Kings Coccidioidomycosis Conference: Coccidioidomycosis In Infants And Children

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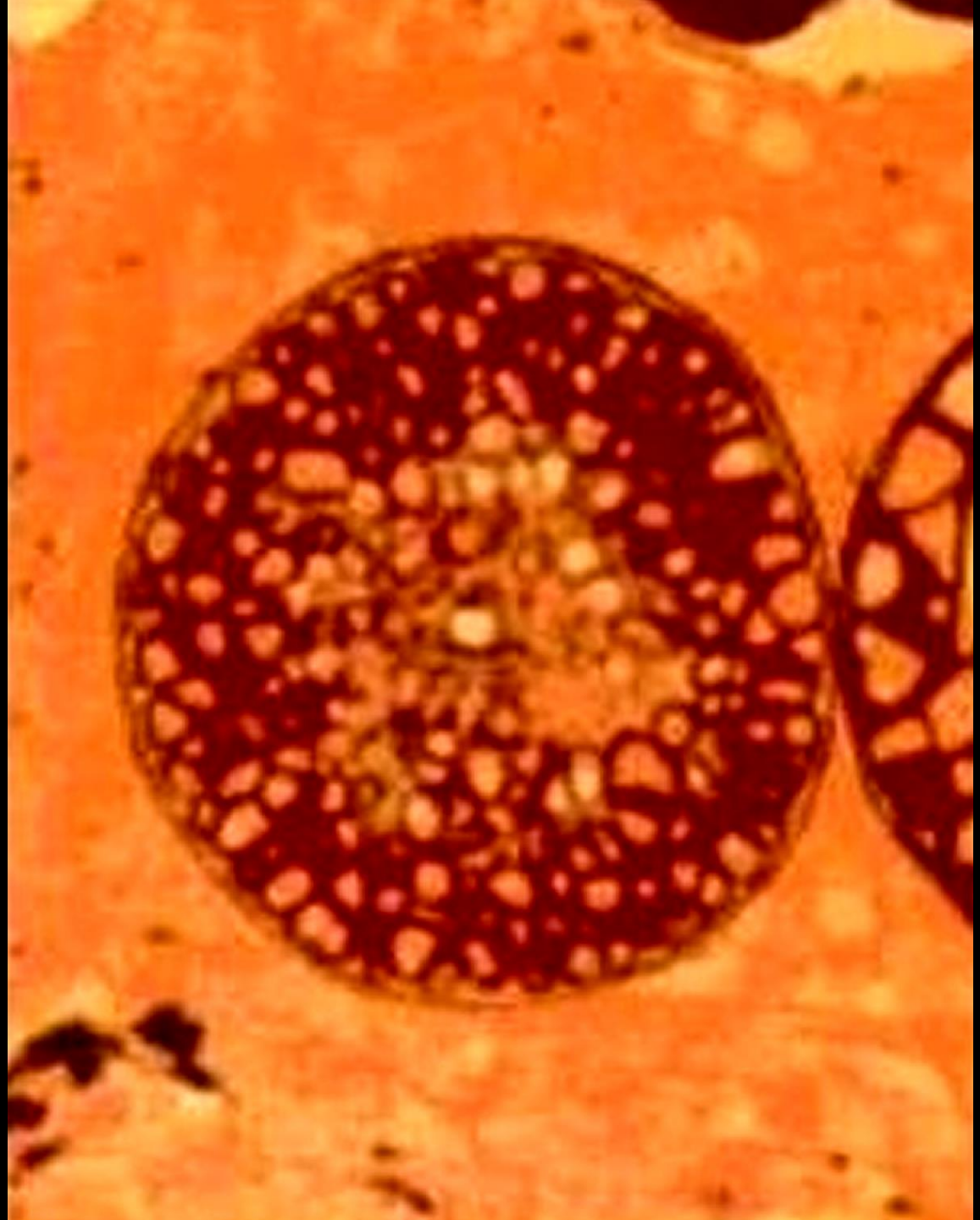
15 Year Review of Pediatric Coccidioidomycosis

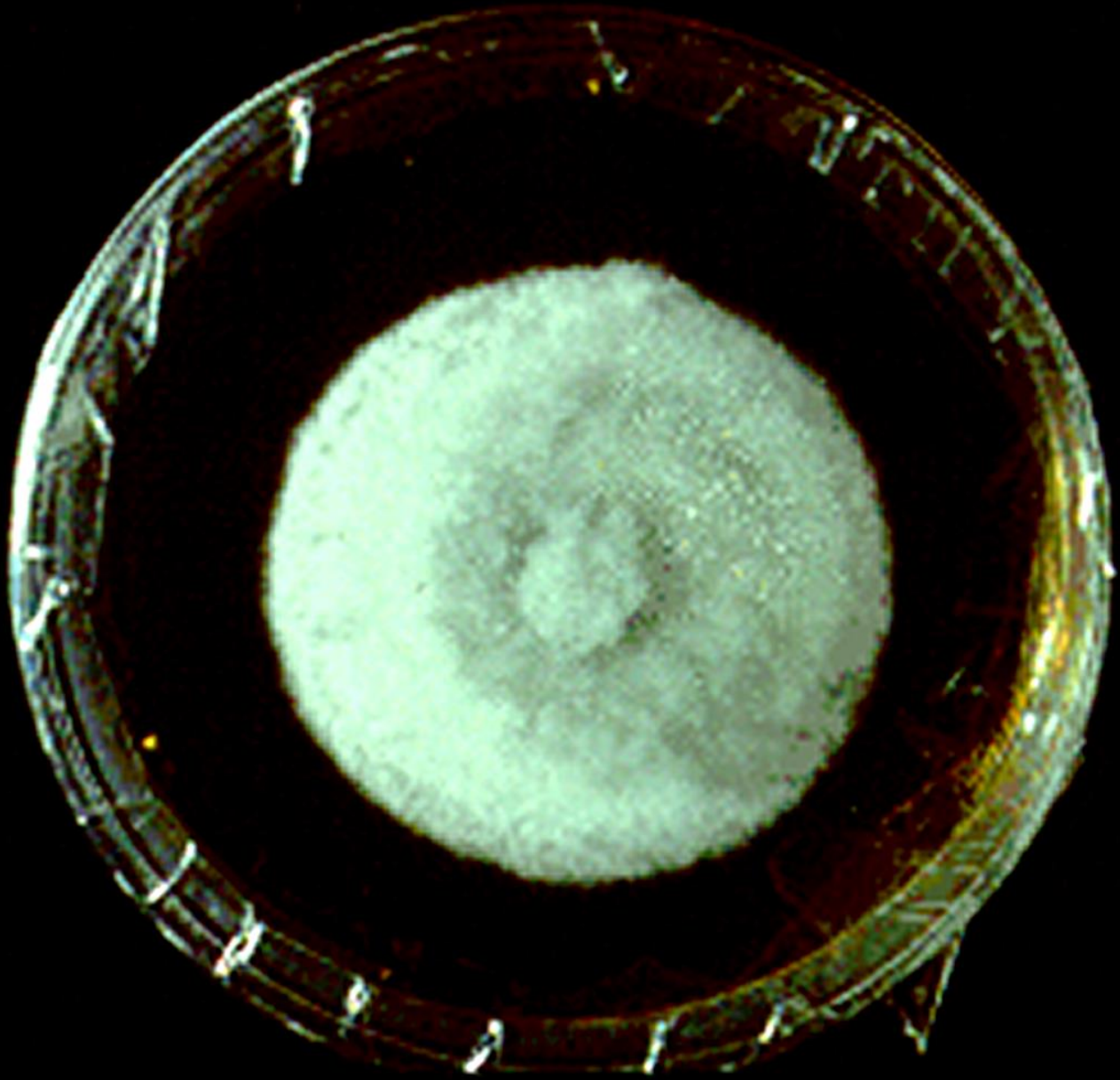
- IRB approved protocol
- Retrospective chart review of all patients seen at Children's Hospital with a discharge diagnosis of coccidioidomycosis (cocci) from 1990-2005
- 298 charts reviewed, 199 met study criteria for diagnosis of cocci and had data available for review

F. Geertsma, S. Wollersheim, J. Moua, J. Nolt, M. Birmingham and W. Fletcher

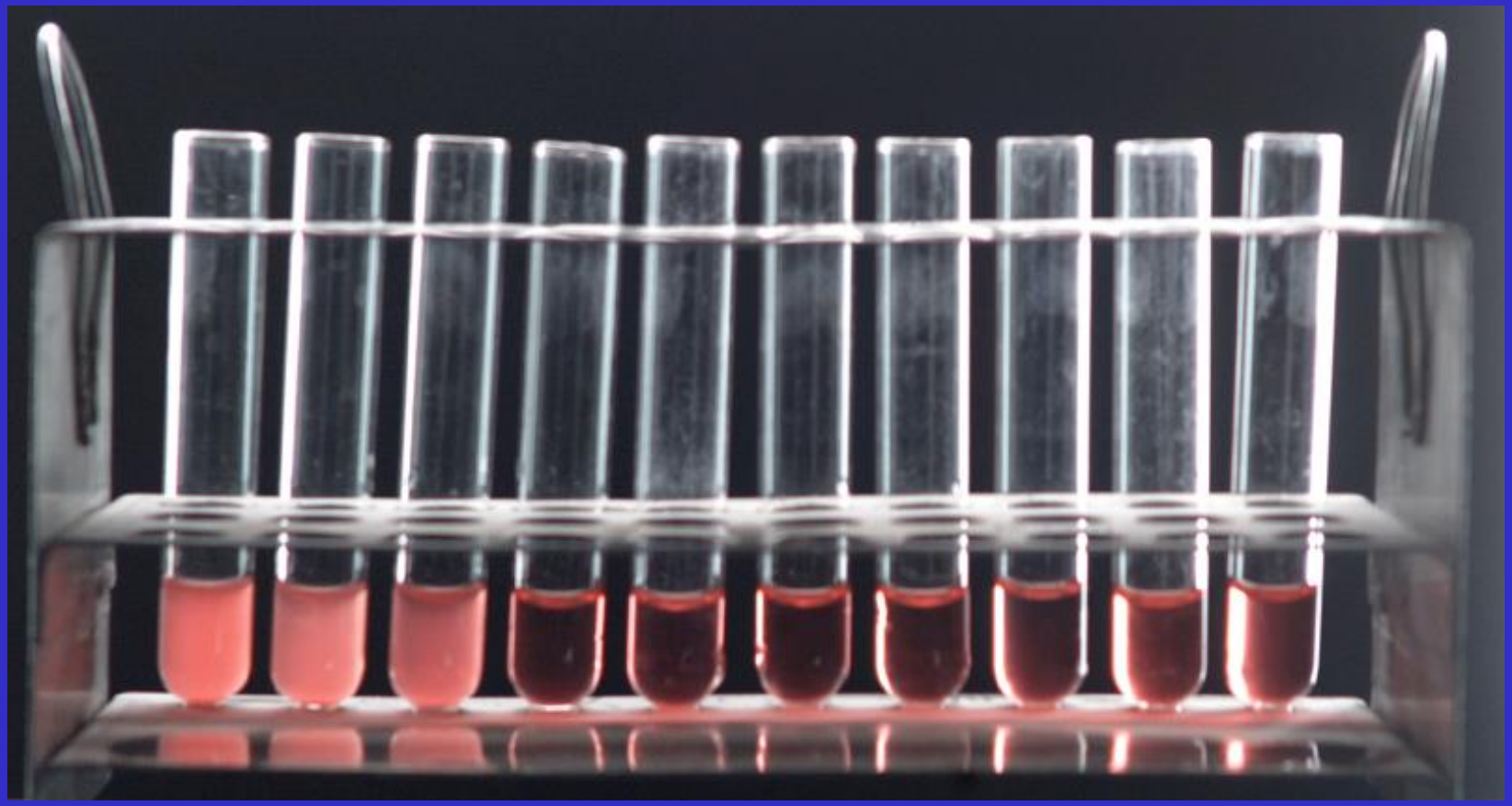
15 Year Review-Continued

- Inclusion criteria
  - Age 0-18 years at time of initial visit
  - Diagnosis of cocci by clinical signs/symptoms AND
    - Histopathology and/or
    - Positive culture and/or
    - Positive serology
- We did not include subjects with diagnosis based on skin testing, only clinical suspicion or screening antibody testing (eg EIA)





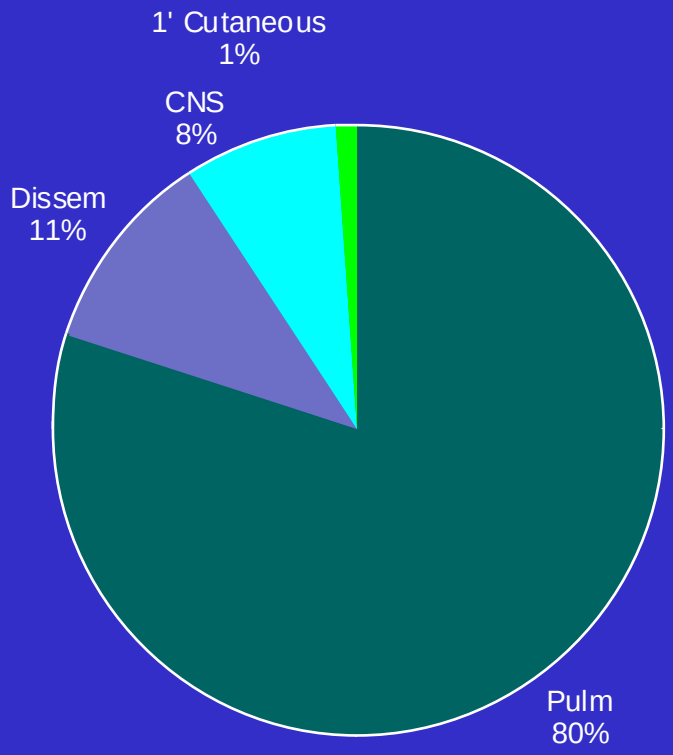
Complement Fixation Assay



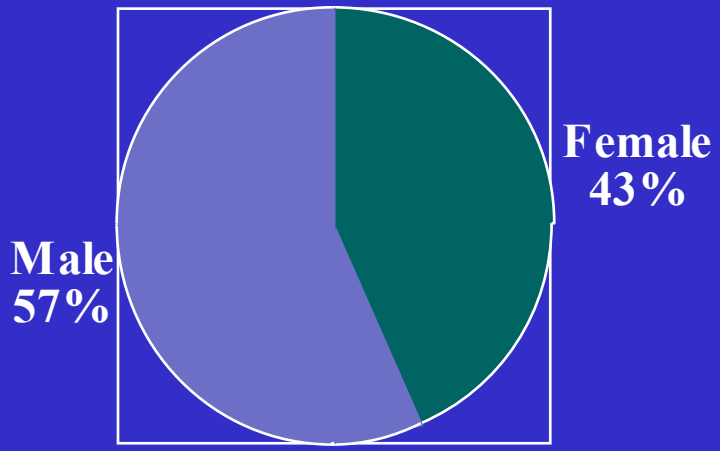
15 Year Review-Data Collection

- Data extracted from charts including information regarding PE, symptoms, demographics, site of infection, laboratory studies, radiographic studies, treatment, follow-up information, hospitalization, ultimate disposition etc.
- Correlations sought to help define clinical disease in this population
- “fishing trip” descriptive design of study hopefully will provide groundwork for more focused inquiries in the future

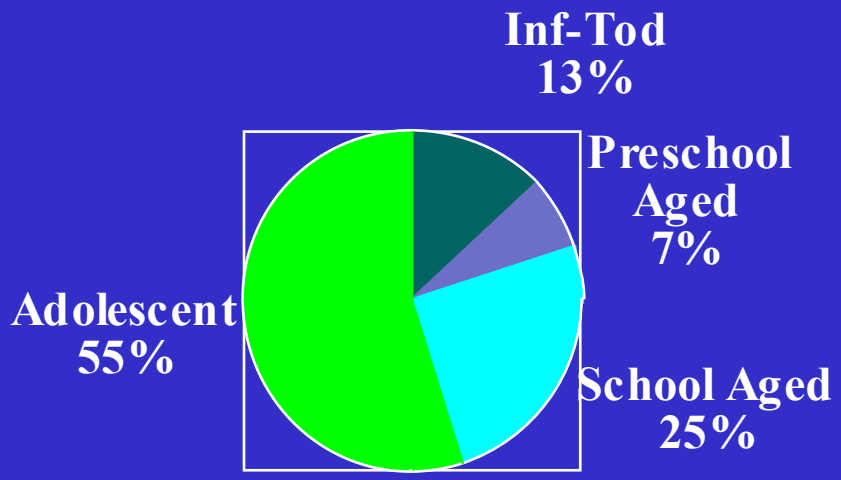
All Patients by Site
n=199



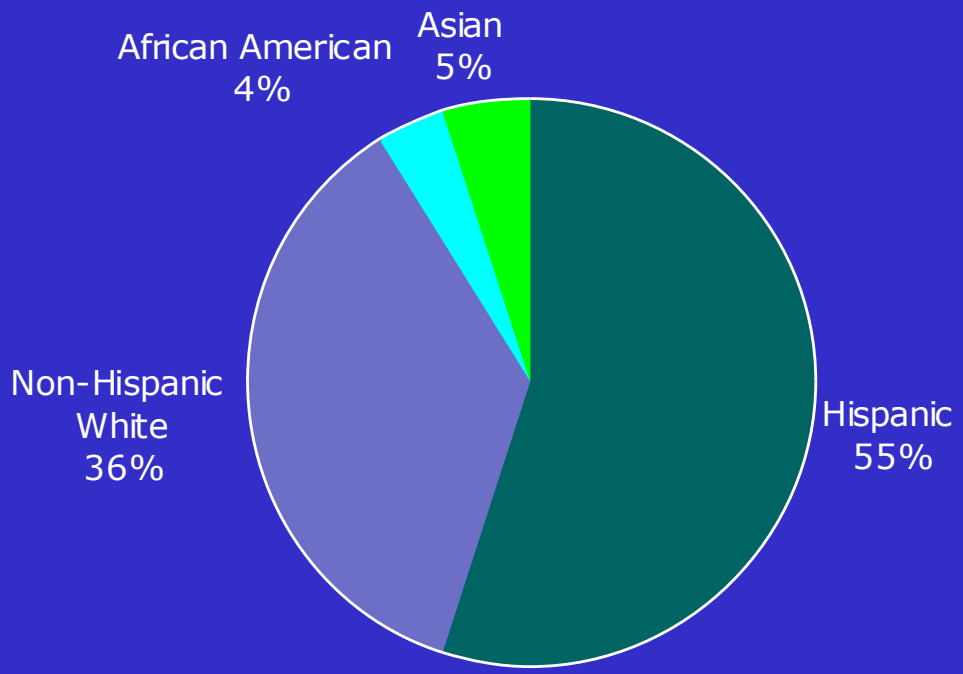
Sex Ratio of Study Group



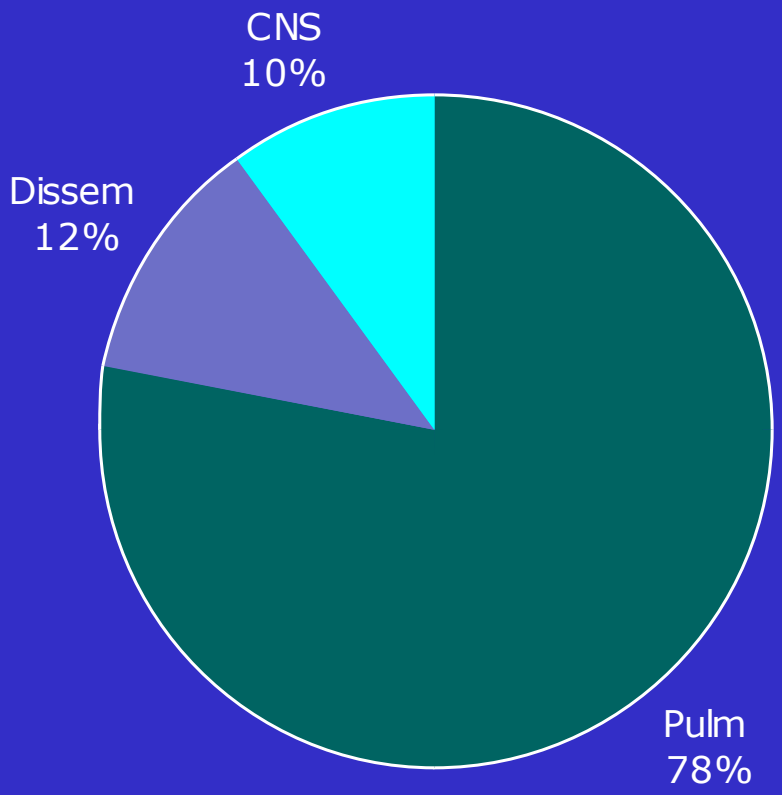
Age Distribution of Study Group



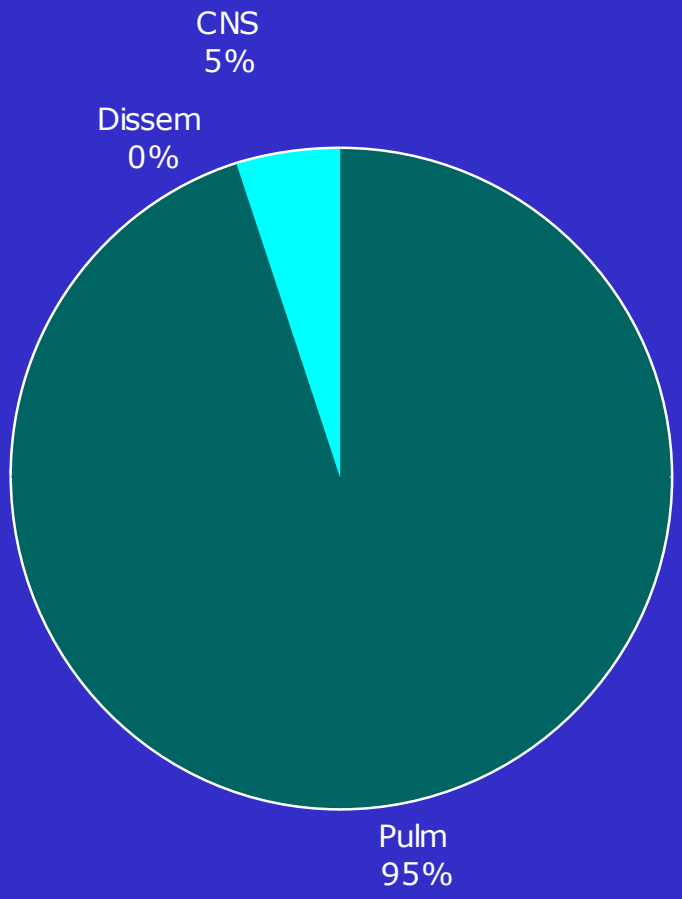
Ethnic Background of Study Group n=199



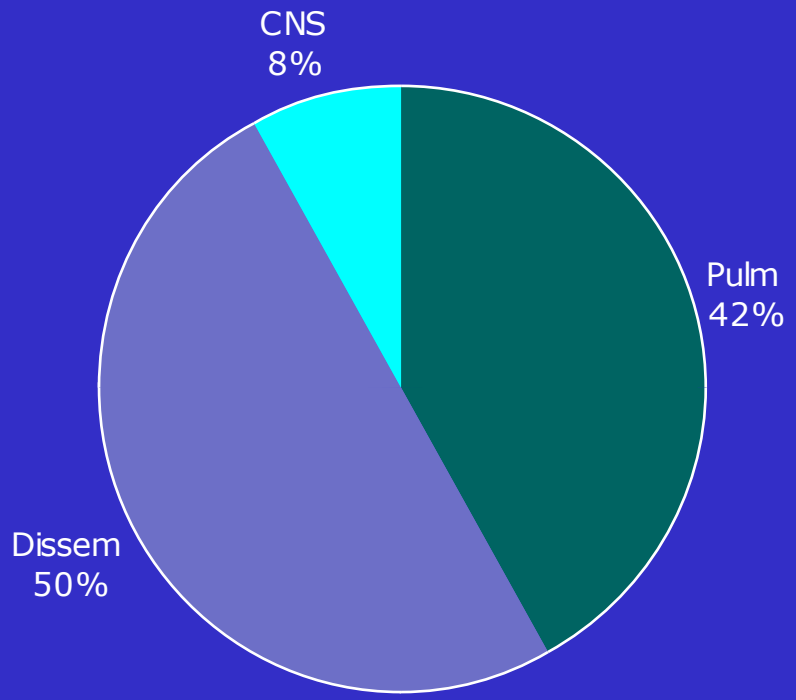
Ethnicity vs Site
Hispanic



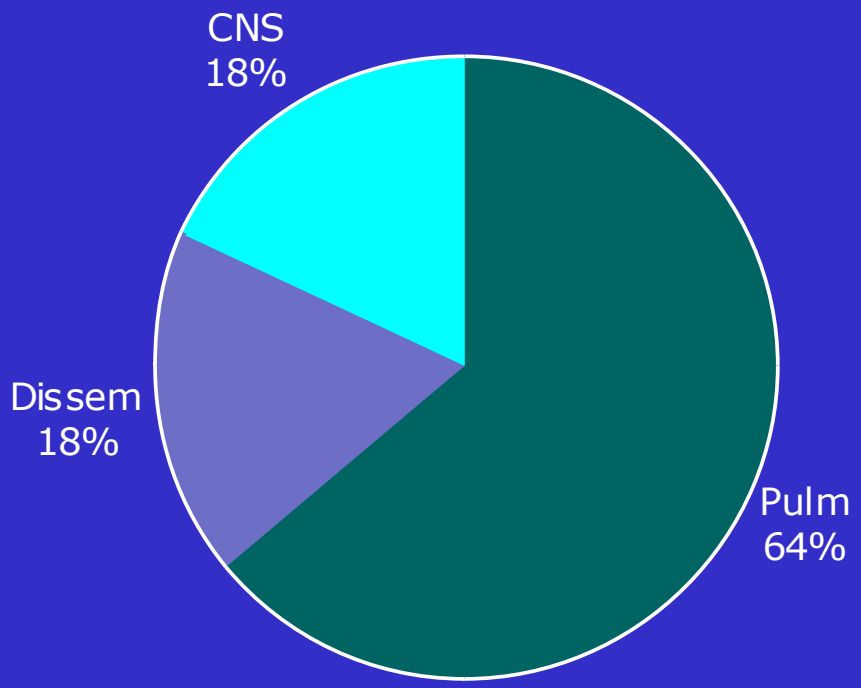
Ethnicity vs Site
Non-Hispanic White



Ethnicity vs Site
African American



Ethnicity vs Site
Asian



15 Year Review- Clinical Characteristics

- Immunsp. 3%
- Fever 67%
- HA 23%
- Wt loss 34%
- Dyspnea 16%
- Hemoptysis 1.5%
- Night sweats 9%
- Rash 31%
- Arthralgias 12%
- Malaise 26%
- Cough 62%
- Chest pain 26%
- Stiff neck 4%
- Alt LOC 3%

15 Year Review- Clinical Characteristics

• Arthritis	2%
• Abn Breath sounds	20%
• Deceased breath sounds	25%
• Abscess or mass	7%
• EN	11%
• EM	1%
• Murmers	3%
• Lymphadenopathy	9%
• HSM	3%

15 Year Review-Associations

PE/History

- HA and alt LOC assoc with CNS dz
- Lymphadenopathy and HSM assoc with dissem dz
- EN assoc with pulm dz
- Hispanics, Asians then African Americans seen with increasing rates of disseminated disease (numbers not large enough for Asians to achieve statistical significance but trend demonstrated)
- African American and Asians more likely to present with a soft tissue mass/abscess than Hispanic or White children
- More likely to see HSM in AA children than others with disseminated disease

15 Year Review-Associations

Imaging

- 18% of cases without dissemination dz had negative chest imaging
- 39% of cases with disseminated cases had negative chest imaging studies
- 44% of cases with CNS disease had negative chest imaging studies

15 Year Review Associations

Associations-laboratories…

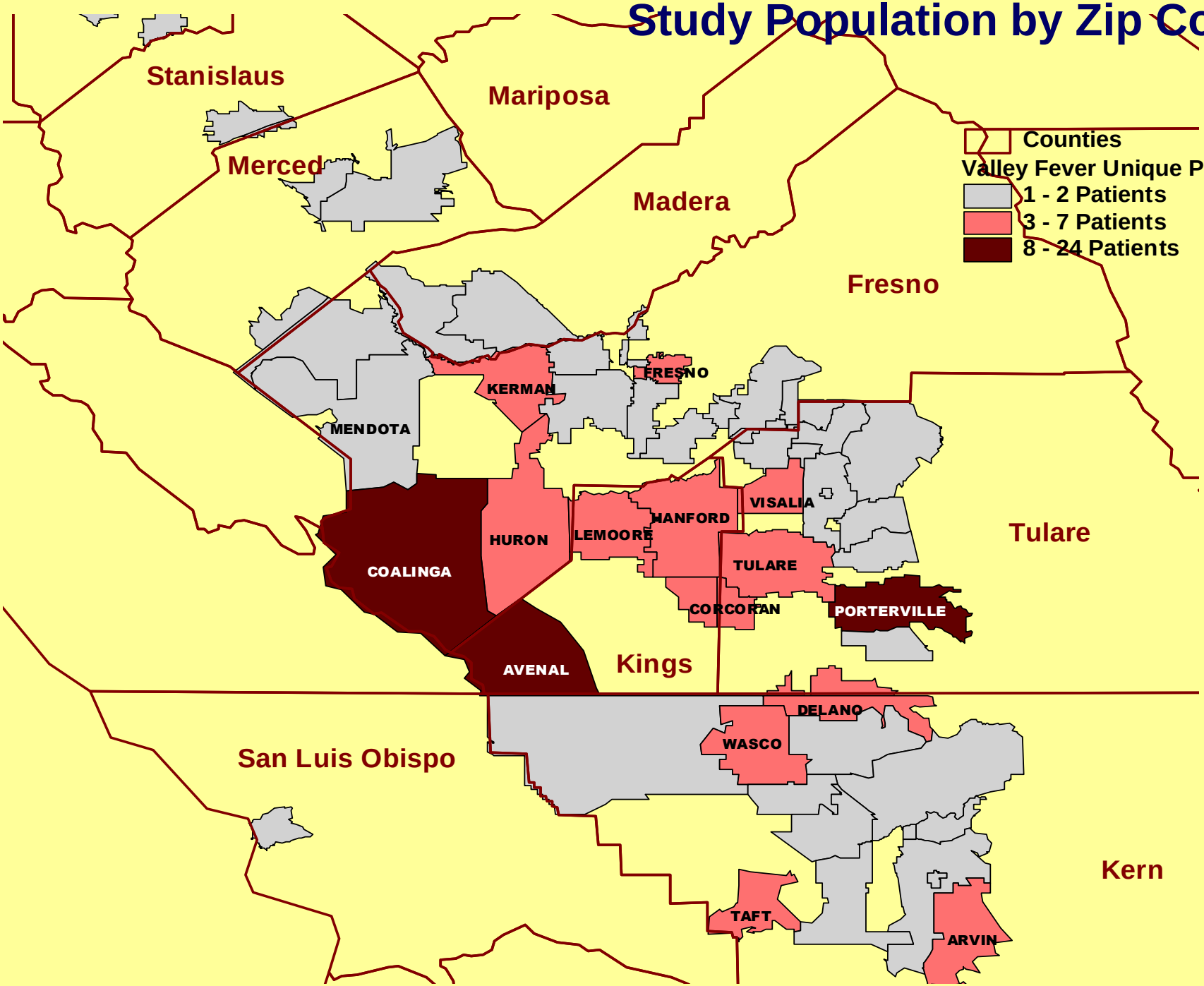
- Markers
  - Differentiate disseminated disease from purely pulmonary dz
    - ESR 36 in Pulm vs 45 in DDZ ($p<.001$)
    - Alk phos 165 Pulm 275 DDZ ($p<0.001$)

15 Year Review-Associations

Complement Fixation Titers-Serum

Pulmonary disease	1:11
Disseminated dz +/-CNS	1:55
	P<0.001

Study Population by Zip Code



Cocci in Kids…

- Issues to consider
  - Immune status of infants
  - Lack of data regarding use of certain antifungals in children and infants
  - Practicality of obtaining certain diagnostic procedures in children and infants
  - Difficulty in interpreting serologic studies in young infants due to presence of maternal antibody

Cocci in Kids-Observations

- Common cause for referral to ID clinic and ID inpatient consultation since ~2000
  - Presentations similar to adult disease except
    - "big spleen" disease in preadolescent/adolescents
    - Disease in young infants-disseminated but not congenital-often with skin disease
      - Well appearing despite high titer disease
      - Respond to outpatient oral therapy

Cocci in Kids

- Therapy
  - Amphotericin B-d
    - Well tolerated in infants and young children
    - Used when large fungal burden suspected/patient very ill systemically
  - Lipid associated Ampho B
    - Used as second line therapy when toxicities encountered with ampho B-d or with treatment failures
      - Less comorbidities in our population
  - Azoles
    - Fluconazole
      - For patients with less severe disease and CNS disease, also when fungal burden not as significant

Cocci in Kids

- Therapy continued
  - Azoles
    - Itraconazole
      - Used in skeletal dz
      - Clinical failure on fluconazole esp with CNS dz
      - Seem to see HTN with chronic use
    - Voriconazole
      - Increasing experience with this drug
        - » CNS failures on other azoles
        - » Inability to use parenteral antifungals in patients with severe systemic disease
        - » Dose we use is up to 11mg/kg orally BID
  - Immunomodulation?
    - IFN γ

Cocci in Kids

Questions that continue to keep us up at night…

- Long term effects of the disease , especially in the young infants we are seeing?
- Long term effects of the treatments we are using on the developing infant/brain?
- Role of Voriconazole?
- Role of immunomodulators?
- What to do with the cohort of young infants we are seeing with disseminated disease?
  - What drugs?
  - How long?
  - Are there marker for evaluation “maturity of their immune response?