

Fever, Cough, Rash: Consider Coccidioidomycosis

BY SHERRY BOSCHERT
San Francisco Bureau

SCOTTSDALE, ARIZ. — Think of coccidioidomycosis in patients with a rash, fever, and cough, even if they don't live in the southwestern United States where *Coccidioides* is endemic.

At least two patients have presented to the Mayo Clinic, Rochester, Minn., with cutaneous manifestations of coccidioidomycosis. Both patients were "snowbirds" who traveled to warmer climates in the southwest during the winter, according to physicians from the Mayo Clinic, Scottsdale, Ariz.

Although this mainly is a lung infection, cutaneous manifestations provide a clue to the diagnosis. "In the last 10 years at the Mayo Clinic in Arizona, I've been impressed by how often the dermatologist has a role to play in the diagnosis of coccidioidomycosis," Dr. David J. DiCaudo said at a dermatology conference sponsored by Skin Disease Education Foundation.

The desert areas of the southwestern United States and northern Mexico are the prime locations of this fungus, which is found in the western United States, Central America, and south to Argentina. Most U.S. infections occur in Arizona and in California's San Joaquin Valley, where a syndrome with the infection was first recognized and dubbed "valley fever," said Dr. DiCaudo of the Mayo Clinic, Scottsdale.

The incidence of coccidioidomycosis in Arizona more than tripled in the past decade, with a 56% increase in the past year alone. Droughts in recent years and construction activity stirring up soil and dust probably have contributed to the increase, he suggested. The organism lives in soil as filamentous mycelia that break down into

arthroconidia, which can be carried on the wind and inhaled. Once inside people or animals, they transform into the spherule form recognized in biopsy specimens.

Most *Coccidioides* infections cause no symptoms. Around 40% of infected people develop a mild to moderate influenzalike illness with fever, cough, chills, and arthralgias. Even healthy people can be severely affected and laid low for weeks by the symptoms. Fewer than 1% develops severe infection or dissemination to the meninges or bones, with some deaths.

People of Filipino heritage are hundreds of times more likely to develop severe infection or dissemination, compared with the general population, and African Americans are at increased risk as well, Dr. DiCaudo said. People with compromised immune systems caused by pregnancy, HIV infection, or organ transplant, or those using steroids or other immunocompromising medications also face greater risk with this infection.

The painful red nodules of erythema nodosum are the most common cutaneous manifestation of coccidioidomycosis. They typically appear on the lower extremities 1-3 weeks after the onset of systemic symptoms and suggest a good prognosis.

Other cutaneous symptoms appear earlier. Acute exanthem may appear within the first 24-48 hours of illness. "I've seen



Sweet's syndrome, presenting as painful plaques, is associated with pulmonary coccidioidomycosis.

COURTESY DR. DAVID J. DICAUDDO

several patients who had a florid eruption even before the onset of any other symptom. Days later, they developed fever and cough," he said.

The acute exanthem can resemble a drug reaction. Associated pruritus may be mild to severe. Lesions on the palms are common. It may last days or weeks.

The infection also can cause Sweet's syndrome, presenting as painful plaques, often but not always on the upper body, associated with fever and peripheral blood leukocytosis. In other settings, Sweet's syndrome commonly is treated with systemic corticosteroids. "It's worth checking to make sure the patient doesn't have coccidioidomycosis first," because an immunosuppressive drug would increase their risk, Dr. DiCaudo said.

Granulomatous dermatitis can develop early in the course of the disease with widely distributed papules and plaques.

All of these cutaneous symptoms are reactive conditions; no *Coccidioides* will be found in the skin. The skin symptoms evolve over a period of weeks or months as the patient recovers from the pulmonary infection.

A skin biopsy can be helpful, however, in rare disseminated infection, which typically develops 1-3 months after the onset of illness and can cause nodules, granulomatous plaques, and ulcers on the skin. It can mimic many other diseases including tuberculosis or acne. Even rarer is primary cutaneous infection at the site of inoculation, typically from injury by a laboratory pipette, a splinter, or even a cactus spine.

Serology is the key to diagnosing coccidioidomycosis. Keep in mind that the rash precedes seroconversion, so you may want to retest some patients with negative serologies 2 weeks later, he said. Low titers are common and shouldn't be dismissed.

The IgG antibody test can be positive and the IgM negative during active infection and shouldn't be interpreted as a past infection, he added. The antibodies tend to disappear following recovery, so a positive titer most likely represents acute infection.

The large spherules (10-80 mcm) are easily seen under microscopy, typically as granulomatous or suppurative inflammatory infiltrate. If needed, an in situ hybridization assay is available to distinguish the organism from *Blastomyces* or *Cryptococcus*.

Patients with coccidioidomycosis generally are managed by primary care physicians or infectious disease specialists.

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Promising Pilot Program Promotes Home-Based STD Testing

BY HEIDI SPLETE
Senior Writer

MIAMI — At-home tests that involve self-collected vaginal samples that are sent to a lab for analysis are effective at identifying women with sexually transmitted diseases, suggest findings from a pilot study presented at the annual meeting of the American College of Preventive Medicine.

"We thought maybe we could reach out and get out of the clinic and encourage asymptomatic women to collect samples at home," said Charlotte A. Gaydos, Dr.P.H., a microbiologist in the division of infectious diseases at Johns Hopkins University, Baltimore.

Surmising that the Internet might be an effective way to promote such at-home tests, the researchers established a Web site (www.iwantthekit.org) and promoted it via the radio, posters, and print ads in local publications in the Baltimore-Washington region. In response, a total of 2,418 at-home test kits for women were mailed between June 2004 and January 2007, and the program is ongoing.

Data from 778 samples that had been analyzed as of Jan. 31, 2007, show 71 samples

(9%) were positive for *Chlamydia trachomatis* and 12 (1%) were positive for *Neisseria gonorrhoeae*. Four samples showed coinfection with chlamydia and gonorrhea. Samples collected since September 2006 were tested for *Trichomonas vaginalis*, and 13 of 115 samples (11%) tested positive.

The test kit includes sterile swabs for collecting vaginal samples and a questionnaire soliciting information on demographics, sexual history, and the participants' opinions about at-home testing and their preferences for methods to receive test results.

"We require two positive assays for a positive diagnosis," Dr. Gaydos said. Samples are analyzed using nucleic acid amplification tests (NAATs), which are more than 90% sensitive, compared with the 85% sensitivity associated with cultures. "The NAATs are the best tests there are today; they are very powerful," Dr. Gaydos said.

Participants received their test results via a toll-free number. A study coordinator arranged treatment appointments at a free local clinic for those women with positive test results.

So far, most of the women who tested positive have been treated, Dr. Gaydos noted. All 11 patients with gonorrhea

were treated, as were 66 of 69 (96%) chlamydia cases.

Of the 760 participants who identified their race, 70% were black, 22% were white, and the remainder were another race or mixed race. Chlamydia rates were significantly higher among black women, compared with white women (12% vs. 2%).

The participants ranged from 14 to 63 years of age, with an average age of 23 years, but those who tested positive tended to be younger, and the average age at first sex was 15 years, Dr. Gaydos noted.

Positive tests were most common in the 15- to 19-year-olds (16%), followed by 20- to 24-year-olds (8.5%) and 25- to 29-year-olds (8%).

After the researchers controlled for multiple factors including age and race, the strongest risk factors for positive test results were use of birth control, nonconsensual sex, and multiple partners.

In addition, more than 50% of the participants reported a history of STDs; 40% reported a history of chlamydia, and 15% reported a history of gonorrhea.

Results of the questionnaires that accompanied the kits suggest participants were receptive to the idea of at-home

STD testing. On a Likert scale of 1 to 5, 96% said that the sampling process was "easy" or "very easy" and 93% said that they would use it again.

Nearly 25% said they preferred to receive results by e-mail, but a secure Web site to provide results is too expensive at this time, Dr. Gaydos said. Under the current protocol, participants calling the toll-free number give the kit number and a password that they chose to ensure confidentiality.

Even with the current phone-in method of requesting results, the success of the Web site in recruiting patients for home sampling and in treating those who test positive is encouraging, she added. "This may be another tool that we can use to reach out of the clinic and to save money. You can save a lot of money if you don't have to pay clinicians to collect the samples."

A test kit for men was recently developed, and it is promoted on www.iwantthekit.org along with the women's kit. Men are asked to submit a urine sample and an optional penile swab. Complete analyses are pending on the 40 samples that have been collected to date; about one-third have tested positive for chlamydia, Dr. Gaydos said. ■