Precision Health in Valley Fever
Does Ancestry Matter?

John N Galgiani MD
Valley Fever Center for Excellence
University of Arizona
Coccidioidomycosis Spectrum of Disease

100 Infections

60 No Symptoms

40 Symptoms

37 Recover

Life-Long Immunity
Valley Fever Problem in Arizona Alone

- Total Infections: 100,000 - 10,000 - 1,000 - 100 - 10
- Seek Medical Attention
- Diagnosed/Reported
- Disseminated Infection
- Deaths
Complications from Coccidioidomycosis

**Pulmonary**
- Diffuse acute pneumonia
  - ARDS
- Peripneumonic effusion
- Nodules
- Cavities
  - Hemoptysis
  - Rupture
- Chronic firbro-cavitary pneumonia

**Disseminated Infection**
- Skin
- Subcutaneous abscesses
- Arthritis
- Osteomyelitis
- Meningitis
Possible Reasons for Complication in Valley Fever

• Infection from lots of fungal spores
  – Archeology dig exposures are high inoculum
  – More likely pneumonia but no more likely to have complications

• Some strains more virulent than others?
  – No evidence for this

• Some people are different from others
  – All evidence points to this
Risk Factors for Coccidioidal Complications

Pulmonary
- Diabetes mellitus
- Cardio-pulmonary or other co-morbidities. (Evidence: “common sense”).

Disseminated Infection
- Deficient cellular immunity
- Males > Females
- Racial background
  - African-American
  - Filipino
- Adults > Children
- Pregnancy
Coccidioidomycosis in Renal Transplantation 1970-1979: 18/260 (6.9%)

<table>
<thead>
<tr>
<th></th>
<th>Kidney Recipients</th>
<th>Tucson Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence/yr</td>
<td>3%</td>
<td>1%</td>
</tr>
<tr>
<td>Dissemin.</td>
<td>75%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Mortality</td>
<td>65%</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

IM Cohen et al, 1982
Sex

% without Dissemination

Months after Transplant

- Female
- Male
p < .03

IM Cohen et al, 1982
<table>
<thead>
<tr>
<th>Publication Date</th>
<th>Antifungals Studied</th>
<th>% Male (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988</td>
<td>Ketoconazole</td>
<td>76% (85)</td>
</tr>
<tr>
<td>1990</td>
<td>Itraconazole (Dissem.)</td>
<td>81% (21)</td>
</tr>
<tr>
<td>1993</td>
<td>Fluconazole (CNS)</td>
<td>82% (50)</td>
</tr>
<tr>
<td>2000</td>
<td>Fluconazole</td>
<td>73% (191)</td>
</tr>
<tr>
<td>2007</td>
<td>Posaconazole</td>
<td>65% (20)</td>
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</tbody>
</table>
Impact of Disseminated Coccidioidomycosis in Arizona, 2007-2008

Coccidioidomycosis Study Group 55th Annual Meeting April 2, 2011
Foley CG, Tsang CA, Christ C, Anderson SM
Overview of Methodology

Every 10th cocci case reported to ADHS interviewed

493 individuals enrolled and interviewed

Medical records requested for same 493 people

324 (65.7%) records reviewed and included in the analysis

26 (8.0%) with evidence of dissemination

169 records not received or inadequate (excluded)

Enhanced Surveillance (ES) Jan 2007-Feb 2008

Validation of dissemination using medical records
## Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Disseminated 26 (8%)</th>
<th>Non-Disseminated 298 (92%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>49.4 yrs</td>
<td>52.5 yrs</td>
<td>0.44</td>
</tr>
<tr>
<td>Male (n=167)</td>
<td>18 (11%)</td>
<td>149 (89%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Female (n=157)</td>
<td>8 (5%)</td>
<td>149 (95%)</td>
<td></td>
</tr>
<tr>
<td>White (n=257)</td>
<td>16 (6%)</td>
<td>241 (94%)</td>
<td></td>
</tr>
<tr>
<td>Black (n=20)</td>
<td>5 (25%)</td>
<td>15 (75%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Asian (n=12)</td>
<td>0 (0%)</td>
<td>12 (100%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Native Am. (n=6)</td>
<td>1 (17%)</td>
<td>5 (83%)</td>
<td>0.40</td>
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</tbody>
</table>
Risk of disseminated Valley Fever in African-Americans as compared to Caucasians.

<table>
<thead>
<tr>
<th>Report</th>
<th>Year</th>
<th>Study type</th>
<th>Fold increased risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smith et al</td>
<td>1946</td>
<td>Retrospective</td>
<td>+14.0</td>
</tr>
<tr>
<td>Flynn et al</td>
<td>1979</td>
<td>Outbreak, retrosp.</td>
<td>+9.5</td>
</tr>
<tr>
<td>Pappagianis</td>
<td>1988</td>
<td>Outbreak, retrosp.</td>
<td>+9.1</td>
</tr>
<tr>
<td>Rosenstein et al</td>
<td>2001</td>
<td>Retrospective</td>
<td>+ 7.0</td>
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<tr>
<td>Crum et al</td>
<td>2004</td>
<td>Retrospective</td>
<td>+41.9</td>
</tr>
<tr>
<td>Drake et al</td>
<td>2009</td>
<td>Retrospective</td>
<td>+11.0</td>
</tr>
<tr>
<td>Foley et al</td>
<td>2011</td>
<td>Prospective</td>
<td>+4.0</td>
</tr>
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Relation of Race/Ethnicity and Genetics?

• Self-Identified Race/Ethnicity is just that:
  – Social/Cultural affinity and identification.
  – Genetically in the U.S. this is nearly always an admixture of various ancestries.

• Approximately 95% of the human genome DNA sequence is not related to any particular ancestral origin.

• However, the remaining 5% is.
% of Genes of West African Ancestry In 3 Self-Identified U.S. Populations

Torres and Kittles, 2007
Fig. 1 Triangle plot showing the distribution of individual admixture estimates obtained by using a maximum likelihood approach in the population of Puerto Rico. Each of the three founder populations constitutes a vertex of the triangle. Each circle represents an individual and its position in the graph depends on the ancestry proportions of the subject.
Two Genetic Studies Now Open

NIH Study (Dr. S Holland)
- Any person with disseminated Valley Fever and normal immunity.
- UA is enrolling for this study; involves collecting a blood specimen.
- Some subjects could be seen at the NIH Clinical Center in Bethesda.

Valley Fever Center Study
- Any person self-identified as African American with normal immunity.
- Involves collecting saliva for DNA and optionally a blood specimen.
- All studies will be conducted in Arizona.
Thank-you
Valley Fever Center for Excellence