

COCCIDIOIDOMYCOSIS *by Bill Wojciechowski, MS, RRT*



Coccidioidomycosis is an endemic fungal disease caused by *Coccidioides immitis* and *Coccidioides posadasii*. *C. immitis* is sometimes called the Californian species, and *C. posadasii* is referred to as the non-Californian species. *C. immitis* and *C. posadasii* are genetically distinct species. However, differences in morphology and pathogenicity have not yet been delineated. *Coccidioides* species prevail in the southwestern United States in arid and semiarid climates. Arid and semiarid climates are characterized as having relatively modest rainfall (less than 10 inches annually), mild winters, and prolonged hot seasons. In the United States, these climates are particularly located in the Lower Sonoran Life Zone, which includes parts of Arizona, Texas, New Mexico, Nevada, Utah, and central and southern California. Northern Mexico and areas of Central and South America are other endemic regions for *Coccidioides*. These fungi are located only in the Western Hemisphere, and reside in the soil in these endemic regions. Disturbances to the soil created by wind, excavation, and even earthquakes cause fungal spores, also called arthroconidia, to become airborne. Approximately, 150,000 people are infected with *Coccidioides* each year in the United States.

History

Coccidioidomycosis, also known as Valley Fever because of its prevalence in the San Joaquin Valley in California, was initially described as a severe disease in 1892 by Alejandro Posadas in South America. Posadas had a patient named Domingo Ezcurra,

an Argentinean soldier, who contracted coccidioidomycosis and was treated for 11 years before succumbing to this disease. In 1894, the first case in California was reported. In 1896, Rixford and Gilchrist identified the causative microorganism, and named it *Coccidioides immitis*. In 1929, a less severe form of the disease was serendipitously recognized when a student from the Stanford University Medical School survived this pulmonary infection. Amphotericin B became available for treating coccidioidomycosis in 1957. In 1987, a number of oral antifungal medications known as azoles such as ketoconazole and itraconazole became available.

Microbiology

The *Coccidioides* species is dimorphic, which means it can change from the room-temperature hyphal form to the body-temperature spherule form. *Coccidioides* also has two life cycles. It is saprophytic (lives off dead decaying organic matter) when in the soil, and is parasitic when in a host. In the soil as a saprophyte, *Coccidioides* spores form mycelia. As mycelia mature, they form more spores. When the soil becomes agitated, the spores become airborne and are inhaled by a host, which can be people, domestic animals, or wildlife. At this point, the saprophytic cycle ends, and the parasitic cycle begins. Once inside the lungs of the host, the spores germinate into spherules filled with endospores. The spherules (30-60 microns) filled with endospores, which are 3 to 5 microns in diameter, ultimately burst releasing the endospores, thereby further invading the host.

Diagnosis

A history of travel or residence in an endemic area is critical in establishing exposure to the microorganism. A *Coccidioides* skin test, similar to the tuberculosis skin test, is available. However, the vast majority of residents of endemic regions demonstrate cutaneous hypersensitivity to coccidioidin or spherulin. Therefore, skin reactivity testing is not a useful diagnostic tool. Coccidioidomycosis should be suspected in persons who present with cough, chest pain, shortness of breath, low-grade fever, arthralgia, fatigue, or skin rashes (erythema nodosum or erythema mutiforme), and who are at increased risk, based on pregnancy, ethnicity, occupational status, or immunocompetence. The following ethnic groups are most susceptible to *Coccidioides* infection: Filipinos, Hispanic, and African-Americans. At risk occupations include farmers, archeologists, and excavators. Immunocompromised persons are also at elevated risk.

Differentiating coccidioidomycosis from other diseases requires a sputum culture and serologic testing. The direct observation of spherules in a sputum sample establishes the diagnosis. A complement-fixation test is used to detect IgE antibodies. Precipitin testing reveals coccidioidal IgM in about 75% of patients having acute infection. Depending on how the host responds to the infection, the chest x-ray may be normal, or reveal nodules, infiltrates, cavities, hilar adenopathy, or pleural effusion. Bronchoscopy is useful when non-invasive procedures fail to render a diagnosis.

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Clinical Manifestations

>60% of people infected with *Coccidioides* are asymptomatic. The remaining 40% range from mild to severe, and are manifested as (1) primary coccidioidal pneumonia, (2) pulmonary nodular, (3) pulmonary cavitary, (4) chronic progressive fibrocavitary pneumonia, and (5) disseminated coccidioidomycosis.

Primary Coccidioidal Pneumonia

Primary coccidioidal pneumonia generally presents as community acquired pneumonia within 7 to 21 days following exposure to *Coccidioides*. Symptoms include low-grade fever, malaise, headache, myalgia, arthralgia, and cough. These symptoms are usually mild and resolve without treatment. However, pregnant women and patients who are immunosuppressed generally receive antifungal medication. The former receive amphotericin B, instead of an azole, because azoles are teratogenic. The immunocompromised patients may be given either amphotericin B or one of the azoles. All patients require monitoring every three months for at least a year to identify those whose infection may worsen.

Pulmonary Nodular

Approximately, 5% of people exposed to *Coccidioides* develop a persistent pulmonary focus, which manifests itself as a nodule, cavity, or chronic progressive pneumonia. Patients with nodule formation, except those pregnant and immunocompromised, tend not to receive antifungal drugs, but require monitoring with chest radiography for two years. If nodular enlargement occurs, measures are taken to ascertain if *Coccidioides* infection is active. If so, antifungal therapy is warranted.

Pulmonary Cavitary

Cavity formation occurs in about 5% of infected patients. These cavities can resolve spontaneously, requiring no treatment.

The presence of a cavity demands monitoring with chest radiography. If after two years of its initial detection, the cavity remains or enlarges consideration is given to resection. These cavities can harbor bacteria, or other fungi, and be a source of hemoptysis. In such cases antifungal medications are warranted.

Chronic Progressive Pneumonia

Patients who present with chronic progressive pneumonia often have a low-grade fever, cough, weight loss, chest pain, and hemoptysis. These patient frequently receive antifungal drugs for about one year despite any apparent resolution. Surgical resection is sometimes considered for patients who demonstrate refractory lesions, or have unresolved hemoptysis.

Disseminated Coccidioidomycosis

An estimated 0.5% to 1.0% of people with coccidioidomycosis develop the disseminated form, which may emerge weeks, months, even years following the primary infection. Interestingly, this form of *Coccidioides* infection may develop long after a person leaves an endemic area. Disseminated coccidioidomycosis is more frequent in males than females. Persons, who are immunocompromised, and those receiving immunosuppressive therapy, are more likely to manifest this condition.

Disseminated coccidioidomycosis entails the spread of the *Coccidioides* infection from the lungs to other parts of the body of the host. Commonly, dissemination involves lungs, skin, joints, meninges, brain, and soft tissue. However, *Coccidioides* infection has been reported in every organ system in the body.

The symptoms associated with disseminated coccidioidomycosis are rather nonspecific. They include low-grade fever, anorexia, weight loss, and general malaise. Patients with pulmonary involvement often produce mucopurulent sputum, and exhibit hemoptysis, dyspnea, and cyanosis.



A recent magazine survey indicated that courtesy has diminished in public places in the United States. People interviewed said they thought that we are no longer as polite as we used to be and this has contributed to the decline of "the quality of life."

Well, the quality of my life is just fine. I don't trust surveys and I'm not sure that we aren't as polite as ever. No way to tell, of course, but I still see a lot of people being courteous. Men often hold the door open for a woman. (This ought to make women mad, not pleased, but that's another matter.) In my office, people in the hallway or at the elevator in the morning usually say "Good morning" as though they meant it. They're polite and it makes the day better.

There may be something false about manners that puts us off being polite. Phrases like, "How do you do?" or "Pleased to meet you" don't ring true. They're devoid of meaning or sentiment and some people don't use them. I don't.

Even though I think we're as polite as ever, we may have diminished the importance of some good words like "please" and "thank you" by using them too often. Sometimes they're just fillers in a conversation. "Have a nice day" doesn't really mean much. No one gives a serious answer to "How are you?" There isn't time in the day to tell everyone who asks how you are.

Computers have contributed to the weakening of words like "please" and "thank you." When I start my computer, it says, "please wait" or "thank you" when it's proceeding with some function that takes time. My old typewriter had the good taste not to say anything.

We get artificially polite recorded messages on the telephone. "We're sorry we are unable to come to the phone right now." They're probably out somewhere having a good time. It's a dumb message. The real message is something like: "Not here. Call back later."

We got off on the wrong foot years ago when some early-day Miss Manners decided we should start all our letters, "Dear Sir,"

"Dear Mr. Rooney" or "Dear Andy." I get 20 letters a day from people who call me "dear" and I'm not dear to any of them. I don't know them and they don't know me, so please knock it off with the "Dear."

I got a letter yesterday from the New York State DMV telling me I had to renew the registration for my car. The letter started with, "Dear Mr. Rooney." I'm just not that close to anyone in the DMV.

It would be better if we were more honest than polite about everything but that isn't going to happen. It would mean that we'd all have to tell the truth all the time. The truth hurts so often that we avoid it. We're polite.

Courtesy is sometimes artificial. We lie in order not to hurt someone's feelings by telling the truth. We don't say, "Boy, you got a bad haircut" to someone who just came from the barber, but it would be a better world if we were all less diplomatic and more direct. If we regularly said what we really think instead of what we think will sound good, people would get used to it and adjust their reaction to the facts and not to a statement we made that they know is not the whole truth.

One of my grandchildren, who does not read this column, sent me something he'd written for a class that I thought was poor. What do I do? I was pleased that he cared enough about what I thought to send the piece to me and I wanted to like it but I did not. What do I say? I lie. In bed that night, I got wondering whether I said the right thing to my grandson. Should I have been honest and direct and told him his writing was poor, or should I have encouraged him by saying it was good when it wasn't?

I hope you like this column. You readers are wonderful.

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Treatment & Prognosis

Most patients infected with *Coccidioides* require no antifungal medication. Patients with pulmonary nodules and cavities usually require no medication, but must be monitored over time. When indicated, ketoconazole, itraconazole, or fluconazole are prescribed for oral administration. Amphotericin B is often used in the initial treatment of life-threatening coccidioidomycosis. Surgical resection is generally reserved for patients who exhibit severe hemoptysis, bronchopleural fistula, or who fail to respond favorably to antifungal medications. Coccidioidomycosis appears to be a reemerging as evidenced by an increase in the number of cases during the past decade. Major outbreaks have emerged in southern California in 1977 and late 1991 through 1994. A new resurgence is indicated by an increase in coccidioidomycosis during the past year in Arizona.

Most coccidioidal infections are self-limiting, and resolve either spontaneously or with treatment with antifungal drugs in a few months. On the other hand, people who have weak cell-mediated immunity and high IgG levels have a bleak prognosis. Relapse is common among patients who have disseminated coccidioidomycosis. Public education in endemic areas is important for early diagnosis of *Coccidioides* infection. Residents, especially those in high-risk groups, within endemic areas, and people traveling through these regions, should be informed of exposure risks, and encouraged to seek medical treatment if respiratory symptoms appear.

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investment and work. But then moving forward, well-planned Service Learning activities can easily take the place of canned lectures, a lab activity and a test or two. That alone will recoup some precious time and bring an extra dimension to the program.

The real challenge for both the teachers and the service sites is to assure the quality of the service learning opportunities. Obviously not all service learning opportunities will be created equal. It's not just busy work. The ultimate success of the endeavor will really depend upon the *quality* of experiences available for students. And it's the quality that will make all the difference in outcomes. To be credible, real learning must occur with real service being provided. The service experience needs to be closely connected to course content. A little training and some supervision should be available. A minimum number of hours needs to be arranged with schedules stated in advance.

At the same time, we can expect that the service sites will be grateful for the contributions of students who are providing some service or benefit that their organizations would otherwise have probably done without.

Something notable about Service Learning is the acceptance it seems to be enjoying among both students and educators. The movement has become quite visible on the nation's college campuses, seeing substantial growth since its inception.

Meeting the needs of a changing student demographic and workplace present some formidable challenges for allied health programs. Service Learning serves as one valuable possibility to realizing the needs of both students and communities at large.