



# **Coccidioidomycosis (San Joaquin Valley Fever, Valley Fever, Desert Fever)**

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## **Disease Plan**

### **Quick Links:**

<http://www.cdc.gov/fungal/diseases/coccidioidomycosis/index.html>

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Last updated: February 25, 2016, by Randon Gruninger

**Questions about this disease plan?**

**Contact the Utah Department of Health Bureau of Epidemiology: 801-538-6191.**

## ✓ WHY IS COCCIDIOIDOMYCOSIS IMPORTANT TO PUBLIC HEALTH?

Valley Fever, also called coccidioidomycosis, is an infection caused by the fungus *Coccidioides*. The fungus is known to live in the soil in the southwestern United States, parts of Mexico, and Central and South America. In Utah, the fungus is known to live in the soil of Washington and Uintah counties. Surveillance of coccidioidomycosis infections in Utah is important to track the extent of the fungus in the different counties, differentiate between locally acquired and imported cases of coccidioidomycosis, and to monitor trends in Utah.

## ✓ DISEASE AND EPIDEMIOLOGY

### Clinical Description

After infection, a wide spectrum of manifestations is possible; it is estimated that more than 50% of infected cases develop symptoms. Typically, coccidioidomycosis first infects a person's lungs. Most people with symptomatic disease will develop a moderate influenza-like illness or pneumonia-like febrile illness with one or more of the following symptoms: chest pain, cough, fever, headache, myalgia (muscle pain), arthralgia (joint pain), and rash (erythema nodosum or erythema multiforme). Other symptoms may include: fatigue, sore throat, shortness of breath (dyspnea), and sputum production (hemoptysis). Symptoms may last for weeks to months, and the majority of infections will resolve without specific antifungal therapy. A smaller proportion of infections result in chronic pulmonary or extrapulmonary infections.

Although coccidioidomycosis primarily involves the pulmonary system, chest x-rays are unremarkable in up to 50% of cases. Dissemination of the disease can occur. Approximately 1/1,000 cases of coccidioidomycosis will progress to disseminated coccidioidomycosis, which is the most severe form of the disease. Disseminated disease forms lesions in the lung and abscesses throughout the body. These abscesses tend to form in the subcutaneous tissues, skin, bone, and the central nervous system (the brain and spinal cord) causing infections such as meningitis and bone and joint infections. There is an increased risk of dissemination for those with HIV infection, diabetes, organ transplants, Hodgkin's disease, chronic corticosteroid therapy, and those who are pregnant. Several studies have shown that men and people of African or Asian descent are also at higher risk.

### Causative Agent

Coccidioidomycosis is caused by spores of a fungus called *Coccidioides* that grows in soil in areas of low rainfall, high summer temperatures, and moderate winter temperatures. Two species of *Coccidioides* fungus have been found, *Coccidioides immitis* and *Coccidioides posadasii*. The spectrum of disease caused by the two species of *Coccidioides* fungus are indistinguishable, and laboratories are not routinely able to determine species. For this reason, it is simplest to refer to all isolates as *Coccidioides* species.

## Differential Diagnosis

The differential diagnosis for coccidioidomycosis includes other fungal infections, lymphoma, tuberculosis, and other granulomatous infections.

## Laboratory Identification

Multiple methods for diagnosing coccidioidomycosis are available.

Recommended commercially available tests to aid in the diagnosis of coccidioidomycosis include serology, histopathology with special stains, or fungal culture.

IgM antibodies are detectable in approximately 50% of patients one week after symptom onset and approximately 90% by three weeks after symptom onset. IgG antibodies are generally detectable by 4-6 weeks after symptom onset, and 85-90% of patients have detectable IgG by three months after symptom onset. Antibodies generally do not persist for more than several months to a year, but may occasionally last longer in association with a pulmonary cavity or disseminated disease. All serology is generally considered acute testing and a marker for current or recent infection. While false positives are rare, false negatives may occur in up to a third of confirmed cases. Therefore, negative serologic results do not rule out coccidioidal disease. One study reported approximately 5% of immunocompromised patients with coccidioidomycosis are seronegative.

<b>Coccidioidomycosis Serological Test Interpretation</b>	
IgM or IgG ELISA	Less than testing platform threshold is <b>Negative</b>
	Greater than negative threshold, but less than positive threshold is <b>Equivocal</b> . Repeat testing in 10-14 days may help eliminate an equivocal result.
	Greater than testing platform threshold is <b>Positive</b> .
ID	<b>Immunodiffusion (ID)</b> measures IgM and a positive result may suggest active or recent infection. Serum precipitins** may be detected within 1-3 weeks after the onset of primary infection, but are rarely detected 6 months after infection. Precipitins may reappear with relapse or persist in disseminated cases. IgG antibody may also be detected.
CF	Any titer suggests past or current infection. Greater than 30% of cases with chronic residual pulmonary disease have negative CF test results. Titers of less than 1:32 or 1:2 may indicate past infection or self-limited disease. Titers greater than or equal to 1:32 may indicate disseminated infection.  <b>Single antibody titers are generally not diagnostic, paired samples are preferred. Acute and convalescent samples drawn at least 21 days apart, showing at least a fourfold rise in titer, are diagnostic.</b>  With <i>Coccidioides</i> complement fixation (CF) tests, there can be false positive testing in patients with other fungal diseases such as histoplasmosis and blastomycosis, and false negative tests in people with single lung masses from coccidioidomycosis.

\*\*An antibody that under suitable conditions combines with and causes its specific and soluble antigen to precipitate from solution.

Cerebrospinal fluid (CSF) should be tested in patients with suspected or diagnosed meningitis.

Fungal culture can be performed on respiratory secretions (sputum, bronchoalveolar lavage (BAL)), normally sterile fluids (e.g., pleural, peritoneal), tissues (fine needle aspirates or biopsies of the lung, brain, skin), or abscesses. If a culture isolate is available, submit to the Utah Public Health Laboratory (UPHL) to be forwarded to CDC for sequencing. Sequencing can determine if the strain matches, or is similar to, other strains found in the southwest United States.

Other tests that can be performed, but are not widely available include urine antigen (available at MiraVista labs only) and PCR testing (not FDA-approved; only done on sputum or tissue).

A positive skin test (spherulin) indicates prior exposure and infection with the fungus. Because reactivity is life-long, skin tests are not generally helpful in diagnosing current infection, but can help determine whether a person is at risk of infection. A conversion from negative to positive after onset of symptoms is considered laboratory evidence of disease.

Whole genome sequencing of the organism can provide useful information about genetic changes, and also help link coccidioidomycosis cases to geographic areas.

## **Treatment**

Mild cases of coccidioidomycosis usually resolve without treatment. However, treatment may shorten the course of illness, or prevent complications to prevent severe cases. Opinion varies about the most relevant factors to consider when judging the severity of illness and necessity of treatment. Commonly used indicators are:

- greater than 10% loss of body weight
- night sweats persisting longer than three weeks
- infiltrates involving more than half of one lung or portions of both lungs
- prominent or persistent hilar adenopathy
- anti-coccidioidal complement fixing antibody concentrations in excess of 1:16
- failure to develop dermal hypersensitivity to coccidioidal antigens
- inability to work
- symptoms persisting for more than two months.

The most frequently used oral antifungals are fluconazole and itraconazole. Surgical removal of cavities in the lung and drainage of abscesses in bones or joints is sometimes necessary. The duration of treatment for uncomplicated primary coccidioidal infection generally ranges from three to six months.

Specific treatment guidance published by the Infectious Disease Society of America (2005) can be found here: <http://cid.oxfordjournals.org/content/41/9/1217.full.pdf+html>.

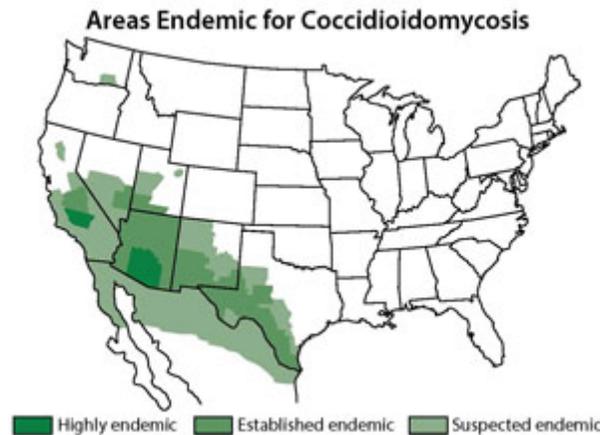
## Case Fatality

Case fatality rate estimates range from 12-17%. Coccidioidal meningitis, the most serious form of disseminated disease, is almost always fatal within two years of diagnosis if left untreated.

## Reservoir

*Coccidioides* lives in dust and soil in some areas in the southwestern United States (U.S.), Mexico, and South America. In the U.S., *Coccidioides* lives in Arizona, California, Nevada, New Mexico, Texas, and Utah. In 2010, the fungus was found in south-central Washington, an area not previously known to have *Coccidioides*.

This map shows the approximate areas (called “endemic areas”) where *Coccidioides* is known to live, or is suspected to live, in the U.S. and Mexico. Much of what is known about where the fungus lives in the southwestern U.S. is based on studies performed in the late 1940s and early 1950s.



## Transmission

Anyone who is around dust-producing activities where soil or other materials contaminated with *Coccidioides* species are located can get coccidioidomycosis if enough spores are inhaled. People can be exposed to *Coccidioides* species spores during recreational or occupational activities including digging, farming, construction work, driving off-road vehicles, riding ATVs, biking, camping, and hiking. Living in, or traveling through, an endemic area can lead to an exposure and illness.

## Susceptibility

Anyone can get coccidioidomycosis. Lifelong immunity almost always develops following infection. Some people can have the infection come back again (a relapse) after getting better the first time, but this is very rare.

## Incubation Period

Symptoms of disease usually start within one to four weeks after exposure. Disseminated disease may develop years after the primary infection (even when the primary infection was so mild that the patient does not remember having it).

## Period of Communicability

The fungus that causes coccidioidomycosis cannot be spread from the lungs between people or animals. However, in extremely rare instances, a wound infection with *Coccidioides* can spread infection to someone else. The infection may also be spread through organ transplant of an infected organ.

## Epidemiology

*Coccidioides* species grow in arid and semiarid areas of the Western Hemisphere. In the U.S., this range extends from California to southern Texas, and includes parts of Utah. The soil conditions in southern Utah are well suited for growing the *Coccidioides* species. From 2008-2013, an average of 51 cases of coccidioidomycosis were reported to the Utah Department of Health (UDOH) each year. The number of cases reported in 2013 and 2014 were slightly lower than the number reported in the previous two years.

## ✓ PUBLIC HEALTH CONTROL MEASURES

### Public Health Responsibility

- Investigate all suspect cases of disease; fill out and submit appropriate disease investigation forms.
- Provide education to the general public, clinicians, and first responders regarding disease transmission and prevention.
- Identify clusters or outbreaks of this disease and determine the source.
- Identify cases and sources of infection to prevent further transmission.
- Identify and evaluate laboratory personnel handling a *Coccidioides* culture. If a *Coccidioides* culture was handled outside of a biological safety cabinet, a list of all persons present in the room should be collected.

### Prevention

The best way to prevent exposures to *Coccidioides* species is to avoid situations where soil that might be contaminated can be inhaled. People living in endemic areas can help prevent illness through decreasing the amount of dust in their environment; this may be accomplished by installing air conditioning, pouring asphalt, or planting grass. It should be noted that these measures will help decrease dust, but will not eliminate *Coccidioides* species from the environment.

Education about the possibility of acquiring infection through exposure to dust or soil, and providing the recommendation to avoid activities that increase the likelihood of dust inhalation (e.g., recreational activities, construction, archaeological digs), is particularly important for

patients at high risk of severe infection (e.g., immunocompromised patients, pregnant women, African Americans, Filipinos, and those with diabetes). It is critical to encourage people who may be exposed to *Coccidioides* species to consult a healthcare provider for early diagnosis and treatment if symptoms develop.

## **Chemoprophylaxis**

There are no chemoprophylaxis agents for coccidioidomycosis cases. Refer to prevention strategies above.

## **Vaccine**

A coccidioidomycosis vaccine is not currently available.

## **Isolation and Quarantine Requirements**

There is no need for patient isolation or quarantine restrictions.

# **CASE INVESTIGATION**

## **Reporting**

All cases of coccidioidomycosis should be reported to public health.

## **Case Definition**

### **Coccidioidomycosis (*Coccidioides species*) (2011)**

#### **Clinical description**

Infection may be asymptomatic or may produce an acute or chronic disease. Although the disease initially resembles an influenza-like or pneumonia-like febrile illness primarily involving the bronchopulmonary system, dissemination can occur to multiple organ systems.

#### **Clinical case definition**

An illness characterized by one or more of the following:

- Influenza-like signs and symptoms (e.g., fever, chest pain, cough, myalgia, arthralgia, and headache)
- Pneumonia or other pulmonary lesion, diagnosed by chest radiograph
- Erythema nodosum or erythema multiforme rash
- Involvement of bones, joints, or skin by dissemination
- Meningitis
- Involvement of viscera and lymph nodes

#### **Laboratory criteria for diagnosis**

- Cultural, histopathologic, or molecular evidence of presence of *Coccidioides* species,  
OR

- Positive serologic test for coccidioidal antibodies in serum, cerebrospinal fluid, or other body fluids by:
  - Detection of coccidioidal immunoglobulin M (IgM) by immunodiffusion, enzyme immunoassay (EIA), latex agglutination, or tube precipitin, OR
  - Detection of coccidioidal immunoglobulin G (IgG) by immunodiffusion, EIA, or complement fixation, OR
- Coccidioidal skin-test conversion from negative to positive after onset of clinical signs and symptoms.

**Case classification**

*Confirmed:* A case that meets the clinical case definition and is laboratory confirmed.

<b>Criterion</b>	<b>Confirmed</b>
<b><i>Clinical evidence</i></b>	
Influenza-like signs and symptoms (e.g., fever, chest pain, cough, myalgia, arthralgia, and headache)	○
Pneumonia or other pulmonary lesion, diagnosed by chest radiograph	○
Erythema nodosum or erythema multiforme rash	○
Involvement of bones, joints, or skin by dissemination	○
Meningitis	○
Involvement of viscera and lymph nodes	○
<b><i>Laboratory evidence</i></b>	
Cultural, histopathologic, or molecular evidence of presence of <i>Coccidioides immitis</i> ,	○
Positive serologic test for coccidioidal antibodies in serum or cerebrospinal fluid by: <ul style="list-style-type: none"> <li>• Detection of coccidioidal immunoglobulin M (IgM) by immunodiffusion, enzyme immunoassay (EIA), latex agglutination, or tube precipitin, or</li> <li>• Detection of rising titer of coccidioidal immunoglobulin G (IgG) by immunodiffusion, EIA, or complement fixation, or</li> <li>• Coccidioidal skin-test conversion from negative to positive after onset of clinical signs and symptoms.</li> </ul>	○

Notes:

○ = At least one of these “O” (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all “N” criteria in the same column—is required to classify a case.

**Case Investigation Process**

- Complete minimum/required fields in UT-NEDSS.
- Verify case status.
- Determine whether the case had travel/exposure history consistent with acquisition of disease in Utah or elsewhere.

- Work with the testing laboratory and UDOH to submit culture-positive specimens to CDC for genomic sequencing.

## **Outbreaks**

Outbreaks due to coccidioidomycosis are not common, but can occur following dust storms, earthquakes, or soil excavation. An outbreak of coccidioidomycosis would be defined by the occurrence of more than the average, or expected, number of cases in a particular non-endemic area.

## **Identifying Case Contacts**

The fungus that causes coccidioidomycosis is not typically spread from person to person. However, in extremely rare instances, a wound infection with *Coccidioides* can spread the infection to someone else, or the infection can be spread through transplant of an infected organ. In the event an organ transplant patient is identified with coccidioidomycosis, it is critical for public health partners to work together to identify other organ recipients.

## **Case Contact Management**

Exposed laboratory workers should be referred to an infectious disease physician for appropriate antibiotic management.

## ✓ REFERENCES

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## ✓ VERSION CONTROL

02.2016 Updated format, links, prevention, disease and epidemiology, case investigation, public health control measures, and references sections.

## ✓ UT-NEDSS Minimum/Required Fields by Tab

### Demographic

- First Name
- Last Name
- Date of Birth
- County
- Birth Gender
- Race

### Clinical

- Date Diagnosed
- Died
- Date of Death
- Disease
- Onset Date
- Does the patient have any of the following symptoms?
  - Headache?
  - Chest pain?
  - Weight loss?
  - Sputum production?
  - Joint Aches?

- Sore Throat?
- Rash?
- Fatigue?
- Cough?

### Laboratory

- Organism
- Result Value
- Test Result
- Test Type

### Epidemiological

- Imported From

### Reporting

- Date first reported to public health

### Administrative

- Outbreak Associated
- Outbreak Name
- State Case Status