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
California Increase in Cases

- 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

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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.
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)

*Body condition score
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!

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

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”

- 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 ≥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 ≥1:256
- Incidental Dx at pre-enrollment evaluation
Asymptomatic Infection?

• “Sonny”
  • Healthy 6 YO M
  • Albumin - low, WBC* -mildly elevated
  • Cocci titer 1:32
• “Kit”
  • Healthy 6 YO M
  • WBC – moderately elevated
  • Cocci titer 1:64

• 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

*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 camels
  • 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](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