

epiTRENDS

A Monthly Bulletin on Epidemiology and Public Health Practice in Washington

Fungal Disease Awareness

August 14–18, 2017, is the nation's first Fungal Disease Awareness Week. This week is organized to highlight the importance of recognizing serious fungal diseases early enough in the course of a patient's illness to provide life-saving treatment.



Only a few fungal infections are notifiable conditions in Washington. Among these are two environmental fungal pathogens emerging in this region: *Cryptococcus gattii* and *Coccidioides immitis*. Other fungal pathogens requested for reporting but not currently known to be endemic to Washington include *Histoplasma* and *Blastomyces*. Outbreaks of any fungal disease are reportable.

Coccidioidomycosis

Coccidioidomycosis, or Valley fever (VF), is caused by infection with the *Coccidioides* fungus, which persists in the soil of warm, arid regions with low rainfall. Infection is generally caused by inhalation of pathogenic spores from disturbed soil or dust, such as through occupational tasks (construction, farming), recreational activities (ATV riding) or weather events (landslides, wind storms). Weather patterns and soil composition appear to affect infection rates. Other transmission routes for *C. immitis* include dirt inoculation directly into a wound, laboratory exposure, or organ transplantation. Recurrent disease resulting from latent infection can also occur. Because spores can easily aerosolize in the laboratory, handling *C. immitis* without correct biosafety measures can result in inhalation of the organism.

Based on community surveys in the Southwest United States through skin testing or serology, an estimated 60% of *Coccidioides* infections are asymptomatic or mild. Disease presentation varies, but in some cases can be severe, including chronic pulmonary disease or disseminated

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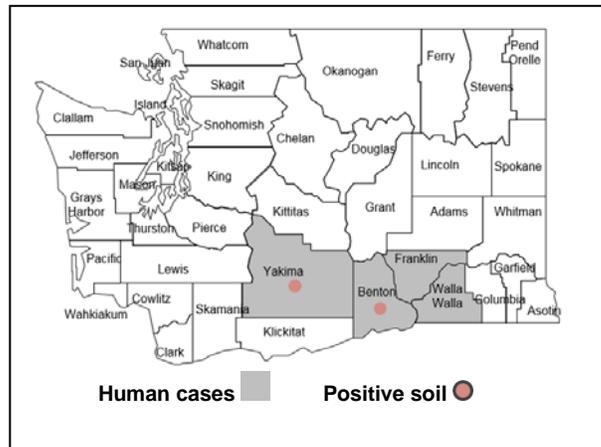
disease. Erythema nodosum or erythema multiforme rash can occur. About 1% of cases have disseminated infection to bones, joints, soft tissues, or the brain. Provider knowledge and clinical suspicion of coccidioidomycosis is vital to timely diagnosis and treatment; the early manifestations of coccidioidomycosis may mimic other respiratory ailments, including influenza-like illness and community-acquired pneumonia. Persons aware of Valley fever before seeking healthcare are more likely to request testing for *Coccidioides* and more likely to receive an earlier diagnosis.

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Diagnosis of coccidioidomycosis is based on serology, histopathology with special stains, or fungal culture. Any positive serology is generally considered a marker for current or recent infection but false negatives may occur in up to a third of confirmed cases. Cultures are encouraged with submission of isolates for further strain typing. Laboratories should take appropriate precautions when handling fungal cultures.

Management of patients with coccidioidomycosis depends on the extent of the infection and presence of risk factors for severe disease. Localized acute pulmonary disease is generally self-limiting and requires only reassessment to demonstrate resolution of symptoms. Extensive or disseminated infection or risk factors for severe disease are indications for treatment, possibly including antifungal drugs such as fluconazole or amphotericin B, surgical debridement, or a combination.

Coccidioidomycosis is an emerging infection in Washington State. As of August, 2017, twelve confirmed cases with suspected or confirmed local exposures have been identified, all in south-central Washington. Among these cases, two deaths were reported. Locally-acquired cases of coccidioidomycosis in Washington have had higher rates of hospitalization and death and longer times to diagnosis compared to infections acquired in other endemic regions. As the majority of people infected with *Coccidioides* are asymptomatic or have only mild illness, and the majority of illness

self-resolves, it is likely that only the most severe cases of coccidioidomycosis with exposure in Washington are being identified and reported to public health authorities. The main risk factor for Valley fever among Washington residents remains travel to the Southwest.

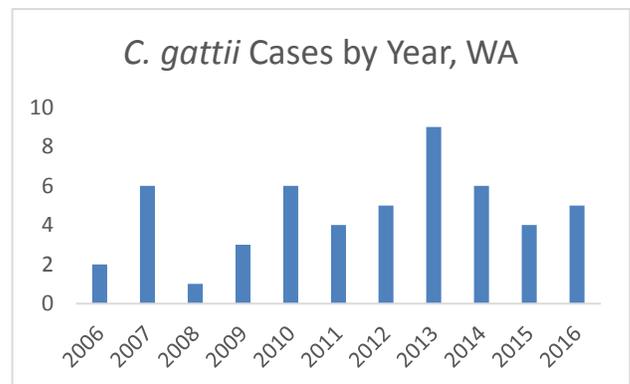
Environmental sampling efforts have identified the fungus in soil from Benton and Yakima counties; limited sampling has been done in other Washington counties, so the geographic range of the organism is still undefined. Domestic and wild animals can be affected, and dogs and a horse without travel outside Washington have been diagnosed with coccidioidomycosis.

Cryptococcus gattii

Of the several dozen known *Cryptococcus* species only a few have been identified as human pathogens. *Cryptococcus neoformans* causes the majority of cryptococcal disease in humans, acting as an opportunistic pathogen in people with weakened immune systems. *Cryptococcus gattii* was more recently identified as a pathogen, affecting both healthy persons and those with weakened immune systems. It is an environmental fungus initially associated with eucalyptus trees in tropical and subtropical areas. The organism was first recognized as causing illness during a 1999 outbreak on Vancouver Island, British Columbia. Subsequent environmental studies found *C. gattii* when sampling trees, soil, air, and water from Vancouver Island, mainland British Columbia, Washington, and Oregon. The endemic area is now thought to extend along the Pacific Coast.

Most clinical infections with *C. gattii* occur as pneumonia, causing severe prolonged cough, fever, and shortness of breath. Infection can result in meningitis which is fatal unless treated. Large mass lesions (cryptococcomas) can develop in the lung, brain, or muscle; organs such as the kidneys, prostate, bone, and skin can also be affected. Asymptomatic infections occur, for example, previously unsuspected cryptococcomas found during imaging studies done for other reasons.

Feline cases of *C. gattii* infection were detected in 2005 in Washington with the first human case in Washington in 2006. As of August, 2017, 52 human cases, including seven deaths, and 60 animal cases have been identified in the state. Most cases were residents of northwestern counties, although travel to an endemic area creates a risk for anybody. In the Pacific Northwest, infected domestic and wild animals include dogs, cats, ferrets, pet birds, horses, sheep, elk, and porpoises.



Clinical suspicion is important in identifying a cryptococcal infection, a particular challenge in a person without obvious risk factors. Cryptococcal meningitis is suggested from microscopic examination of cerebral spinal fluid (CSF) mixed with India ink, revealing fungal forms having outer capsules. Cryptococcal antigen in serum or CSF establishes a preliminary diagnosis. Confirmation is via histopathology or culture. Standard clinical diagnostic methods do not distinguish *C. gattii* and *C. neoformans*; speciation is done on a culture. Genotyping provides useful information about genetic changes and geographic distribution. To assist with speciation and additional typing, cryptococcal isolates not specifically identified as *C. neoformans* should be submitted to Washington State Public Health Laboratories for speciation. Surveillance in

Washington is only for *C. gattii*, so an infection that is confirmed as *C. neoformans* is not reportable.

Those infected with *C. gattii*, including people with identified asymptomatic infections, are treated with prescription antifungal medication. Type and duration of treatment depends on severity of infection and body region affected, but could include fluconazole (for asymptomatic and mild infections) or amphotericin B (for severe infections). Surgery may be required to remove cryptococcomas. Since the incubation period can be long, determining exposure location may be difficult. Local health jurisdictions can report cases through PHIMS as a Rare Disease of Public Health Significance and should also complete the supplemental CDC case report form.

Other Fungal Pathogens

Histoplasma and *Blastomyces* are soil fungi found in central and eastern states. The associated diseases, histoplasmosis and blastomycosis, are similar to coccidioidomycosis in that the majority of infections are asymptomatic or mild. Some people infected with *Histoplasma* may experience severe lung disease that can spread to other parts of the body, including the central nervous system. Likewise, infection with *Blastomyces* can sometimes be severe, and may spread to the skin and bones. Laboratory tests for *Histoplasma* antigen can cross-react with *Coccidioides* antigen, so fungal culture and detailed travel history are important for accurate diagnosis. Rare cases of histoplasmosis without travel history have been reported in Washington, raising concern that local acquisition is possible. Further data is needed to ascertain whether *Histoplasma* exists in the environment in Washington. Local health jurisdictions can report cases through PHIMS as a Rare Disease of Public Health Significance.

Public health agencies have an essential role in characterizing emerging diseases. Information provided by local health jurisdictions in Washington has improved our understanding of fungal pathogens in our state.

Healthcare providers should be aware which fungal infections can be acquired in Washington. We encourage healthcare providers and their patients to “**Think Fungus**” when symptoms of infection do not get better with treatment.

