Valley Fever Research

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USGS science for a changing world

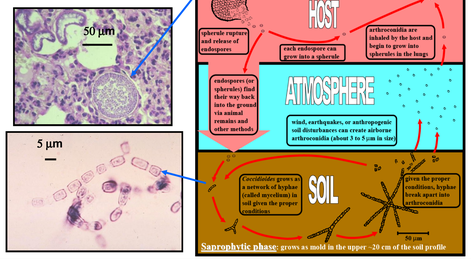
Background:

The etiological agent of Valley Fever (coccidioidomycosis) is *Coccidioides*

- ***Coccidioides is*** **a dimorphic soil inhabiting fungus found in the southwest U.S., northern Mexico, and parts of Central and South America**
- **In the environment, *Coccidioides* lives in the upper 20 cm of some soils**
- **As a parasite, *Coccidioides* infects all vertebrates including humans**
- ***Coccidioides*** **is the only eukaryote regulated under the U.S. Anti-terrorism and Effective Death Penalty Act (It is a Select Agent)**

Coccidioides life cycle

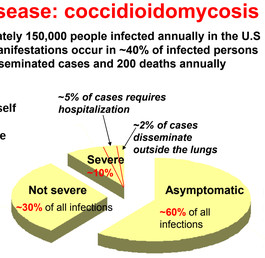
Coccidioidomycosis: A systemic infection caused by the inhalation of airborne arthroconidia (spores) of *Coccidioides*



The disease: coccidioidomycosis

- **Approximately 150,000 people infected annually in the U.S**
- **Clinical manifestations occur in ~40% of infected persons**
- **~3,500 disseminated cases and 200 deaths annually**

Symptoms range from self-limited influenza-like illness to pneumonia including:
- **fatigue**
- **cough**
- **chest pain**
- **fever**
- **rash**
- **headache**
- **joint ache**



An opportunistic disease

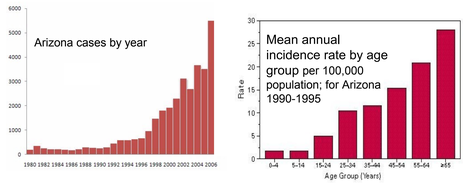
Disseminated form of coccidioidomycosis:
- Skin
- Bones and joints
- Meninges
- Organs and tissues

Coccidioidomycosis epidemiology and infectivity

Annual cost of > $60 million but hard to estimate and quite variable

Higher risk of the disseminated form of coccidioidomycosis among: African-Americans, Native Americans, Filipinos, Hispanics, Asians, pregnant women, immunosuppressed, males, elderly

A reemerging infectious disease: National surveillance started in 1995. Reportable in some states with endemic disease; California, New Mexico, Arizona



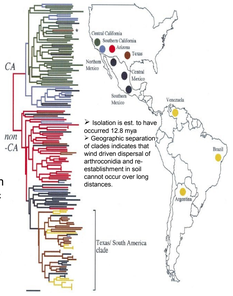
Coccidioidomycosis Endemic Area

Two species of *Coccidioides* are now known to exist:

1) Coccidioides immitis
(C. immitis) is found in the central valley of California, southern California, and MX.

2) Coccidioides posadasii
(C. posadasii) is found in the parts of the endemic area outside the central valley of CA California

Based on hematology of infected individuals- We are now testing with environmental isolates



INFECTIVITY: U.S. Army research in the1960s with *Coccidioides:*

	Bacillus anthracis	***Coccidioides***
Human median infectious (inhalation dose-spores)	8,000-10,000 (Nicas and Hubbard, 2002)	1-10

Rhesus monkey data:

Dose (spores inhaled)	Exposed	Infections	Mortality
10		5 100%	NR
10	10	100%	30%
50	5	100%	0
100	5	100%	NR
300	5	100%	60%
1,000	5	100%	NR
10,000	5	100%	80%

Coccidioides Infection

1. Dust storms and high winds

Centennial dust storm, California Central Valley, 12/20/77.
- **Infected people in Portland, OR, over 700 km away**
- **Dust plume rising to 1,500 m elevation**
- **Winds > 120 mph**

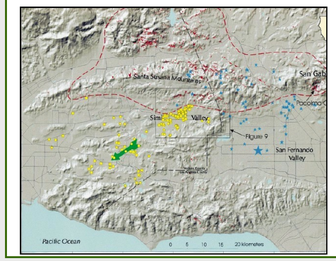


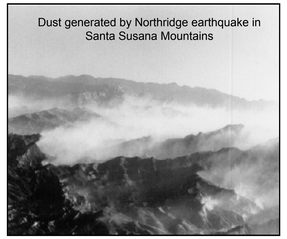

2. Anthropogenic dust

Construction and archeological surveys

3. Earthquakes

The Northridge earthquake (1994, M 6.7 epicenter shown by large blue star below) caused landslides in the Santa Susana Mtns. (red patches). Prevailing winds (green arrow) blew arthroconidia over the Simi Valley and caused 203 infections (yellow dots) including 3 deaths.





Participants (2001-2006)

USGS: Mark Bultman, Mark Gettings, MRP
UofA: Fred Fisher, Neil Ampel, Andrew Comrie, Donna Wolk, Bernard Zeigler, Rajanikanth Jammalamadaka, Marc Orbach
UC Davis: Demosthenes Pappagianis, Suzanne Johnson

Relevant USGS and other projects

USGS ESD program, Effects of climatic variability and land use on American drylands project: Rich Reynolds project chief; This project has provided us some funding in the past and is in part responsible for many *Coccidioides* related products including Bultman and others, 2005.
University of California-Davis Department of Medical Microbiology and Immunology: Ongoing coccidioidomycosis research. This project offers us in-kind access to BL-3 laboratories used to isolate *Coccidioides* from soil, specially bred highly susceptible mice, DNA analysis, and the ability to store genetic material in return for bringing them possibly infected soils. In some cases they do Coccidioides soil analysis and DNA analysis for us. Demosthenes Pappagianis M.D., Ph.D. and Suzanne Johnson, Ph.D.
Valley Fever Center for Excellence, Tucson, Arizona, *Coccidioides* Study Group: This is a formal group that meets annually that we have participated in every year since 2002. It confers on research on both the medical and environmental aspects of coccidioidomycosis. John Galgiani, M.D.
University of Arizona, *Coccidioides* Study Group: This is an informal group that meets regularly to discuss and develop Coccidioides related research. It has generated a number of UA-USGS studies and publications.
NPS-Dinosaur National Monument: Provided information on soil infectivity at Swelter Shelter and the likelihood of the existence of other infectious sites.
BLM: Investigated infectious sites in California with Erik Zaborsky
BIA: Working on an outbreak at Zuni NM with Timothy Naimi, Indian Health Services

Potential Projects:

CDC has asked us to redefine the endemic zone (Tom Chiller)
Lawrence Livermore: Interested in soil isolation (Wendy Wilson)
New York Department of Health, Div. of Infectious Disease: Soil isolation (Vishnu Chaturdedi, Director of Mycology)

Selected Publications:

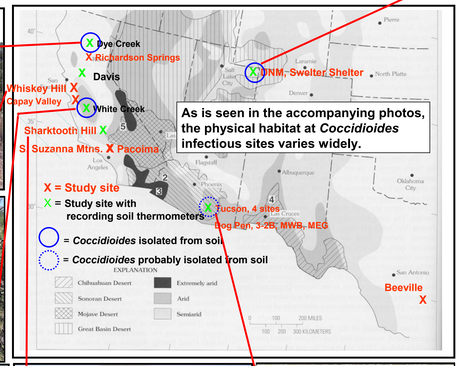
Gettings, ME, 2007, Agent based modeling of physical factor that may control the growth of *Coccidioides* in soils, submitted to JGR.
Fisher, F. S., Bultman, M.W., Johnson, S.M., Pappagianis Demosthenes, and Zaborsky, Eric, 2007, Coccidioides niches and habitat parameters in the southwestern United States, a matter of scale: Ann. N.Y. Acad. Sci. 1111, pp 47-72.
Fisher, F. S., Bultman, M.W., Johnson, S.M., Pappagianis Demosthenes, and Zaborsky, Eric, 2006, Habitat parameters of Coccidioides occurrence sites in northern Utah, southern Arizona, Central and northern California: Proceedings of the sixth international symposium on coccidioidomycosis, Aug. 23-26, 2006, Stanford Univ., Stanford, CA.
Bultman, M.W., Fisher, F.S., and Pappagianis, Demosthenes, 2005, An overview of the ecology of soil-borne human pathogens, *in* Essentials of Medical Geology: Impacts of the Natural Environment on Public Health: Elsevier Academic Press, New York.

Objective: to develop a model of the physical habitat of *Coccidioides*

- **Habitat model can be used to develop maps depicting the favorableness of soils for hosting *Coccidioides***
  - **These maps can serve as tools for coccidioidomycosis risk mitigation**
- **Habitat models can be combined with infectivity models to predict spread of the *Coccidioides* and coccidioidomycosis**
- *Coccidioides* is extremely difficult to identify in the environment (Kern county air sampling story)
  - BSL 3 animal laboratory
  - PCR analysis post animal isolation
- Concentrated on looking at know coccidioidomycosis infectious sites, places where people got sick
- Confirmed the presence of *Coccidioides* at 4 of our sites (blue circles below)
- Redefined the habitat model of *Coccidioides* based on the wide variety of habitats found at the known infectious sites

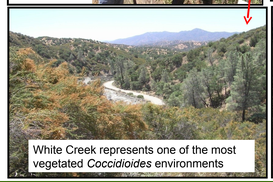
Development of *Coccidioides* habitat based on know infectious sites:

The Dye Creek *Coccidioides* site is the only known site in soil derived from volcanic rocks



As is seen in the accompanying photos, the physical habitat at *Coccidioides* infectious sites varies widely.

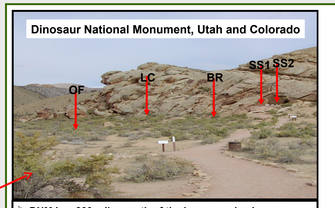
Demosthenes Pappagianis M.D. (UC-Davis) and Fred Fisher (UofA) at Whiskey Hill, CA, a heavily vegetated infectious site



White Creek represents one of the most vegetated *Coccidioides* environments

Sharktooth Hill represents one of the driest *Coccidioides* environments

Tucson has been the traditional model for *Coccidioides* habitat



- **DNM is > 200 miles north of the known endemic area**
- **High desert with hot summers and cold winters**
- **Elevation: 4825 ft**
- **Vegetation: Greasewood *Sarcobatus vermiculatus* and sparse grasses; (similar to Larrea tridentata in AZ)**
- **Site faces south –excellent sun exposure**
- **Represents an ecological niche due to microclimate**

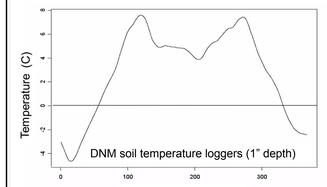
Coccidioidomycosis outbreak, June 2001

8 seasonal workers and 2 DNM archeologists were working on improving the public viewing of an archeological site called Swelter Shelter. This work included sifting soil to search for archeological objects of interest.

Dates (2001)	Total # people	# people exposed to dust	#protected	# sick
June 16 – 29	10	10	0	10
July 2	2	2	2	0
Sept 24 – 27	4	2	0	1
Sept 25	2	1	1	0
Totals	18	15	3	11

1964 Archeological Study: 5 exposed to dust, 5 infected

Due to the microclimate created by the south facing cliff, soils in and near Swelter Shelter are 5-7 degrees C warmer than surrounding areas in the winter and up to 4 degrees C cooler in summer.



How did *Coccidioides* get into soils at Swelter Shelter?

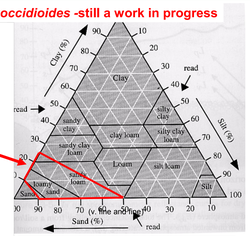
1. **PALEO-INDIANS** (25-10,000 B.C.) Big-Game Hunters -- Rocky Mountains/Great Plains
2. **ARCHAIC CULTURE** (10,000-0 B.C.) Hunting and Gathering Economy -- Great Basin/Colorado Plateau
   - **ANASAZI** (0-1700 A.D.) Horticultural Society -- Four Corners Area *
3. **FREMONT PEOPLE** (500-1200 A.D.) Horticultural Society -- Great Basin/Colorado Plateau
   - **NAVAJO** (1400 A.D. - present) Hunting and Gathering Economy -- Four Corners Area/Colorado Plateau *
4. **UTE-INDIANS** (1300 A.D. - present) Hunting and Gathering Economy -- northeastern Utah

Results so far:

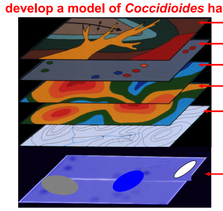
By using the data from known coccidioidomycosis infectious sites we have developed:
2.A revised physical habitat model for *Coccidioides*
3.A fuzzy spatial system at that predicts *Coccidioides* habitat at Organ Pipe Cactus National Monument, Arizona
4.Agent based models that depict how *Coccidioides* may spread
5.We hope to continue habitat modeling as well as build models that show how the *Coccidioides* endemic zone may change with changing climate, potentially putting million of Americans at risk of infection.

1. Revised habitat parameters of *Coccidioides* -still a work in progress

- **Soil**
- **Type**
  Hyperthermic or thermic Aridisols or Entisols with mean annual soil temperatures ranging from 15° C to over 22° C.
  Sites outside of these areas but with favorable microclimates have been found
- **Texture** (very important)
- **Mineralogy**
  Want low cation exchange capacity
  Low clay content, low organic content
- **pH** (~~8.5 to 11.0~~) (6.5 to 8.5)
- **Depth of occurrence (up to 20 cm.)**
  All positive samples from 10-20cm depth
- **Less than 2% organic material**
  (not true for CA soils)
- **Low water holding capacity**
- **Salinity: 8 to 16 mmhos/cm (EC)**
  (.35 to 4 in positive samples or infectious sites)
- **Abundance and types of soluble salts**
  •likes elevated sodium, potassium, calcium, chloride (not observed in all + samples)
- **Elevation (1000-5000 ft.)**
- **Slope** (+ samples low-moderate)
- **Aspect** (South facing slopes)
- **Associated vegetation types (*Larrea tridentata* and salt associated vegetation** (no))
- **Associated vegetation density-low** (only in AZ)
- Favorable parent material for soil
  - **siltstones and sandstones**
  - **•Miocene sedimentary rocks**
  - **•Volcanic rocks**
  - **•Presence of borates (not seen)**
- **Low abundance of biological soil crusts**
- **Buoyant arthroconidia may be washed up from soils in heavy rains and be moved by sheet wash accumulating in piles of organic debris commonly found in the desert. These may be the main source of wind-borne arthroconidia.**



2. A fuzzy spatial system is a rule-based model that can combine spatial data using the rules of fuzzy logic including lingual variable. It is used here to develop a model of *Coccidioides* habitat based on spatial data

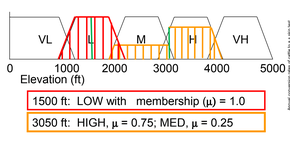


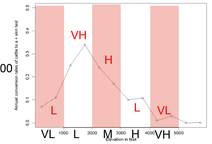
Fuzzy spatial systems are based on rules created by experts (expert system), are reproducible, can be easily adapted to deal with new data, and produce spatial or cumulative results

No or limited statistics

Favorableness of soils for the growth of *Coccidioides*

Step 1: Elevation example - Map Fuzzy Elevation to Fuzzy Favorableness



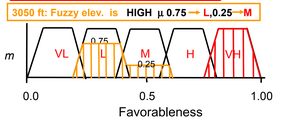


1500 ft: LOW with membership (μ) = 1.0
3050 ft: HIGH, μ = 0.75; MED, μ = 0.25

Step 2: Create relational FAM rules: if elevation A; then favorableness B

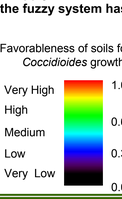
FUZZY ELEVATION	FAVORABLENESS
VL	L
L	VH
M	H
H	L
VH	VL

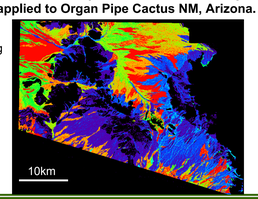
Recall the two elevations:
1500 ft: Fuzzy elev. is LOW μ 1.0 → VH
3050 ft: Fuzzy elev. is HIGH μ 0.75 → L,0.25 → M



Step 3: Apply all rules to all spatial cells in study area, sum and defuzzify. Here the fuzzy system has been applied to Organ Pipe Cactus NM, Arizona.

Favorableness of soils for hosting *Coccidioides* growth sites

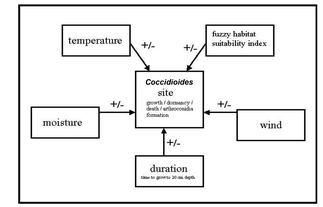


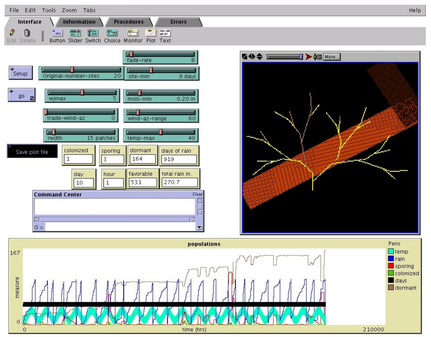


3. Agent based life cycle modeling

Complex Systems modeling of the saprophytic *Coccidioides* life cycle

A fuzzy cognitive map based model of the spread and survival of the fungus *Coccidioides* in soil via windborne spore transport





4. Future project development:

- **Continue to refine the habitat model based on known infectious sites**
- **Develop, with collaborators, better way to isolate *Coccidioides* from soils**
- **Develop better models of infectivity based on *Coccidioides* life cycle models, soil habitat models, wind erosion models, and agent based models**
- **Use what is known about *Coccidioides* habitat coupled with published models of changes in temperature and precipitation in the U.S. to model and map possible changes in the *Coccidioides* endemic zone as a function of climate change. The endemic zone may move north, east, and up in elevation. These changes, over time, could put millions of individuals with no immunity at risk of infection.**