# Valley Fever Management in Rural Arizona Primary Care

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THE UNIVERSITY OF ARIZONA
College of Nursing

# Objectives

1. Review Valley fever epidemiology, clinical presentation, and risk factors.
2. Describe Valley fever diagnosis, treatment, and management in rural primary care settings.
3. Discuss aspects of Valley fever detection and management in rural and tribal communities.

# Case Study # 1

- 8 yo Hispanic boy with fever (38.7) and intermittent, non-productive cough.  No known sick contacts.
- Azithromycin was prescribed for likely PNA. Despite treatment, his symptoms persisted, and after 7 days Amoxicillin-clavulanate was prescribed.

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- On the 14th day of illness, he was seen in the Emergency Department. In addition to his cough and fever, erythematous nodules noted over both shins.
- CXR revealed right lower lobe infiltrate.

Image Source: https://www.healthdirect.gov.au/erythema-nodosum

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A. Asthma
B. Tuberculosis
C. Coccidioidomycosis
D. Histoplasmosis

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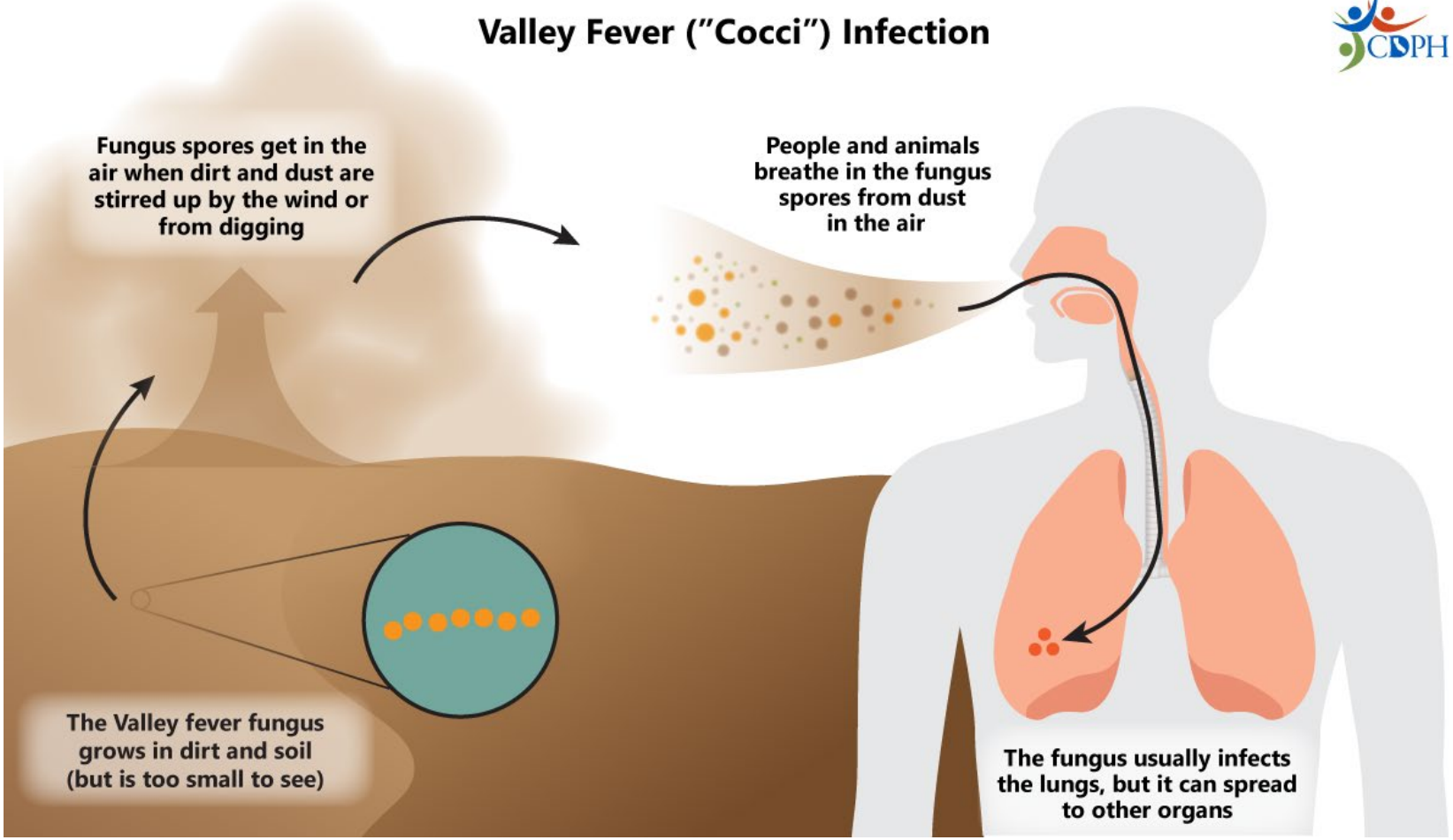
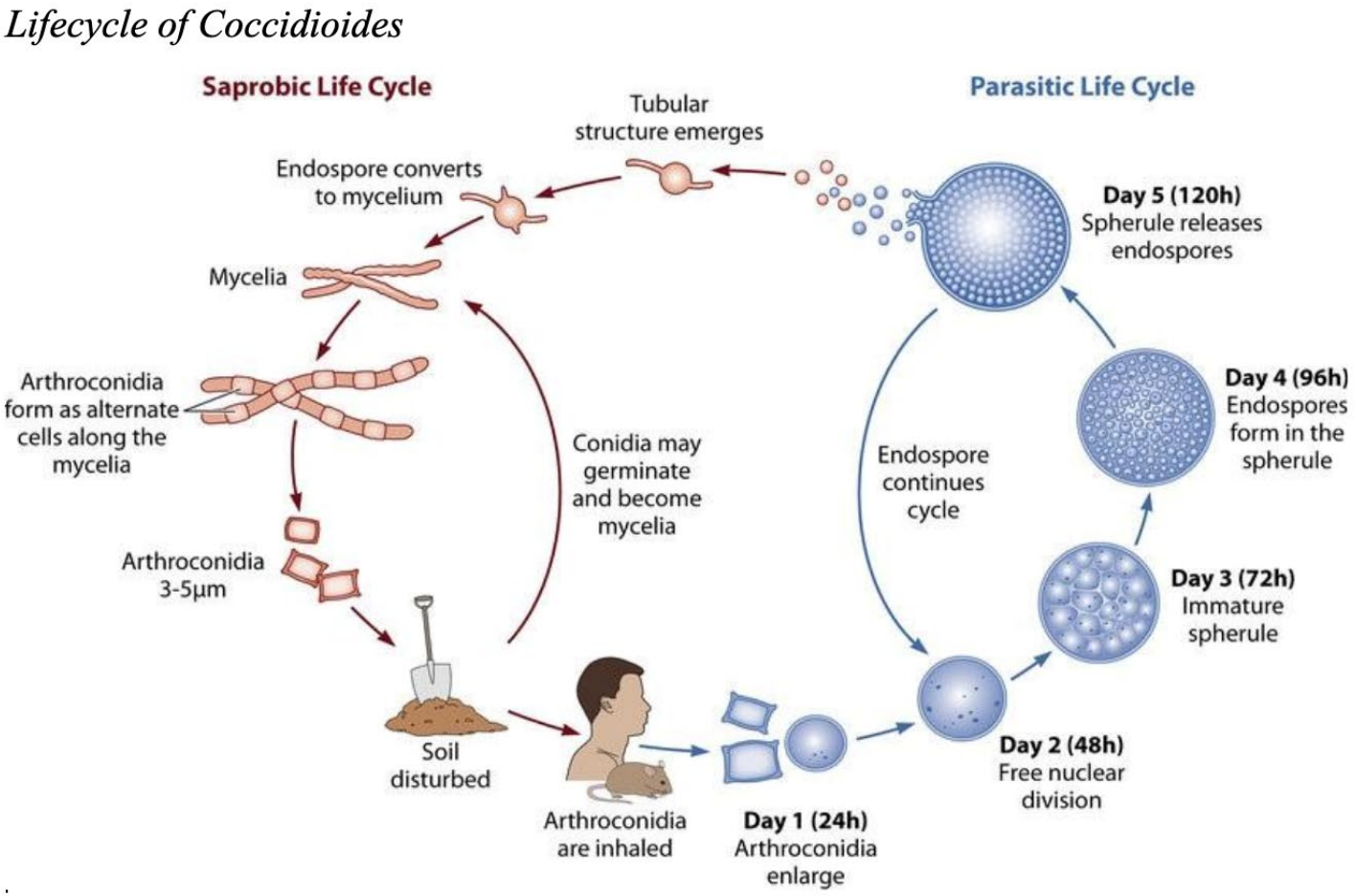
# Valley Fever (Coccidioidomycosis)

## Etiology



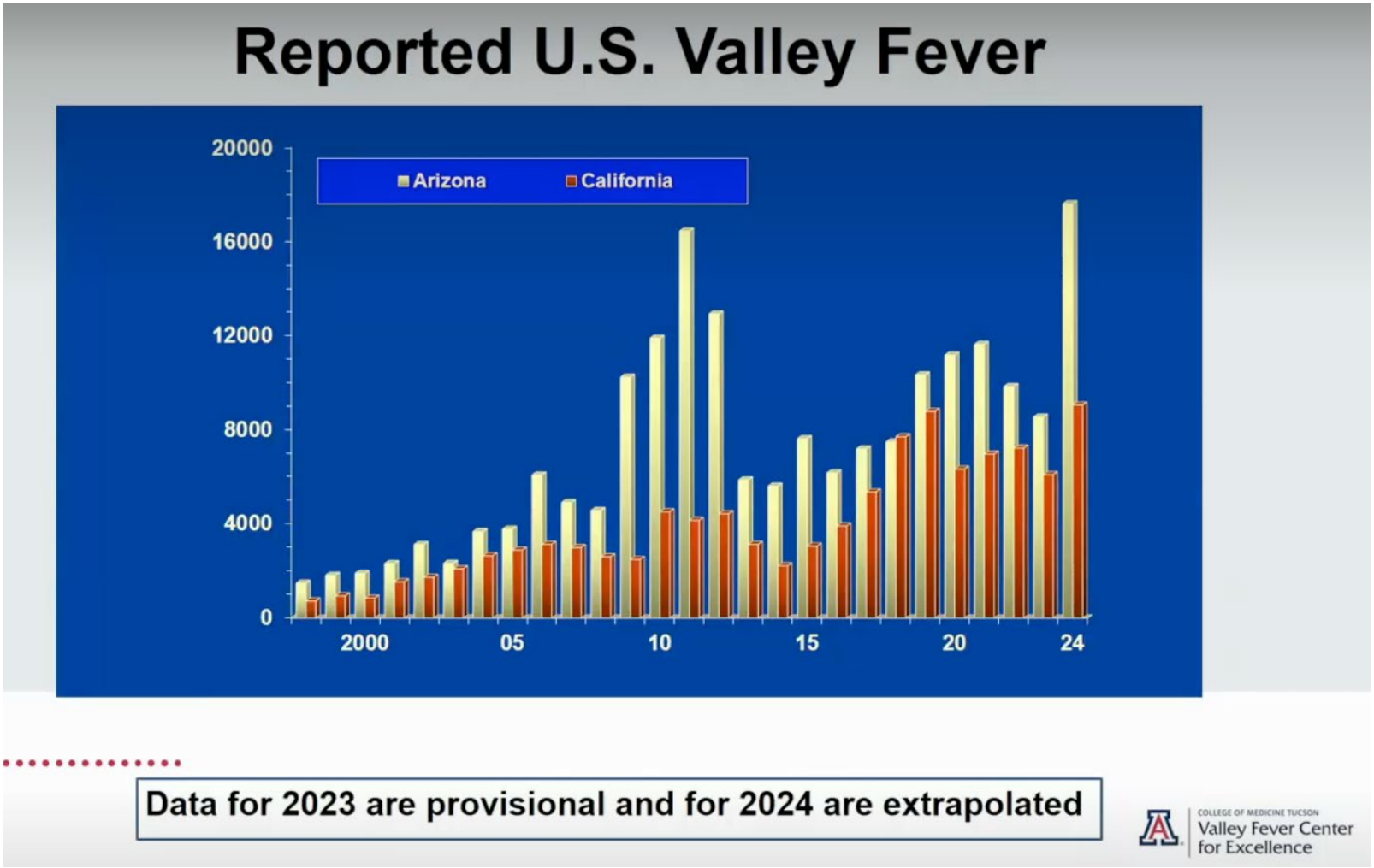

(California Department of Public Health, 2023)

# Lifecycle of *Coccidioides*



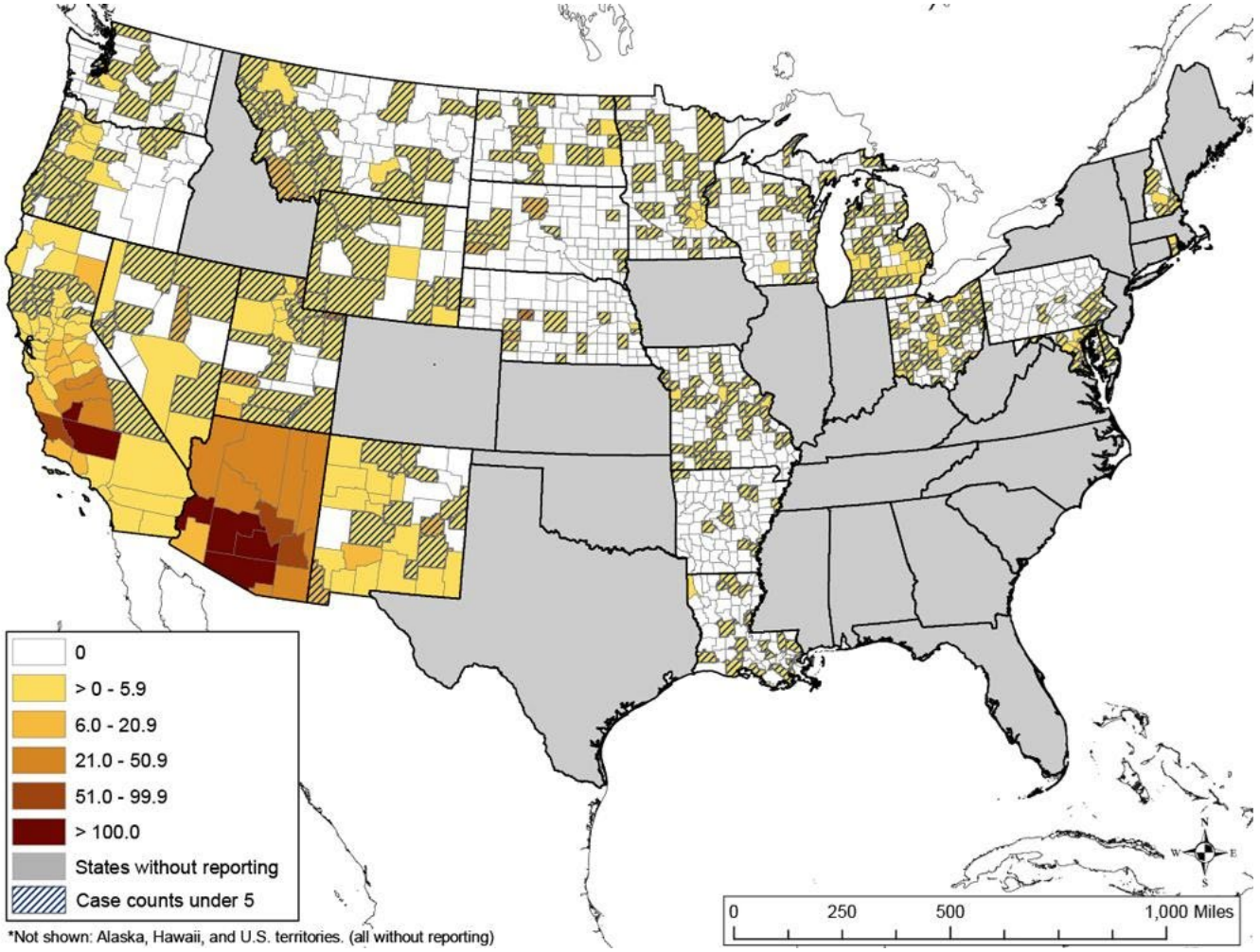

(Donovan et al., 2019)

# CDC: up to 500,000 cases/year




(Galgiani, 2024)

# Valley Fever Cases in the US




(CDC, 2017)

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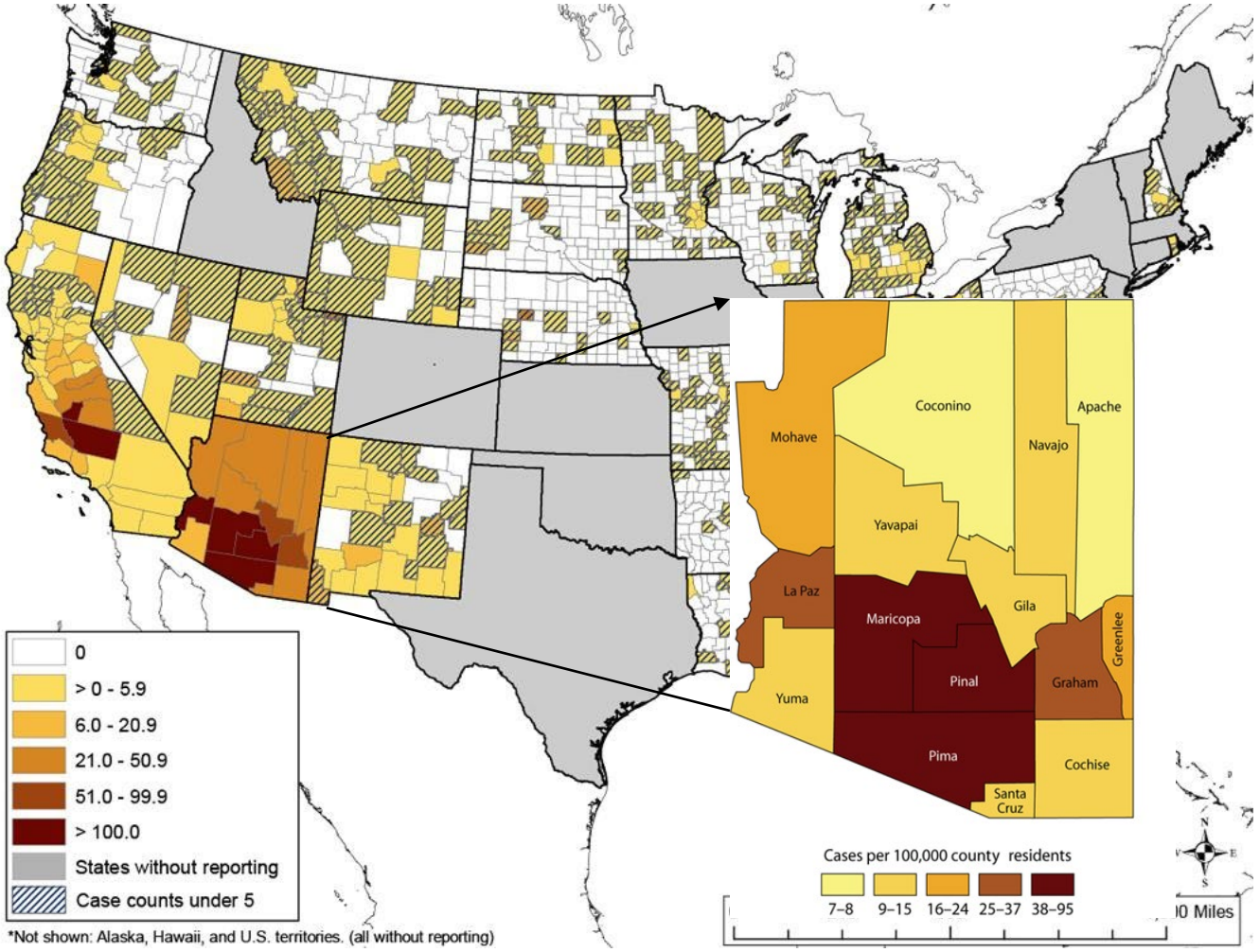


(CDC, 2017)

# One third of all CAP in Arizona is likely Coccidioidomycosis

(Benedict et al., 2018; Valdiva et al., 2006)

# Arizona Provider Statistics

- Only 3 out of 10 providers in Arizona appropriately test for Cocci

(Chen et al., 2011; Pu et al., 2021)

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## Arizona CAP patients tested:

- Primary Care: 2-13%
- Urgent Care: 7.9%
- Emergency Department: 2.8%

(Chang, 2008; Khan, 2018; Pu et al., 2023)

# Results:

- Avg 1 month delay to diagnosis
- > 80% misdiagnosed, given antibiotics
- Delayed diagnosis = increased morbidity and mortality/ significant health care costs

(Donovan et al., 2019; Ginn et al., 2019; Pu et al., 2021)

# Infectious Disease Society of America: CAP Guidelines

**Knowledge Gap:** IDSA does not include fungal infections in their guidelines for CAP

(Metlay et al., 2019)

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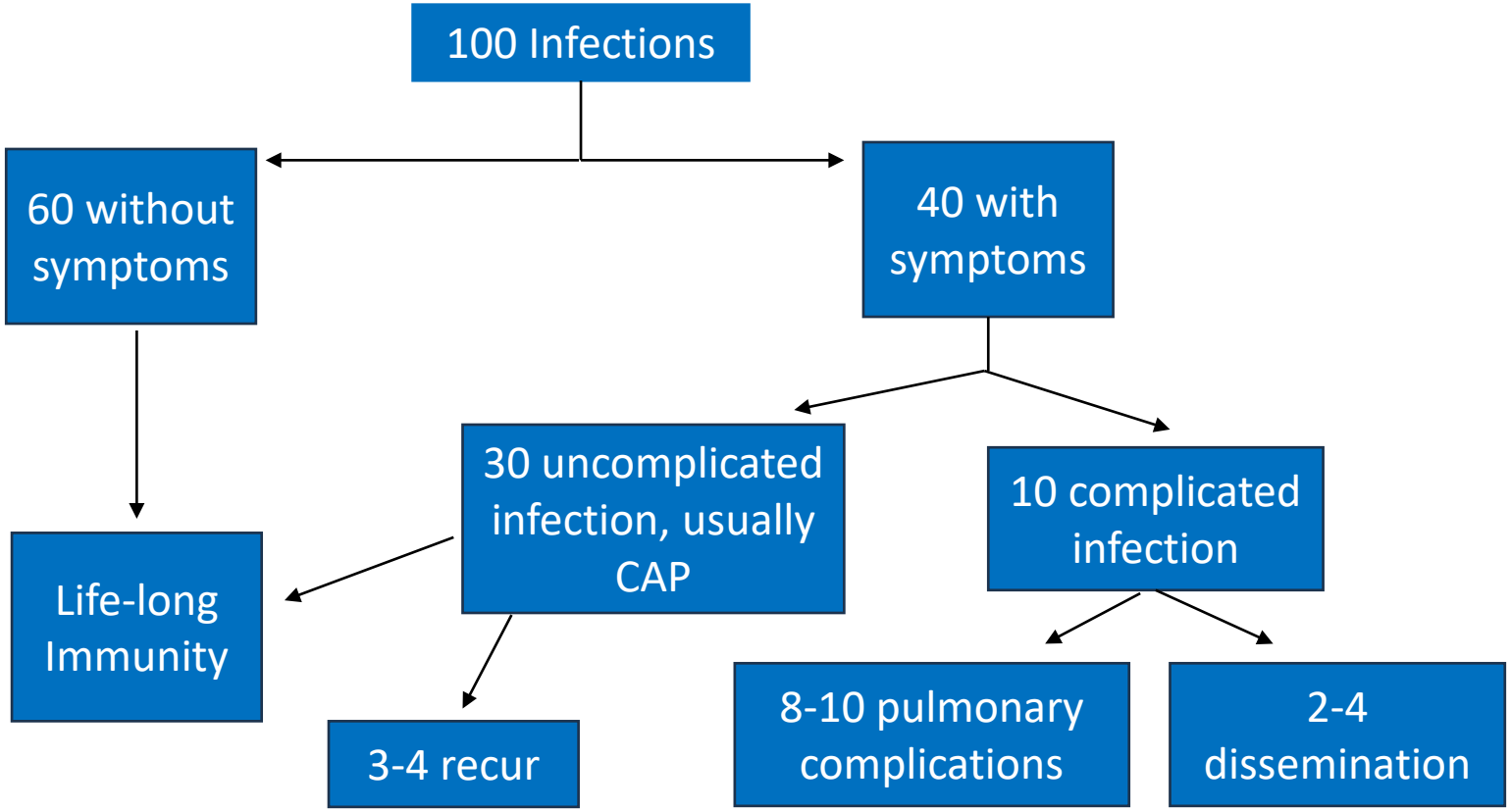
**….“What’s in Your Community? Rethinking CAP”** *Open Forum Infectious Diseases*

*- editorial by Thompson & Heidari (2021)*

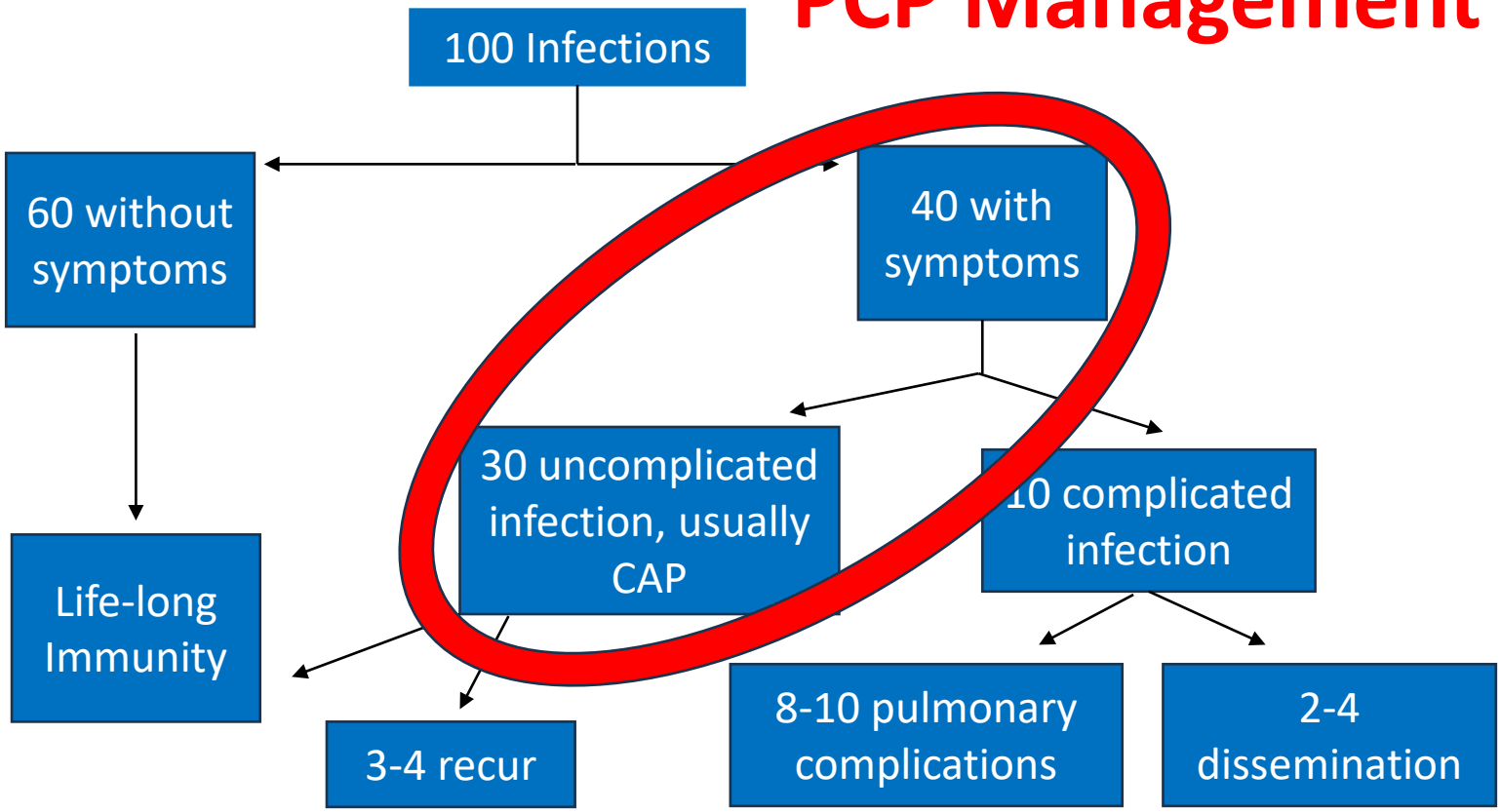
# Pattern of Valley Fever Progression




(VFCE, 2019)

# Pattern of Valley Fever Progression

**PCP Management**




**Specialist Care**

(VFCE, 2019)

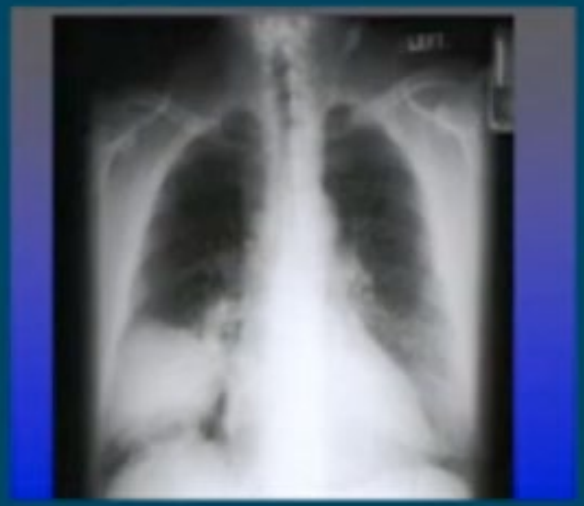
# Devin's Story

- U of Arizona student from Chicago
- Spring 2018- rapid weight loss, extreme fatigue
- Campus health, urgent care: no diagnosis
- Intubated in ICU during Spring break
- Finally diagnosed at 6 weeks from onset
- Disseminated cocci- on lifelong antifungals

# Community-Acquired Pneumonia

- Most common pulmonary presentation
- Symptoms 1-3 weeks after exposure
- Self-limited, most resolve without treatment

Chest radiographs often show abnormalities, such as patchy, unilateral pulmonary infiltrates, hilar adenopathy, and pleural effusions. Lung disease can be bilateral.



(Chiller, 2017)

# Valley Fever Clinical Presentation

- Pulmonary symptoms common, but may not be most prominent
- For example, triad of fever, erythema nodosum, and arthralgia (desert rheumatism)

| Symptoms | Signs |
| --- | --- |
| • Pulmonary<br>– Cough<br>– Chest pain<br>– Dyspnea<br>– Hemoptysis<br>• Arthralgias<br>• Headache<br>• Fatigue<br>• Night sweats | • Fever<br>• Weight loss<br>• Rash<br>– Erythema multiforme<br>– Erythema nodosum |



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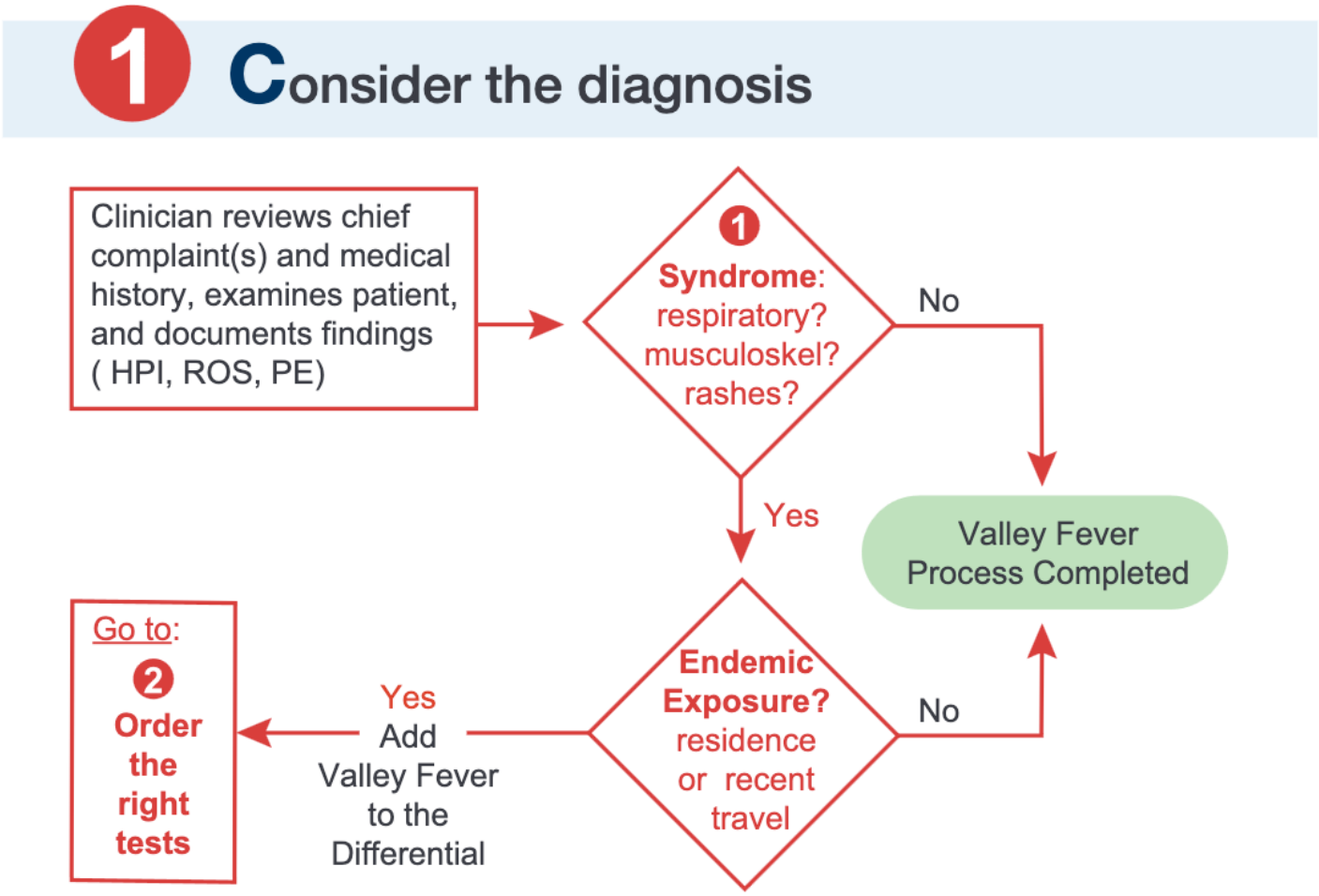
# Valley Fever (Coccidioidomycosis): Training Manual for PCPs


(Valley Fever Center for Excellence, 2019)

# VFCE Guidelines




(VFCE, 2019)

# C: onsider the Diagnosis

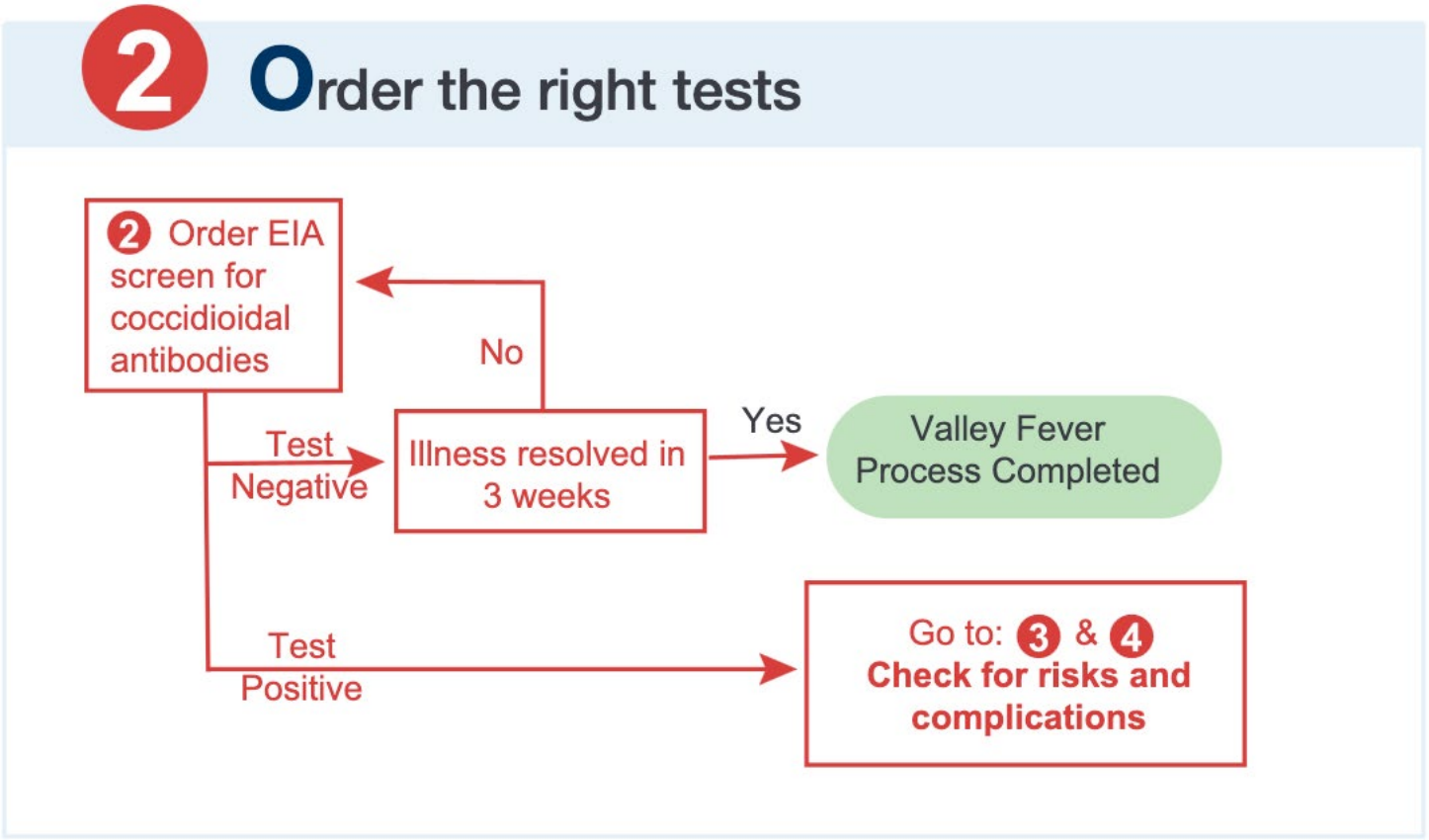
## Consider Testing with Any of Following:

- Respiratory symptoms and at least one of the following:
  - More than 1 office visit
  - Chest X-ray ordered
  - Antibiotic prescribed
- Two of the following for more than one week:
  - Fever
  - Fatigue
  - Arthralgia
- Unexplained peripheral blood eosinophilia
- Skin lesions of:
  - *Erythema nodosum*
  - *Erythema multiforme*



(VFCE, 2019)

# VFCE Guidelines




(VFCE, 2019)

# O: rder the Right Tests

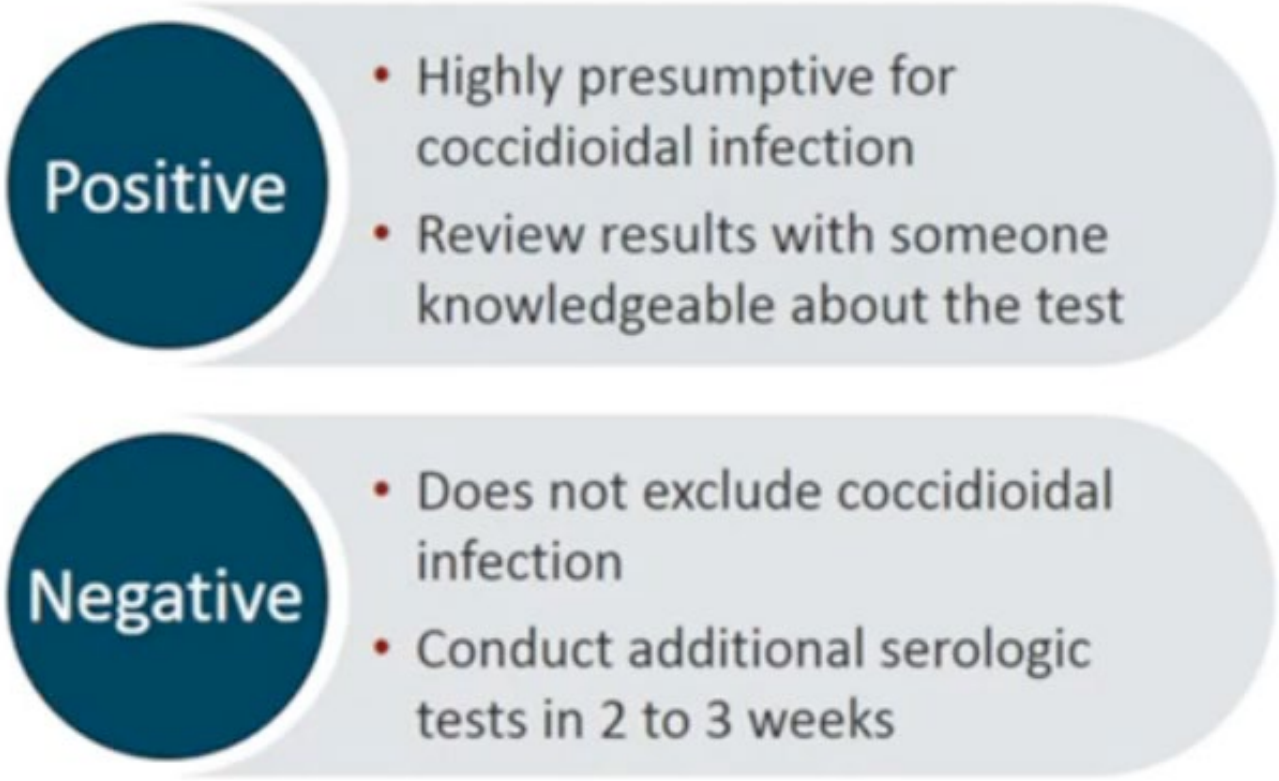
- Serologic tests are the mainstay
- EIA: least expensive, high sensitivity

| Serologic Test | Relative Diagnostic Value |
|---|---|
| Enzyme immunoassay (EIA) | • Highly sensitive for IgM or IgG antibodies<br>• Less specific; positives may require ID or CF confirmation |
| Latex (LA) | • Highly sensitive for IgM<br>• False positives are common<br>• Least specific of the standard serologic tests |
| Complement fixation (CF) | • Quantitative test for CF antibodies<br>• More sensitive but less specific than ID<br>• Has prognostic value<br>– Higher CF titers = more extensive infection<br>– Rising CF antibody levels = worsening disease |
| Immunodiffusion | • Qualitative test for IgM or IgG antibodies<br>• More specific than EIA, LA, or CF but less sensitive<br>• False negatives may occur in late infections |



(VFCE, 2019)

# EIA Test Interpretation




- Immunocompromised patients less likely to have initial positive serology

(VFCE, 2019)

# Which patient(s) would you send to a specialist?

A. Positive EIA test

B. Pt with unilateral PNA

C. Diabetic patient

D. Pt. with bilateral PNA

E. Pregnant Patient

F. Immunocompromised patient

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# VFCE Guidelines


High Risk Patients: Immunosuppression, Diabetes, Pregnancy ➡ Refer to Specialist

(VFCE, 2019)

# **C:** heck for Risk Factors

## Immunosuppression

- Complications from Cocci more likely:
  - HIV/AIDS
  - Solid organ or bone marrow recipient
  - Chemotherapy
  - TNF-alpha blockers
- BRMs may increase risk of severe disease as much as 150-fold

(Donovan et al., 2022; VFCE, 2019)

# **C:** heck for Risk Factors

## Diabetes

- High risk for pulmonary complications
  - Lung cavitations
  - Chronic fibrocavitary pneumonia
  - Pleural Effusion
- Not at higher risk for dissemination unless severely uncontrolled DM

(VFCE, 2019)

# C: heck for Risk Factors

## Pregnancy

- Cocci is serious/ life-threatening in pregnancy
  - Disease course longer
  - Complications more frequent
  - Fungi may disseminate outside lung
- Highest risk: 3rd trimester or immediately post-partum
- Azoles teratogenic

(VFCE, 2019)

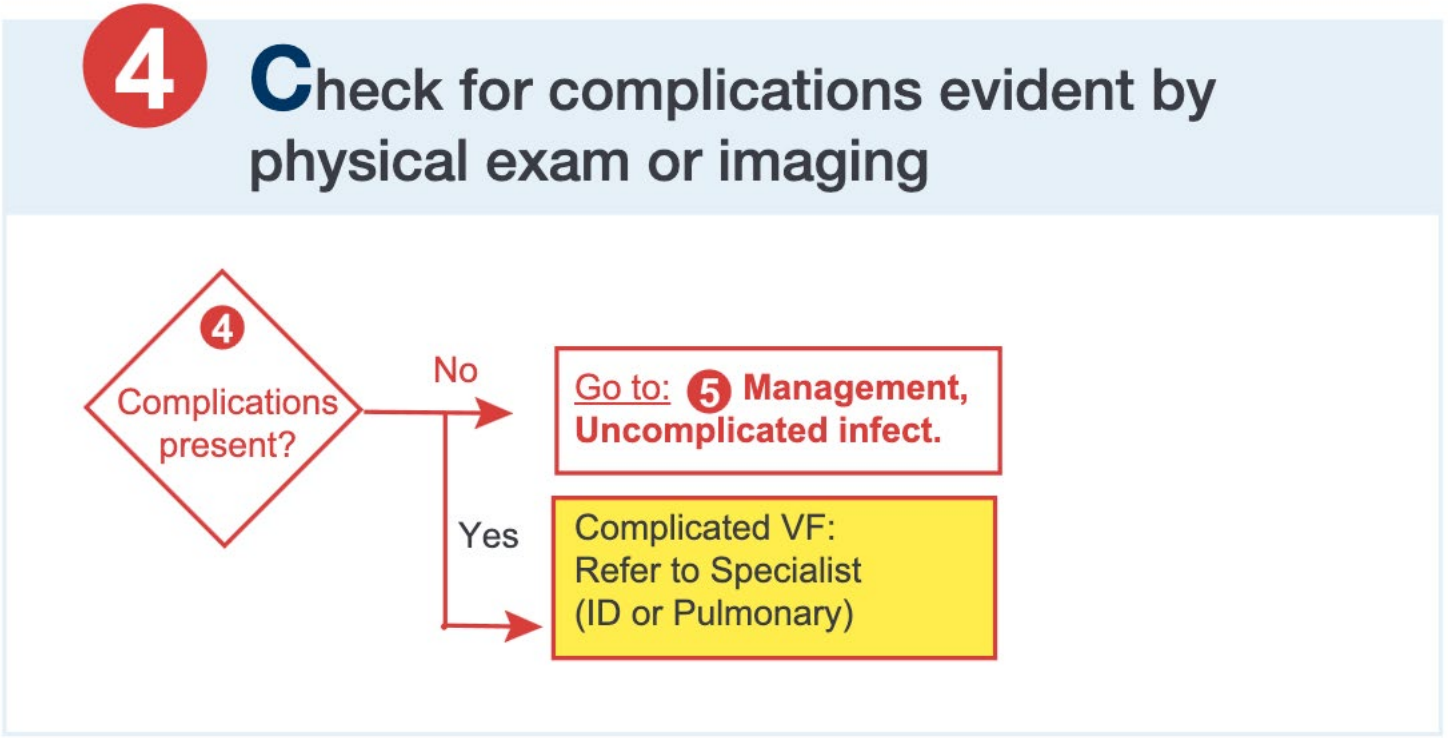
# **C:** heck for Risk Factors

**Other Risk Factors** (Not as significant, no specialist needed):

- Ethnicity
  - Higher complication risk with Filipinos, African Americans
  - Higher incidence: Native Americans, Hispanics
- Gender: men slightly higher risk
- Age:
  - Elderly- higher risk of serious disease
  - Higher incidence in adults versus children

(VFCE, 2019)

# VFCE Guidelines




A careful history, physical exam, and review of imaging is important after any positive serology

(VFCE, 2019)

# **C:** heck for Complications

## Pulmonary Complications ~ 10%

Symptoms may include cough, chest pain, dyspnea, and hemoptysis

- Lung cavities, which may rupture
- Pleural Effusion
- Chronic fibrocavitary pneumonia
- ARDS- less common, usually fatal

- Benign residual pulmonary nodules may remain after resolution

(VFCE, 2019)

# Benign Coccidioidal Lung Nodules

Image source: https://www.youtube.com/watch?v=5FMtgRMT1MI&list=PLeL9ROmy1WLQrk7UvsQUuHkuDpXoJouYS&index=3

Residual nodules may be mistaken for lung cancer

(Ampel, 2012; Peterson et al., 2023)

# C: heck for Complications

## Extrapulmonary Dissemination

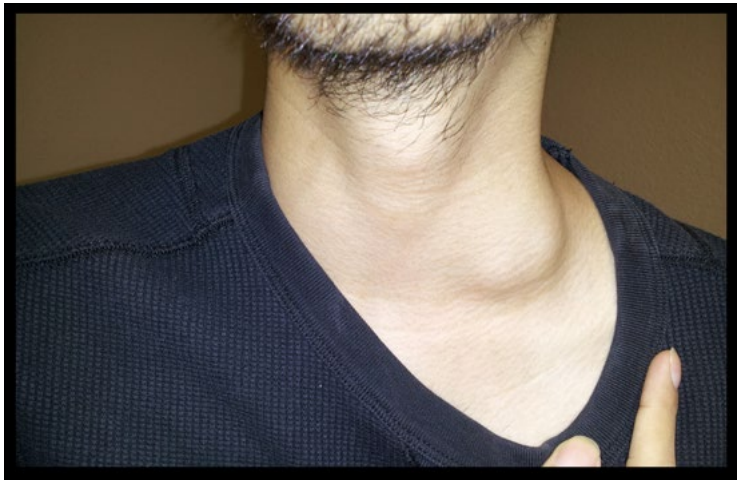
- Typically manifest within a few weeks to months

**Sites of Extrapulmonary Dissemination**

| | |
|---|---|
| Skin or soft tissue | • Most common site of extrapulmonary disease<br>• Ask about new or persistent skin lesions |
| Bone or joints | • Indicated by bone pain or mass<br>• Common symptoms:<br>– Low back pain (vertebral disease)<br>– Joint pain or effusion (often in 1 knee or the other) |
| Meninges or CNS | • Rare, but carries a high risk of mortality<br>• May cause worsening headache, vomiting, or altered mental status |
| Other organs | • Any organ can be affected<br>• Symptoms are often nonspecific |

(Chiller, 2017; VFCE, 2019)

# Dissemination examples



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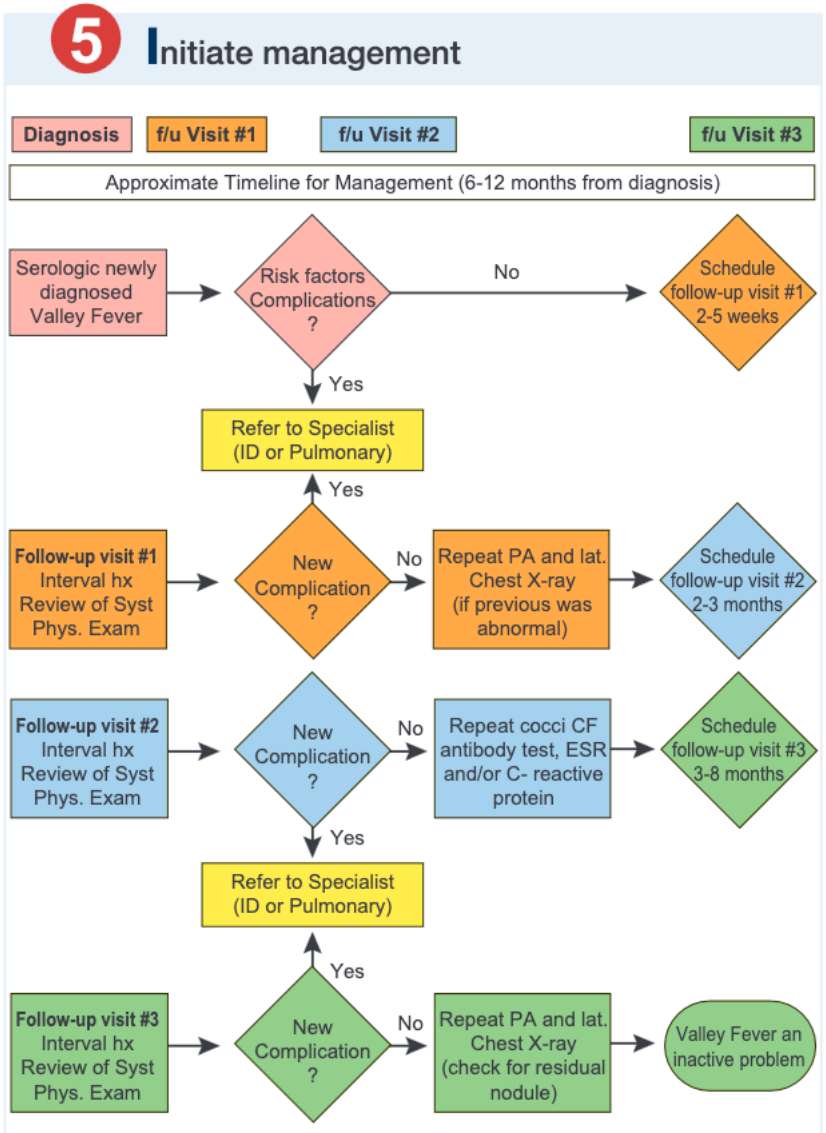



My patient has a positive serology without risk factors or signs of complications….

**Now what?**

(VFCE, 2019)

# I: nitiate Management

## Managing Uncomplicated Cocci

Key role of Primary Care Provider

- Patient education
- Monitor for complications
- Consideration of antifungals, physical therapy
- Follow-up visits:

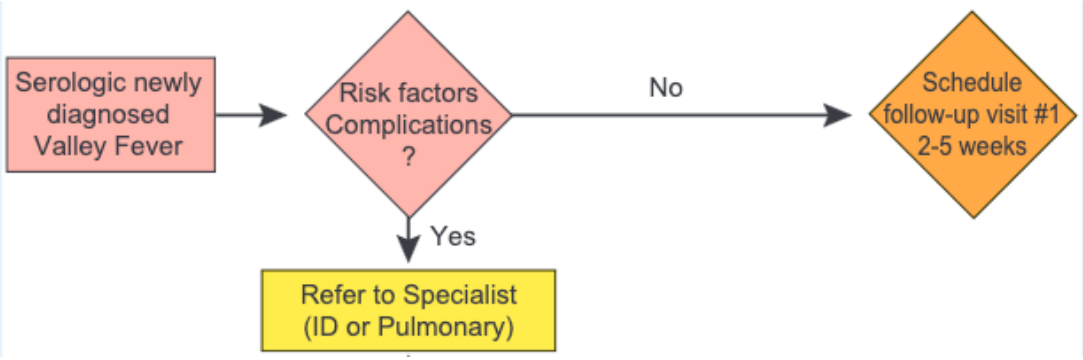
**Table 6. Suggested Plan for Follow-up Visits.**

| Visit | Time From Diagnosis | ROS, Phys Exam | Coccidioidal Serology | Chest X-ray (PA and Lat.) |
|---|---|---|---|---|
| 1 | 2-5 weeks | X | | X |
| 2 | 2-3 months | X | X | |
| 3 | 3-6 months | X | | |
| 4 | 12 months | X | | X |



(VFCE, 2019)

# First Visit: Diagnosis




- **Patient Education**
  - Review how cocci contracted (not contagious)
  - Most illness improves over weeks to months
  - Monitor for:
    - Worsening respiratory symptoms
    - New focal symptoms outside chest
- **Baseline CXR and CF titer**

Schedule follow-up in 2-5 weeks



(VFCE, 2019)

# Complement Fixation (CF) titers

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| Complement fixation (CF) | • Quantitative test for CF antibodies<br>• More sensitive but less specific than ID<br>• Has prognostic value<br>– Higher CF titers = more extensive infection<br>– Rising CF antibody levels = worsening disease |

- Useful for detecting extensive infection / worsening disease
- Rising levels or levels > 1:16 may indicate dissemination
- Patient's clinical presentation important to consider



(VFCE, 2019)

# To treat or not to treat?

Experts have different opinions on whether to treat uncomplicated pulmonary cocci with antifungals

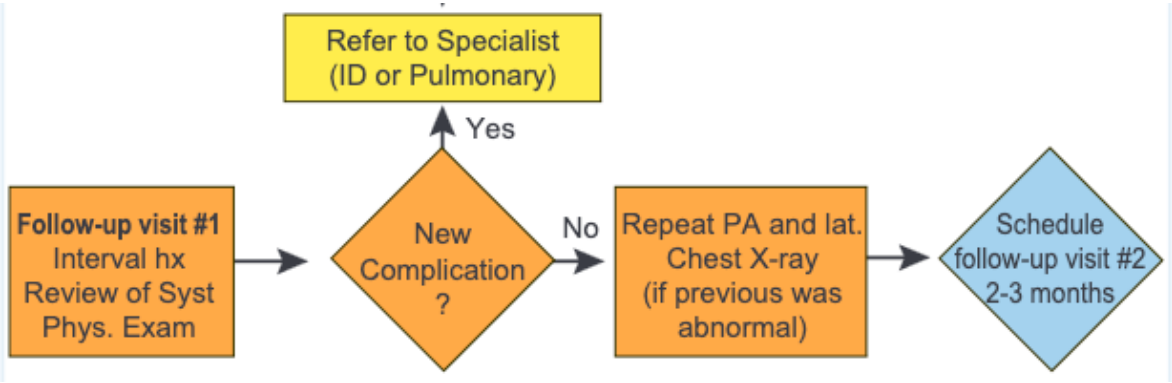
- No RCTs have been done to prove benefit

If antifungal treatment desired:

Typically Fluconazole 400mg daily for 3-6 months

(VFCE, 2019)

# Follow-up Visit: 2-5 weeks

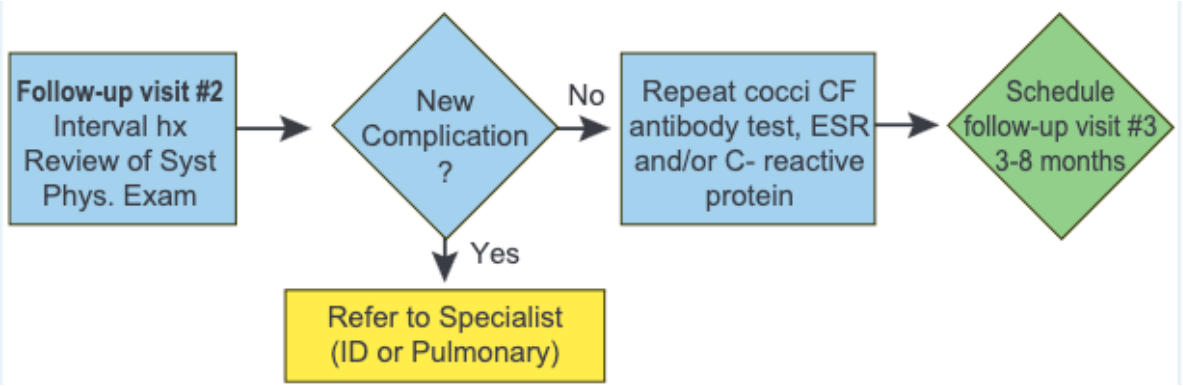



- **Review interval history, ROS and PE for new complications**
  - New complications- specialist referral
  - Repeat CXR if previous was abnormal

Schedule follow-up in 2-3 months

(VFCE, 2019)

# Follow-up Visit: 2-3 months

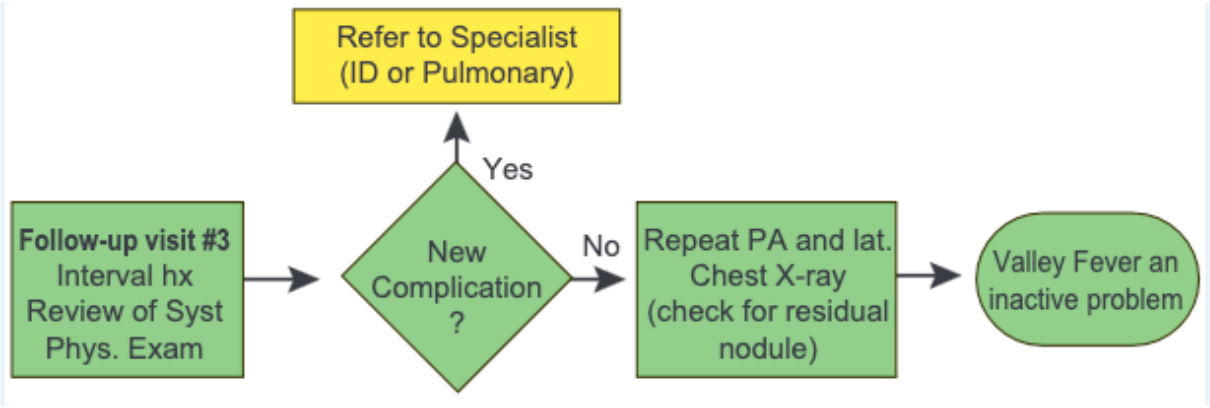



- **Review interval history, ROS and PE for new complications**
  - New complications- specialist referral
  - Repeat CF titers, ESR or C-reactive protein

Schedule follow-up in 3-8 months

(VFCE, 2019)

# Follow-up Visit: 3-8 months



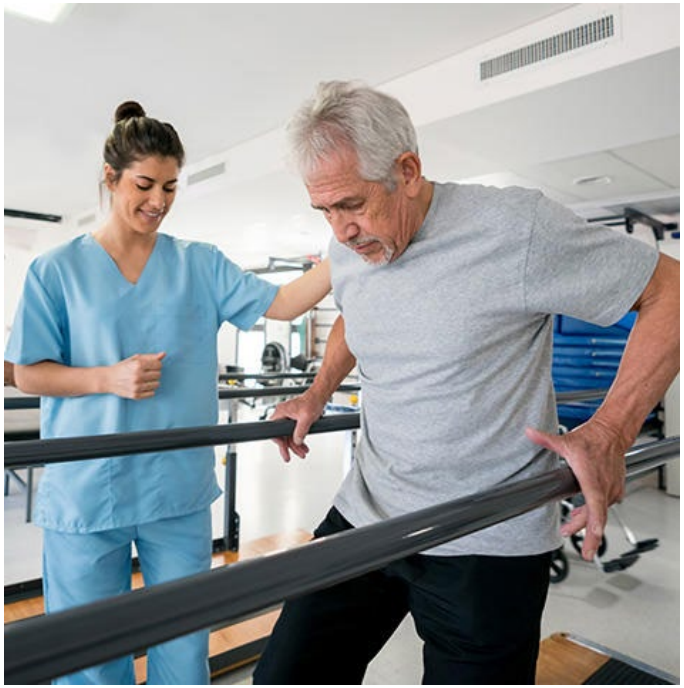

- **Review interval history, ROS and PE for new complications**
  - New complications- specialist referral
  - Repeat CXR (check for residual nodules)

Complications unlikely after 1-2 years

(VFCE, 2019)

# Residual Fatigue Syndrome

- Chronic fatigue often debilitating, one of the last symptoms to resolve
- Consider Physical Therapy for prevention or to reverse fatigue-related deconditioning



(VFCE, 2019)

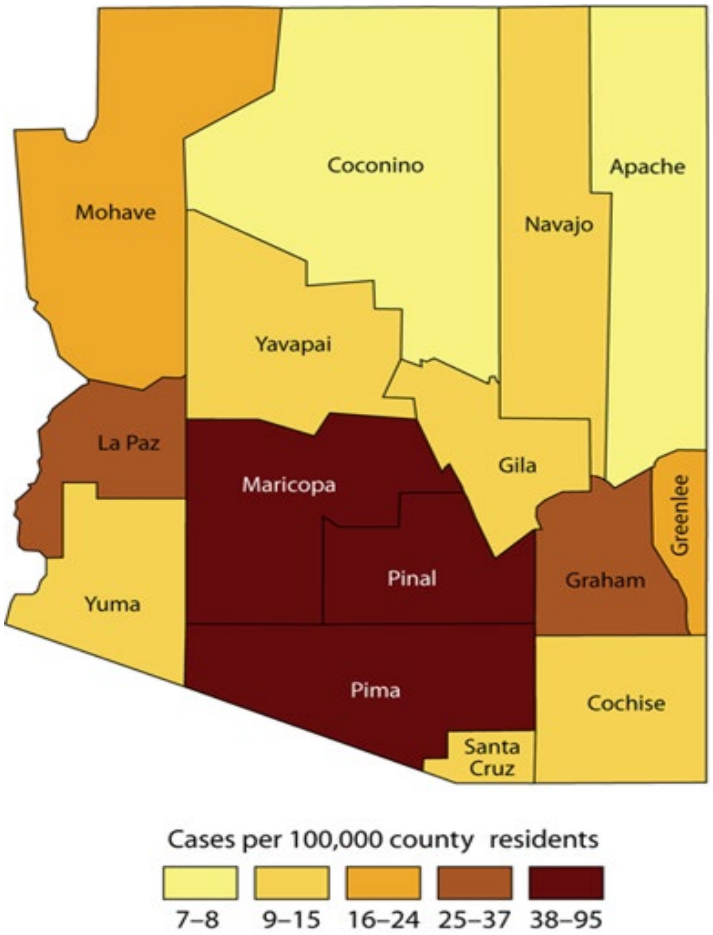
# Rural Health and Valley Fever

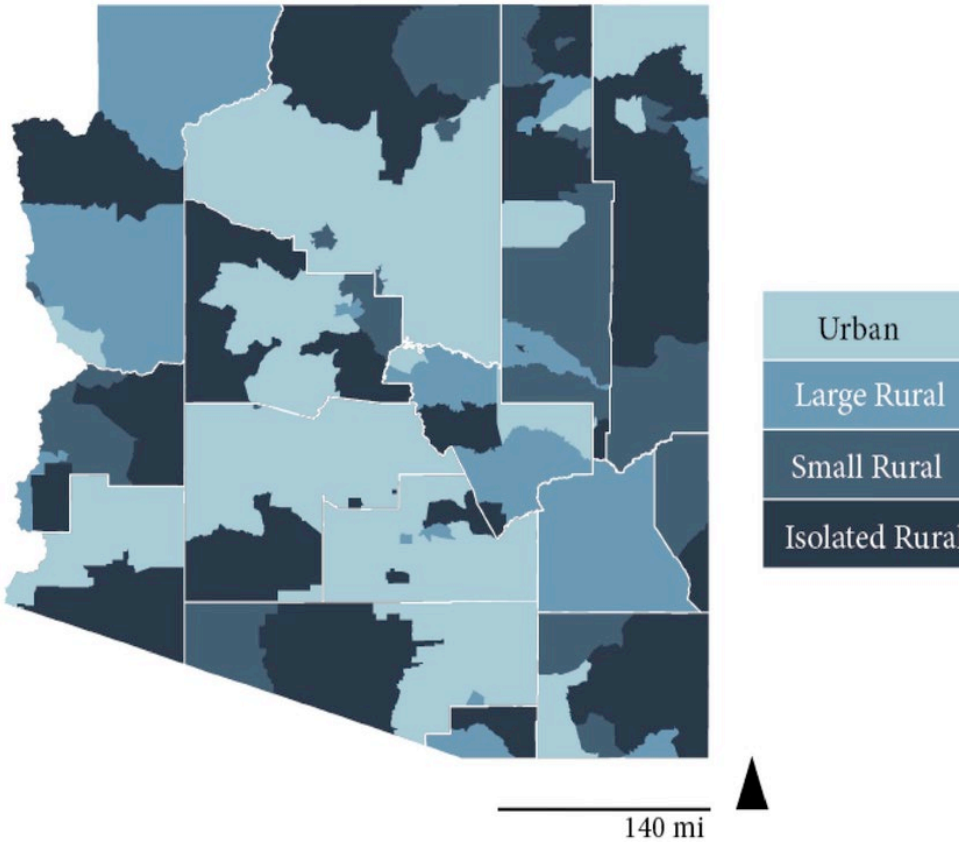
How does Cocci impact rural and tribal communities?

# Danny's Story

- June 2020- COVID
- 4 weeks later, dx CAP at IHS, given antibiotics
- Weeks out for pulmonology specialist- no rural specialist
- Lung Cavitations, admitted; Dx with Cocci
- Rapid 60 lb weight loss, extreme fatigue, night sweats
- Pulmonologist noted lump on chest- concerned for cancer, later found it was disseminated cocci
- On potentially life-long antifungal treatment

# Arizona Valley Fever Cases and Rurality




(Brady et al., 2021; CDC, 2017)

# Rural Risk Factors

- **Occupations that disrupt soil**
  - Agricultural or construction
- **Lack of paved roads**
- **Poor access to specialty services**
- **Higher risk population demographics**
  - Ethnic minorities, those living with diabetes mellitus, pregnancy

# Increased risk from dirt and dust exposure

Of 410 cocci patients:

- 49% reported dust storm or high dust event

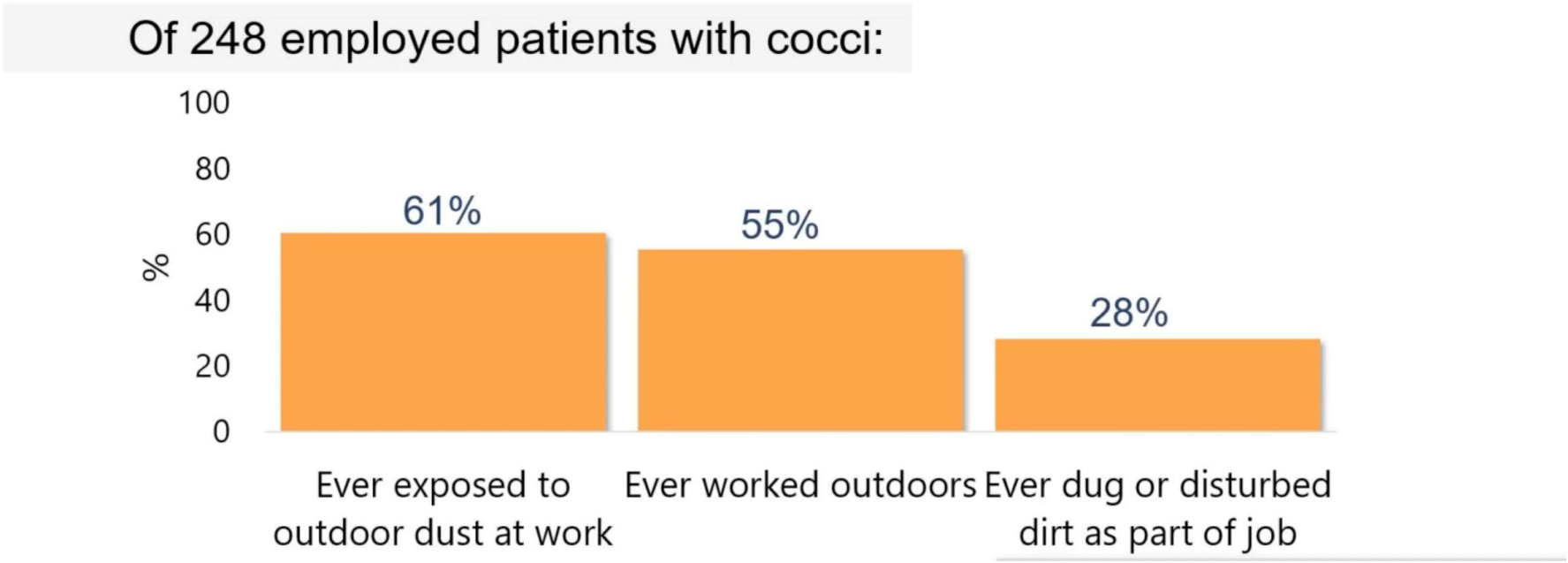
- 39% reported construction near home, work, school, or commute

- 13% reported participating in outdoor event

Two months prior to onset/testing

**Preliminary data**:
CDPH Cocci Enhanced Surveillance (2022-2023)

# Occupational exposure




(California Department of Public Health, 2023)

# Impact of Wildfires?

## Pyroaerobiology

- Impact of smoke on pathogen spread?
- Smoke is “living” component – easily able to spread soil dwelling pathogens
- Drone sampling of smoke
  - High-quantity bacteria and fungal pathogens
    - *Aspergillus*
    - *Mucorales*
    - *Cryptococcus*
    - *Cladophialphora* etc

Kobziar and Thompson, ***Science***, 2020;370(6523):1408-10.

# Rural Health Professions Program


AMERICAN INDIAN HEALTH-AHEC

# Key Stakeholder Interviews

- Interviews with rural PCPs, rural hospital/ FQHC leadership, lab managers, PTs
- Survey Results:
  - Varied knowledge of VF per rural health professional interviews: from minimal to moderate; all indicated value of further education/resources
  - Lack of lab infrastructure in remote areas causes delay of results or long travel distances to get tested
  - Rural patients often travel to urban centers for treatment/specialists

# Recommendations from Survey

- **Infrastructure**
  - Improve lab testing capability
  - Self-ordered VF testing option
  - Address rural dust exposure

- **Rural Provider Education**
  - Inservice training, particularly in primary care

- **Expert Consultation**
  - Support rural Telehealth capability
  - Connect rural health professionals with experts such as VFCE
  - Utilizing language translators when addressing native communities.

# Key Takeaways for Providers

Consider Cocci in patients with respiratory complaints and/or *E nodosum*

Refer Valley fever patients with high risk (T2DM, immunosuppression, pregnancy) or signs of complications to specialists

Uncomplicated Cocci can be managed successfully in primary care without need for specialists

# Key Takeaways for Rural Health

Further evaluation of Valley fever in rural and tribal communities is needed- interplay of rural risk factors and disease, management in rural settings

Developing infrastructure to support rural providers/patients: lab testing capabilities, telehealth options for specialists, rural physical therapy options

Support for rural PCPs can include in-service training, expert consultation services

*Special thank you to Dr. Galgiani and the Valley Fever Center for Excellence*


https://vfce.arizona.edu/

# Questions?

## References

## Resources

American Indian Health-AHEC

Arizona Telemedicine Program

Southwest Telehealth Resource Center TRC

The University of Arizona College of Nursing