Coccidioidomycosis

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KEYWORDS

• Coccidioidomycosis • Coccidioides • Epidemiology • Treatment • Meningitis
• Primary infection

KEY POINTS

- The incidence and geographic range of coccidioidomycosis continues to expand.
- Coccidioidomycosis is responsible for up to 25% of all community-acquired pneumonia within the endemic region.
- Pulmonary nodules secondary to prior coccidioidal infection represent a significant problem within the endemic region and are not easily distinguishable from malignancy.
- Disseminated coccidioidal infection requires long courses of antifungal therapy increasing toxicity concerns.

INTRODUCTION

Coccidioidomycosis is a fungal disease caused by *Coccidioides immitis* and *C posadasii*. These dimorphic saprophytic fungi lay latent as a mycelial form in dry desert soil developing into arthroconidia. The organism seems to survive well in areas with lower amounts of rainfall (12–50 cm per year), few winter freezes, and alkaline soils. Initial human infection occurs primarily by inhalation of aerosolized spores and in rare cases through direct cutaneous inoculation.[1,2] The inoculum needed for infection can be quite small, even a few arthroconidia.[3] Following inhalation, arthroconidia undergo morphologic change and turn into spherules (large structures containing endospores).[4] This structure can rupture, leading to the spread of endospores hematogenously or through the lymphatics into virtually any organ, which in turn may develop into a new spherule. Human disease can range from asymptomatic to severe,

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disseminated disease, and death. Individual control of disease depends greatly on that host's immune response.

EPIDEMIOLOGY

The geographic range of *Coccidioides* has been derived from clinical cases, soil testing, and from skin testing performed in 1957 throughout the Southwestern United States.[5,6] The exact ecologic niche remains to be determined. Endemic areas where disease is prevalent include Arizona, California, New Mexico, Nevada, Utah, Washington, Texas, Mexico, and some areas in Guatemala, Honduras, Venezuela, Brazil, Argentina, and Paraguay.[7,8] In the United States, the annual incidence of coccidioidomycosis is variable but overall is increasing, from a rate of 5.3 per 100,000 in 1998 to a rate of 42.6 in 2011.[9] Of these cases reported to the Centers for Disease Control and Prevention, 66% were from Arizona and 31% from California. Despite the increased incidence, from an analysis of death certificates, the age-adjusted mortality rate from 1990 to 2008 has remained stable at approximately 0.59 per million person years.[10] There were 1451 coccidioidomycosis-related deaths in California compared with 1010 in Arizona despite its higher annual reported case rate.

The incidence of coccidioidomycosis in California and Arizona can vary greatly by geographic region and may be seasonal in pattern. In a yearly summary by the California Department of Health, the overall incidence of coccidioidal infection in the state increased from 4.3 to 11.6 per 100,000 population between 2001 and 2010.[11] In Kern County, however, the rate reported in 2011 was much higher, 241 per 100,000 population.[12] Similar increases have been observed in Arizona.[13,14] The reasons for the overall increase are not fully clear and have been attributed to changing environmental conditions, human activities in endemic areas, changing surveillance methods and definitions, increased numbers of immunosuppressed individuals, and even improved awareness and diagnostic testing rates.[15] In endemic regions, the people most affected are construction and farm workers, military personnel, archaeologists, excavators, inmates, and officers in correctional facilities.

Epidemics in endemic regions have occurred after dust storms, earthquakes, and earth excavation where dispersion of arthroconidia is facilitated.[2,13] In Washington State, 3 cases were recently reported, an area not previously considered endemic; follow-up soil testing showed the presence of *Coccidioides immitis*, suggesting the geographic range of this organism is larger than previously thought.[16,17] After coccidioidomycosis became a reportable condition, the case rate even in nonendemic regions (eg, recent report in Missouri) increased substantially; but many cases were among people who never previously traveled to an endemic region and were diagnosed serologically rather than by culture, polymerase chain reaction (PCR), or histopathologically.[18] Clinical cases of coccidioidomycosis in patients from nonendemic regions are often reported; but frequently a link is established, however brief the transit, to an endemic region.[19] There is even a case report of coccidioidomycosis in Hong Kong in a patient who is thought to have contracted the disease by sweeping shipping containers from the United States with no other link to the endemic region.[20]

DIAGNOSTIC TESTING

Currently, diagnosis can be established using immunologic assays, culture, or histopathology of tissues involved.[21] In mammalian tissues, coccidioidomycosis exists nearly exclusively as a characteristic spherule with endospores (**Fig. 1**). Spherules are approximately 60 to 100 μm in diameter and can contain hundreds of variable-sized daughter endospores, each capable of propagating infection. Rarely, hyphae