

ANIMAL AND HUMAN HEALTH PREVENTION OPPORTUNITIES

Histoplasmosis in Montana — A New Fungal Frontier?

Histoplasmosis occurs among animals or humans following infection with the dimorphic fungus, *Histoplasma capsulatum*. Infection occurs after inhalation or ingestion of soil contaminated with *H. capsulatum*. The majority of infections in animals and humans are asymptomatic or result in mild illness not recognized as histoplasmosis. Clinical presentations are diverse and range from self-limited to severe disease requiring antifungal therapy. In the United States, *H. capsulatum* is endemic to the Mississippi and Ohio River valleys. The recognized endemic areas are not known to include the Rocky Mountain region. Animals and humans in Montana typically are diagnosed with histoplasmosis following recent travel to recognized endemic areas. During June 2012–November 2013, 6 unrelated human cases of histoplasmosis were reported among Idaho (n=1) and Montana residents (n=5) who had no recent travel to recognized endemic areas. (Table). During the past 7 years, histoplasmosis has also been diagnosed in a dog and cat without previous travel histories in Idaho and Wyoming, respectively. These case reports suggest *H. capsulatum* might exist in Montana and in other Rocky Mountain states.

In this issue of *Montana One Health*, we describe how histoplasmosis might be an emerging fungal disease in Montana, review diagnostic and treatment considerations, and remind Montana veterinarians and clinicians to consider the diagnosis.

Histoplasmosis in domestic dogs and cats

Clinical presentation

The incidence of histoplasmosis is equal among dogs and cats. Risk factors for infection include outdoor activities in endemic areas and disturbing nitrogen-rich soil that contains bird and bat excrement. Transmission of *H. capsulatum* from infected animals to humans is not known to occur, but common source infections involving both animals and humans is possible. Clinical presentation usually includes anorexia, weight loss, depression, diarrhea, dyspnea, and other non-specific signs. Clinical examination often reveals fever, tachypnea, coughing, emaciation, hepatosplenomegaly, and rarely dermal lesions.

Diagnostics

Fungal culture remains the gold standard for diagnosis, but takes 4–6 weeks and is non-sensitive. Diagnosis is often made using **cytology** of a peripheral blood smear, or after rectal scrapings or fine needle aspiration. If cytology is inconclusive, then **histopathology** might be required for diagnosis. For diagnosis in animals, **enzyme immunoassay (EIA)** or **polymerase chain reaction (PCR)** are associated with false negative results and not yet readily available. **Serology** is not recommended for use in animals.

Treatment and prognosis

Treatment for histoplasmosis typically includes oral azole antifungal agents for 4–6 weeks. Itraconazole is the preferred agent, but fluconazole is preferred if disease involves ocular lesions or the central nervous system. Severe disseminated disease often requires intravenous antifungal therapy for up to 60 days. Prognosis depends on the extent and severity of disease. Pulmonary infections usually have better outcomes compared with gastrointestinal or disseminated disease.

Animal cases in Montana

No known animal cases of histoplasmosis have occurred since at least January 1, 2009. Animals can be sentinels for human illness; therefore, knowledge of animal cases of

histoplasmosis can assist public health officials in increasing awareness for the disease in humans. Veterinarians who diagnose histoplasmosis in an animal without a history of travel to recognized endemic areas should report the case to the Department of Livestock by calling 406-444-2043.

Histoplasmosis in humans

Clinical presentation

The majority of infections are asymptomatic or result in mild illness not requiring a healthcare provider visit. The primary clinical presentation of histoplasmosis is pneumonia. The most common symptoms include fever, dyspnea, chest pain, and cough. Infected patients with immunocompromising conditions are at-risk for disseminated histoplasmosis. The clinical presentation of disseminated histoplasmosis often includes fever, chills, malaise, anorexia, and weight loss, but can have a wide range of signs based upon organ system involvement. Illness can progress to a severe sepsis syndrome.

Diagnostics

Fungal culture is the gold standard test but requires 4–6 weeks and is non-sensitive. Tissue biopsy with **histopathology** can be used to make a presumptive diagnosis, but specificity depends on pathologist experience. **Antibody testing** can be used to diagnose acute histoplasmosis. A four-fold change in titers indicates acute infection. Antibody testing should only be performed by reference laboratories experienced in this assay and is not useful in severe disease because of a delay in obtaining results. **Urine EIA** is a non-invasive, relatively sensitive, and specific assay for the diagnosis of histoplasmosis. While urine EIA is highly specific, false-positive results can occur in the presence of certain fungal infections (e.g., blastomycosis). Urine EIA can be used to follow the course of illness. **PCR** is not widely used for the diagnosis of histoplasmosis.

Treatment

Refer to the Infectious Disease Society of America (IDSA) treatment guidelines at <http://www.idsociety.org/organism/>.

Human cases in Idaho and Montana

Each of the recently reported histoplasmosis cases in Idaho and Montana occurred among patients with immunocompromising

conditions and without recent travel to known endemic areas (Table). However, 4 patients reported activities that likely increased their risk for *H. capsulatum* infection. Lack of travel to known endemic areas contributed substantial delays in diagnosis and initiation of treatment for 3 patients. Notably, 2 patients were diagnosed within 30 days of clinical presentation via the clinician's use of urine EIA. Clinicians should report any case of histoplasmosis not associated with recent travel to known endemic areas immediately to your local health department (ARM 37.114.203)

Table. Characteristics of human histoplasmosis cases reported in Idaho and Montana, 2012–2013

Characteristic	n (%)
No. cases	6
Male	3 (50)
Median age in years (range)	68 (17–79)
<i>State of residence (geographical area within state)</i>	
Idaho (southwest)	1 (17)
Montana (east [n=2], southwest [n=3])	5 (83)
Presence of immunocompromising condition	6 (100)
Hospitalized	3 (50)
Died	1 (17)
<i>Positive laboratory results contributing to diagnosis</i>	
Culture	2 (33)
Urine enzyme immunoassay	2 (33)
Histopathology*	2 (33)
Diagnosis delayed >6 months	3 (50)
<i>At-risk activities</i>	
Potting plants with bat guano-containing potting soil	1 (17)
Exploring caves	1 (17)
Mowing grass in pasture/attending a rodeo	1 (17)
Cleaning pigeon cages	1 (17)
None known	2 (33)
Travel to recognized endemic areas within 3 years of illness	0 (0)

*One patient with a culture positive for *Histoplasma capsulatum* also had histopathology results consistent with *H. capsulatum* infection (results not shown in table).

References available on web version. Visit <http://www.dphhs.mt.gov/publichealth/publications.shtml>.

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Histoplasmosis Key Points

Animal health

- Histoplasmosis cases have occurred among domestic animals in Idaho and Wyoming; none of the animals had recently traveled to areas recognized as being endemic for *Histoplasma capsulatum*.
- Montana veterinarians should consider the diagnosis of histoplasmosis among domestic dogs and cats with compatible clinical illnesses, even in the absence of known travel to recognized endemic areas.
- Because domestic animals can serve as sentinels for human infections, veterinarians should report histoplasmosis cases without recent travel to known endemic areas to the Department of Livestock at 406-444-2043.

Human health

- Histoplasmosis cases have been diagnosed among Idaho and Montana residents; none of the patients had recently traveled to areas recognized as being endemic for *H. capsulatum*.
- Montana clinicians should consider histoplasmosis as a diagnosis among patients with compatible clinical illnesses, even in absence of recent travel to known endemic areas.
- When testing for histoplasmosis, clinicians should consider using the urine enzyme immunoassay (EIA) for detection of *H. capsulatum* antigen; urine EIA is a non-invasive, sensitive, and highly specific assay.
- Clinicians should immediately report cases of histoplasmosis not associated with recent travel to endemic areas to your local health department. For more information, contact the Communicable Disease Epidemiology Section at 406-444-0273.