Coccidioides spp. Exposure/Injury Response Protocol

Organism or Agent: Coccidioides spp. (Coccidioides immitis and posadasii)
Exposure Risk: Coccidioidomycosis
UCSF Occupational Health Services: 415/885-7580 (Available during work hours)
Exposure Hotline Pager: 415/353-7842 (Available 24 hours)
Office of Environmental Health & Safety: 415/476-1300 (Main number; available during work hours) or 9-911 (Available 24 hours)
EH&S Public Health Officer: 415/514-3531
Biosafety Officer: 415/514-2824

PROTOCOL SUMMARY

In the event of an accidental exposure or injury, the protocol is as follows:

1. Modes of Transmission:
   a. Skin puncture or injection
   b. Ingestion
   c. Contact with mucous membranes (eyes, nose, mouth)
   d. Contact with non-intact skin
   e. Exposure to aerosols
   f. Respiratory exposure involving inhalation of the mold/arthroconidia form

2. First Aid:
   a. Skin Exposure, immediately go to the sink and thoroughly wash the skin with soap and water. Decontaminate any exposed skin surfaces with an antiseptic scrub solution.
   b. Skin Wound, immediately go to the sink and thoroughly wash the wound with soap and water and pat dry.
   c. Splash to Eye(s), Nose or Mouth, immediately flush the area with running water for at least 5-10 minutes.
   d. Splash Affecting Garments, remove garments that may have become soiled or contaminated and place them in a double red plastic bag.

3. Treatment:
   a. In the event of an acute injury resulting from a laboratory incident where the injury requires immediate medical care, the injured employee/student should report to the emergency department for medical treatment. The injured individual must take a copy of this entire protocol document to the Emergency Department, including information regarding the specific strain associated with exposure.
   b. In the event of exposure, with or without an injury, call the Exposure Hotline in order to get access to medical care for the exposure. The Exposure Hotline responder will provide guidance to the injured individual on necessary medical treatment and post exposure follow-up.

4. Follow up is needed in the event of any Laboratory Exposure:
   a. After first aid has been administered, immediately inform your supervisor of the exposure.
   b. In the event of a large spill, contact the emergency response team (9-911) for clean-up.
   c. Contact Occupational Health Services, after first aid is complete, for follow-up care by contacting the Exposure Hotline.
   d. Contact the Biosafety Officer at 415/514-2824 to report the injury or exposure.
ROLES & RESPONSIBILITIES
AFTER ACCIDENTAL EXPOSURE TO COCCIDIOIDES

1. WORKER’S RESPONSIBILITIES (Employee/Student Initial Self-Care)
   a. First Aid: Perform the recommended first aid and decontamination according to the posted instructions.
   b. Treatment: i) In the event of an acute injury resulting from a laboratory incident which requires immediate medical care, the injured individual should report to the Emergency Department for acute medical treatment. ii) In the event of an exposure, with or without an injury, call the Exposure Hotline in order to get access to medical care for the exposure and evaluation for possible post exposure prophylaxis.
   c. Access to Exposure Hotline: Call the Exposure Hotline in order to get access to medical care for the exposure. Dial 415 /353-7842.
   e. Secure the laboratory: Identify the equipment involved in the exposure and the mechanism of exposure. Make sure that the laboratory area has been secured and that notification of contamination has been posted to prevent other individuals from entering the area.
   f. Follow up: Students and workers should contact Occupational Health Services (OHS) at 415 / 885-7580 for any needed follow up care.

2. SUPERVISOR’S/PI’S RESPONSIBILITIES
   a. First Aid and Decontamination: Verify that the worker has washed and decontaminated himself/herself. Ensure that appropriate medical treatment has been received.
   b. Secure the laboratory: Confirm that the laboratory area has been secured and that notification of contamination has been posted to prevent other individuals from entering the area.
   c. Laboratory clean-up (as needed): Contact the Office of Environmental Health & Safety (OEH&S) through the UC Police Department Emergency Dispatch (from a campus telephone 9-911, from a non-campus phone 415/476-1414).
   d. Report the exposure: Call the Biosafety Officer at 415/514-2824 during regular hours to discuss the exposure. A report summarizing any suspected Coccidioides exposure needs to be submitted to the Biosafety Committee by the Principal Investigator (PI). The report must include the following:
      • A brief description of the exposure event, a description of the area involved, and the extent of employee exposure
      • If applicable, specification of the amount of infectious material released, time involved, and explanation of procedures used to determine the amount involved
      • Corrective action taken to prevent the re-occurrence of the incident
      • Coccidioides decontamination procedures
   e. Follow Up: Confirm that the worker has called the Exposure Hotline and has scheduled for an appointment at the UCSF Occupational Health Clinic as necessary.
SECTION I – Infectious Agent
Organism or Agent: Coccidioides spp (immitis or posadasii)
Synonym or Cross Reference: Coccidioidomycosis
Characteristics: Dimorphic fungus, mold form in soil which produces infectious arthroconidia, spherule form in animals and human hosts

SECTION II – Recommended Precautions
Containment Requirements: According to BMBL5: BSL-3 practices, containment equipment, and facilities are recommended for propagating and manipulating sporulating cultures already identified as Coccidioides spp. and for processing soil or other environmental materials known to contain infectious arthroconidia.

UCSF Required Personal Protective Equipment: BSL 3 procedures for work involving the mold form, arthroconidia, and spherules. Use personal protective equipment standards as detailed in the Biosafety Use Authorization (BUA).

SECTION III – Handling Information
Spills: Allow aerosols to settle; wearing protective clothing, gently cover spill with paper towel and apply 10% bleach (0.5% sodium hypochlorite) solution, starting at perimeter and working towards the center; allow sufficient contact time (30 min) before clean up.
Disposal: Decontaminate waste contaminated with known or suspected Coccidioides in the mold form before disposal. Dispose as biohazardous waste.
Storage: Store in sealed containers that are appropriately labeled.

SECTION IV – Health Hazards (from Canadian Pathogen Safety Data Sheet)
Pathogenicity: The majority (around 60%) of individuals infected is asymptomatic or develops a very mild illness, with symptoms including cough, fever, arthralgias, myalgias, and fatigue that can last 2-6 weeks. Symptomatic individuals develop acute pneumonia or valley fever. In a small percentage of cases acute pneumonia can become chronic progressive pneumonia or pulmonary nodules and cavities can develop in the lungs, characterized by pneumonia, pleural effusion, and hilar lymphadenopathy. Dissemination occurs in 1% of infections and can affect the skin, lymph nodes, bones, and joints, causing systemic symptoms such as fever, cough, and night sweats. Meningitis is the most serious complication of coccidioidomycosis, with symptoms including headache, nausea, vomiting, and affected mental status. This may occur in 30-50% of disseminated infections, and is fatal without treatment. Coccidioidomyces infection may also lead to erythema nodosum, acute exanthema (“Toxic erythema”), erythema multiforme, Sweet’s syndrome, and interstitial granulomatous dermatitis

Epidemiology: Coccidioides spp. are geographically limited to the alkaline soil of semiarid climates, and in regions with hot, dry summers, and low annual rainfall. C. immitis is confined mainly to California, whereas C. posadasii occurs in the southwestern United States, northern Mexico and areas of Central and South America. The major risk factor for infection is environmental exposure to dust and soil. Disseminated infection is more common among black, Asian or Filipino individuals, pregnant women in the third trimester and immunocompromised individuals.
Host Range: Humans, nearly all mammals, and some reptiles.
Infectious Dose: Estimated to be 1-10 arthroconidia per Canadian MSDS.
**Modes of Transmission:** Inhalation of arthroconidia, although secondary transmission via fomites and organ transplants may occur.

**Incubation Period:** 1 to 3 weeks, although some infections are asymptomatic.

**Communicability:** Not contagious but has occasionally been transmitted from person-to-person via fomites or organ transplants.

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**SECTION V – Viability**

**Drug Susceptibility:** Susceptible to amphotericin B and the azole group of antifungal drugs including fluconazole, itraconazole, voriconazole, and posaconazole. Drug resistance is uncommon.

**Susceptibility to Disinfectants:** Susceptible to 1:10 dilution of bleach, ≥6% hydrogen peroxide, 8% formaldehyde or 3% phenolics with a contact time of 20 minutes or more.

**Physical Inactivation:** Fungi in soil can be inactivated by heat at 120 °C for 30 minutes.

**Survival Outside Host:** Coccidioidal arthroconidia are hardy and can survive for long periods of time on inanimate surfaces. They can grow in the soil in semiarid climates.

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**FOR THE USE OF THE EXPOSURE HOTLINE**

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**SECTION VI – Medical**

**Surveillance:** Monitor for symptoms. Diagnosis of coccidioidomycosis can be established using serologic, histopathologic and culture methods. Skin tests can be used to identify the disease. Any pregnant or immunocompromised worker should be evaluated by an infectious disease specialist.

**First Aid/Treatment:** Coccidioidomycosis is generally self-limiting and will resolve without treatment. Disseminated infections, or patients who experience excessive morbidity, should be treated with antifungal medication. The type of drug and length of treatment depends on the site of infection and clinical response.

**Immunization:** None.

**Prophylaxis:** Exposed personnel should be given fluconazole (400 mg daily for 6 weeks).

1. **Prophylaxis Recommended For:**
   a. Significant inhalational exposure to arthroconidia.
   b. Percutaneous injury with *Coccidioides*, materials contaminated by *Coccidioides*, or mucous membrane exposure.

2. **Prophylaxis Considered For:**
   a. Potential inhalational exposures to arthroconidia in individuals with risk factors for development of systemic disease.
   b. Potential mucous membrane exposure.

3. **Prophylaxis Not Recommended For:**
   a. Intact skin exposure associated with the spherule form of *Coccidioides*, where there is no inhalation or percutaneous or mucous membrane exposure.

Medication: Fluconazole – 400 mg once daily, given with food, for 6 weeks. This drug may have significant side effects and multiple drug interactions. Fluconazole is contraindicated in pregnancy. If there is any question regarding early pregnancy, a pregnancy test should be performed before starting prophylaxis.

The person who was exposed will need close follow up in UCSF Occupational Health Services. Further details on prophylactic treatment schedules and follow up as recommended by Stevens, D. A., Clemons, K. V., Levine, H. B., Pappagianis, D., Baron, E. J., Hamilton, J. R., et al. (2009) are outlined on page 5.

**Reporting:** All laboratory exposures must be reported to the Biosafety Officer. Any known cases of coccidioides exposure must be reported to the Public Health Officer. Reporting to the San Francisco Department of Public Health is not required.
SECTION VII – Laboratory Hazards

LABORATORY-ACQUIRED INFECTIONS: 93 cases of laboratory-acquired coccidioidomycosis infections and two deaths were reported prior to 1978. An additional 15 cases were asymptomatic but identified with skin tests during that period. One symptomatic case was reported from 1979-2004.

SOURCES / SPECIMENS: Lower respiratory tract samples, cerebrospinal fluid, sputum, skin and visceral lesions, and soil samples from infected areas (southwestern United States, parts of Central and South America).

PRIMARY HAZARD: Inhalation of spores, parenteral inoculation or contact with mucous membranes.

SPECIAL HAZARD: None.

FOR THE USE OF THE EMERGENCY DEPARTMENT

SECTION VIII – Emergency Medical Treatment

Treatment Indications: Emergency department treatment will be required for injuries that require immediate medical care. The treatment needs to consist of the following: 1) decontaminate and debride wound, 2) repair wound, 3) consult with infectious disease specialist for high risk exposure, 4) contact the Exposure Hotline to discuss the need to start post exposure prophylaxis, if indicated (see section VI above), and 4) have patient follow up with UCSF-OHS. For significant exposures, baseline labs should be drawn.


- Baseline serum samples should be obtained promptly from exposed persons. These samples should be stored for future testing for coccidioidal immunoglobulin G and M antibodies by an experienced laboratory.
- Persons with prior exposures are at a lower risk of infection.
- All potentially exposed persons should be given a therapeutic dose of oral fluconazole (400mg daily for adults) for 6 weeks.

Pregnant Women

- Azoles are considered teratogenic, making infection in pregnant women more complicated and the results of greater concern.
- If it is certain the pregnant woman was exposed, she should be treated with a prophylactic dose of intravenous amphotericin B therapy (which is safe during pregnancy) once a week until the pregnancy has concluded (then azoles could be given instead); the 6-week period concluded without any sign of coccidioidal disease; or coccidioidal infection was confirmed (then daily administration of amphotericin would be recommended).
- If it is uncertain if the pregnant woman was exposed, it is recommended to observe her health until coccidioidal symptoms appear at which time she should be treated with intravenous amphotericin B therapy.

Post Exposure Period

- The potentially exposed persons should be monitored during the 6 weeks of prophylaxis and for some months after.
- If the person was to develop a fever or cough, the persons should visit a clinician, specifying a possible exposure to Coccidioides. Retesting initial serum samples may be necessary, as the development of coccidioidal seropositivity can be delayed.
• If the person receiving azole is diagnosed with a primary infection, then several months of treatment should be considered, in combination with an alternative antifungal agent. It is also recommended then to use an intravenous amphotericin B preparation, because no other azoles have the favorable clinical experience as itraconazole and fluconazole has in treating coccidioidal infection. In vitro susceptibility testing of an isolate could also be useful in choosing a therapeutic option.
• Patients with disseminated coccidioidomycosis would require longer-term therapy and follow up
• If there is no clinical suspicion of coccidioidomycosis after the 6week prophylaxis period, testing for coccidioidal immunoglobulin G and M antibodies along with concurrent baseline serum samples should be performed. If there is no seroconversion, prophylaxis can be stopped. If there is serological evidence of a subclinical infection prophylaxis can probably also be stopped, although continuing treatment may be considered for those with comorbidities or other risk factors.
• Natural exposures to Coccidioides may result in undiagnosed primary infections and disease arising later. It is then recommended that individuals with Coccidioides exposure, subclinical or not, be observed for one year for the possibility of developing disseminated disease.

**Exposure Indications:** In the event of an exposure, with or without an injury, the Exposure Hotline must be called.

**SECTION VIII – References**


Appendix I.
CDC/NIH RECOMMENDATIONS FOR LABORATORY EXPOSURE TO COCCIDIOIDES

_Coccidioides immitis_ and _Coccidioides posadasii_

_Coccidioides_ spp. is endemic to lower sonoran deserts of the western hemisphere including northern Mexico, southern Arizona, central and southern California, and west Texas. The original species (_C. immitis_) has been divided into _C. immitis_ and _C. posadasii_. These species are dimorphic fungal pathogens existing in nature and in laboratory cultures at room temperature as filamentous molds with asexual spores (single-cell arthroconidia three to five microns in size) that are the infectious particles that convert to spherules under the appropriate culture conditions _in vitro_ at 37°C and _in vivo_ in warm-blooded animals.

**Occupational Infections**

Laboratory-associated coccidioidomycosis is a documented hazard of working with sporulating cultures of _Coccidioides_ spp. Occupational exposure has also been associated in endemic regions with archeology and high dust exposure. Attack rates for laboratory and occupational exposure are higher than for ambient exposure when large numbers of spores are inhaled. Smith reported that 28 of 31 (90%) laboratory-associated infections in his institution resulted in clinical disease, whereas more than half of infections acquired in nature were asymptomatic. Risk of respiratory infection from exposure to infected tissue or aerosols of infected secretions is very low. Accidental percutaneous inoculation has typically resulted in local granuloma formation.

**Natural Modes of Infection**

Single spores can produce ambient infections by the respiratory route. Peak exposures occur during arid seasons. _Coccidioides_ spp. grow in infected tissue as larger multicellular spherules, up to 70 microns in diameter and pose little or no risk of infection from direct exposure. The majority of ambient infections is subclinical and results in life-long protection from subsequent exposures. The incubation period is one to three weeks and manifests as a community-acquired pneumonia with immunologically mediated fatigue, skin rashes, and joint pain. One of the synonyms for coccidioidomycosis is desert rheumatism. A small proportion of infections is complicated by hematogenous dissemination from the lungs to other organs, most frequently skin, the skeleton, and the meninges. Disseminated infection is much more likely in persons with cellular immunodeficiencies (AIDS, organ transplant recipient, lymphoma).

**Laboratory Safety and Containment Recommendations**

Because of their size, the arthroconidia are conducive to ready dispersal in air and retention in the deep pulmonary spaces. The much larger size of the spherule considerably reduces the effectiveness of this form of the fungus as an airborne pathogen.

Spherules of the fungus may be present in clinical specimens and animal tissues, and infectious arthroconidia in mold cultures and soil or other samples from natural sites. Inhalation of arthroconidia from environmental samples or cultures of the mold form is a serious laboratory hazard. Personnel should be aware that infected animal or human clinical specimens or tissues stored or shipped in such a manner as to promote germination of arthroconidia pose a theoretical laboratory hazard. BSL-2 practices, containment equipment, and facilities are recommended for handling and processing clinical specimens, identifying isolates, and processing animal tissues. BSL-3 practices, containment equipment, and facilities are recommended for experimental animal studies when the route of challenge is parenteral.
other environmental materials known to contain infectious arthroconidia. Experimental animal studies should be done at BSL-3 when challenge is via the intranasal or pulmonary route.

**Special Issues**

**Transfer of Agent:** Importation of this agent may require CDC and/or USDA importation permits. Domestic transport of this agent may require a permit from USDA/APHIS/VS. A DoC permit may be required for the export of this agent to another country. See Appendix C of BMBL5 for additional information.

Taken directly from: [http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm](http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm)