

# *epi*TRENDS

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## Fungal Pathogens

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Only a few of the notifiable conditions in Washington State are fungal infections. Among these are two fungal pathogens emerging in this region: *Cryptococcus gattii* and *Coccidioides immitis*.

### *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. It is an environmental fungus initially associated with eucalyptus trees in tropical and subtropical areas. In 1999 the organism was first recognized as causing illness during an 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 may 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 can develop in the lung, brain, or muscle (cryptococcomas); 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.

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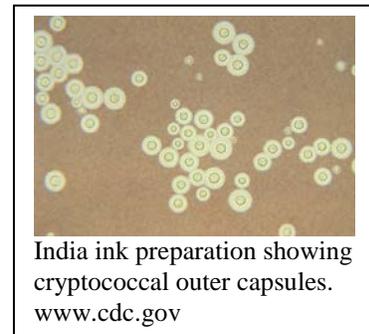
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Feline cases of *C. gattii* infection were detected in 2005 in Washington with the first human case in Washington in 2006. As of July, 2015, 44 human cases (including six deaths) and 59 animal cases have been identified in the state. Pneumonia accounted for 39% of human cases, meningitis for 33%, and 4% had both pneumonia and meningitis. The overall case fatality rate was 14%. 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. Surveillance 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.

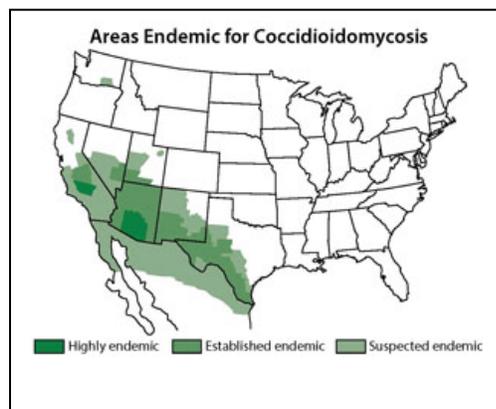
Since the incubation period can be long, determining exposure location may be difficult. Of Washington's 44 human *C. gattii* cases, 16 did not travel out of state during their exposure period or only traveled to areas not known to be endemic, indicating likely in-state acquisition. An additional 11 residents had limited travel and were probably exposed in Washington. 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.

## ***Coccidioides***

Infection with *Coccidioides* species results in coccidioidomycosis, commonly called Valley fever. *Coccidioides* are fungi that persist in the soil of warm arid regions. Infection is generally through inhaling spores but can also result from wound contamination or organ transplant. Disturbing soil, such as through construction, farming, wind, or landslides, causes the spores to become airborne. Weather patterns and soil composition appear to affect infection rates.

Based on community surveys through skin testing or serology, an estimated 60% of *Coccidioides* infections are asymptomatic or mild. Illness may occur as pneumonia or localized wound infections. Erythema nodosum or erythema multiforme rash can occur. About 1% of cases have disseminated infection to bones, joints, soft tissues, or the brain.

Diagnosis of coccidioidomycosis is based on serology, histopathology with special stains, or fungal culture. All 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.



In Washington State, coccidioidomycosis typically was associated with exposures in southwestern states. As of July 2015, nine confirmed cases with suspected or confirmed local exposures have been identified, all in south-central Washington. Environmental sampling efforts have identified the fungus in soil from Benton County; 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.

## **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 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. No cases with exposure to these pathogens in Washington have been identified. Local health jurisdictions can report cases through PHIMS as a Rare Disease of Public Health Significance.

*Cryptococcus gattii* and *Coccidioides immitis* are rare but potentially severe pathogenic fungi endemic to Washington. Many healthcare providers are unfamiliar with these notifiable infections and may need assistance with diagnosis and laboratory testing. Office of

Communicable Disease Epidemiology can assist with investigation of suspected or confirmed cases. The DOH Zoonotic Disease Program can be consulted regarding infections in animals.

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.

## Resources

*C. gattii* in the Pacific Northwest: [http://wwwnc.cdc.gov/eid/article/15/8/08-1384\\_article](http://wwwnc.cdc.gov/eid/article/15/8/08-1384_article)

Medical management of cryptococcosis:

<http://cid.oxfordjournals.org/content/50/3/291.full.pdf+html>

Identification of *C. immitis* in Washington:

<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6320a3.htm>

Medical management of coccidioidomycosis:

<http://cid.oxfordjournals.org/content/41/9/1217.full.pdf+html>