

to expand worldwide at an increasingly rapid rate. The IMGA should enable the community to better respond to numerous opportunities, to rapidly pass information to those interested in Medical Geology issues, and to make critical decisions that will benefit this emerging scientific discipline.

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Coccidioidomycosis: Mitigating the Risk

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Introduction

In the upper 20 cm of some desert soils in the southwestern U.S., northern Mexico, and parts of Central and South America lives a dimorphic fungus that is the only eukaryote regulated under the U.S. Anti-terrorism and Effective Death Penalty Act. This fungus is *Coccidioides* and it is the etiological agent of coccidioidomycosis, also called valley fever. As it grows in the soil in its saprophytic phase, it is characterized by branching segmented hyphae that form a network of mycelium. As the fungus matures arthroconidia (spores), 2 to 5 microns in size, are formed as barrel shaped segments of the hypha (figure 1). The arthroconidia can be easily separated from the hypha by soil disturbance (natural or anthropogenic) and consequently dispersed by the wind. If an appropriate host inhales airborne arthroconidia, primary infection may occur and the parasitic phase of the *Coccidioides* lifecycle is initiated. Appropriate hosts include humans and other vertebrates. The life cycle of *Coccidioides* concludes with the death and subsequent decay of the infected host, returning the fungus to its saprophytic form in the soil.



Figure 1. *Coccidioides* sp. hyphae showing initial formation of arthroconidia



Figure 2. Cutaneous coccidioidomycosis Source: Mycology online, University of Adelaide, Australia.

Character of coccidioidomycosis in humans

Coccidioidomycosis begins with the inhaled arthroconidia growing into spherules in the host's lung tissue. The spherules mature, rupture, and release up to thousands of endospores. Each endospore can grow into a mature spherule and the infection propagates by this method. About 100,000 people are infected annually in the United States (Valley Fever Center for Excellence, 2002). Sixty to seventy percent of infected individuals will be asymptomatic and will develop long-lasting immunity. The remainder display symptoms that range from an influenza-like illness to over-whelming pneumonia starting 7-28 days after exposure. Most recover completely and develop long-lasting immunity. In a small number of cases (<1 percent), a progressive pneumonia can persist for months to years (Ampel, 2000). In about 0.5 percent of cases, the disease may disseminate into the skin, bones, soft tissue, or meninges (figure 2) and may require lifelong anti-fungal therapy. It can also disfigure, disable, or kill the infected individual.

The risk of developing active pulmonary coccidioidomycosis varies by age, gender, and, possibly, the level of exposure to the fungus. Figure 3 displays the incidence rate for coccidioidomycosis by age in Arizona from 1990 through 1995. Figure 3 clearly shows that elderly individuals are more susceptible to acquiring active coccidioidomycosis (CDC, 1996). Males tend to get coccidioidomycosis at a higher rate than females and diabetics tend to get a more serious form of pulmonary coccidioidomycosis than non-diabetics (Ampel, 2000). Also, in cases where there is a large exposure to inhaled arthroconidia, such as workers at an archeological dig, almost everyone exposed comes down with active pulmonary coccidioidomycosis (CDC, 2001). The risk of developing disseminated coccidioidomycosis varies by ethnicity and other factors. Blacks, Filipinos, Native Americans, males, and pregnant women in the second and third trimester are at an elevated risk for disseminated infection (Ampel, 2000). Those at the greatest risk from coccidioidomycosis (pulmonary and disseminated) are individuals with an underlying immunosuppressive condition (HIV/AIDS, lupus, organ transplants, chemotherapy, etc). In fact, disseminated coccidioidomycosis is commonly fatal in HIV patients. HIV infected patients with the non-meningitis form of disseminated coccidioidomycosis had a fatality rate of 68 percent and a median survival of 54 days (Aberg, 2003). Those with coccidioidal meningitis had a 33% fatality rate and a median survival of 6 months (Aberg, 2003).

Coccidioidomycosis is a dangerous and expensive disease. Pappagianis (1980) estimated that the overall annual cost to the nation was one million person-days of labor. A review by the United States Centers for Disease Control and Prevention in Atlanta, Georgia (Goodman, ed., 1994) of the medical records in Kern County, California showed that coccidioidomycosis accounted for approximately \$66 million in direct costs of hospitalization and outpatient care during the period 1991-1993.

Based on demographic trends in the United States an increasing number of previously un-exposed high-risk individuals (mostly elderly) are moving into endemic areas. In addition, recent changes in climate may favor infection. These factors have combined to create an increasing number of cases of coccidioidomycosis in the U.S. In 2001, the Arizona Department of Health Services reported an incidence of 43 cases per 100,000 population, a 186 percent increase in the incidence rate since 1998 (CDC, 2003).

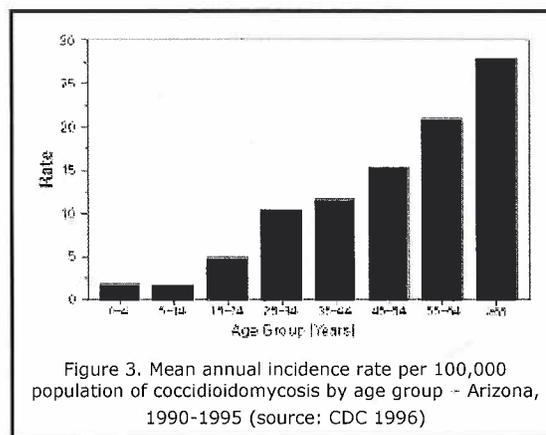


Figure 3. Mean annual incidence rate per 100,000 population of coccidioidomycosis by age group - Arizona, 1990-1995 (source: CDC 1996)

Geology and ecology of *Coccidioides sp.*

The coccidioidomycosis endemic area is shown in figure 4. This area represents the geographical extent of environmental conditions favorable for *Coccidioides* to complete its life cycle in the soil. Coccidioidomycosis was entirely attributed to *Coccidioides immitis* until recently. Work by Fisher and others (2002) has provided evidence of two species of *Coccidioides*; *Coccidioides immitis* and *Coccidioides posadasii*. *Coccidioides immitis* is found in the central valley of California, southern California, and Mexico. *Coccidioides posadasii* is found in the parts of the endemic area outside the central valley of California (Fisher and others, 2002).

Ongoing project work at the USGS Mineral Resource Program's Southwest Field Office in Tucson, Arizona is aimed at 1) defining the geological/ecological habitat of *Coccidioides sp.*; 2) modeling that habitat with spatial and temporal models in order to map soils favorable for hosting *Coccidioides sp.* and delineating conditions where arthroconidia may be released into the atmosphere; and 3) with USGS Earth Surface Dynamics Program, to monitor and



model dust emissions. The goal is to use this information to help mitigate coccidioidomycosis by predicting possible epidemics, sighting public facilities in areas where the fungus is not likely to be found, allowing biological and chemical control methods to be effectively utilized, and by allowing dust abatement methods to be used with greater effectiveness.

Laboratory and site-specific field studies have shown that many physical, chemical, climatic, and biological factors influence the growth of *Coccidioides* in the soil and the consequent development and deployment of arthroconidia.

With some exceptions endemic areas are generally arid to semiarid with low to moderate rainfall, mild winters, and long hot seasons. Mean annual soil temperatures range from 150° C to over 220°C. The presence of soils with textures that provide adequate pore space in the upper (20 cm) parts of the soil profile, for moisture, oxygen, and growing room is very important. Small amounts of clay foster water holding capacity, but large amounts of clay may be detrimental for *Coccidioides* growth. The presence of some organic material is needed for carbon and nitrogen but in most known occurrences it is generally sparse, less than 2%. Large amounts of organic compounds may be detrimental because they would foster the growth of bacteria and other fungal species that would compete with *Coccidioides*. Many *Coccidioides* growth sites have soils with elevated salinity, which may act an inhibitor of microbial competitors (Egeberg and others, 1964).

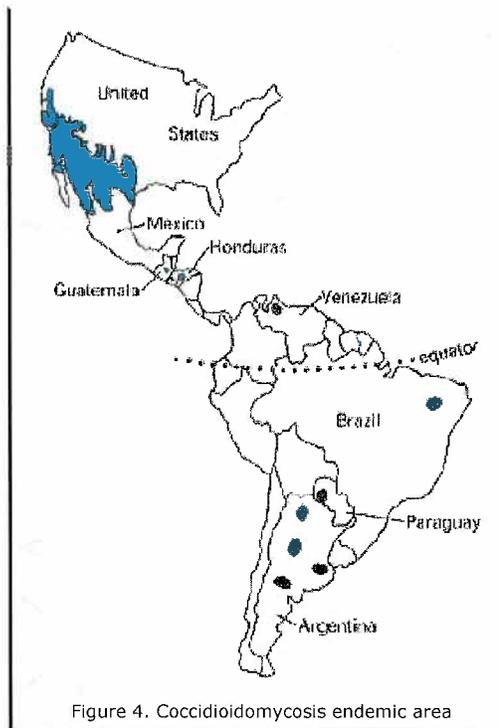


Figure 4. Coccidioidomycosis endemic area

Detection of *Coccidioides* in the environment is difficult. Traditionally mice are inoculated with isolates from suspect soil. After a pre-determined time period the mice are sacrificed and their organs examined for evidence of infection as seen by the formation of the unique spherule form of *Coccidioides*. Recently, laboratories have turned to DNA analysis in an attempt to identify the cultured fungus. While there have been some successes using DNA, there is no standardized procedure and results so far are unreliable. Scientist collaborating with the USGS at the University of Arizona and the University of California Davis are working on the development and improvement of these new techniques. Presently, testing soil for the presence of *Coccidioides* is time consuming and difficult, thus there are few locations where it has been identified in the soil.

***Coccidioides* sp. habitat modeling**

Habitat modeling of the saprophytic phase of *Coccidioides* is difficult, because of the limited number of places where it is known to exist in soil. This prevents the establishment of statistical relationships between growth sites and their physical, chemical, and biological habitat parameters. Therefore habitat modeling is accomplished using analysis of the physical properties of known *Coccidioides* sites within a spatial fuzzy system. A spatial fuzzy system is a system of spatial variables where some or all of the spatial variables are described with fuzzy sets. The fuzzy system is capable of translating structured knowledge into a flexible numerical framework and processing it with a series of if-then rules.

Fuzzy systems can describe non-linear numerical processes with linguistic common sense terms and can handle differing precision and accuracy in the data. They produce models that can be repeated and updated easily.

A fuzzy system analysis was applied in Organ Pipe Cactus National Monument, Arizona. The resulting product is a map (Figure 5) depicting



the favorableness of areas for hosting *Coccidioides* in soils based on a scale of 0 to 1, which we define as its fuzzy habitat suitability index. An important property of this kind of analysis is that "what if" scenarios can be used to predict changes in habitat with changing climate.

Complex systems modeling of the life cycle of *Coccidioides*

Like all environmental systems, the life cycle of *Coccidioides* is determined by a complex set of interactions between the organism and its surroundings. One concept that we are now testing is the possibility that saprophytic *Coccidioides* can reestablish itself in soil after arthroconidia have been blown to a new location

by an extreme wind event. Fisher and others (2001) have shown that there is spatial genetic differentiation in *Coccidioides* and geographically separate genetic clades are recognized in central California, southern California, Arizona, Mexico, Texas, and South America. This genetic differentiation argues against the ability of *Coccidioides* arthroconidia to reestablish themselves in soils, at least over long distances. But, spread of the fungus by wind may still be an important local process. In an attempt to model the spread and survival of the fungus *Coccidioides* in soil via wind-borne arthroconidia transport, a complex systems model has been developed using public domain agent-based modeling software. The hypothetical model posits that for a successful new site to become established, four factors must be simultaneously satisfied. 1) There must be transport of arthroconidia from a source site to sites with favorable soil (physical, chemical, and biological properties). 2) There must be sufficient moisture for fungal growth. 3) Soil temperatures at the surface and at depth must be favorable for growth. Finally, 4) the temperature and moisture must remain in favorable ranges for a long enough time interval for the fungus to grow down to depths at which arthroconidia will survive subsequent heat, aridity, and ultraviolet radiation of the hot, dry season typical of the Southwest U.S. climate.

Numerous model runs have shown that the probability of new sites depends on the four factors in a Bayesian way. These results indicate that the complexity introduced in the model from site favorableness, temperature, moisture, and duration of favorable temperature and moisture conditions is adequate to explain distributions of real sites described in the literature and that wind transport at a local scale may be possible. We are now working on integrating more physical habitat factors as well as soil favorableness information into the complex systems model.

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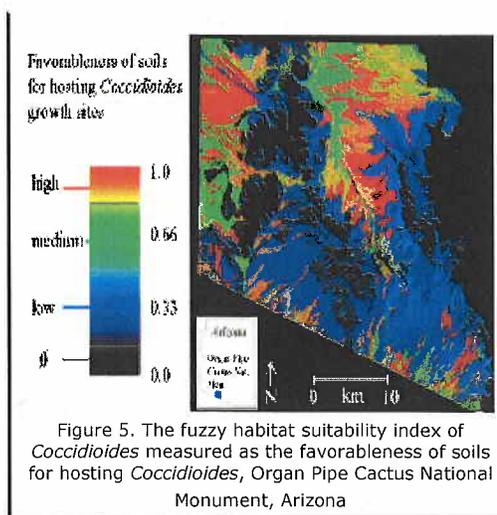


Figure 5. The fuzzy habitat suitability index of *Coccidioides* measured as the favorableness of soils for hosting *Coccidioides*, Organ Pipe Cactus National Monument, Arizona

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Formation of new USGS Human Health Coordination Committee

Charles G. Groat (signed) Chip Groat Director, USGS

I am pleased to announce that Herb Buxton has agreed to chair a USGS Human Health Coordination Committee. This committee, comprising program coordinators who currently support Human Health research, will work to increase coordination with human health agencies and coordination among USGS human health related activities. Some of the committee's first tasks will be to develop long-term strategies to identify focused research areas for the USGS, to strengthen our partnerships with human health agencies, and to identify opportunities for additional funding and growth. As chair of the Human Health Coordination Committee, Herb's first task will be to work with the Associate Directors to assemble the group. He will also serve as the USGS point of contact for health agencies and facilitate interdisciplinary response to their needs. Currently, Herb manages the Toxic Substances Hydrology Program and he will continue in that role concurrently.

Human health issues are a high priority for the American people, and, as a Federal agency, the USGS can provide critical science information in this area. However, many of our capabilities are underutilized, particularly in the areas of wildlife health-human health interactions and the use of our environmental databases (water quality, rock and soil geochemistry, land cover, etc). To maximize our impact, we must partner with the health sciences and medical fields to understand their information needs and to educate them about the value USGS can add.

As the Toxics Program Coordinator, Herb has worked closely with environmental and human health agencies on topics such as mercury cycling in aquatic ecosystems, contamination from hardrock mining, MTBE, pesticides and their degradation products, and pharmaceutically and hormonally active contaminants. He received his B.S. in Geology from Rensselaer Polytechnic Institute, and his M.S. in Geology from the State University of New York. After working as a research associate at the University of South Carolina's Hydrogeology Program, he has had a 25-year career with the USGS as a scientist and manager.

Please join me in welcoming Herb to this new leadership role.

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