JOURNAL OF CLINICAL MICROBIOLOGY, Oct. 2004, p. 4552–4555 Vol. 42, No. 10
0095-1137/04/$08.00+0 DOI: 10.1128/JCM.42.10.4552–4555.2004


# Seroincidence of Coccidioidomycosis during Military Desert Training Exercises

Nancy F. Crum,[1]* Mark Potter,[2] and Demosthenes Pappagianis[3]

*Infectious Disease Division, Naval Medical Center San Diego, San Diego,[1] Internal Medicine Department, Fort Irwin U.S. Army Training Center, Fort Irwin,[2] and Department of Medical Microbiology and Immunology, School of Medicine, University of California, Davis,[3] California*

Received 5 September 2003/Returned for modification 15 December 2003/Accepted 17 July 2004

**Coccidioidomycosis is a common fungal infection acquired in the southwestern United States. This is the first study in over 2 decades to determine the seroincidence of *Coccidioides immitis* infections among U.S. military members performing training exercises in an area of endemicity. Only 8% of participants were aware of coccidioidomycosis, despite the majority having visited or lived previously in an area of endemicity. One (0.6%) of the 178 participants developed "definite" serologic evidence of infection over a 5-week training period; four (2.3%) additional patients developed "possible" coccidioidomycosis infections. None had complicated disease. The calculated annual incidence ranged from 6 to 32%. This study suggests that the risk of serious coccidioidomycosis is low among military personnel during desert training exercises; however, disease incidence may vary depending on specific activities and geographic factors. Due to the potential morbidity and mortality of this infection, preventative strategies, including vaccine development, are advocated.**

An estimated 100,000 cases of coccidioidomycosis occur annually in areas of the southwestern United States; however, since *Coccidioides immitis* infection is not a nationally reportable disease (reportable only in Arizona and California), the exact incidence is unknown. Persons at highest risk for infection include those who perform activities leading to dust formation resulting in aerosolization of fungal arthroconidia. Professions at highest risk include archeology, farming, construction work, and the military. Disease is more likely in men, a fact related to occupational exposures. Disseminated disease is more common in African-Americans, Filipinos, and those with cellular immunodeficiencies; however, there is no evidence that asymptomatic infections are more common in these groups (4, 11, 15, 18; D. Pappagianis, S. Lindsay, and S. Beall, Letter, Am. Rev. Respir. Dis. **120:**959–961, 1979). The seroincidence of coccidioidomycosis in high-risk groups, such as military personnel performing desert training exercises, has not recently been studied. Smith et al. found an annual incidence of up to 25% among military personnel training in the southwestern United States during World War II (14), and skin test conversion rates for coccidioidomycosis were as high as 34% during a 7-month period in the 1970s (5). However, a study during the 1960s at Lemoore Naval Air Station showed an annual incidence rate of less than 2% (3). Since the incidence of coccidioidomycosis has varied among studies and is reportedly increasing (1, 9), we designed a prospective cohort study to determine the seroincidence of coccidioidomycosis in military personnel performing desert training exercises.

## MATERIALS AND METHODS

Military members, as part of routine tactical exercises, participated in a 5-week training exercise at Fort Irwin U.S. Army Training Center, located in the Central Valley of California. This exercise included 3 weeks of intense military maneuvers, including camping on the desert soil, hiking and running, riding in open vehicles, artillery use, and tank driving. These activities produced intense dust exposures. Personnel did not wear face masks during training.

After obtaining approval from the Navy and Army Institutional Review Boards, we offered enrollment to 400 consecutive persons among the 4,000 persons training during the month of August 2002. Enrollment was conducted over a 5-day period before the desert training began. All military members training at the military desert facility were eligible; the only exclusion factor was the current use of an oral antifungal medication. After each participant signed the informed consent, demographic information, medical history, travel history, and any symptoms were recorded. Each participant donated 10 ml of serum for *C. immitis* testing, which included an enzyme immunoassay (EIA; Meridian Diagnostics) performed at the Naval Medical Center San Diego and a complement fixation (CF) test performed at the Veteran's Administration Hospital, La Jolla, Calif. One week after completion of the 5-week training exercise, a second sample of blood was obtained for EIA and CF testing. Participants provided information through responses to questionnaires regarding specific activities performed during their training, amount of dust exposure, and symptoms during training. All personnel then returned to duty stations, which were not located in areas where coccidioidomycosis was endemic. A third specimen was collected from a subset of participants, 6 to 8 weeks after departure from the training site, for repeat EIA and CF testing. Positive specimens by EIA or CF testing on the second or third blood draws were tested using immunodiffusion at the University of California, Davis (10). A "definite" case of acute coccidioidomycosis was defined by an EIA immunoglobulin G (IgG) seroconversion or positive immunodiffusion test. A "possible" case was defined by an isolated EIA IgM seroconversion with negative EIA IgG, CF, and immunodiffusion tests. Medical care was provided on-site during the training exercise and at each participant's home military base.

The seroincidence of coccidioidomycosis was calculated using the number of new infections divided by the number of participants available for follow-up testing. Descriptive analysis was performed, and relative risk and *P* values were calculated using chi-square testing with Yates' corrected *P* values (SPSS).

## RESULTS

Three hundred seventy-eight military personnel (9.5% of the total number of personnel training at the site) were enrolled. The median age of the participants was 24 years (range, 18 to 51 years). Ninety-five percent were male. There were 253 (66.9%) white/non-Hispanics, 57 (15.1%) African-Americans, 53 white/Hispanics (14.0%), 6 Asians (1.6%), and 3 Pacific

* Corresponding author. Mailing address: Clinical Investigation Department, Naval Medical Center San Diego, 34800 Bob Wilson Dr., Ste. 5, San Diego, CA 92134-1005. Phone: (619) 532-8134, ext. 40. Fax: (619) 532-8137. E-mail: nfcrum@nmcsd.med.navy.mil.

TABLE 1. Symptoms reported before and after training exercises

| Symptom | No. of participants with symptoms/total no. of participants (%) | | No. of participants with incident symptoms/total no. of participants (%) after training | RR (*P* value)[a] |
|---|---|---|---|---|
| | Before training | After training | | |
| Fevers | 7/378 (1.9) | 18/337 (5.3) | 16/337 (4.7) | 2.6 (0.03) |
| Night sweats | 20/378 (5.3) | 28/337 (8.3) | 24/337 (7.1) | 1.4 (0.31) |
| Chills | 8/378 (2.1) | 27/337 (8.0) | 19/337 (5.6) | 2.7 (0.02) |
| Cough | 46/378 (12.2) | 87/337 (25.8) | 60/337 (17.8) | 1.5 (0.04) |
| Dyspnea | 2/378 (0.5) | 39/337 (11.6) | 38/337 (11.3) | 21.3 (<0.01) |
| Chest pain | 14/378 (3.7) | 25/337 (7.4) | 22/337 (6.5) | 1.8 (0.12) |
| Anorexia | 0/378 (0) | 3/337 (0.9) | 3/337 (0.9) | (0.10) |
| Nausea or vomiting | 1/378 (0.3) | 26/337 (7.7) | 25/337 (7.4) | 28.0 (<0.01) |
| Myalgias | 0/378 (0) | 75/337 (22.3) | 75/337 (22.3) | (<0.01) |
| Arthralgias | 1/378 (0.3) | 69/337 (20.5) | 69/337 (20.5) | 77.4 (<0.01) |
| Rash | 10/378 (2.6) | 29/337 (8.6) | 23/337 (6.8) | 2.6 (0.01) |
| Swollen joints | 16/378 (4.2) | 15/337 (4.5) | 7/337 (2.1) | 0.5 (0.16) |
| Headache | 43/378 (11.4) | 114/337 (33.8) | 88/337 (26.1) | 2.6 (<0.01) |
| Weight loss | 3/378 (0.8) | 72/337 (21.4) | 69/337 (20.5) | 25.8 (<0.01) |
| Bone pain | 16/378 (4.2) | 8/337 (2.4) | 6/378 (1.6) | 0.4 (0.05) |

[a] RR, relative risk. *P* value indicates significance of number of participants with symptoms at initial visit versus those with incident symptoms 1 week after completion of training.

Islanders (0.8%), while 6 participants (1.6%) gave no response. Of those who provided a travel history, 56.6% had lived or traveled to an area of endemicity before this training exercise, 39% had previously trained at the desert site where the study was conducted, and 15.3% were born in an area of endemicity. No participant had significant underlying medical conditions, and all were seronegative for human immunodeficiency virus.

Eight percent of the participants had heard of coccidioidomycosis or valley fever before entering the study, and one person (0.3%) reported a history of coccidioidomycosis. Of the 378 participants, 8 (2.1%) had evidence of a prior infection based on a positive EIA IgG or CF antibody titer for the initial blood sample, including the individual with a history of prior coccidioidomycosis.

One week after the conclusion of training, 334 persons (88.4%) reported for their follow-up visit. Dust exposures during the training were reported as extensive by 209 participants (62.6%), moderate by 96 (28.7%), and mild by 29 (8.7%). The duration of dust exposure was greater than 10 days for 282 participants (84.4%). Ninety-nine percent of the military personnel reported dust exposure due to vehicle traffic, 30.6% was from marching, 39.2% was from digging, 11.7% was from artillery fire, 8.6% was from ground detonations, and 19.3% was from dust storms. Most of the personnel had dust exposures from multiple sources. Forty-five percent noticed burrowing animals in the sand near training sites. The symptoms before and after training are shown in Table 1. The signs and symptoms, including fever, chills, cough, dyspnea, nausea, myalgias, arthralgias, rash, headache, and weight loss, were statistically significantly more common after training after the data for those who had preexisting symptoms had been excluded. The mean weight loss reported during training was 8.2 lb (range, 3 to 20 lb).

A third evaluation was performed with a subset of participants 6 to 8 weeks after training to ensure adequate time to develop an immune response to an infection and to attempt to capture those not available for the second evaluation: 178 (47.1%) provided serum samples. Overall, 349 of 378 participants (92.1%) had an evaluation for symptoms and *C. immitis* testing at 1 week and/or 6 to 8 weeks posttraining.

One (0.6%) of the 178 participants evaluated 6 to 8 weeks after training developed definite acute coccidioidomycosis during the 5-week training exercise. The participant with an acute *C. immitis* infection tested positive (for both IgM and IgG by EIA) at both 1 and 6 weeks after training with a CF antibody titer of 1:2; his immunodiffusion test was positive. This case occurred in a 24-year-old Caucasian male who reported extensive dust exposures of greater than 10 days' duration due to vehicle movement, marching, detonations, and artillery fire. He reported no symptoms before training but developed myalgias, arthralgias, and headaches shortly after training, symptoms which resolved over a 2-week period; he missed no workdays. The results of a physical examination and chest radiograph were negative, and no therapy was instituted. Four (2.3%) additional patients developed possible coccidioidomycosis, with an isolated EIA IgM seroconversion; two (50%) were African-American, one (25%) developed symptoms (including chills, myalgias, weight loss, and headache), and all were observed without being given therapy. All other participants tested negative for coccidioidomycosis. During the 2 months after the training, medical personnel at the various duty stations of the study participants were astutely aware of the possibility of coccidioidomycosis among those reporting to sick call; with the exception of the cases noted above, none were found to have an illness consistent with coccidioidomycosis, and the results of chest radiographs performed for respiratory symptoms were all negative.

## DISCUSSION

This is the first study in more than 2 decades to examine the incidence of coccidioidomycosis in U.S. military personnel. Our study surveyed 10% of the participants at a large military training exercise in central California and found a lower-than-expected incidence (one definite case) of coccidioidomycosis within this high-risk group; four additional participants had possible infections. All cases were uncomplicated, and none required therapy. The annual incidence rate was calculated as 6 to 32% among those performing military maneuvers within the desert. This figure is similar to that found in other military studies, but it exceeds the rates of 43 to 86 cases per 100,000 in studies of exposed civilian populations (1, 11).

*C. immitis* infections have increased over the past decade and are currently labeled as an emerging infectious disease (6). Military members are at particular risk for this infection due to their training activities in desert locations (16); we have recently reported an outbreak among U.S. Navy SEALS training in a similar desert terrain (2). In addition, Standaert et al. reported an outbreak of coccidioidomycosis in a Marine Corps reserve unit training in southern California (17). With over 350,000 personnel stationed in areas of endemicity and thousands more training in these areas, we sought to determine the disease incidence to assess whether preventative measures, including the potential use of prophylactic antifungals, were warranted during military maneuvers in regions of coccidioidomycosis endemicity (7). Previous incidence studies among military members in the southwestern United States showed annual rates of 1.5 to 34% (3, 5, 7, 14). *C. immitis* infections may cause decreased military readiness due to acute illness. In addition, this infection has the potential to cause disseminated disease, leading to substantial disability, including forced military retirements (7, 8, 12, 13).

Clinical manifestations occur in 40 to 60% of the cases of coccidioidomycosis and typically present as a flu-like illness. Several of the military members developed illnesses during training, although only one was found to have coccidioidomycosis. The high rate of reported symptoms may have been due to bacterial or viral pathogens or the dusty and arid training conditions. Our only definite case did develop symptoms of myalgias and headaches after his *C. immitis* infection, but given the high incidence of symptoms among other participants, it is uncertain if his symptoms were due to the infection. Like our patients, most persons with coccidioidomycosis have no sequelae and miss few workdays (11).

This study had several strengths in its design. It was a prospective cohort study conducted among a well-defined population at high risk for coccidioidomycosis. The study relied on three distinct laboratory methods (EIA, including both IgM and IgG; CF antibody titers; and immunodiffusion) to diagnose coccidioidomycosis cases and sampled participants before training and twice after training (10). Skin testing would have been useful to aid in the diagnosis of asymptomatic cases but is not currently available. Those with a clinical illness were carefully examined to exclude disease. It is unlikely that participants who developed a clinical illness were evaluated by an outside medical facility, given the no-cost, convenient care provided by the military.

The limitations of the study include its small sample size and the low number of acute infections, making it difficult to assess risk factors such as demographics and activities for disease development. For instance, some studies have suggested that tobacco use increases the risk of serious pulmonary coccidioidomycosis (11). Our patient with definite coccidioidomycosis did use tobacco; however, since he was only one patient in the study who developed the infection, and 61% of participants were tobacco users, this study could not evaluate tobacco use as a potential risk factor. Although a broad range of ages (18 to 51 years) was studied, most participants were in their early 20s; studies have shown that coccidioidomycosis incidence, as well as the occurrence of significant pulmonary disease, is more common at later ages (1, 11). All enrollees trained during the month of August, and, therefore, seasonality could not be assessed. The late summer and fall months have been shown to have the highest infection rates due to the dry desert soil conditions (1, 16); hence, the peak time of infectivity may have occurred after our study (exposure in August). Furthermore, coccidioidomycosis rates may vary from year to year. Thus, a single incidence study may not capture the true risk of this infection. Since we studied a specific training experience involving tank driving and artillery use, our findings may not reflect the risk of coccidioidomycosis during other military or civilian desert activities.

Based on our study findings, military training exercises seem to place personnel at risk for coccidioidomycosis, albeit a low risk. Preventative measures, such as wearing face masks during dusty conditions, using closed-cab vehicles, camping on vegetated soil, and educating personnel regarding the infection, are advocated; more elaborate schemes of disease prevention (such as the prophylactic use of antifungal medications) are not supported by the low incidence found in this study. The development of a coccidioidomycosis vaccine should be pursued, since *C. immitis* causes over 100,000 infections annually within the United States and occasionally leads to disabling and life-threatening disease.

## ACKNOWLEDGMENTS

The Department of Defense Global Emerging Infections Surveillance and Response System (GEIS) provided funding for this study.

We express gratitude to Margaret Bilsom and Dorothy Hochnein at the Naval Medical Center San Diego, San Diego, Calif., and Joshua Fierer and Jerry Wopschall at the Veteran's Administration Hospital, La Jolla, Calif., for performing the laboratory testing for coccidioidomycosis. We also thank Brad Hale, April Truett, Bret Smith, and Joshua Hilliard for their assistance with data collection.

The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Navy, the Department of Defense, or the U.S. Government.

## REFERENCES

1. **Centers for Disease Control and Prevention.** 2003. Increase in coccidioidomycosis—Arizona, 1998–2001. Morb. Mortal. Wkly. Rep. **52:**109–112.
2. **Crum, N. F., C. Lamb, G. Utz, D. Amundson, and M. Wallace.** 2002. Coccidioidomycosis outbreak in Navy SEALs during training in an endemic area—Coalinga, California. J. Infect. Dis. **186:**865–868.
3. **Drips, W., Jr., and C. E. Smith.** 1964. Epidemiology of coccidioidomycosis. JAMA **190:**1010–1012.
4. **Gray, G. C., E. F. Fogly, and K. L. Albright.** 1998. Risk factors for primary pulmonary coccidioidomycosis hospitalizations among United States Navy and Marine Corps personnel, 1981–1994. Am. J. Trop. Med. Hyg. **58:**301–312.
5. **Hooper, R., G. Poppell, R. Curley, S. Husted, and R. Schillaci.** 1980. Coccidioidomycosis among military personnel in Southern California. Mil. Med. **145:**620–623.
6. **Kirkland, T. N., and J. Fierer.** 1996. Coccidioidomycosis: a reemerging infectious disease. Emerg. Infect. Dis. **3:**192–199.
7. **Olivere, J. W., P. A. Meier, S. L. Fraser, W. B. Morrison, T. W. Parsons, and D. M. Drehner.** 1999. Coccidioidomycosis—the airborne assault continues: an unusual presentation with a review of the history, epidemiology and military relevance. Aviat. Space Environ. Med. **70:**790–796.
8. **Olson, P. E., W. D. Bone, R. C. LaBarre, C. R. Martin, G. C. Utz, L. K. Miller, and L. Gresham.** 1995. Coccidioidomycosis in California: regional outbreak, global diagnostic challenge. Mil. Med. **160:**304–308.
9. **Pappagianis, D.** 1994. Marked increase in cases of coccidioidomycosis in California: 1991, 1992, and 1993. Clin. Infect. Dis. **19:**S14–S18.
10. **Pappagianis, D.** 2001. Serologic studies in coccidioidomycosis. Semin. Respir. Infect. **16:**242–250.

11. **Rosenstein, N. E., K. W. Emery, B. Werner, A. A. Kao, R. Johnson, D. Rogers, D. Vugia, A. Reingold, R. Talbot, B. D. Plikaytis, B. A. Perkins, and R. A. Hajjeh.** 2001. Risk factors for severe pulmonary and disseminated coccidioidomycosis: Kern County, California, 1995–1996. Clin. Infect. Dis. **32:**708–715.
12. **Rush, W. L., D. P. Dooley, S. P. Blatt, and D. M. Drehner.** 1993. Coccidioidomycosis: a persistent threat to deployed populations. Aviat. Space Environ. Med. **64:**653–657.
13. **Shelton, R. M.** 1942. A survey of coccidioidomycosis at Camp Roberts, California. JAMA **118:**1186–1190.
14. **Smith, C. E., R. R. Beard, H. G. Rosenberger, and E. G. Whiting.** 1946. Effect of season and dust control on coccidioidomycosis. JAMA **132:**833–838.
15. **Smith, C. E., R. R. Beard, E. G. Whiting, H. G. Rosenberger.** 1946. Varieties of coccidioidal infection in relation to epidemiology and control of diseases. Am. J. Public Health **36:**1394–1402.
16. **Smith, C. E.** 1958. Coccidioidomycosis, p. 285–316. *In* S. B. Hayes and J. B. Coates, Jr. (ed.), Preventive medicine in World War II, vol. IV. Office of the Surgeon General, Washington, D.C.
17. **Standaert, S. M., W. Schaffner, J. N. Galgiani, R. W. Pinner, L. Kaufman, E. Durrey, and R. H. Hutcheson.** 1995. Coccidioidomycosis among visitors to a Coccidioides immitis-endemic area: an outbreak in a military reserve unit. J. Infect. Dis. **171:**1672–1675.
18. **Williams, P. L., D. L. Sable, P. Mendez, and L. T. Smyth.** 1979. Symptomatic coccidioidomycosis following a severe natural dust storm. An outbreak at the Naval Air Station, Lemoore, Calif. Chest **76:**566–570.