infect* 2001; 16: 109-118.
3. Wheat LJ, Freifeld AG, Kleiman AB, et al. Clinical practice guidelines for the management of patients with histoplasmosis: 2007 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2007; 45: 807-25.