

Coccidioidomycosis: an overview of Valley Fever and the fungus that causes the disease



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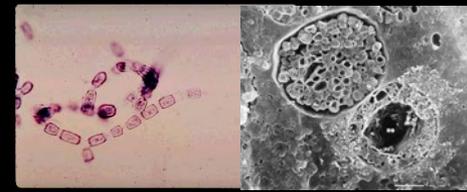
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What Is Valley Fever?



- Caused by a soil fungus (not a virus or bacterium)
 - *Coccidioides immitis* (CA, Baja-CA)
 - *Coccidioides posadasii* (AZ, TX, MX, Central and South America)
(Coccidium-like not mild (immitis))
- Also known as: San Joaquin Valley Fever, Desert Fever, Desert Rheumatism, Cocci
- True pathogenic fungus –
 - Causes disease in healthy hosts
 - Dimorphic – two forms
 - Other pathogens are *Histoplasma*, *Blastomyces*, *Paracoccidioides*

What are the Fungi?

QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.

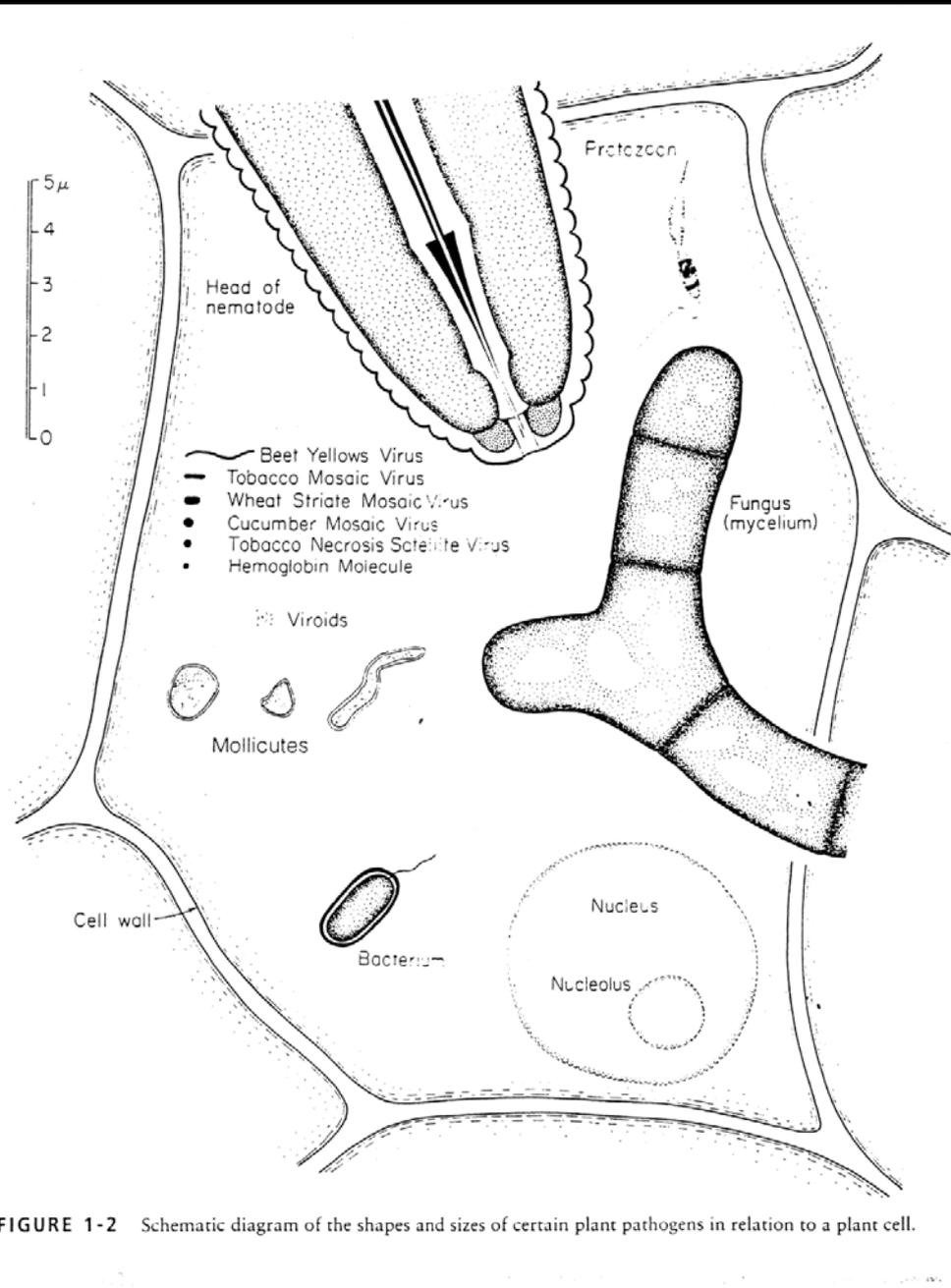
QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.

- Eukaryotic organisms, unlike bacteria and viruses
- Ubiquitous
- Reproduce asexually and sexually by spores
- Heterotrophs: rely on other organisms for nutrients carbon and nitrogen, like animals and many bacteria
- Rely on absorptive nutrition for food
- Filamentous growth (threadlike strands called hyphae), often branching. Exception: yeasts which are unicellular
- Lack chlorophyll, stems, leaves, roots so they are not plants
- Actually more closely related to animals than plants
- Rigid cell walls
- Food: most rely on dead organic material. ~10% are plant pathogens, 0.14% cause disease on animals

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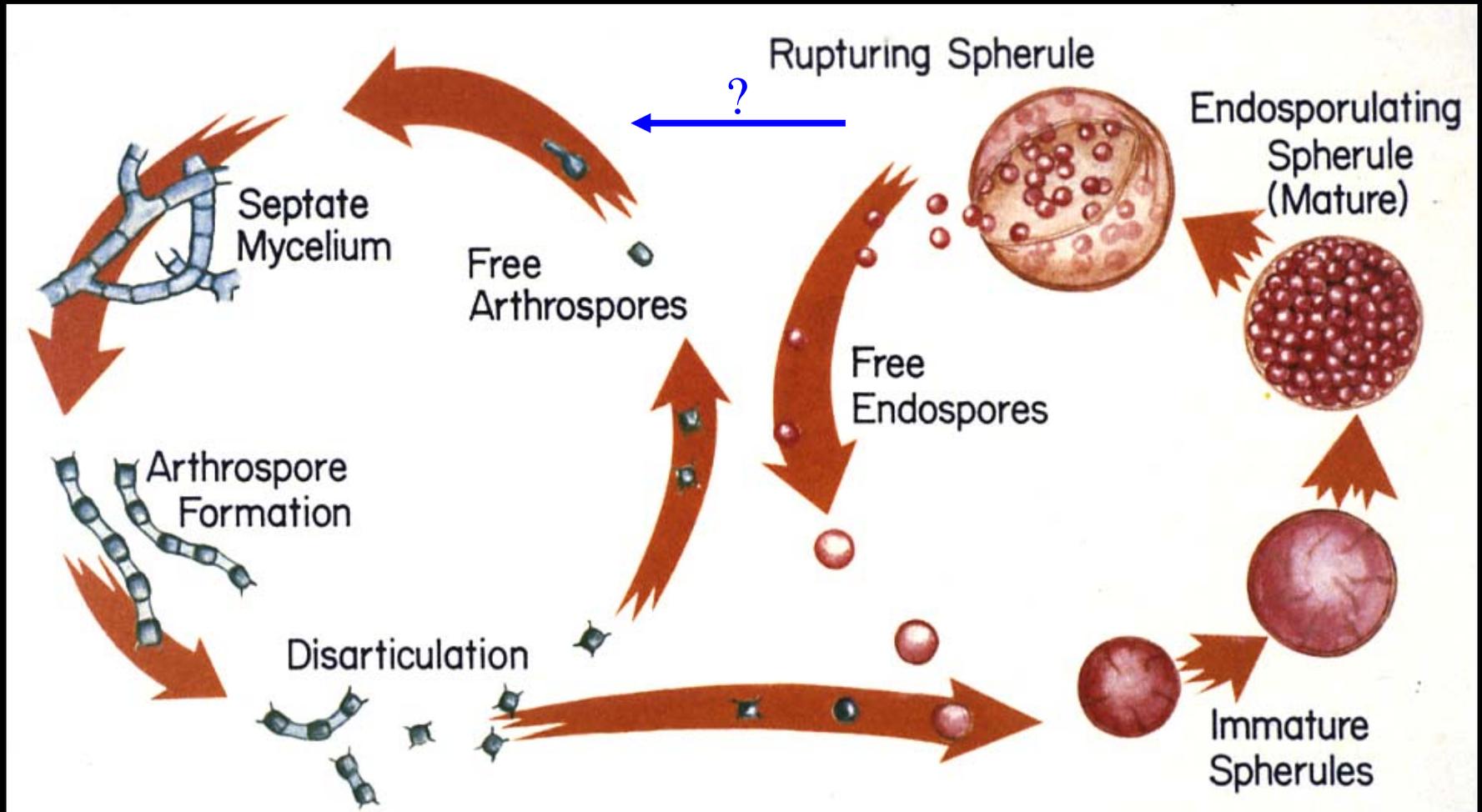
How big are they?



Diseases and the pathogen

- Valley Fever - fungus
- Tuberculosis - bacterium
- West Nile - virus
- Hanta - virus
- Anthrax - bacterium
- Legionnaires disease - bacterium
- Malaria - protozoan
- HIV/AIDS - virus

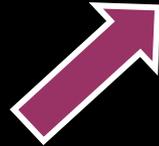
The *Coccidioides* spp. lifecycle



Saprobic (in soil)
Polar growth

Parasitic (in the lungs)
Isotropic growth

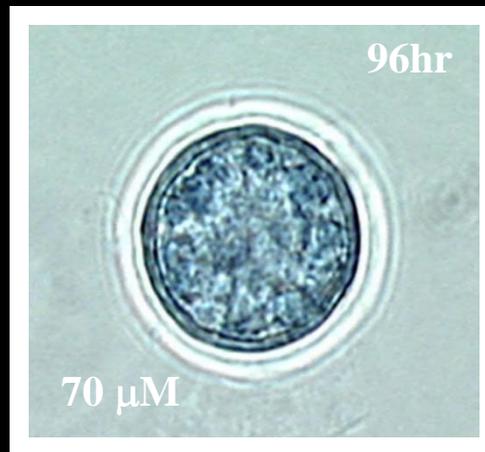
Saprobic Soil phase



And on media
In the lab



Parasitic Host-phase



Who is susceptible?

- A true pathogen that infects healthy mammals
 - Humans
 - Some are more susceptible to serious disease:
 - Immunosuppressed people, the elderly, some racial groups
 - Dogs (most important) and cats
 - Domestic livestock
 - Exotic pets and zoo animals
 - Primates are particularly susceptible
 - Boris, Tucson Reid Park Zoo Polar Bear

AZ Daily Star 2-2-02



Boris was diagnosed with valley fever last fall and will continue taking medication until blood tests show he's better.

Valley fever makes Boris an official desert denizen

Reid Park Zoo polar bear gets Twinkies laced with pills

By Sarah Garrecht Gasson
ARIZONA DAILY STAR

Boris the polar bear encounters things at the Reid Park Zoo that he would never experience in the wild — 100-degree summers, adoring crowds, peanut butter sandwiches.



keep higher primates, such as gorillas or orangutans, because they mask symptoms of valley fever, which can become fatal if left untreated, VanPeenen said.

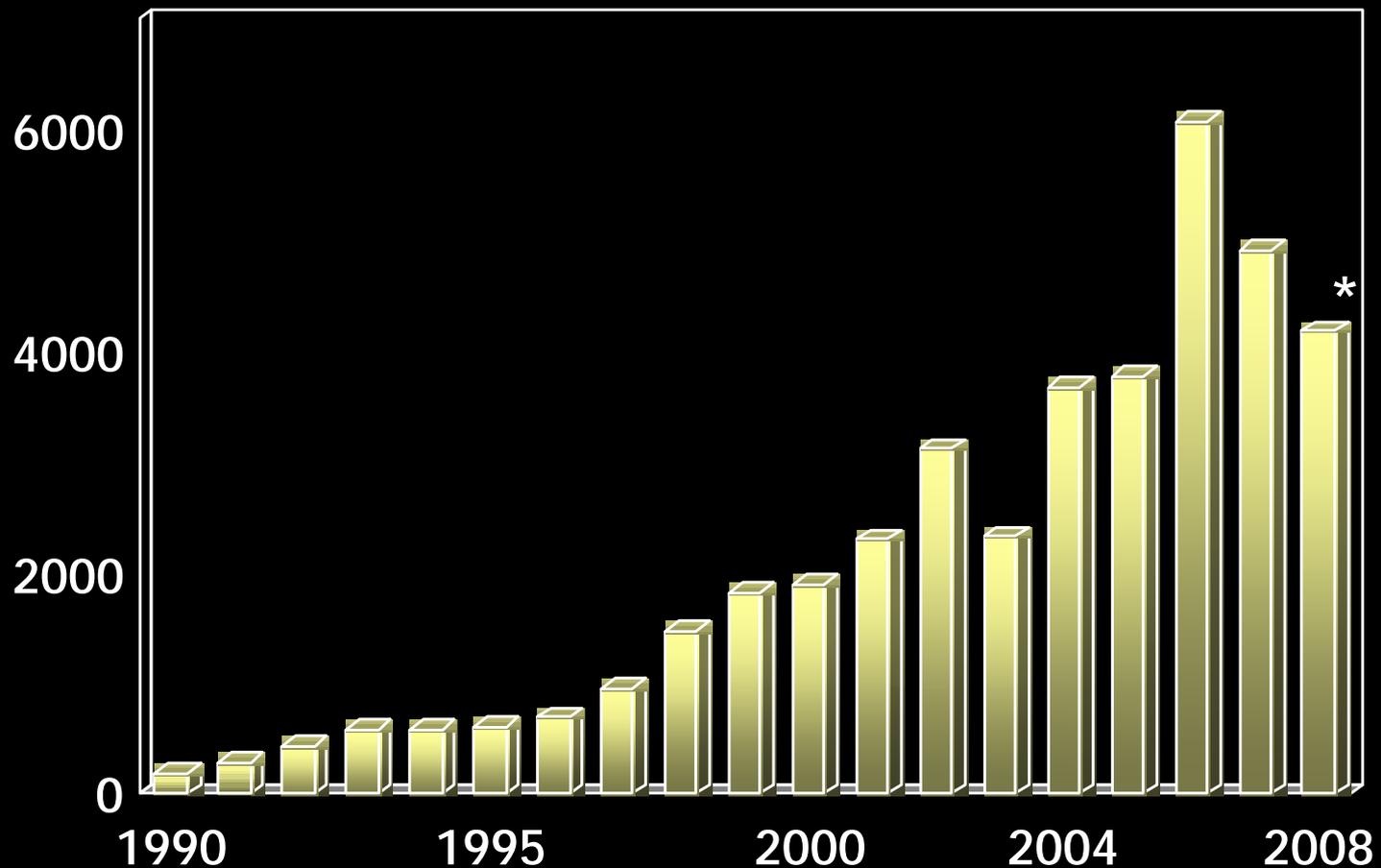
Once an animal shows that something is wrong, keepers watch closely.

"But after about three weeks everybody becomes suspicious and we try to rule out anything else prior to having to tranquilize them and do the blood work" to test for valley fever, Flint said.

Then comes the challenge of figuring out how to get pills into a polar bear.

Keepers first gave Boris his

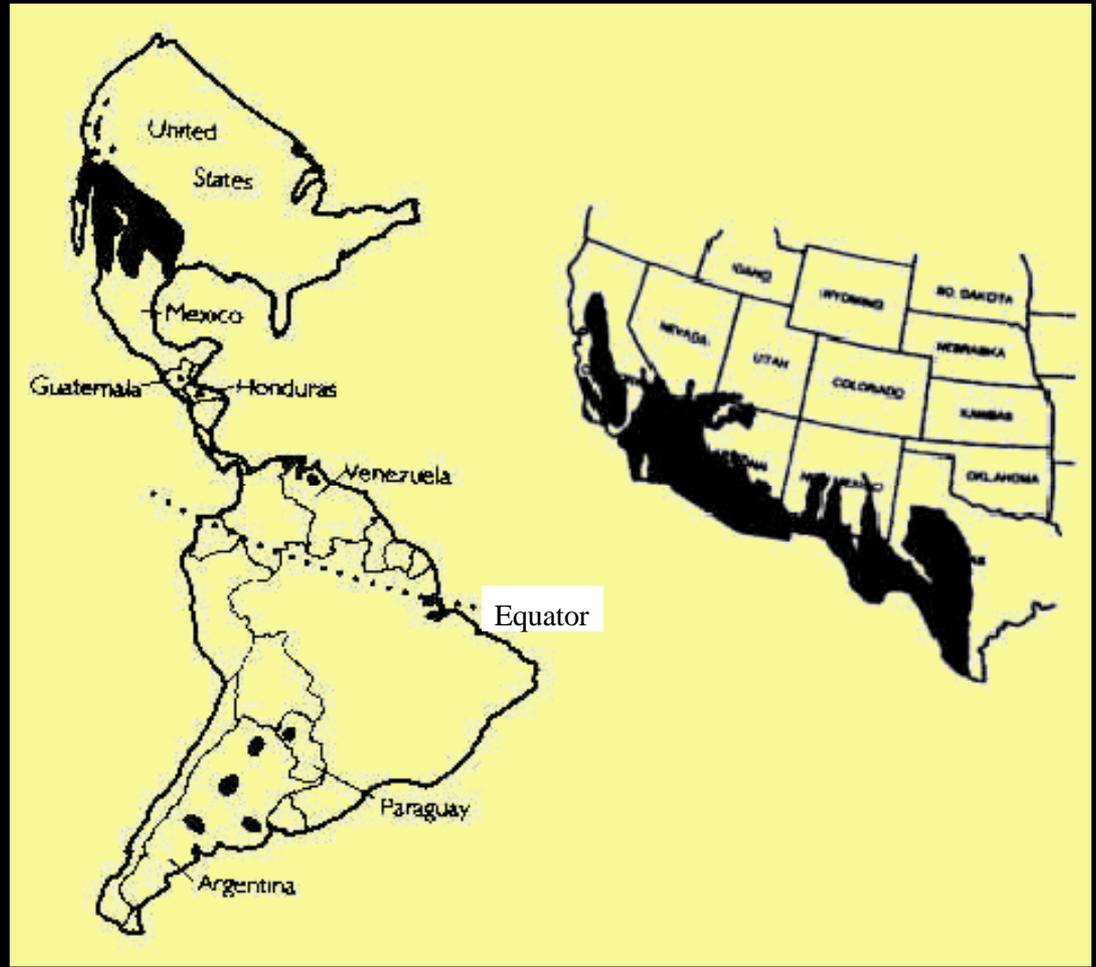
Reported Arizona Valley Fever



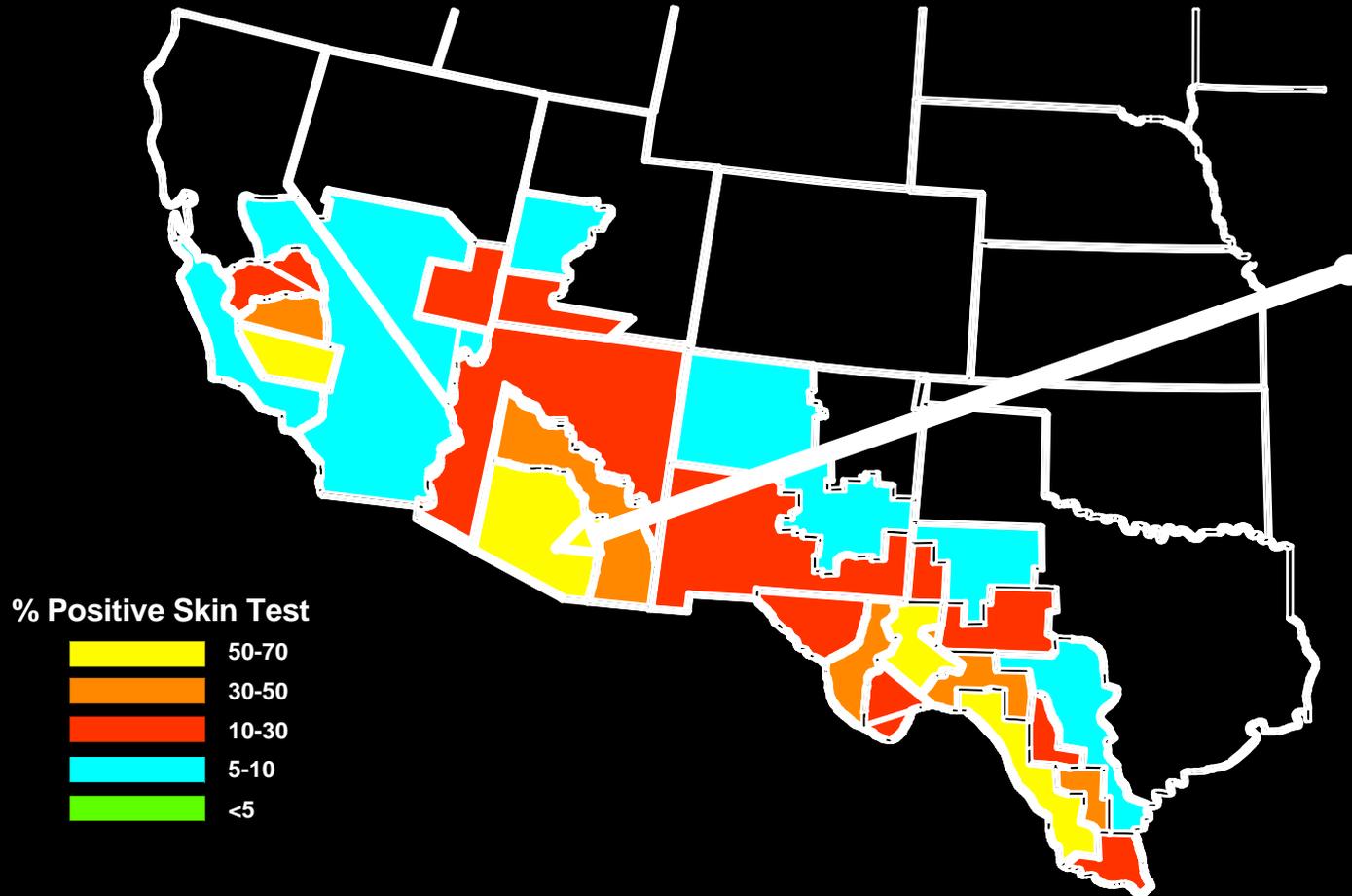
*Extrapolated from reports through Oct 31st

Where does the fungus live?

- Limited to the Western hemisphere
- Typically, hot desert
- low elevation
- low rainfall
- sandy, alkaline soil
- specifically where it lives is of great interest and an active area of research



Valley Fever in the US



Where does the fungus live (on a local level)?

- We know less than we don't know
- The range of the fungus is the same as the creosote bush (but it is not found with the bush)
- Rodent burrows seem to be more likely to contain the fungus than other areas
- Active attempts to isolate the fungus from soils have limited success
 - It is sporadically distributed.
 - Using a mouse biosensor, 8.9% of sites were shown to contain the fungus
- A hypothesis: sporadic distribution is because desert rodents are resistant carriers of the pathogen. When the rodents die, the fungus colonizes their body to create a point source for spread of spores

What we read about Valley Fever in the news

SPORTS SHORTS

Player sues PGA, says he contracted illness in Tucson

THE ASSOCIATED PRESS

CLEARWATER, Fla. — Pro golfer **Greg Kraft** has sued the PGA Tour for failing to warn players about the risk of contracting a fungal infection at a tournament in Tucson, the St. Petersburg Times reported Thursday.

Kraft, 39, filed the lawsuit earlier this week. He said he believes he got valley fever, an illness most common in the southwestern United States, at the Tucson Open in February 2002.

"The tour had a responsibility to its players," Kraft's attorney, **Leonard Decof**, told the newspaper. "They should have known about this. If golfers are going to be playing under conditions that could be dangerous or life threatening, the tour should know about it and warn them."

Omni Hotels Management Corp., which operates the resort where the tournament took place, also was named as a defendant.

The PGA Tour and Omni Hotels did not immediately return phone calls from the newspaper seeking comment.

Because valley fever is not well known outside of the southwestern states, doctors elsewhere often misdiagnose it, Decof said Wednesday.

Doctors originally suspected Kraft had cancer, Decof said, adding that because Kraft wasn't diagnosed with valley fever quickly, he is at greater risk of suffering from it for the rest of his life.

Kraft, an 11-year tour player, earned \$71,756 this past year, placing him 220th on the PGA money list. Kraft has lost his tour card, and the PGA Tour has refused to give him a medical waiver.

► **Herman Keiser**, the 1946 Masters champion, died from complications of Alzheimer's disease in Copely, Ohio. He was 89.

The five-time PGA Tour winner beat **Ben Hogan** by a stroke in the 1946 Masters

TOP WORLD STORIES

Beckham transfer first in poll

LONDON — **David Beckham**, the most recognizable face in the world's most popular game,

was the biggest newsmaker in international sports in 2003.

The England captain's \$43 million transfer from Manchester United to Real Madrid was voted the top sports story of the year in a worldwide poll of subscribers to The Associated Press.

The Beckham saga finished comfortably ahead of the doping scandals that rocked sports, **Michael Schumacher's** record sixth Formula One title, **Lance Armstrong's** fifth straight Tour de France victory and England's World Cup rugby triumph.

Beckham received 15 first-place votes and 321 points from 55 ballots cast from sports editors and broadcasters on all continents — not counting the United States, which has its own survey.

In June, Beckham was transferred from Manchester United, his home for 13 years, to Real Madrid, a nine-time European champion.

A series of high-profile drug cases finished second in the AP voting with 13 first-place votes and 297 points. British sprinter **Dwain Chambers**, four U.S. track and field athletes and four NFL players

have tested positive for THG, a previously undetectable steroid.

Third in the voting with 279 points, including seven first-place votes, was Schumacher's F-1 title. **Kobe Bryant's** arrest on sexual assault charge was voted eighth.

SOCCER

Player's brother could be alive

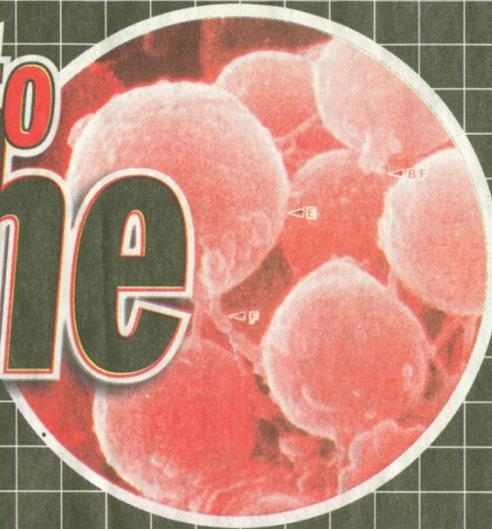
TBILISI, Georgia — A defender for Italian soccer power AC Milan thinks his kidnapped brother is still alive and will be released soon.

Kakha Kaladze returned to his homeland and met Georgian Interior Minister **Georgy Baramidze**. The player said Thursday authorities received information with "90 percent" certainty that **Levan Kaladze**, a university student at the time of his abduction in 2001, was still alive.

An investigator in the prosecutor general's office said the family had paid \$200,000 in ransom to the kidnapers in the spring of this year.

The Arizona Daily Star
December 26, 2003

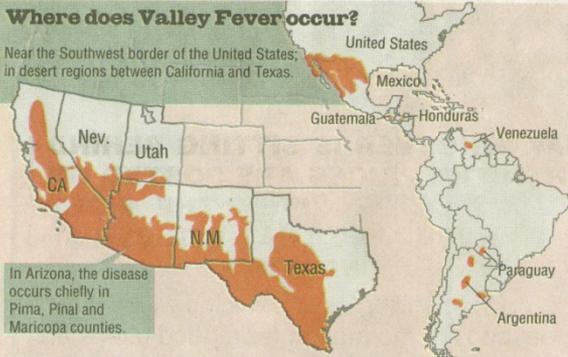
Hazardous to breathe



There's no sure way to avoid exposure, and there's no quick recovery from the disease we've come to know as Valley Fever

Where does Valley Fever occur?

Near the Southwest border of the United States; in desert regions between California and Texas.



Guillermo Munro/Staff

Electron micrographs supply an up-close look at *Coccidioides immitis*, the fungus that causes Valley Fever. When the narrow, stringy organism lives in dry soils, it can be brittle and easily broken into spores that float in the air. Inside the lung, the spores change into large, multicellular structures, called spherules, that multiply and can cause respiratory problems.

part-
ment of
Health
Services.

Valley Fever also presents serious risks for pets, especially dogs, for whom it can be a life-threatening illness requiring costly medication. As with many diseases, early detection is vital.

Who gets Valley Fever?

Sixty years ago, exposure to



“There’s no sure way to avoid exposure, and there’s no quick recovery from the disease we’ve come to know as Valley Fever.”

Arizona Daily Star
September 27,
2002

A Little Dirt Never Hurt Anyone, Right?

A warning to all desert rats: If you're hiking in the arid West, you're going to get dusty, but try to keep from breathing the stuff. Turns out the soil-borne Valley Fever—once isolated to southern Arizona and low California valleys—is spreading.

Last June, this illness struck 10 fossil diggers in northeastern Utah. At first, doc-

Relative risk of infectious diseases in the news - AZ (2006)

- West Nile Virus - 150 cases, 11 deaths
- Hanta Virus - 13 cases, 5 deaths
- Valley Fever - 5,535 cases, 33 deaths

How to avoid exposure, or what is the reservoir of disease inocula?

- West Nile Virus - avoid mosquito bites
- Hanta Virus - avoid deer mouse droppings
- Valley Fever - unknown
 - avoid breathing?

Human disease

- Coccidioidomycosis is underreported!!
 - 30% of cases of community acquired pneumonia are actually valley fever

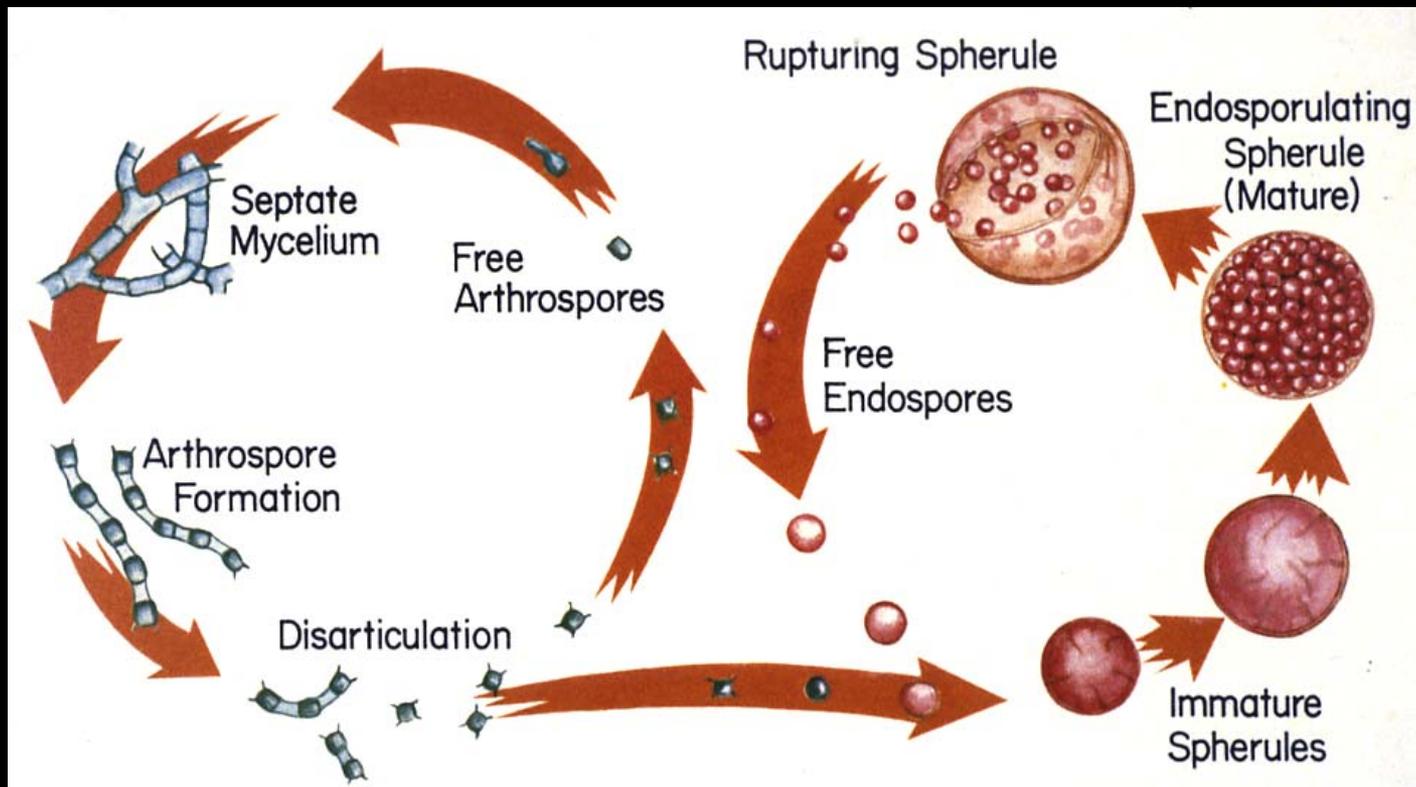
Risk factors for disease

- Risk factors for infection
 - Construction
 - Agricultural occupation
 - Archeological excavation
 - Outdoor recreation in undisturbed endemic areas
- Risk factors for severe or disseminated disease
 - Diabetes mellitus
 - Age >65 yrs
 - Male gender
 - Pregnancy
 - Underlying disease
 - Immunosuppression
 - Black or Filipino race

Areas of Research

- Biology/Genomics of the fungus
 - targets for controlling the disease through understanding what is important for the pathogen to grow
- Vaccine development
 - Prevent infections for those living in the endemic region
- Identifying the environmental niche of *Coccidioides*
 - Knowing where the fungus is in the environment would allow one to know the relative risk of exposure

Gene expression analyses of *Coccidioides*



- Specific genes promote the transition to, and growth during the parasitic phase
 - goal: block those genes to prevent the parasitic phase
- We are using genomics to identify these genes

Environmental Studies: How to avoid exposure

- Don't Breathe, or move from the endemic region
- Where exactly does this fungus live in the soil? What is its niche?
- Why is it restricted to the Lower Sonoran Life Zone?
 - ❖ Is there a specific soil type, moisture regime, or ecological association that is connected with *Coccidioides*?
 - ❖ Is there an animal association? Previous researchers suggested rodent burrows as sources. Others suggested associated with creosote (not correct).
 - ❖ Distribution of fungus overlaps distribution of the rodent family Heteromyidae (pocket mouse, kangaroo rat)
- Resistant infection often results in a granuloma containing quiescent fungus
 - ❖ Speculation: Could the death of resistant rodents serve as the point source for spore dispersal?
- Are clinical and environmental samples different? What about samples from animals other than humans?

How to Prevent Valley Fever

- Don't breath (!)
- Don't live in the southwest
- Risk reduction based upon predictive models
 - Climatology
 - Soil, Geology
 - Microbial ecology
 - Anthroprogenic Factors
 - Construction, urbanization, agriculture
- Vaccines

Acknowledgements

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Mouse Model

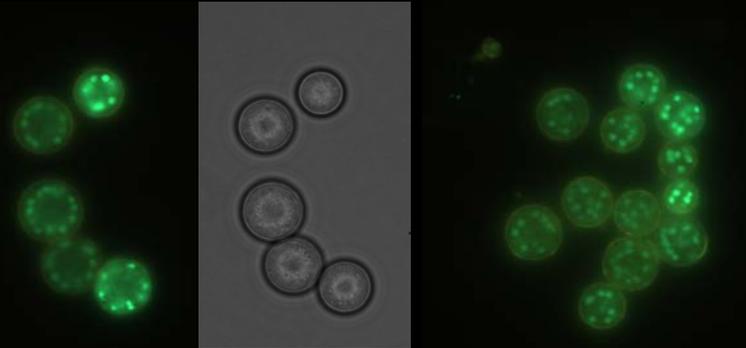
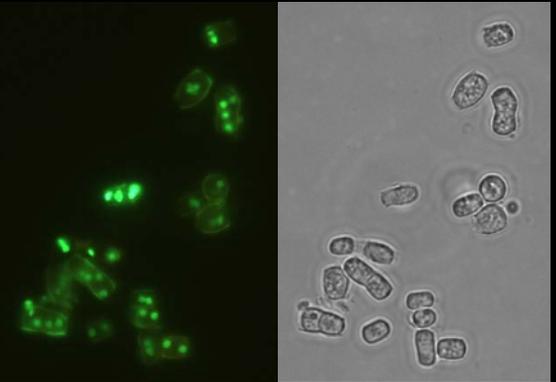
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What Is Valley Fever?

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Arizona Daily Star
September 26, 2004

Future Treatments

- New Drugs
 - Nikkomycin Z - targets fungus cell wall chitin
 - Successful in mice, clinical trials are in progress
- Vaccine Development*
 - Fungal cell surface molecules are recognized by the immune system are called “antigens”
 - Immunization with these molecules may be protective
 - Dozens of antigens have been identified through biochemistry, genomics
 - They have been cloned and many tested for protection
 - Potential Vaccine Recipients
 - Southwest residents and tourists (~50K primary infections, ~ 750 disseminated cases)
 - Military
 - Homeland Security
 - Dogs

* Funded by State of CA, CA Healthcare foundation and CA private foundations, \$15.1 million