

# COCCIDIOIDOMYCOSIS

## (San Joaquin Valley fever, Valley fever, Desert fever)

### ✓ DISEASE AND EPIDEMIOLOGY

#### **Clinical Description:**

After infection, a wide spectrum of manifestations is possible. Coccidioidomycosis first infects a person's lungs, and 50-60% of people that become infected will not develop symptoms. Most persons 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 percent of infections result in chronic pulmonary or extrapulmonary infections. Cutaneous manifestations include erythema nodosum and erythema multiforme. Erythema nodosum is much more common in women than in men.

Although coccidioidomycosis primarily involves the bronchopulmonary system, dissemination can occur to multiple organ systems. Approximately 1 in 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 infection, such as meningitis, and bone and joint infection. People of African or Asian descent, pregnant women and people who are immunocompromised are at increased risk for developing disseminated coccidioidomycosis

#### **Causative Agent:**

Coccidioidomycosis is caused by spores of a fungus called *Coccidioides*. Two species of *Coccidioides* fungus have been found, *Coccidioides immitis* and *Coccidioides posadasii*. The spectrum of diseases caused by the two species of *Coccidioides* fungi 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.

#### **Culture:**

Isolation of *Coccidioides* species in culture is definitive evidence of infection. When a specimen is sent from a patient with possible coccidioidomycosis, the receiving

laboratory should be notified, since secondary cases have been reported in laboratory workers opening the plates for inspection. However, healthcare workers collecting the specimen are at no risk, since coccidioidomycosis is not transmitted person-to-person.

**Serology:**

Serologic testing is the most common means of diagnosing coccidioidomycosis, and several serologic tests, including ELISA, complement fixation (CF), and immunodiffusion (ID) assays, are available. ID assays primarily measure IgM antibodies, however IgG antibodies may also be detected. ELISA and CF measure both IgG and IgM. While IgM antibodies are produced early in illness, IgG antibodies generally appear 2-6 weeks after infection. Most tests are highly specific for active infection. Any positive serologic result, even minimally reactive, is likely to be clinically relevant. Most patients lose serologic reactivity within months of an infection unless residual lesions are evident or infection is active. A negative serologic result, however, never excludes the diagnosis of coccidioidomycosis. Although most tests for coccidioidal antibodies are very specific, they are relatively insensitive, especially during the first one to two weeks after infection. Repeating tests, if a first serologic test is negative over the course of 2 months will improve diagnostic sensitivity.

Coccidioidomycosis Serological Test Interpretation	
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	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. 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.

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

**Microscopy:**

The diagnosis of coccidioidomycosis can be made by identifying fungal spherules in tissue specimens.

**Skin testing:** (reagents for skin tests are currently not available in the United States)

The coccidioidomycosis skin test can generate an immune response if the patient has antibodies to *C immitis* circulating in their blood. The immune response indicates an exposure to *C. immitis*. Two antigens used in the skin test are coccidioidin prepared from *C. immitis* mycelium and spherulin prepared from spherule-endospores. The test includes injecting the antigens just below the skin surface and then waiting 24 to 48 hours to read the test result. If the test result is positive there is an immune response at the injection site. The immune response includes inflammation and swelling. If the test is negative there is no immune response to the coccidioidin or spherulin antigens.

### **Treatment:**

Mild cases of coccidioidomycosis usually resolve without treatment. However, treatment may shorten the course of illness or prevent complications and thus is necessary for severe cases. Opinion varies about the most relevant factors to judge the severity of illness. However, commonly used indicators are:

- Greater than 10 percent loss of body weight;
- Night sweats persisting greater 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; or
- Persisting symptoms 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.

### **Case fatality:**

Case fatality rate estimates range from 12-17%. Coccidioidal meningitis, the most serious form of disseminated disease, is almost always fatal within 2 years of diagnosis if left untreated.

### **Reservoir:**

*C. immitis* and *C. posadasii* grow in the soil.

### **Transmission:**

Anyone who is present near dust-producing activities where soil or other materials contaminated with *Coccidioides species* are present 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.

Coccidioidomycosis is not contagious; it cannot be transmitted from an infected person or animal to someone else.

### **Susceptibility:**

Anyone can get coccidioidomycosis. Those with any condition that compromises cellular immunity, including people with HIV infection, patients with organ transplants or hematologic malignancies, and patients on immunosuppressant agents are more vulnerable to more severe illness.

Life-long immunity almost always develops following infection. However, reactivation can occur in those who become immunosuppressed.

**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:**

NA

**Epidemiology:**

*Coccidioides* species grow in arid and semiarid areas of the Western Hemisphere. In the US, 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 fungus *Coccidioides* species. From 2005-2009, an average of 41 cases of coccidioidomycosis were reported to the Utah Department of Health each year; in 2006 and 2007 there were 58 and 69 cases of coccidioidomycosis reported to the Utah Department of Health more than twice as many as were reported for the previous two years.

 **PUBLIC HEALTH CONTROL MEASURES**

**Public health responsibility:**

- Investigate all suspect cases of disease and 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 to prevent further transmission.

**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 with decreasing the amount of dust in their environment by installing air conditioning, pouring asphalt, or planting grass. These measures will help decrease dust but will not eliminate *Coccidioides* species from their environment.

**Chemoprophylaxis:**

None.

**Vaccine:**

None.

**Isolation and quarantine requirements:**

**Isolation:** NA

**Hospital:** NA

**Quarantine:** NA

## ✓ CASE INVESTIGATION

### Reporting:

All cases of coccidioidomycosis should be reported to public health.

### Case definition:

#### **Coccidioidomycosis (*Coccidioides species*) (2009)**

##### **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 (microscopic examination), 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.

*Probable:* Culture confirmed without symptoms or identified through histopathologic examination (microscopic examination) without symptoms.

### Case Investigation Process:

- Fill out a morbidity form.

### Outbreaks:

Outbreaks due to coccidioidomycosis are not common, but can occur following dust storms, earthquakes and soil excavation.

**Identification of case contacts and management:**

NA

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