Outcomes among Inmates Treated for Coccidioidomycosis at a Correctional Institution during a Community Outbreak, Kern County, California, 2004

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Background. Treatment of pulmonary coccidioidomycosis is typically limited to patients with severe disease or those with increased risk of dissemination. In response to an increase of coccidioidomycosis at a correctional institution in an endemic area, physicians initiated an enhanced diagnosis and treatment program.

Methods. Case patients were inmates with laboratory-confirmed coccidioidomycosis during January 1, 2003, through October 31, 2004. We abstracted medical record data, including demographics, IgG complement fixation (CF) titers, treatment, and clinical outcome for initial and follow-up visits. Case patients receiving antifungal treatment were categorized into early (<4 weeks from symptom onset) and late treatment groups (>4 weeks after symptom onset). We evaluated clinical outcome, median IgG CF titer, and time to clinical improvement.

Results. Eighty-seven persons were diagnosed with coccidioidomycosis; 79 (91%) records were available. Median age was 36 years (range, 21–71 years), 34 (43%) were black, and all were male. Median time from symptom onset to diagnosis was 3 weeks (range, <1–36 weeks). Most (95%) received antifungal therapy; 32 were in the early treatment and 43 were in the late treatment group. Good clinical outcome was equally likely. In both groups, median peak IgG CF titers were 1:64. Titers in patients with early treatment did not decrease more rapidly. Median time to improvement was similar in early and late treatment groups (7 and 6 months, respectively; P = .6).

Conclusions. Persons incarcerated in endemic areas constitute a susceptible population that should be considered at risk for coccidioidomycosis. Further studies are needed to identify populations that may benefit from early antifungal treatment for pulmonary coccidioidomycosis.

Coccidioidomycosis, or valley fever, is an infection caused by Coccidioides immitis or Coccidioides posadasii. The soil-dwelling fungus is endemic in the southwestern United States, northern Mexico, and areas of Central and South America. Coccidioidomycosis is a reportable disease in the southwestern United States.

Infection occurs after inhalation of conidia [1, 2]. Sixty percent of persons who are infected are asymptomatic [3]. The remainder develop an influenza-like illness characterized by cough, fever, fatigue, and myalgias. Disseminated disease occurs in less than 1% of infected persons and may be manifested by skin, bone, or meningeal involvement. Risk factors for disseminated disease include immunosuppression, pregnancy, black race, or Filipino ancestry [1, 3, 4].

Most symptomatic patients will experience a self-limited infection that resolves without treatment. Though there are no data from randomized controlled trials, In-
fectious Diseases Society of America guidelines for the treatment of uncomplicated primary pulmonary coccidioidomycosis state that treatment is considered warranted in patients who are immunosuppressed, those who have diabetes or pre-existing cardiopulmonary disease, and for those patients who are at increased risk of developing disseminated disease, including those who are pregnant, black, Filipino, or have severe infection. Treatment is usually with an oral azole at a daily dose of 200–400 mg for 3–6 months [5].

As populations in endemic areas expand, reports of coccidioidomycosis have increased, possibly due in part to increased construction activity or increases in the susceptible population [6]. Furthermore, outbreaks of coccidioidomycosis have occurred among immunonaive persons who have traveled temporarily to endemic areas. This includes military recruits training or stationed in endemic areas [7, 8]; persons performing archeological excavations [9]; members of church groups performing construction [10, 11]; or persons performing recreational activities, such as model airplane flying [12]. Other groups, including prisoners incarcerated in endemic areas, especially those who may have previously lived in nonendemic areas, might be an underrecognized, susceptible population.

Taft, California is located approximately 35 miles southwest of Bakersfield in Kern County, a highly endemic region for coccidioidomycosis. The incidence of coccidioidomycosis in the city of Taft had increased ~4-fold in 2003 compared with 2002, an increase possibly due to climate and environmental factors. Similarly, a previous study of increased incidence of coccidioidomycosis in California, including Kern County, in 1991–1993 had also attributed the increase in disease to several years of drought followed by rainy winter and spring seasons [13].

In 2003, officials at a federal correctional institution in Taft, California, were concerned with an apparent increase in the frequency with which inmates were diagnosed with coccidioidomycosis. In response to this increase, treating physicians instituted a plan to enhance diagnosis and treatment of inmates with coccidioidomycosis. We describe the increase in coccidioidomycosis cases at the prison and evaluate the potential impact of the timing of treatment on outcome in inmates with coccidioidomycosis.

METHODS

Case definition and case finding. We defined a case patient as an inmate of the correctional institution with laboratory confirmation of coccidioidomycosis during January 1, 2003, through October 31, 2004. Laboratory findings indicative of disease included culture or histopathological evidence of Coccidioides species or a serologic test positive for coccidioidal antibodies, including (1) a single positive IgM by enzyme immunoassay (EIA) or immunodiffusion (ID), or (2) a single positive IgG by ID or complement fixation (CF) titer ≥1:2.

Since coccidioidomycosis is a reportable disease in Kern County, any positive coccidioidomycosis laboratory finding is reported to the Kern County Department of Public Health (KCDPH). The laboratory at the KCDPH performed all antibody testing on serum from persons incarcerated at the correctional institution. Case patients were identified by using the database at the KCDPH.

When the increase in the number of inmates diagnosed with coccidioidomycosis was recognized by the physicians at the prison clinic in the summer and fall of 2003, they increased efforts to identify and treat patients with the infection; inmates who came to the prison clinic and complained of at least 4 days of consistent symptoms, such as cough, fever, or pleuritic chest pain, were evaluated for coccidioidomycosis with serologic testing and a chest radiograph. Serologic test results were received within 1 week. If serologic tests were positive, the clinician made the treatment decisions on an individual case basis.

Patients diagnosed with coccidioidomycosis were evaluated in the prison clinic and IgG CF titer levels were drawn approximately once per month. Changes in antifungal regimen were based on patients’ clinical status and laboratory testing results. Patients continued to be followed in clinic until they had been off antifungal medication for 3 months and were clinically stable.

Case patients’ medical records at the prison were reviewed and data were abstracted by using a standardized data collection form. The standardized form included patients’ demographics, clinical information, laboratory tests, radiologic studies, and antimicrobial treatment while at the correctional institution or other federal prisons. Medical records for inmates who had been transferred to other federal correctional facilities were reviewed, and the standardized form was completed by a Federal Bureau of Prisons’ physician. This investigation constituted an evaluation of public health practice in response to an urgent public health response; as such, our investigation was not human subjects research and not subject to review and approval by an ethics committee.

Incidence analysis. Incidence of coccidioidomycosis in Taft was calculated by using reports of persons with coccidioidomycosis from the KCDPH and population data from the US Census 2000; incidence data for Taft and population data from the Census 2000 did not include the inmate population at the federal correctional institution. To estimate the incidence rates at the prison in 2002 and 2003, we used the population of the prison on November 1, 2004 (2232 inmates), as the denominator. Race-specific incidence was calculated by using the racial makeup of the prison population on November 1, 2004. Race
was classified as white, black, or other; ethnicity was categorized as Hispanic or non-Hispanic. As we had current information on the total number of cases only through October 2004, the partial incidence for 2004 was calculated by dividing annual incidence by 0.83.

Outcome study. Case patients who received antifungal treatment were categorized into early and late treatment groups; patients who did not receive antifungal treatment were excluded from the outcome study. Case patients were categorized in the early treatment group if they received treatment ≤4 weeks from symptom onset while the late treatment group received treatment >4 weeks after symptom onset.

Outcomes were compared between the case patients in the 2 treatment groups to evaluate whether early treatment was associated with improved outcomes. Three main outcomes were evaluated, including (1) clinical outcome, (2) median IgG CF titer, and (3) the time to clinical improvement. Good clinical outcome was defined as subjective improvement in symptoms, as documented in medical records, one year after diagnosis (or at the last clinic visit, if the patient was followed for <1 year). Poor clinical outcome was defined as the development of new, worsened, or no change in symptoms, or if death due to coccidioidomycosis infection occurred during this time period.

Individual patient’s IgG CF titers were documented at the time of diagnosis and at each subsequent monthly clinic visit. Patients’ IgG CF titers were plotted at monthly intervals from the time of symptom onset. If a patient had >1 IgG CF titer measured during a 1-month period of time, the higher IgG CF titer was plotted. The median IgG CF titer at each monthly interval was calculated for the case patients by treatment group. Time to improvement was defined as the time in months from initiation of fluconazole to a decrease in dose or discontinuation of fluconazole due to improved symptoms or a decrease in IgG CF titer, as decided by the physician at the correctional institution.

Statistical analysis. Data were entered into Microsoft Access databases and analyzed in SAS, version 9.1 (SAS Institute). The 3 outcome analyses were limited to those patients who received antifungal treatment. In addition, persons were excluded from analysis of clinical outcome if they did not have a documented clinical outcome. The χ² test was performed to test for independence between clinical outcome and various demographic and clinical variables. The median IgG CF titers at each monthly interval were compared between the early and late treatment groups using the Wilcoxon test.

A log-rank test was used to test whether there was a difference in the time in months to improvement in the two treatment groups. Persons were excluded from the time to improvement analysis if initial antifungal treatment was with amphotericin B, or if they did not have any follow up clinic visit documented at the correctional institution (or at another federal correctional facility if they had been transferred).

RESULTS

Description of correctional institution. The correctional institution was built in 1997 and houses approximately 2200 inmates; all are male. Inmates at this federal correctional institution may have initially resided in another part of the country or may have been transferred from another facility. Inmates spend much of the day outside and participate in recreational sports, including soccer, basketball, and softball. Inmates are also employed at the prison in jobs such as janitorial work, food service, or laundry service.

Descriptive epidemiology. The incidence of coccidioidomycosis at the correctional institution increased ∼7-fold from 314 cases per 100,000 in 2002 to 2240 cases per 100,000 in 2003. At the correctional institution, 87 persons were diagnosed with coccidioidomycosis and reported to the KCDPH during the study period January 1, 2003, through October 31, 2004 (Figure 1), compared with 7 persons at the correctional institution who were diagnosed with coccidioidomycosis in 2002.

By comparison, the incidence of coccidioidomycosis in the city of Taft (excluding inmates at the correctional institution) increased ∼4-fold from 221 cases per 100,000 in 2002 to 850 cases per 100,000 in 2003. A total of 186 Taft residents were diagnosed during January 1, 2003, through October 31, 2004 (Figure 1). Of these, 100 (54%) were male and 115 (62%) were at least 18 years of age or older. There was a peak of Taft residents diagnosed with coccidioidomycosis during August through November 2003 and a similar peak among inmates during September through November 2003; a total of 126 (46%) persons were diagnosed in the city of Taft and at the correctional institution during the peak months.

Description of patients at correctional institution with coccidioidomycosis. Of the 87 case patients identified, 79 (91%) medical records were available for review. The case patients were of varied race and ethnicity; many were black or Hispanic white (Table 1). Very few case patients were immunosuppressed. The most frequent symptoms at the time of diagnosis included cough, subjective fever, or night sweats. The median time from symptom onset to diagnosis was 3 weeks (range, <1–36 weeks). Almost all of the inmates (78 [99%]) were diagnosed by IgM and/or IgG antibody testing, and 1 inmate was diagnosed by bronchoscopy and culture. Most (68 [86%]) had a chest radiograph performed at the time of diagnosis, 51 (75%) of these had a pulmonary infiltrate present.

Fifty-five patients (70%) were treated with an antibacterial agent prior to establishment of a diagnosis of coccidioidomycosis; the most commonly prescribed antibacterial agents were trimethoprim-sulfamethoxazole, erythromycin, or doxy-
Figure 1. Histogram of persons with coccidioidomycosis in the city of Taft (excluding correctional institution) and at correctional institution, and percentage of total cases at each site by month of diagnosis, January 2003–October 2004. Two persons in the city of Taft had only a documented year of diagnosis and have been excluded from the histogram.

cycline (Table 1). More than one-half (28 [51%]) of the patients continued to receive antibiotics, even after the diagnosis of coccidioidomycosis had been established.

The majority (95%) of patients received antifungal therapy. All received fluconazole, and 4 patients also received amphotericin B at some point during the course of their treatment (Table 1). Of the 71 patients who received only fluconazole therapy, 68 (96%) received an initial dose of 400 mg. The median time from symptom onset to the initiation of an antifungal agent was 5 weeks (range, <1–40 weeks). At the time of the on-site investigation, 20 patients had discontinued fluconazole therapy due to a physician’s order; the median duration of therapy was 27 weeks (range, <1–62 weeks).

Of the 79 case patients for whom records were available, 4 did not receive any antifungal treatment and were therefore classified neither in the early nor late treatment group. A total of 32 persons (41%) were classified in the early (<4 weeks) treatment group and 43 persons (54%) in the late (>4 weeks) treatment group. The early and late treatment groups did not vary by age, race, history of diabetes, immunosuppression, hospitalization, initial IgG CF titer, presence of an infiltrate on initial chest radiograph, or initial dose of fluconazole therapy.

**Outcome analysis.** Of the 74 case patients for whom clinical outcomes were known, 67 case patients’ (85%) symptoms improved at the last clinic visit up to 1 year after diagnosis. Six case patients had no change, new, or worsening symptoms, and 1 case patient died. The case patient who died was immunosuppressed because of a history of renal transplantation and subsequent treatment with immunosuppressive medications. He was hospitalized soon after being diagnosed with coccidioidomycosis and died in December 2003 from complications due to the infection.

Clinical outcome was documented for 71 of the 75 case patients who received antifungal treatment. Patients who were
treated early were as likely as those treated late to have a good clinical outcome (42% vs 58%; P = .7).

All 75 case patients who received antifungal treatment were included in the analysis of IgG CF titer levels. The number of patients with an IgG CF titer measured and documented at a clinic visit at any specific month after diagnosis varied; it ranged from 5 to 26 patients in the early treatment group and from 9 to 24 patients in the late treatment group. The median IgG CF titer was highest at 2 months after symptom onset in the early treatment group (1:64; Figure 2). There was no difference between the median titers at each monthly interval since symptom onset in the early and late treatment groups (Figure 2). In addition, the IgG CF titers in patients who received early treatment did not decrease more rapidly than the titers of those in the late treatment group.

The 70 patients who were treated initially with fluconazole and had at least 1 follow-up visit were included in the time to improvement analysis. Eleven case patients had a decrease or discontinuation of fluconazole treatment due to improved symptoms or a decreased titer; 4 patients were in the early treatment group, and 7 patients were in the late treatment group. The median time to improvement was similar among the patients in the early treatment group (7 months) and the late treatment group (6 months) (P = .6).

**DISCUSSION**

We investigated a coccidioidomycosis outbreak among inmates incarcerated at a correctional institution in Kern County, an area known to be highly endemic for the disease. This investigation identified prisoners at a correctional institution located in an endemic area for coccidioidomycosis as a susceptible population, similar to military recruits, workers, and travelers to endemic areas [7–12]. Prison officials and public health authorities should be aware that this population may be highly susceptible to coccidioidomycosis and should consider this diagnosis in inmates in endemic areas. Since the time of this investigation, the correctional institution has implemented a local policy in an effort to decrease morbidity and mortality due to coccidioidomycosis. Staff members review new inmates’ medical records prior to their arrival, identify inmates who are immunosuppressed, and relocate them to another institution in a nonendemic area.

The burden of coccidioidomycosis among prisoners in this study was found to be quite high, with an incidence of over 2%. Although poor clinical outcomes were infrequent, many prisoners nonetheless had significant and prolonged symptoms as well as radiographically confirmed pneumonia. Although only limited information was available regarding residence prior to incarceration, it is likely that many of the prisoners were from outside an endemic area. State and federal prison authorities should consider prior residence in a nonendemic area when deciding where to place inmates, especially with inmates who are immunosuppressed and are at higher risk of developing severe coccidioidomycosis should they become infected.

This investigation evaluated differences in outcome among a cohort of persons with primary pulmonary coccidioidomycosis. The data do not demonstrate any significant differences in outcomes among patients who received early (≤4 weeks) treatment compared to those who received late (>4 weeks) treatment. Three prior, nonrandomized studies have considered the impact of timing of treatment on patients’ outcome, although the outcomes in these analyses were limited by the ability to control for the decision to use antifungal medication. In the retrospective study by Caldwell et al [14], patients who were treated early had significantly decreased peak IgG complement fixation titer, dissemination, and chronic disease.

**Table 1. Characteristics of Patients with Coccidioidomycosis at a Correctional Institution, January 2003–October 2004**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients (n = 79)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic</strong></td>
<td></td>
</tr>
<tr>
<td>Median age (range), years</td>
<td>36 (21–71)</td>
</tr>
<tr>
<td>Male sex</td>
<td>79 (100)</td>
</tr>
<tr>
<td><strong>Race/ethnicity</strong></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>34 (43)</td>
</tr>
<tr>
<td>Hispanic white</td>
<td>22 (28)</td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>12 (15)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>7 (9)</td>
</tr>
<tr>
<td>Immunosuppressed</td>
<td>2 (3)</td>
</tr>
<tr>
<td><strong>Symptom</strong></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>57 (72)</td>
</tr>
<tr>
<td>Subjective fever</td>
<td>40 (51)</td>
</tr>
<tr>
<td>Night sweats</td>
<td>25 (32)</td>
</tr>
<tr>
<td><strong>Positive serology</strong></td>
<td></td>
</tr>
<tr>
<td>IgM EIA</td>
<td>57 (72)</td>
</tr>
<tr>
<td>IgM ID</td>
<td>39 (49)</td>
</tr>
<tr>
<td>IgG ID</td>
<td>57 (72)</td>
</tr>
<tr>
<td>IgG CF titer ≥1:2</td>
<td>67 (85)</td>
</tr>
<tr>
<td><strong>Antibacterial agent prior to diagnosis</strong></td>
<td></td>
</tr>
<tr>
<td>Any antibiotic</td>
<td>55 (70)</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>29 (39)</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>28 (35)</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>15 (19)</td>
</tr>
<tr>
<td><strong>Antifungal therapy</strong></td>
<td></td>
</tr>
<tr>
<td>Any antifungal agent</td>
<td>75 (95)</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>75 (100)</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Early treatmenta</td>
<td>32 (41)</td>
</tr>
<tr>
<td>Late treatmentb</td>
<td>43 (54)</td>
</tr>
</tbody>
</table>

**NOTE.** Data are no. (%) of patients, unless otherwise indicated. CF, complement fixation; EIA, enzyme immunoassay; ID, immunodiffusion.

a Defined as ≤4 weeks after symptom onset.

b Defined as >4 weeks after symptom onset.
Figure 2. Median IgG complement fixation (CF) titers among patients receiving early (dashed line) and late (solid line) treatment by month since onset of symptoms. The subset of patients at month 0 reported that their symptom onset date corresponded to the date the initial CF fixation titer was performed.

In another study, oral antifungal therapy for patients with mild coccidioidomycosis prevented severe disease [4]. Another more recent study did not find a difference among treated and untreated persons, although it clearly demonstrated the factors associated with the decision to use therapy [15]. Our findings highlight the controversy surrounding this issue, and emphasize the need for a randomized, clinical trial to determine the effectiveness and timing of antifungal therapy. Newer antifungal agents, such as posaconazole, have been shown to be safe and effective in salvage studies and may be worthy of further study [16, 17].

When the outbreak was recognized at the prison, physicians aggressively tested for coccidioidomycosis in patients who had several days of influenza-like symptoms. Although the issue of antifungal treatment in acute pulmonary coccidioidomycosis is controversial, early diagnosis of disease does provide benefit in that it facilitates appropriate patient management and prevents further diagnostic testing and unnecessary treatment with the use of antibacterial agents [18]. Of note, in this patient population, slightly over one-half of the patients who initially received antibacterial agents continued to receive them even after the diagnosis of coccidioidomycosis was made. This finding highlights the need for further education on appropriate antimicrobial use.

This investigation had several limitations. As mentioned above, we had only limited information on prisoners’ residences prior to incarceration at the correctional institution. Thus, we were not able to determine whether the case patients had been living in nonendemic areas. Additionally, prison physicians may have tested for coccidioidomycosis more frequently in response to the outbreak; this may have introduced mild surveillance artifact in the case counts. As the majority of the case patients received antifungal treatment, we were unable to determine whether early antifungal treatment was beneficial compared with no antifungal treatment. Lastly, the cohort of case patients was confined to 1 prison, so the findings may not be representative of all patients with coccidioidomycosis.

In conclusion, immunologically naive prisoners incarcerated in areas that are endemic for coccidioidomycosis are a population susceptible for infection. Upon arrival at any correctional institution located in an area endemic for coccidioidomycosis, prisoners should receive education regarding symptoms of coccidioidomycosis so they may obtain medical care early should they develop symptoms consistent with the disease. Clinicians working at the prison clinic should also be aware of coccidioidomycosis in order to facilitate early diagnosis. Although we did not find that early treatment was beneficial in this population, early diagnosis can facilitate appropriate management. Once a vaccine for coccidioidomycosis is available, persons incarcerated in endemic areas may represent a segment of the population that would benefit from vaccination.
Acknowledgments

We thank Zachary Currier, Dr. Royce Johnson, Glen Harvey, Kelly Hugunin, Corey Watts, and the medical staff at the correctional institution for their assistance with this investigation.

Potential conflicts of interest. All authors: no conflicts.

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