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**Coccidioidomycosis**

*Valley Fever,  
San Joaquin Fever,  
Desert Rheumatism*




Coccidioidomycosis is also known as valley fever, San Joaquin fever, and desert rheumatism.

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**Overview**


- Organism
- Economic Impact
- Epidemiology
- Transmission
- Clinical Signs
- Diagnosis and Treatment
- Prevention and Control
- Actions to take



In today's presentation we will cover information regarding the organism that causes coccidioidomycosis and its epidemiology. We will also talk about the economic impact the disease has had in the past and could have in the future. Additionally, we will talk about how it is transmitted, the species it affects, clinical findings and necropsy signs, and diagnosis and treatment of the disease. Finally, we will address prevention and control measures for the disease as well as actions to take if coccidioidomycosis is suspected.

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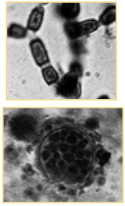

**The Organism**



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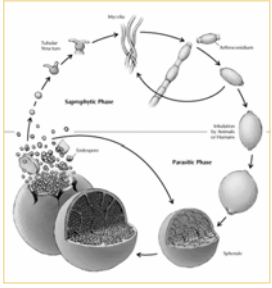
**Coccidioides immitis**

- Dimorphic fungus
  - Saprophytic phase
  - Parasitic phase
- From soil or dust
  - Arthroconidia become airborne, inhaled
  - Transform into spherule and endospore

Coccidioidomycosis results from direct inhalation of the spores of the dimorphic fungus *Coccidioides immitis* from the soil or from dust in the air. *C. immitis* has both a saprophytic and parasitic phase in its life cycle. It grows as a mold in the soil, and when disturbed, the hyphae fragment forms a durable structure called arthroconidia which becomes airborne. When the arthroconidia are inhaled, they transform into thick-walled multinucleate spherules that then separate to produce thousands of endospores, which can then produce a new spherule and begin the cycle anew. Photo on top hyphae and arthroconidia. Photo on bottom spherules containing endospores. Photo source: [http://botit.botany.wisc.edu/toms\\_fungi/jan2002.html](http://botit.botany.wisc.edu/toms_fungi/jan2002.html)

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**Coccidioides immitis**  
Lifecycle phases




Photo from [www.hosprract.com](http://www.hosprract.com)

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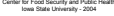
**Importance**



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**History**

- 1892: First reported as disease
- 1920-1930
  - Soil recognized as reservoir for agent
- 1987
  - CDC adds coccidioidomycosis to annual survey of HIV-associated diseases
- 1991-1995
  - Incidence increases tenfold in San Joaquin Valley, CA

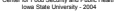


*C. immitis* was the first fungal pathogen recognized as dimorphic and coccidioidomycosis was first reported as a defined disease in 1892. In the 1920's and 1930's, soil was recognized as a reservoir for the agent, and in 1987 the Centers for Disease Control and Prevention (CDC) added coccidioidomycosis to its annual survey of HIV-associated diseases. Awareness of the disease was raised in the early 1990s, when the incidence of coccidioidomycosis increased tenfold in San Joaquin Valley, California, after heavy rainfalls were followed by drought conditions, resulting in increased dust in the air.

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**Economic Impact**


- Infection is costly
  - Time lost from work
  - Direct medical costs
- 1990: Kern County, CA
  - Cost more than \$66 million
- Costly to livestock industry
  - Infection can be widespread
  - Diagnosis/treatment can be significant



Coccidioidomycosis can be a devastating disease, in terms of both direct medical costs, and time of productivity lost from work while the patient is ill. The outbreak of *C. immitis* infections in Kern County (located in the San Joaquin Valley of California) in the 1990's cost more than \$66 million dollars in medical care alone. Coccidioidomycosis also has an effect on the livestock industry and measures should be taken to decrease the animals' exposure to dust. Should infection occur, is usually widespread. The cost of diagnosis and treatment of afflicted animals can be significant.

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**Epidemiology**



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**Geographic Distribution**

- Endemic areas
  - Southwestern U.S.
    - New Mexico, Texas, California, Arizona
  - Northern Mexico
  - Central America
  - Argentina
- 10-50% skin test positive

Coccidioidomycosis is endemic in the southwestern U.S., including parts of New Mexico, Texas (west of El Paso), the central valley of California, and Arizona, where the incidence in humans is particularly high. The endemic area extends into northern Mexico, and foci of infection are present in parts of Central America and Argentina. In endemic areas, 10-50% of the human population skin-test positive for coccidioidomycosis infection. Photo from Rippon JW. Medical Mycology, 3<sup>rd</sup> ed. WB Saunders, 1988, p436 – shaded areas indicate prevalence areas for Coccidioidomycosis.

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**Morbidity/Mortality**

- Two forms in humans
  - 60% asymptomatic
    - Only identified with positive skin test
  - 40% mild to severe disease
    - Can be fatal
    - Immuno-compromised persons highly susceptible to serious infection
- Difficult to assess morbidity in animals

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The rate of infection is directly proportional to the degree of exposure to airborne spores, that is, individuals exposed to large amounts of dust in endemic areas have higher rates of infection. Sixty percent of *Coccidioides immitis* infections are asymptomatic and are recognized by a positive skin test. The remaining 40% of cases can range from mild to severe symptoms and are usually pulmonary. About 90% of these cases will resolve their pulmonary infection without sequelae. Immunocompromised persons are more susceptible to serious infection, and the mortality rate in HIV-infected persons exceeds 70% within one month of diagnosis. Very little is known regarding the prevalence rate of *C. immitis* infections in animals. Infections may be asymptomatic and thus clinically undetectable. Mortality is not common in the primary form of the disease, but can be rather high in the disseminate form depending on the location and severity of the infection.

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**Transmission**

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Transmission in animals only occurs with direct inhalation of *C. immitis* spores from contaminated soil or dust. There is virtually no animal-to-animal transmission. Placental infection has been reported in horses, but is rare. As with humans, the incidence of coccidioidomycosis infection rises following an environmental disturbance. Most animal infections result from exposure to dusty conditions such as dusty feedlots.

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**Animal Transmission**

- Direct inhalation of *C. immitis* spores from soil or dust
  - Rare animal-to-animal transmission
    - Placental infection reported in horses
  - Incidence increases after disturbance
- Dusty conditions
  - Most bovine infections contracted from dusty feedlot

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Transmission in animals only occurs with direct inhalation of *C. immitis* spores from contaminated soil or dust. There is virtually no animal-to-animal transmission. Placental infection has been reported in horses, but is rare. As with humans, the incidence of coccidioidomycosis infection rises following an environmental disturbance. Most animal infections result from exposure to dusty conditions such as dusty feedlots.

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**Human Transmission**

- Direct inhalation of *C. immitis* spores
  - Present in contaminated soil and dust
  - Only established mode of transmission
- Not person-to-person
- Not animal-to-person
- Increased incidence after disturbance



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Coccidioidomycosis is not communicable from one person to another, or from animal to man. Direct inhalation of *C. immitis* spores, which may be carried on dust particles or present in contaminated soil, is the only established mode of transmission. The rate of infection is often increased following a disturbance of soil contaminated with fungal spores.

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**Human Transmission**

- Natural disturbances
  - Dust storms
  - Earthquakes
- Human disturbances
  - Construction sites
  - Archaeological digs





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The incidence of coccidioidomycosis increases following an environmental disturbance. Soil is commonly disturbed either by natural causes such as an earthquake or dust storm (top photo), or by humans (as in an archaeological dig or construction site, bottom photo).

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**Animals and  
Coccidioidomycosis**



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**Clinical Signs**

- Disease varies in severity and species affected
- Incubation period: 1-3 weeks
- Asymptomatic to disseminated
- Signs of primary form
  - Fever (104-105°F)
  - Lethargy, inappetence
  - Dry, harsh cough
    - May be confused with kennel cough

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In animals, disease varies from asymptomatic to disseminated and fatal. Clinical signs vary depending on the severity of infection and the species affected. Dogs are the most severely affected species. Signs of the primary form of coccidioidomycosis include an elevated temperature (104-105°F), lethargy, loss of appetite, and a dry, harsh cough. The cough is pronounced and can be mistaken for kennel cough in dogs.

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**Clinical Signs: Dogs**

- Signs of disseminate form
  - Fever, anorexia, weight loss
  - Infection of the bones
    - Lameness, limping
    - Joint swelling
  - Chronic coughing
  - Abscesses and draining skin lesions
  - Diarrhea

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While coccidioidomycosis is primarily a respiratory disease, the infection can disseminate to many tissues, especially in dogs. Infection of the bones is most common, resulting in lameness and/or limping. Other signs of disseminate infection in dogs include joint swelling, anorexia, chronic coughing, skin abscesses and draining skin lesions, fever, and intermittent diarrhea. Seizures and incoordination may also be seen.

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**Clinical Signs: Other Animals**

- Cats
  - Draining skin lesions, abscesses, subcutaneous granulomatous masses
  - Fever, loss of appetite, weight loss
  - Dyspnea, lameness, neuropathies
- Horses
  - Abortion, osteomyelitis
- Pigs and ruminants
  - Usually asymptomatic

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In cats, dermatologic problems such as draining skin lesions, abscesses, and subcutaneous granulomatous masses are the most common presenting symptoms. Other signs of *C. immitis* infections in cats include fever, loss of appetite and weight loss; dyspnea, lameness and neurological abnormalities may also be seen. In horses, abortion and osteomyelitis have resulted from placental infection, and pigs and ruminants are known to have asymptomatic infections, with lesions limited to the lungs and thoracic lymph nodes.

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**Post Mortem Lesions**

- Gross lesions
  - Disseminated or limited to lungs, mediastinum, thoracic lymph nodes
- Resemble tuberculosis lesions
  - Discrete, variable sized, firm, grayish on cut surface
- Pyogranulomatous lesions
  - Contain purulent exudates and fungal spores

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Gross lesions resulting from coccidioidomycosis infections may either be disseminated or limited to the lungs, mediastinum, and thoracic lymph nodes. The lesions may resemble those of tuberculosis infection, as they vary in size, are discrete and have a firm, graying cut surface. Epithelioid and giant cells may be present in pyogranulomatous lesions, which may contain purulent exudates and fungal spores. Mineralized focal lesions may also be present.

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**Diagnosis**

- Clinical
  - C. immitis infection should be suspected
    - In endemic areas
    - With characteristic clinical signs
- Laboratory Tests
  - Fungal spores found in exudates
  - Serology
    - Complement-fixing antibody tests

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In endemic areas, coccidioidomycosis should be suspected in dogs presenting with chronic bronchopulmonary disease, and when pulmonary nodules and enlarged lymph nodes are identified radiographically. *C. immitis* spores found free in the exudates draining from pyogranulomatous lesions can be helpful in diagnosis: the organisms may vary in size, appearing as 20-200µm spherules with a characteristically double-walled appearance, and diagnosis can be confirmed by demonstrating the spherules in tissues. Alternatively, detection of complement fixing antibodies present in the serum can also aid in diagnosis.

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**Treatment**


- Should be initiated immediately
- For disseminated infections
  - Long-term therapy for at least one year
  - Antifungal agents
- Likelihood of recovery
  - Primary form: Good prognosis
  - Disseminated form: Guarded prognosis

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Treatment should be initiated immediately following diagnosis of coccidioidomycosis infection, and may vary depending upon the location of the infection and its severity. Long-term antifungal therapy is necessary, and should continue for at least one year for disseminated infections. Pharmaceutical treatment with antifungal agents has proven effective in both man and animals. The likelihood of recovery from the primary form of coccidioidomycosis is quite high with therapy, while the chance of recovery from the disseminated form varies with the location and severity of infection; thus, prognosis must be considered guarded.

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**Coccidioidomycosis  
in Humans**



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**Clinical Signs: Primary Form**

- Incubation period: 1-4 weeks
- Usually subclinical
- Fever, chills, cough, sore throat
- Chest pain
- Nodular lesions
- Nonspecific respiratory symptoms
- Complications less common
  - Pneumonia, pleural effusion

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The incubation period is usually 1-4 weeks. In the primary and less severe form of coccidioidomycosis, the disease is usually subclinical. When present, symptoms include fever, cough, chest pain, chills, sputum production and sore throat. Nodular lesions may result from the resolution of primary pulmonary lesions and must be distinguished from nodules associated with tuberculosis or other granulomatous infections. Nonspecific respiratory symptoms resembling acute bronchitis or influenza may occur, and complications such as pneumonia or pleural effusion occur less commonly.

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**Clinical Signs:  
Disseminate Form**

- Severe form of disease
- Weeks to months to years after primary infection
- Symptoms include
  - Low-grade fever, anorexia, weight loss
  - Muscle aches and stiffness, weakness
  - Excessive sweating
  - Widespread focal lesions
- In HIV-infected persons
  - Mucopurulent or bloody sputum

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Progressive or disseminate coccidioidomycosis is the more severe form of the disease, and may develop weeks, months or years after the primary infection. Symptoms include a low-grade fever, anorexia, weight loss, muscle aches and stiffness, excessive sweating, and weakness. Mucopurulent or bloody sputum may be present when there is extensive pulmonary involvement, which may develop in HIV-infected persons. Focal lesions may be found in the bones, joints, skin, subcutaneous tissues, liver, kidneys, lymph nodes, brain and meninges; deeper lesions in the skin may result from connections of draining sinus tracts.

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### Post Mortem Lesions

- Skin lesions
  - Exanthems, maculopapular lesions
- Pulmonary signs
  - Bronchitis, pneumonia, pleural effusion
- Bone and joint lesions
- Lymphadenopathy
- Abdomen
  - Masses, hepatomegaly, splenomegaly

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A wide variety of exanthems, including maculopapular lesions, may be present on the skin. Signs indicating bronchitis, pneumonia, pleural effusions and reactive airway disease are common in the pulmonary system. Bone lesions are unifocal in the majority of cases (60%), and joint lesions are unifocal in 90% of cases. Lymphadenopathy has also been seen, and masses are sometimes present in the abdomen. Hepatomegaly and splenomegaly may also be present.

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### Sampling

- Before collecting or sending any samples, the proper authorities should be contacted
- Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease

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Before collecting or sending any samples from animals with a suspected foreign animal disease, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease.

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### Diagnosis

- Differentials
  - Tuberculosis
- Clinical
  - Coccidioidomycosis should be considered
    - In endemic areas
    - Following a dust/soil disturbance
    - With characteristic clinical signs

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Coccidioidomycosis should be considered when the patient presents with the characteristic clinical signs, and in endemic areas, especially following an environmental disturbance such as a dust storm, earthquake, or archaeological dig. The differential diagnoses include other diseases with respiratory symptoms or other granulomatous infections, such as tuberculosis.

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### Diagnosis

- *C. immitis* spherules visualized in
  - Sputum, pleural fluid, cerebrospinal fluid or exudates from draining lesions
- Complement fixation
  - IgG anticoccidioidal antibodies
    - Titer  $\geq 1:4$  = current or recent infection
    - Titer  $\geq 1:32$  = increased risk of extrapulmonary dissemination
- Skin test of epidemiological value

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Immediately following inhalation, *Coccidioides immitis* spores convert to large tissue-invasive spherules (ranging from 20-80  $\mu\text{m}$  in diameter) which can be visualized in sputum, pleural fluid, cerebrospinal fluid, and exudates from draining lesions. Diagnosis can also be established by culturing the infected body fluids or tissue specimens. Complement fixation for IgG anticoccidioidal antibodies is the most useful diagnostic test, as the severity of infection can be assessed by the titer. Titers  $\square 1:4$  in serum indicate current or recent infection, while higher titers ( $\square 1:32$ ) indicate an increased risk of extrapulmonary dissemination. Titers also reflect the efficacy of treatment, as they generally decline with successful therapy. Coccidioidal meningitis is diagnosed by presence of complement fixing antibodies in the cerebrospinal fluid. The coccidioidin skin test is more valuable in epidemiologic studies than in diagnosis because it is positive in most persons in endemic areas.

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### Treatment

- Primary coccidioidomycosis
  - Treatment generally unnecessary
- Severe/chronic coccidioidomycosis
  - Antifungal agents effective
  - Prognosis generally good
- Disseminate coccidioidomycosis
  - May require invasive or long-term therapy
  - Prognosis poor to guarded

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Treatment for patients with primary coccidioidomycosis is generally unnecessary (usually only about 5% of cases require treatment), unless complement fixation titers indicate the spread of the infection, which requires treatment with antifungal agents. Disseminate cases can also be treated with antifungal agents. The prognosis is generally good for severe and chronic cases if the immune system is healthy and the infection is caught early, although relapses may occur. Severe cases may require more invasive therapy, such as surgery to cure osteomyelitis or excision of pulmonary cavitation. If the infection is severe (such as an HIV/AIDS-associated case), maintenance therapy to prevent relapse may be necessary.

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### Public Health Significance

- Reportable disease
  - Humans in endemic areas
    - California
    - New Mexico
    - Arizona
  - Notify state department of health
- Serious threat to immunocompromised persons
  - High mortality rate

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Coccidioidomycosis is a reportable disease in humans in some endemic areas, such as California, New Mexico and Arizona. The state department of health should be notified if there is a human case in these areas. Infections can result not only in high direct medical costs and lost productivity time, but will also have a high emotional impact should the infection become serious. *Coccidioides immitis* infection also poses a significant threat to immunosuppressed persons, as the disease can have a high mortality rate in these cases.

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### Prevention and Control



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### Recommended Actions

- Notification of Authorities
  - Federal:
    - Area Veterinarian in Charge (AVIC)
    - [www.aphis.usda.gov/vs/area\\_offices.htm](http://www.aphis.usda.gov/vs/area_offices.htm)
  - State veterinarian
  - [www.aphis.usda.gov/vs/sregs/official.htm](http://www.aphis.usda.gov/vs/sregs/official.htm)
- State or local health department

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If you suspect a case or outbreak of Coccidioidomycosis, contact your state and/or federal veterinarian or state or local health department immediately.

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### Quarantine and Disinfection

- Quarantine not necessary
  - Coccidioidomycosis not communicable
- Disinfection
  - Iodine
  - Chlorine
    - Hypochlorite (5.25% is household bleach)
  - Phenolics: Tek-Trol®
  - Quaternary ammoniums
    - Di-Quat 10-S and Roccal®-D Plus

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As coccidioidomycosis is not a communicable disease (it cannot be transmitted between humans, animals, or from animal to human), quarantine is not necessary. Although fungal agents such as *Coccidioides immitis* are highly resistant to most disinfectants, halogens (such as iodine, and chlorine in the form of bleach), phenolics (such as Tek-Trol®), and quaternary ammoniums (Di-Quat 10-S and Roccal®-D Plus) have proven effective against *C. immitis*.

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### Vaccination

- No effective immunization available
  - Efforts being made to develop vaccine
- Precautionary measures should be taken to avoid infection
  - Reduce exposure to soil and dust
    - Man and animal
    - Of particular importance in endemic areas

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Although efforts are being made to develop a successful vaccine, there is no effective immunization available yet to either man or animal to protect against coccidioidomycosis infections. Therefore, precautionary measures should be taken by persons in endemic areas or who have significant exposure to dust and dirt, such as archaeologists and construction workers. Persons afflicted with any disease which weakens the immune system and therefore increases susceptibility to infection and subsequent complications need to decrease exposure to dusty conditions. To prevent animal infection, care should be taken to protect the animal from significant exposure to contaminated soil and dusty conditions, such as a dusty feedlot.

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## Acknowledgments

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## Acknowledgments

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