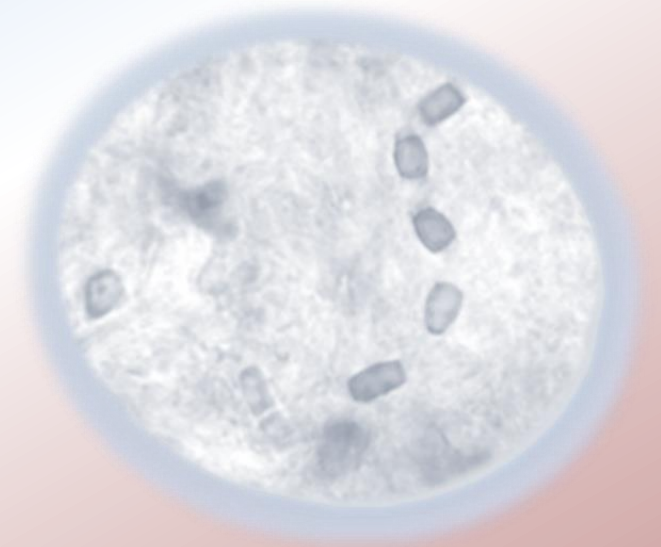


Coccidioidomycosis in Alpacas and Llamas

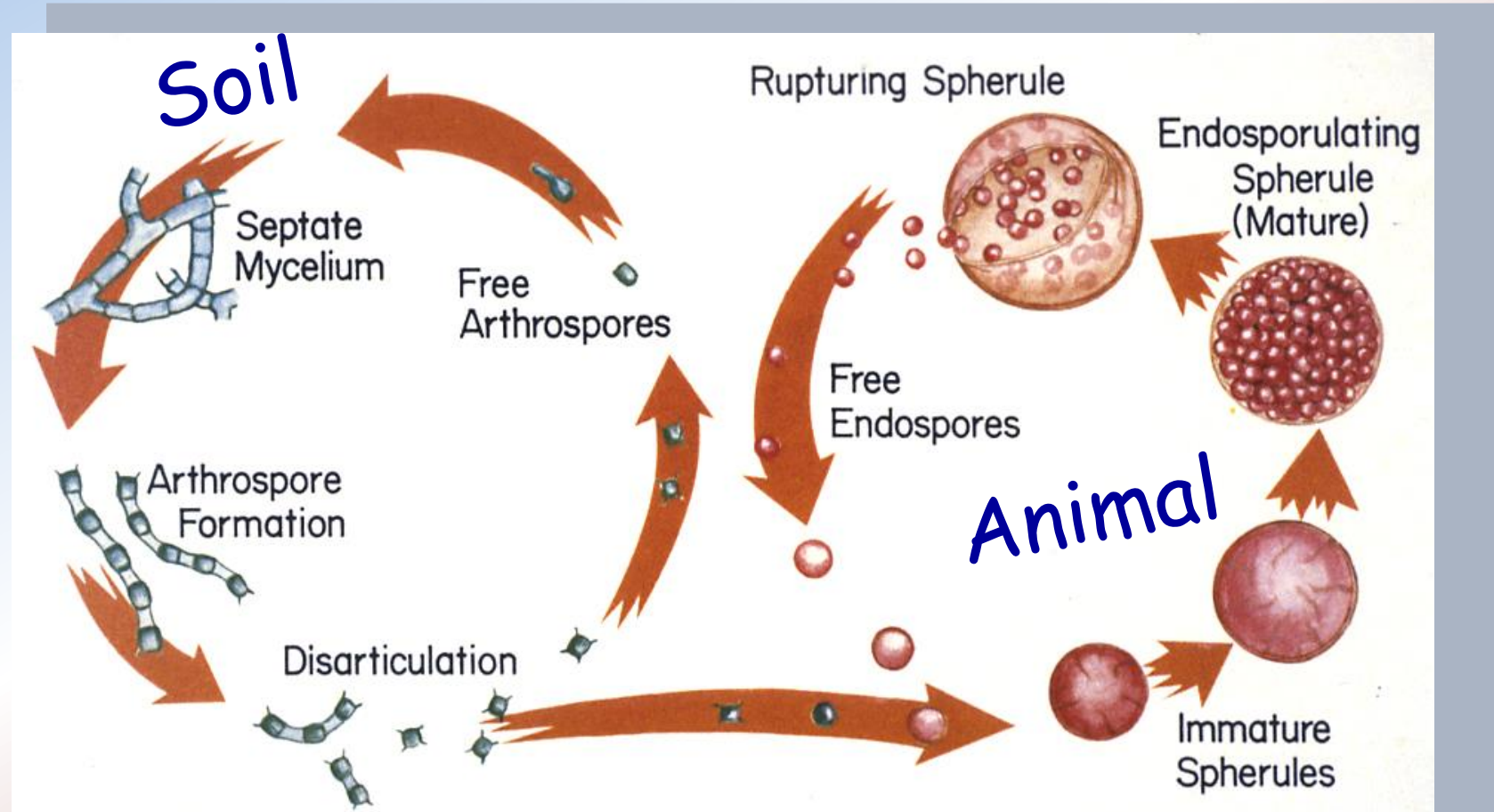


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What is it?

- Fungal infection – *Coccidioides immitis* (CA, WA), *Coccidioides posadasii* (AZ, TX, NM, NV, UT)
- True pathogenic fungus
 - Causes disease in healthy host
- Commonly referred to as Valley Fever or Cocci (vet/medical slang)
- Almost always acquired by inhalation of fungal spores in air/soil

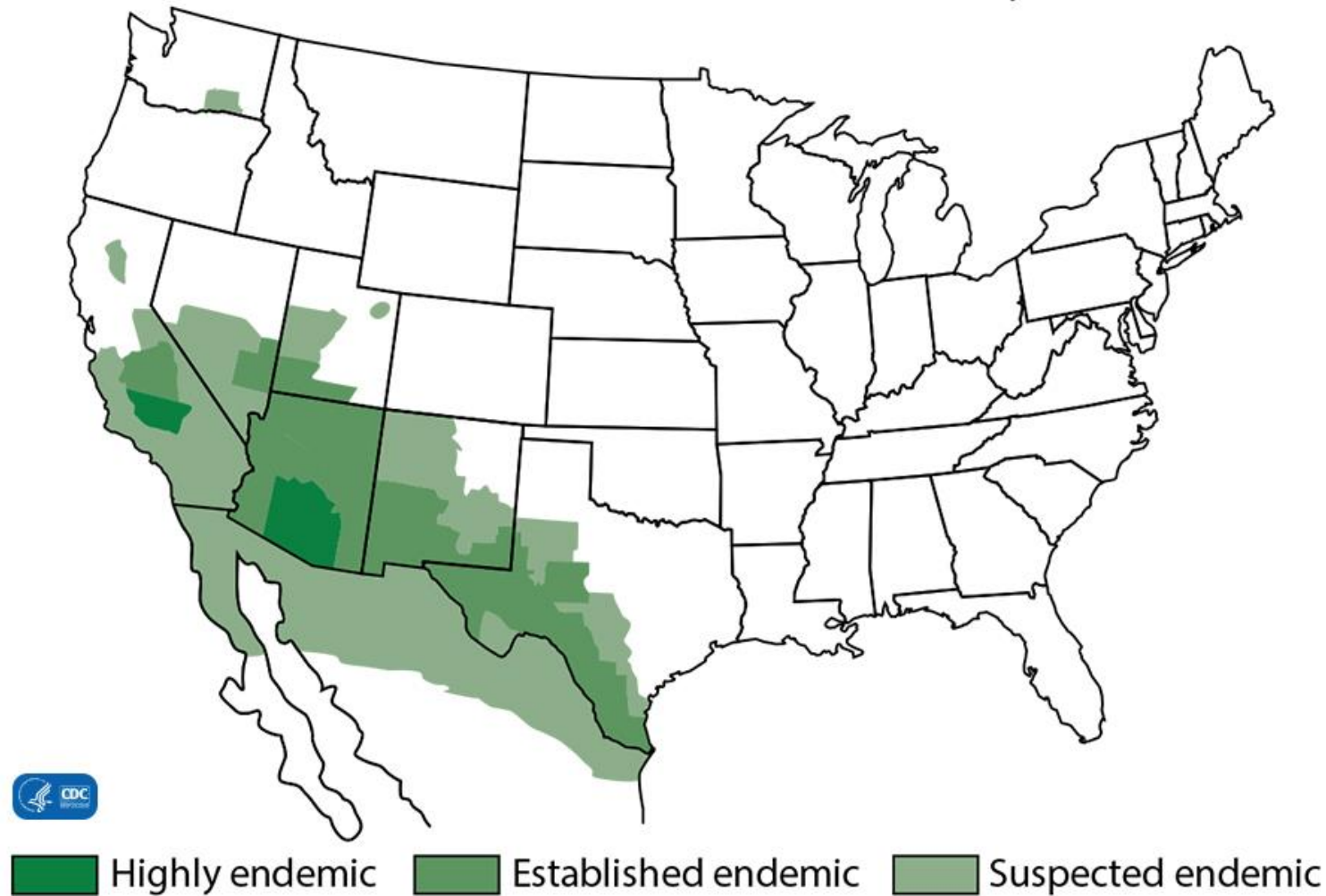
Life Cycle



Coccidioides is **dimorphic** – environmental and host forms

Geographic Distribution

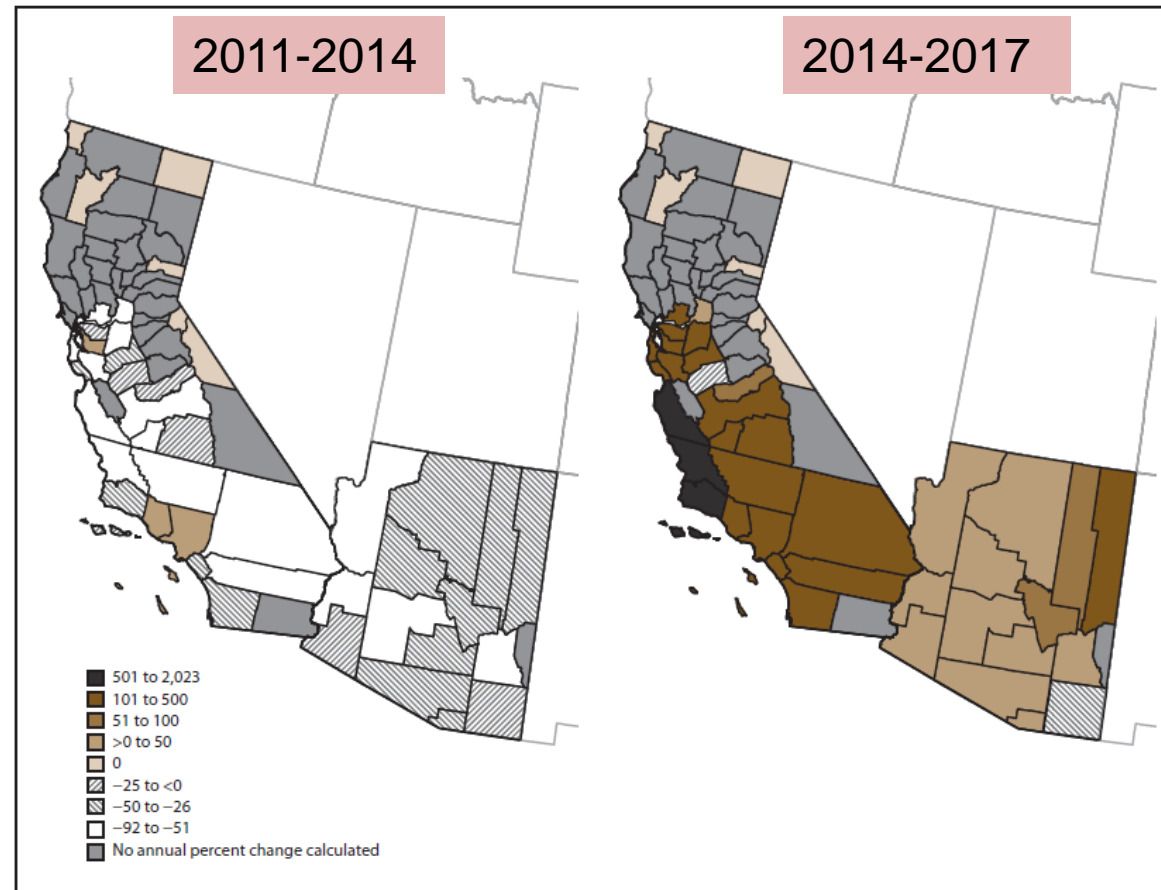
Areas Endemic for Coccidioidomycosis



CDC website:
<https://www.cdc.gov/fungal/diseases/coccidioidomycosis/maps.html>

California Increase in Cases

FIGURE 3. Annual percent change* in coccidioidomycosis incidence, by county — Arizona and California, 2011 to 2014 and 2014 to 2017



* Breaks were manually determined to best represent the range of the data shown. No annual percent change was calculated for counties that reported no cases in endpoint years or reported <25 cases overall during 2011-2017.

- Ventura Cty, SLO Cty, Monterey Cty have huge increases in human cases from 2014-2017
- Animal cases will also be increased, though are not reportable
- Improved awareness of this disease will lead to earlier diagnosis

Who gets Valley Fever?

- Humans
 - Dogs
 - Alpacas/Llamas
 - Cats
 - Horses
 - Non-human primates
 - Marine mammals
 - Zoo/exotic animals
 - NO Birds!
- } Most of VF cases, greatest economic impact



Boris was diagnosed with valley fever last fall and still continues making meowman until Boris starts slow to better.
Scott A. Latham / The

Valley fever makes Boris an official desert denizen

Overview of Disease in Dogs/Humans

- VF pneumonia is most common
 - Cough, fever, lethargy (fatigue), weight loss, lack of appetite
- Disseminated disease 1-5% in humans, ~25% in dogs
 - Outside of lungs, can go virtually anywhere, very serious and does not resolve on its own
 - Effects of race, age, gender on severity of disease in humans
 - Some breeds of dogs are more susceptible to severe/disseminated disease

What do we know about VF in SA Camelids?

- Not very much
- Appear to be very susceptible to severe/fatal disease
- 6 articles total in the peer-reviewed literature regarding cocci in llamas (3), alpacas (2), or both (1)
 - Most reports are of fatal infections
 - In the owner-based survey VFCE (Tucson, AZ) performed, 78% of diagnosed animals died
 - In the report from the California Animal and Food Safety laboratories, 4% of SA camelid deaths were due to VF*

*Fernandez, et.al, *J Vet Diagn Investigation*, 2018; DOI:10.1177/1040638718777282

Necropsy Findings

- 9 alpacas from AZVDL (2007-2016)
- Age range - 8 mos-17 yrs; BCS* poor - 8/9
- Spherules (abundant to florid) and lesions observed in lungs (9/9), lymph nodes (7/9), liver (6/9), heart/pericardium (5/9), other sites (spleen, kidney, brain, stifle joint)
- 79 alpacas and llamas from CAHFS lab. system (1992-2013)
- Age range – neonate-20 yrs
- Lung only – 20%; disseminated 80%
 - 25% and 13% of pneumonia in llamas and alpacas, respectively, was caused by coccidioidomycosis in this necropsy population
 - Organs: Lungs (84%); liver (78%), lymph nodes (54%), heart (34%), spleen and kidney 47%, other (brain, skin, skeletal muscle)

3 Older Literature Reports – Case Series

- 1 alpaca and 19 of 20 llamas reported had disseminated disease
 - Nearly all also had **relevant lung lesions** but not coughing
 - Sites included skin, eye, bones, joints, internal organs, mucous membranes, reproductive organs, and spinal cord and brain
- 2 crias (1 llama, 1 alpaca) were born with Valley Fever and died
 - Born to dams with disseminated disease – dams died/euthanized as well
 - Strongly suspect transplacental transmission in both of these cases

Signs of Illness

- Variable dependent on organs affected
- May have few or no symptoms
 - “found dead” is relatively common
- Owner survey revealed top 3 clinical signs are weight loss, lethargy and reduced appetite (23 animals)
 - Not very specific!

Frequency of reported clinical signs noted by owners of alpacas with coccidioidomycosis

Clinical Sign	Frequency
Weight loss	15
Decreased energy	9
Decreased appetite	8
Coughing	6
Lameness	5
Inability to stand/walk	5
Non-healing sores	3
Fever	2
Joint swelling	2
Enlarged lymph nodes	2
Fiber loss	2
Nose bleed	1

Butkiewicz, Shubitz; *Transbound Emerg Dis*
2019;66:807-812

Signs of Illness – Organ systems

- Weight loss – anywhere!
- Coughing, wheezing, incr. resp rate/effort – lungs
- Lameness – infection of bones or joints
- Paralysis, weakness, difficulty walking – backbones, brain or spinal cord
- Seizures or mental stupor – brain
- Uveitis – ocular tissues
- Draining lesions/abscesses – dermal and subcutaneous tissues, underlying muscle or bone

“Dazzel”



Diagnosis
(above)
and after 9
mos of
treatment
(right)



- 2 YO F
- Was acquired from farm west of Phoenix, AZ (Maricopa Cty)
- At shearing (3 wks after purchase), discovered she was emaciated, weighed 75 lbs
- Dx with Valley Fever, titer $\geq 1:256$
- Was started on fluconazole 600 mg twice daily
- After 9 mos on medication, she weighs more than 100 lbs

Diagnosis

- Clinical history, including travel history/origin of animal if it becomes ill outside endemic area
- Physical examination findings
- Blood tests for inflammation?
 - May see changes, often normal
- Valley Fever-specific blood test – serology, “titer”
- X-rays, if possible
- Biopsy, cytology, culture
 - These are definitive if positive but may require invasive sampling

Diagnosis

- “Desperado”
- 13 YO M – reduced condition
- Incr. lung sounds, incr. RR, occ. cough
- Albumin – L, Globulin – H, WBC – N, cocci titer $\geq 1:256$
- Incidental Dx at pre-enrollment evaluation



Asymptomatic Infection?

- “Sonny”
 - Healthy 6 YO M
 - Albumin - low, WBC* -mildly elevated
 - Cocci titer 1:32
 - Both incidental diagnoses at pre-enrollment screening for fluconazole study
 - Both animals in good body condition, normal appetite and attitude
 - Owners elected to give both animals fluconazole though they were asymptomatic
 - Not known if this would progress to severe illness, but it could
- “Kit”
 - Healthy 6 YO M
 - WBC – moderately elevated
 - Cocci titer 1:64

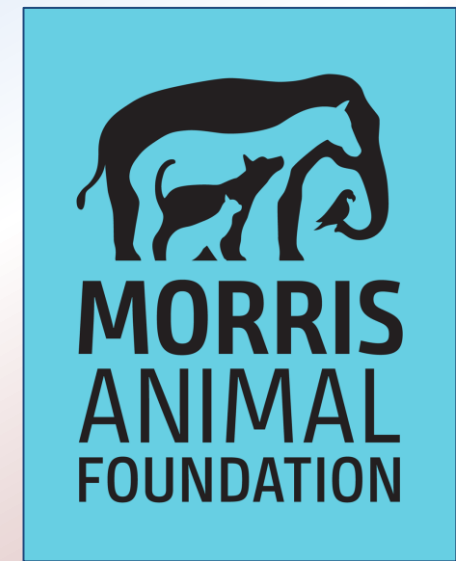
*white blood cell count

Treatment

- Oral antifungal medication (**fluconazole**, itraconazole, ketoconazole)
- Intravenous amphotericin B – impractical, 3X weekly
- Limited information on treatment is that it is unsuccessful at least half the time
- Reasons may include:
 - Poor absorption of oral medication from complex digestive tract of SA camelids
 - Animals have widespread disease at time of initiation of treatment due to late diagnosis

What can we do?

- Education – increase awareness of Valley Fever among owners and veterinarians in the regions where the disease occurs
 - Educate buyers of animals originating in the endemic regions
- Improve understanding of the diagnosis and treatment of disease
- Research treatments and systematically catalog outcomes
 - Determine if therapeutic levels of orally administered drugs show up in bloodstream
 - Define appropriate drugs and treatment doses for SA camelids
 - Find out if treatment is efficacious (follow lots of cases over time)



Pharmacokinetics of Fluconazole in Alpacas

Morris Animal Foundation Grant #D19LA-005

Valley Fever Center for Excellence

Christine Butkiewicz, DVM, Lisa Shubitz, DVM, David Nix, PharmD

Fluconazole in Alpacas

- This study is completed and the manuscript is under review
- A brief summary of the study can be accessed on the Valley Fever Center for Excellence website,
https://vfce.arizona.edu/sites/default/files/alpaca_for_website.pdf
- We are very grateful for the support of the Morris Animal Foundation to perform this study to improve care of Valley Fever in alpacas and llamas