DOH 420-146

# Washington State Annual Report on Fungal Disease, 2014

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Office of Communicable Disease Epidemiology

Washington State Department of Health

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# Executive Summary

Only a few fungal infections are reportable to the Washington State Department of Health (DOH); outbreaks of fungal disease are also reportable. This report summarizes surveillance data through 2014 for reportable fungal pathogens. Among these are two fungal pathogens emerging in this region: *Cryptococcus gattii* and *Coccidioides immitis*. Other fungal pathogens reportable to DOH but not known to be endemic to Washington include *Histoplasma* and *Blastomyces*.

Fungal diseases are a public health concern because of increasing numbers of people with weakened immune systems who may be more susceptible to severe fungal infections, alternations in the environment related to climate change that may be affecting soil habitats of fungi, and changes in healthcare practices that many provide opportunities for new and drug-resistant fungi to emerge in healthcare settings.

*Cryptococcus gattii* is an environmental fungus that has been isolated from native trees, soil, and air in the Pacific Northwest. In 1999 the organism was first recognized as causing human illness in the region during an outbreak on Vancouver Island, British Columbia. Exposure is through inhalation of spores from the environment. *Cryptococcus* is not transmissible from person to person or animal to person. Infection with *Cryptococcus gattii* can cause variable symptoms, such as severe cough with shortness of breath, fever or chills, night sweats, and loss of appetite. Asymptomatic infections can occur; typical presentations are meningitis and pneumonia. Treatment is with antifungals, and may need to be continued for many months.

In 2006, the first human case was detected in Washington. Surveillance has found the majority of cases occur west of the Cascade Range. Only three cases have been reported in counties east of the Cascades and two of these case-patients had extensive travel histories. Over 40% of cases reported in Washington reside in Whatcom County. Since the first identification of human cases of *C. gattii* in 2006, DOH has received between two and ten case reports each year.

*Coccidioides immitis* is an environmental fungus that grows in soil and becomes airborne when the soil is disturbed. Exposure is generally through inhalation of spores from the environment; infection from handling of laboratory cultures can also occur. Coccidioidomycosis is not transmissible from person to person or animal to person. Most infections with *Coccidioides* are subclinical, with no or mild symptoms. Approximately 40% of infections are symptomatic; these cases generally present with fever, fatigue, cough, headache, night sweats, myalgias, or rash. Self-limiting pneumonia is the most common presentation; some patients fail to recover and develop complications or chronic pulmonary disease. Treatment is with antifungals and may need to be continued for many months or possibly life.

During 2010-2011, the first three endemically acquired cases of coccidioidomycosis in Washington were recognized. State-wide surveillance started in April 2014. A unique clade of *Coccidioides* was found to be endemic in a small region of south-central Washington but the geographic range of the fungus is still not fully understood.

# Introduction: *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. It acts as an opportunistic pathogen and most cases of infection occur in people who have weakened immune systems. Another *Cryptococcus* species, *C. gattii,* was more recently identified as causing illness in people with both normal and weakened immune systems. *C. gattii* is an environmental fungus initially associated with eucalyptus trees in tropical and subtropical areas. In 1999 the organism was first recognized as causing human illness in the Pacific Northwest during an outbreak on Vancouver Island, British Columbia. Subsequent environmental studies found the organism in sampled trees, soil, air, and water from Vancouver Island, mainland British Columbia, Washington, and Oregon. The endemic area probably extends along the Pacific Coast.

Most clinical infections with *C. gattii* occur as pneumonia, with symptoms including severe prolonged cough, fever, and shortness of breath. Infection can result in meningitis which is fatal unless treated. Large mass lesions in the lung, brain, or muscle (cryptococcomas) can develop; infections can also affect other organs such as the kidneys, prostate, bone, and skin. In published studies, mortality rates range from 13-33%. The incubation period of *C. gattii* is not well established; symptoms generally begin 2-13 months after exposure with an average of 6-7 months. Asymptomatic infections can occur, for example previously unsuspected cryptococcomas found during imaging studies done for other reasons. Clinical suspicion is important in identifying the cause of a cryptococcal infection, which can be particularly challenging in a person without obvious risk factors.

People who are infected with *C. gattii*, including people identified with asymptomatic infections, need to take prescription antifungal medication. The type and length of treatment depends on the severity of infection and the parts of the body that are affected, but could

include fluconazole (for asymptomatic or mild infections) or amphotericin B (for severe infections). Some people may require surgery to remove cryptococcomas.

Surveillance in Washington is only for *C. gattii*, so an infection confirmed as *C. neoformans* is not reportable. Healthcare providers and laboratories are required to report a case of or positive test result for *C. gattii* infection to the local health jurisdiction within 24 hours.

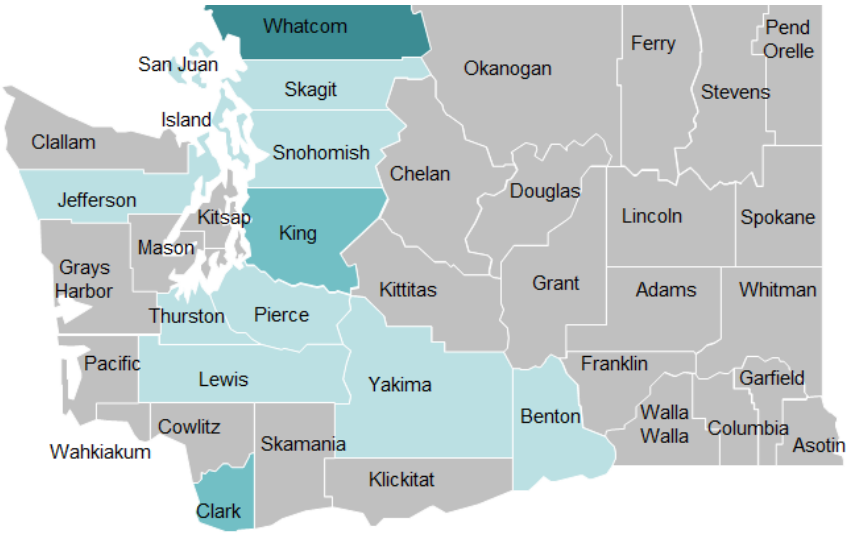
## Epidemiology in Washington

After the initial outbreak of human cases in Canada, feline cases of *C. gattii* infection in Washington were detected in 2005. The first identified human case of *C. gattii* infection in Washington was in 2006. The majority of cases occur west of the Cascade Range; only three cases have been reported in counties east of the Cascades and two of these case-patients had extensive travel histories. Over 40% of cases reported in Washington reside in Whatcom County. Since the first identification of human cases of *C. gattii* in 2006, Washington State Department of Health (DOH) has received between two and ten case reports each year. During 2014, six cases were reported to DOH, including one death.

**Table 1: Reported *C. gattii* Cases by Year of onset**

| Year | Reported Cases |
|---|---|
| 2006 | 2 |
| 2007 | 6 |
| 2008 | 2 |
| 2009 | 3 |
| 2010 | 5 |
| 2011 | 4 |
| 2012 | 5 |
| 2013 | 10 |
| 2014 | 6 |

**Figure 1: Confirmed cases of *C. gattii* infection, 2006-2014**

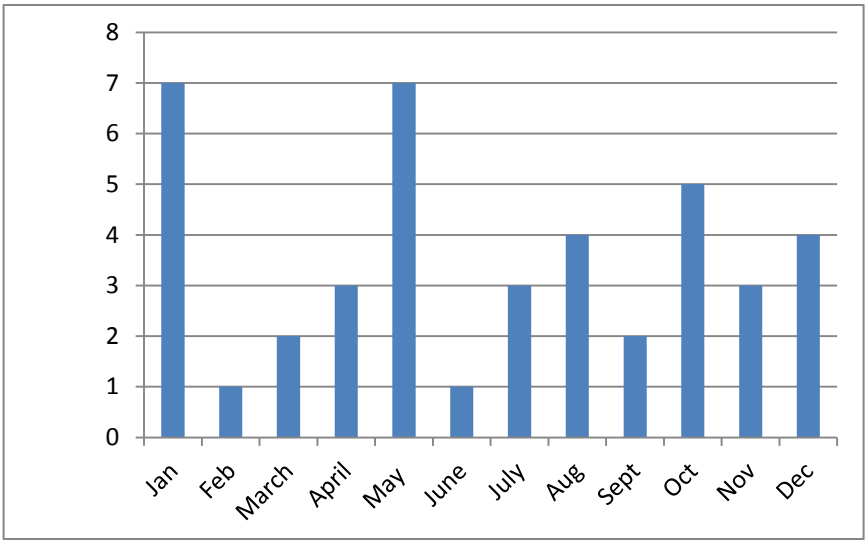


Approximately two-thirds of all cases to-date were reported by laboratories; likewise, in 2014, 67% of cases were reported by laboratories. Cases were reported by six counties in 2014: Whatcom, Skagit, Snohomish, Thurston, Clark, and Pierce counties.

Since the incubation period can be prolonged, determining timing and location of an exposure may be difficult. Of the 43 human cases in Washington reported 2006-2014, 15 residents did not travel out of state during their exposure period or only had travel to areas not known to be endemic for *C. gattii*, indicating likely in-state acquisition. An additional 10 residents had limited travel and were likely exposed in Washington, but exposure could not be determined with certainty. The remaining 18 cases were likely exposed in other endemic areas, such as British Columbia, Oregon, or California, or during international travel.

In 2014, the age of reported *C. gattii* cases ranged from 29 to 68 years, with a median age of 51 years. Sixty-seven percent of cases were male. For 2006-2014, the age of reported cases ranged from 10 to 76 years with a median age of 50 years; overall 56% of reported cases are male. No clear seasonal pattern emerges when looking at case counts by onset month.
Pneumonia accounts for 39% of the human cases, meningitis for 33%, and 4% had both pneumonia and meningitis. Of the 43 human *C. gattii* cases reported in Washington through 2014, seven deaths have been reported, giving a case fatality rate among all cases of 16%. In 2014, 67% of cases were hospitalized and one case died. Overall, 77% of reported cases are hospitalized.

**Figure 2: *C. gattii* Case Count by Month of Onset, 2006-2014**



# Introduction: *Coccidioides immitis*

Infection with *Coccidioides* species results in coccidioidomycosis, commonly called Valley fever. *Coccidioides* are fungi that persist in the soil of warm arid regions with low rainfall. Infection is generally caused by inhalation of pathogenic spores from the environment, but can also be from wound contamination or organ transplant. Disturbed soil, such as through construction, farming, recreational activities, wind, or landslides, cause the spores to become airborne. Weather patterns and soil composition appear to affect the ability of the environmental form of the fungus to survive.

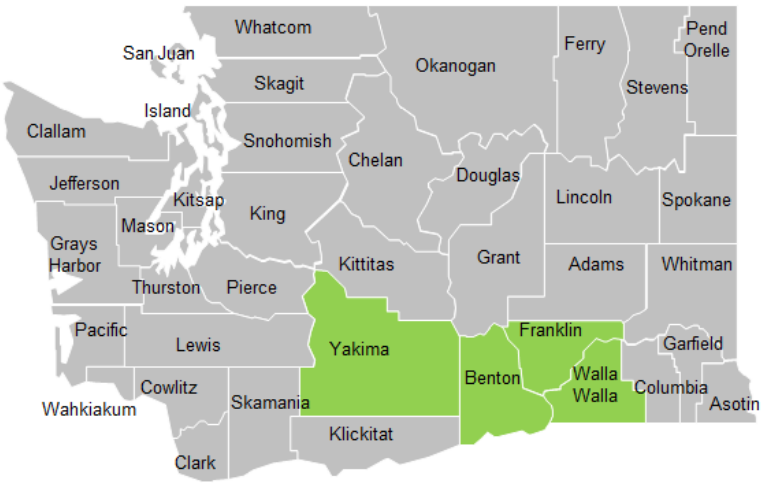
Based on community surveys through skin testing or serology in endemic areas, an estimated 60% of *Coccidioides* infections are asymptomatic or only have mild symptoms. Illness may occur as pneumonia, an influenza-like illness, or localized wound infections. Erythema nodosum or erythema multiforme rash can occur. About 1% of cases have disseminated infection to bones, joints, soft tissues, and the central nervous system. Increased risk for disseminated disease also occurs for persons with weakened immune systems caused by HIV infection, diabetes, pregnancy, organ transplants, or chronic corticosteroid therapy. Men have a higher rate of dissemination and several studies indicate that African Americans and Filipinos are also at higher risk.

In Washington State, coccidioidomycosis was considered a travel-associated condition occurring mainly in people who spent winters in southwestern states. The first identification of endemically acquired coccidioidomycosis in Washington occurred in 2010. Environmental sampling efforts have identified the fungus in the soil of Benton County; limited sampling has been completed in other Washington counties, and the geographic range of the organism is yet to be defined. Whole genome sequencing has identified a unique Washington clade differing from those in the southwestern United States.

Domestic and wild animals can be affected by *Coccidioides*, and dogs and a horse without travel outside Washington have been diagnosed with the disease. Surveillance in Washington is for both *Coccidioides* species, although only *Coccidioides immitis* is thought to be endemic in the state. Washington healthcare providers and laboratories are required to report a case of or positive test result for coccidioidomycosis to the local health jurisdiction within 24 hours.

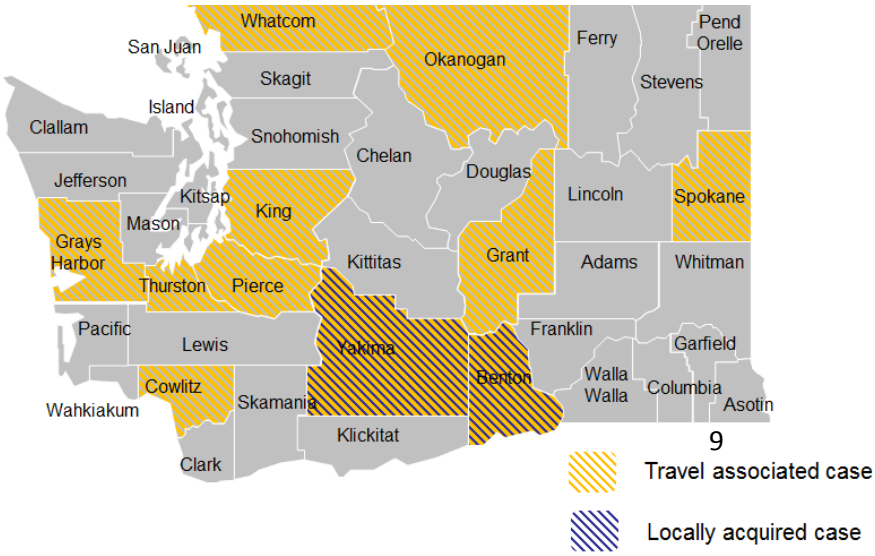
## Epidemiology in Washington

The first endemically-acquired human case of coccidioidomycosis was recognized in 2010. Three counties in Washington made coccidioidomycosis a reportable condition in 2011: Benton, Franklin, and Walla Walla counties. In April 2014, coccidioidomycosis was made reportable statewide. All cases thought to be endemically acquired have been reported from four counties in south-central Washington. Prior to 2014, cases of coccidioidomycosis were reported sporadically, but no standardized reporting procedure was in place.




During 2014, 21 cases were reported to DOH. Approximately two-thirds of all 2014 cases were reported by laboratories. Of the 21 cases, 18 were travel-related and 3 were exposed in south-central Washington. Exposure in Washington is determined in one of two ways: 1) if the case has acute onset of disease with limited or no recent travel history to an endemic

**Figure 4: Counties Reporting Coccidioidomycosis Cases, 2014**



area, 2) if an isolate is available for a case and it matches the Washington clade as determined by whole genome sequencing.

Cases are interviewed to determine detailed travel history; among the 18 travel-related cases in 2014, 5 reported travel to California, 7 reported travel to Arizona, one reported travel to Mexico, one reported travel to the US Southwest, and the remaining 4 cases had unknown location of exposure.

**Table 2: Characteristics of Coccidioidomycosis Cases, 2014 (N=21)**

| | | N (%) |
|---|---|---|
| **Gender** | Male | 17 (81) |
| | Female | 4 (19) |
| **Age Category** | Age 0-19 | 1 (5) |
| | Age 20-39 | 4 (19) |
| | Age 40-59 | 5 (24) |
| | Age 60+ | 11 (52) |

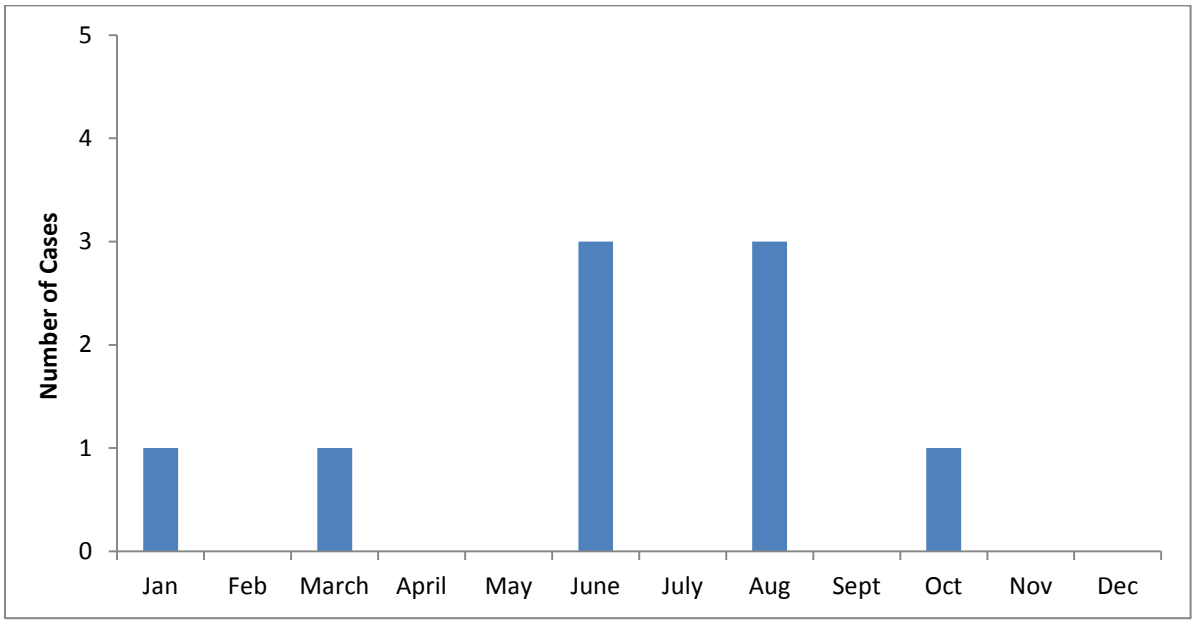
In 2014, the age of reported coccidioidomycosis cases ranged from 18 to 82 years with a median age of 60 years. Eighty-one percent of cases were male.

Of the 9 endemically acquired cases reported during 2010-2014, ages ranged from 12 to 59 years with a median age of 54 years. Eighty-nine percent of these cases were male. This epidemiology differs from what has been reported elsewhere; on average, men represent 55-66% of cases, although male gender is also a risk factor for severe or disseminated disease. It is likely that only very severe cases of coccidioidomycosis are being identified and reported; this may

explain some of the discrepancy, along with small numbers.

There have been too few endemically acquired cases reported to determine if there is a clear seasonal pattern; two-thirds of cases had symptom onset during June or August.

**Figure 5: Cases of Locally Acquired Coccidioidomycosis by Month of Onset, 2010-2014**




Of the 9 locally acquired cases reported in Washington through 2014, one death was reported. Pneumonia accounts for 78% of cases, meningitis for 11%, and cutaneous wound infection for 11%. Two-thirds of cases were hospitalized. In 2014, 52% of all reported cases were hospitalized and three cases (14%) died.

Nationally, coccidioidomycosis is described as “rarely lethal,” with less than 1% of all infections leading to death. Investigations in Arizona indicate that about 40% of coccidioidomycosis cases require hospitalization. In comparison, Washington cases have higher rates of hospitalization and death, indicating there may still be deficiencies in reporting of less-severe cases. Ongoing provider and public education may increase reporting over time as awareness of this emerging infection grows.

# Other Fungal Pathogens

*Histoplasma* and *Blastomyces* are environmental fungi found in the soil in central and eastern states; these fungi are not known to be endemic in Washington. Both diseases caused by these organisms, histoplasmosis and blastomycosis, are similar to coccidioidomycosis in that the majority of infected people will not experience symptoms, or will have only mild symptoms. 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 the collection of a detailed travel history are important for accurate diagnosis. No cases with exposure to these pathogens in Washington have been definitively identified. No cases of histoplasmosis or blastomycosis were reported in 2014. Local health jurisdictions in Washington State can report cases or suspected outbreaks of fungal disease through PHIMS as a Rare Disease of Public Health Significance.

## Acknowledgments

Case follow-up and reporting by local health jurisdictions is vital to fungal disease surveillance in Washington State. Case reporting by providers and laboratories is likewise key. All staff at local health jurisdictions are acknowledged for their contributions to data collection and data entry. Funds and technical assistance from CDC supported this work.

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