Coccidioidomycosis Update for Primary Care

SW Conference on Medicine
April 26, 2018

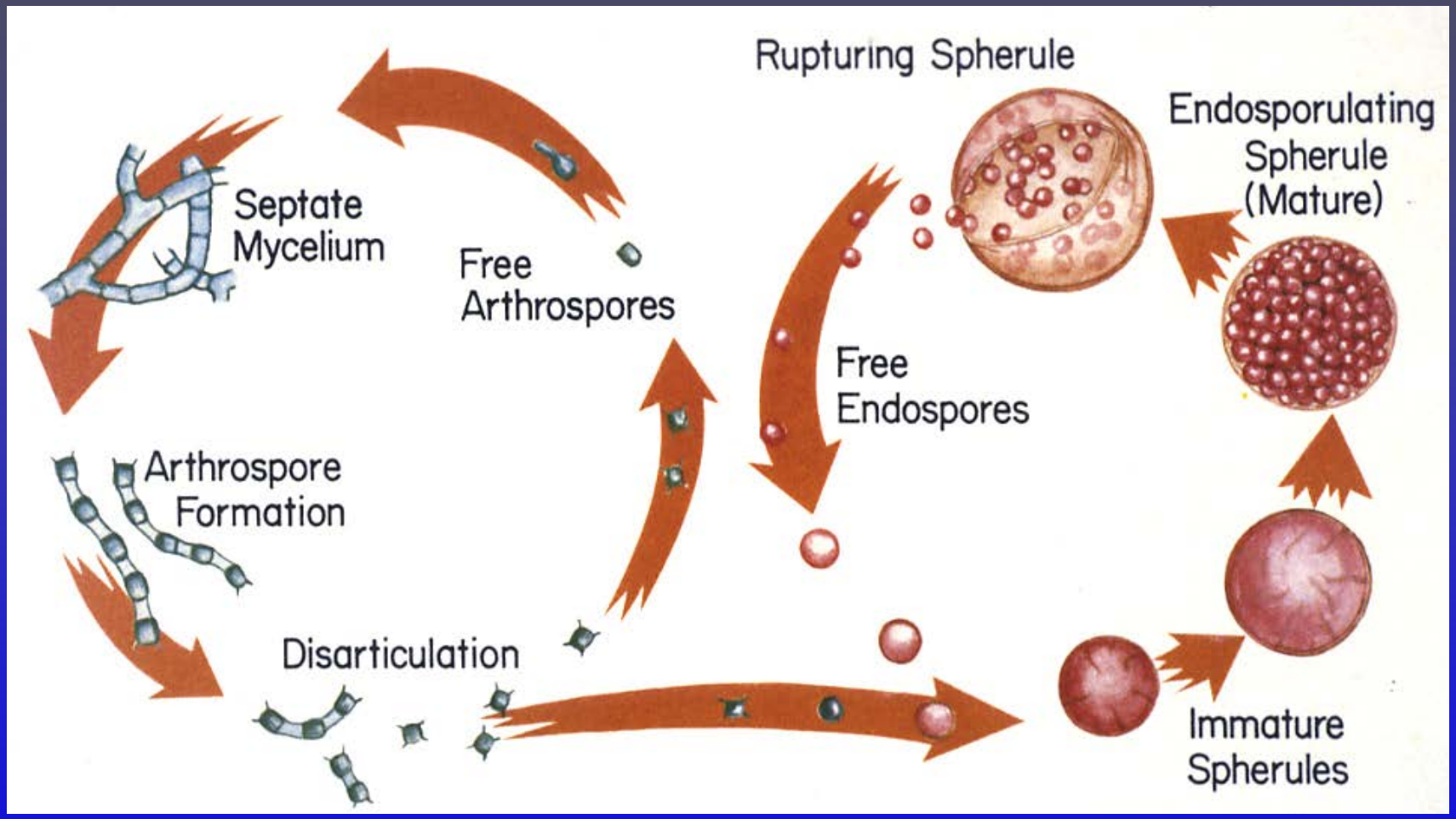
John N Galgiani MD
Valley Fever Center for Excellence
University of Arizona

What Is Valley Fever?

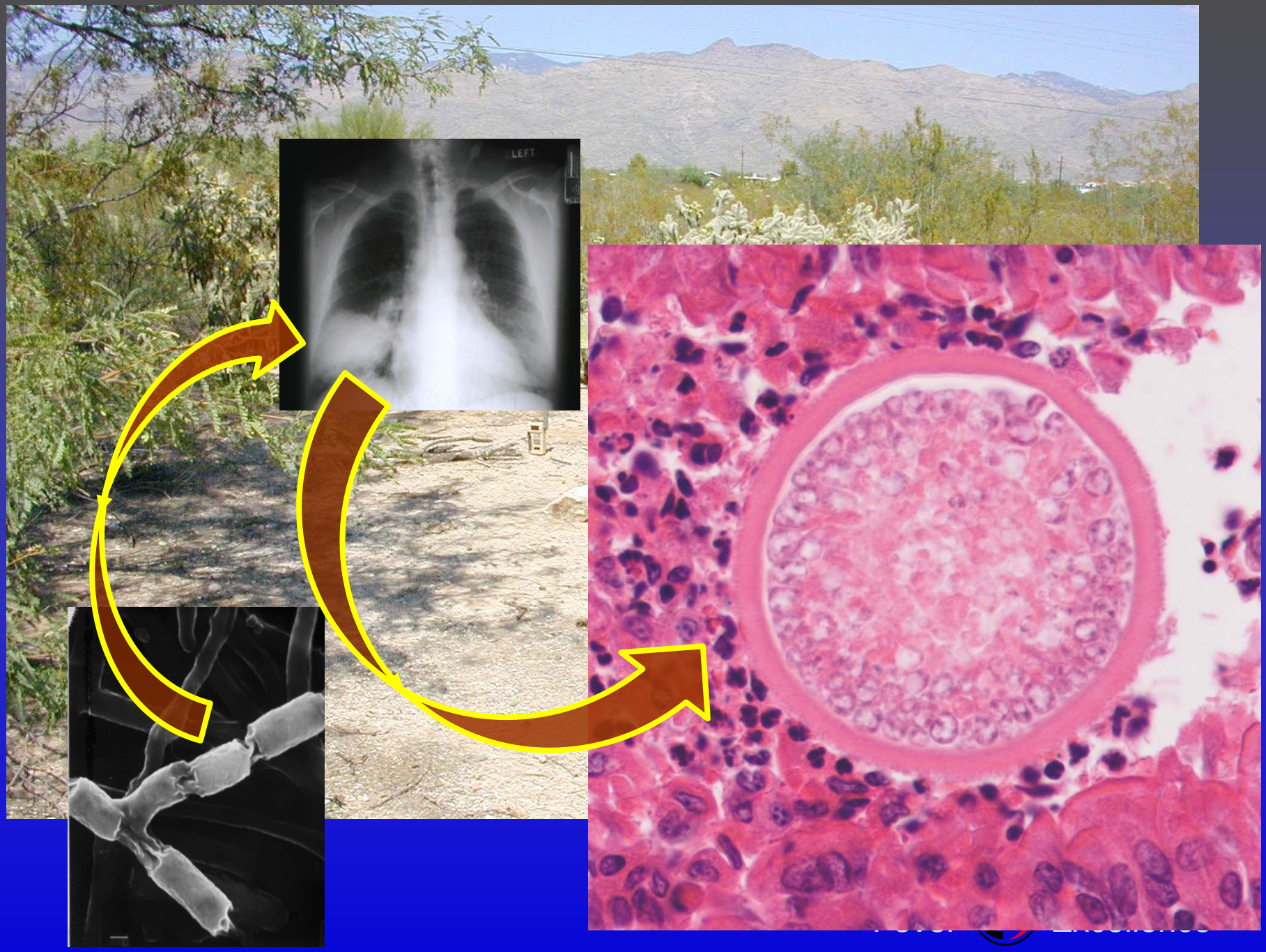
- Caused by soil fungi
  Coccidioides immitis
  Coccidioides posadasii
- Other names:
  - Coccidioidomycosis (cocci)
  - Desert Rheumatism
- Infection results from inhaling a spore
- Severity varies
  - Mild: 60%
  - Moderate: 30%
  - Complicated: 10%
- After infection, most persons develop life-long immunity to a second infection

Morphology of *Coccidioides* spp.

In the Soil **In infected tissue**



Arthroconidia (transmission & scanning EM)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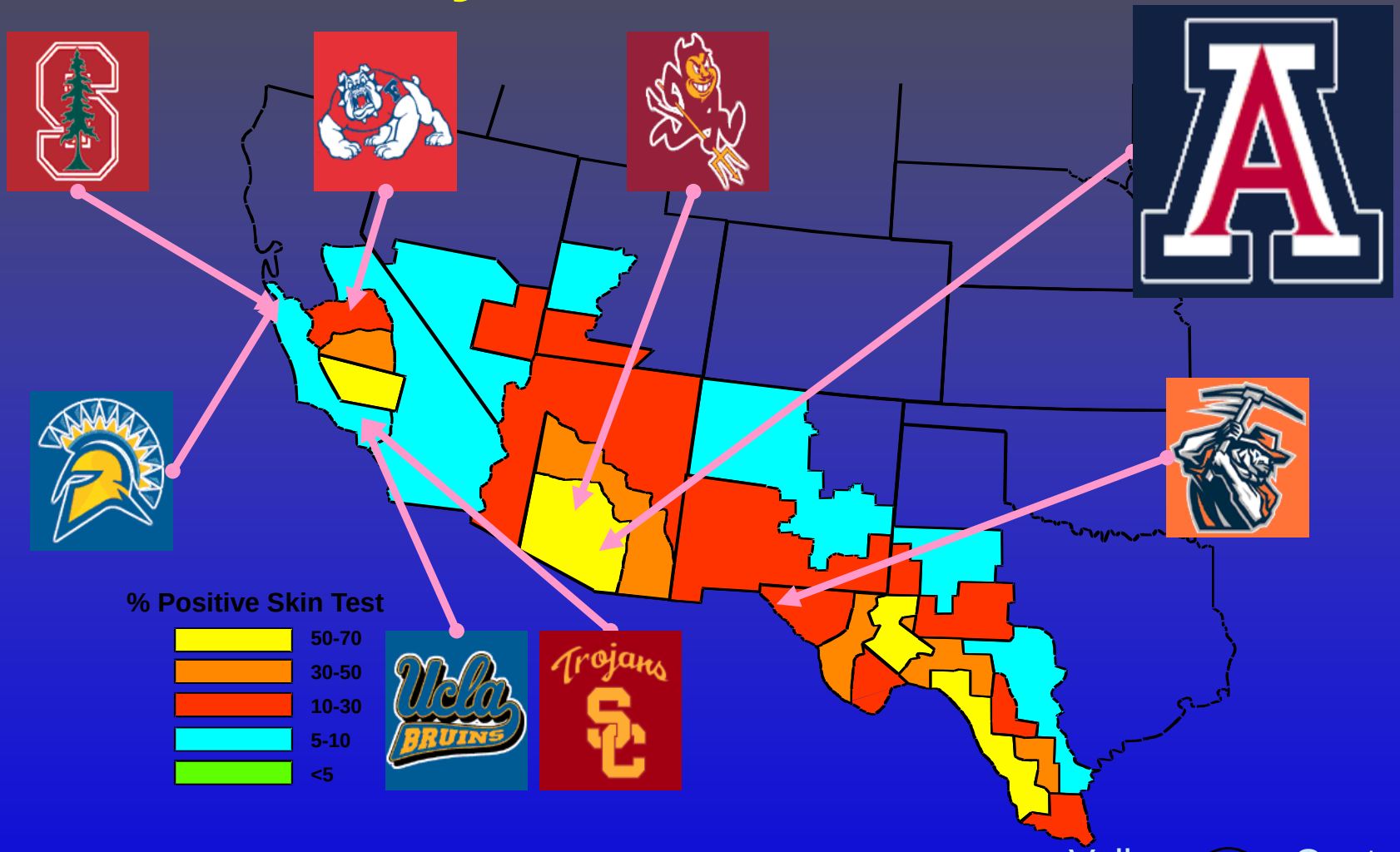
Valley Fever in the U.S.



•www.vfce.arizona.edu

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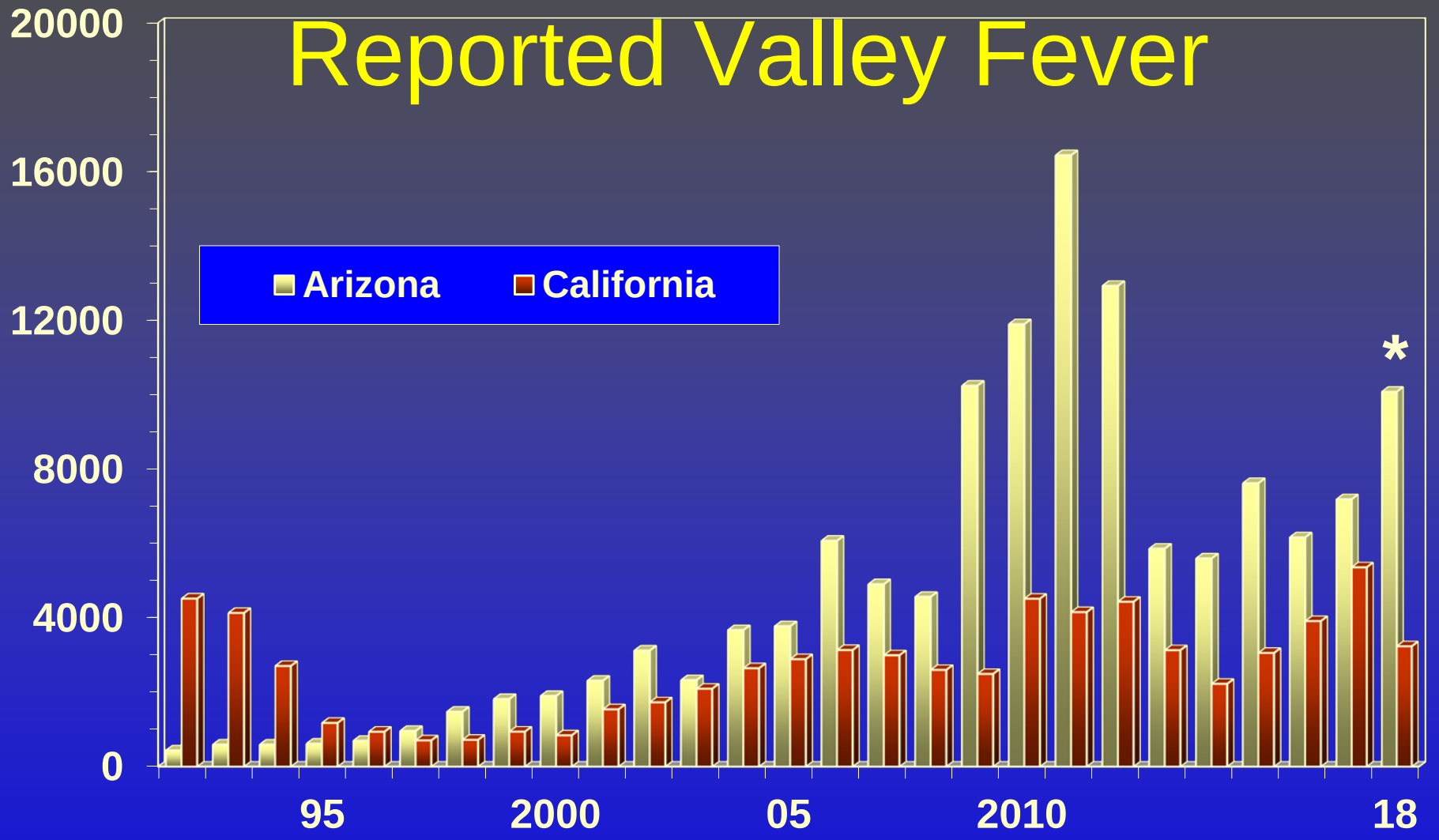
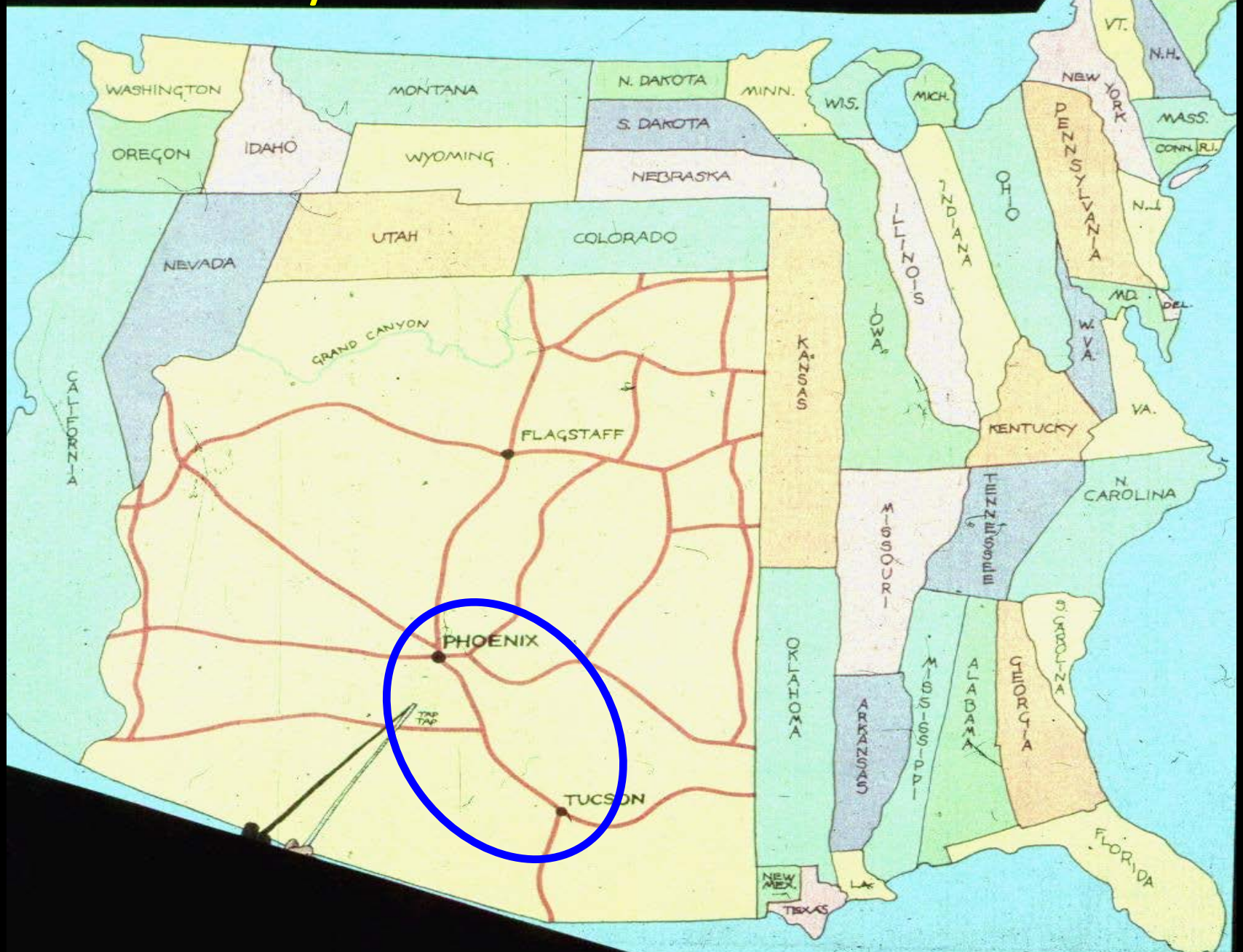
Reported Valley Fever

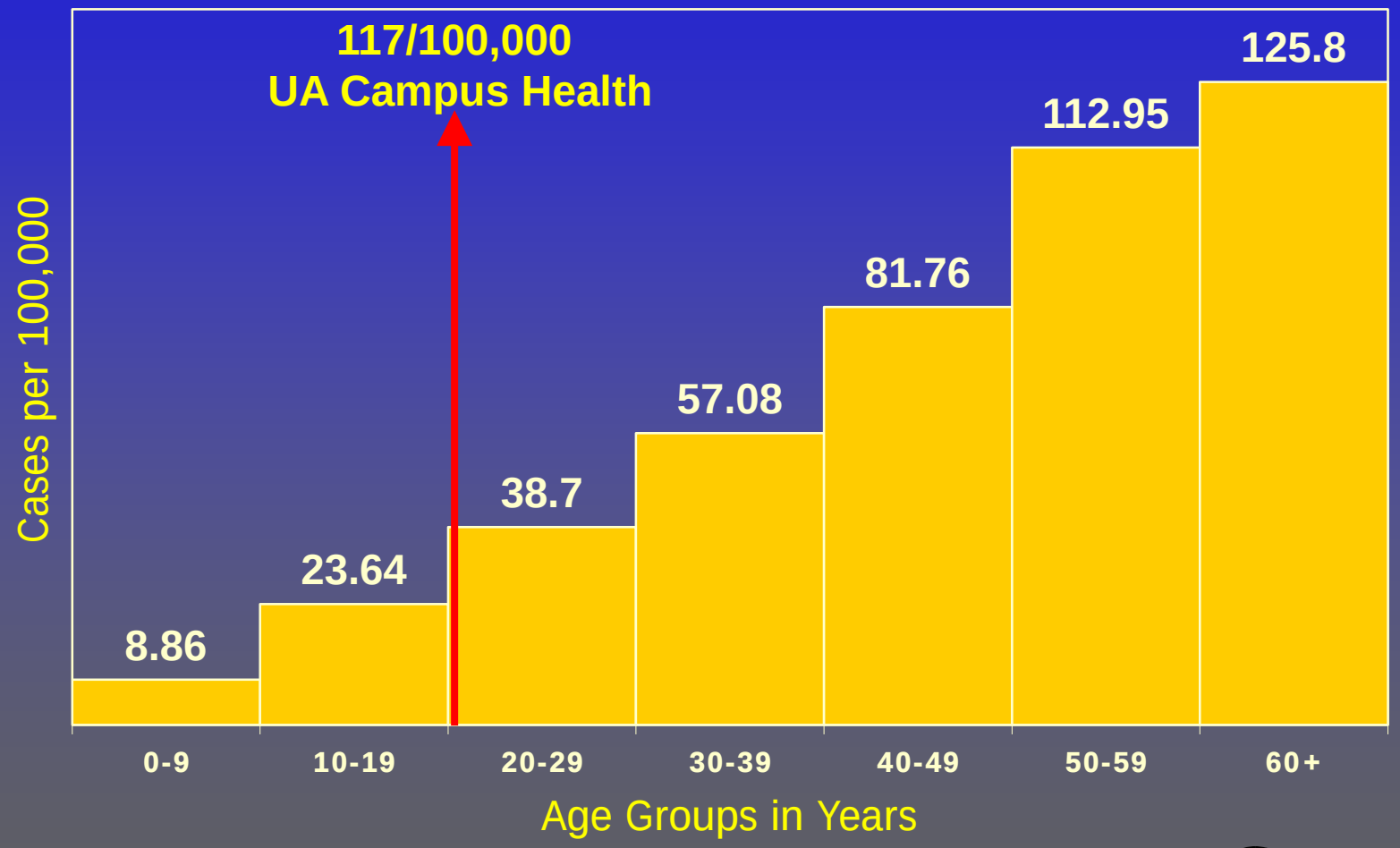


*Extrapolated from week 13

The Valley Fever Corridor:
2/3 of all US disease occur here



Age Specific Rates of Reported Coccidioidomycosis in Arizona, 2004*



N Stern Emerg. Inf. Dis. 2010

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Infectious Disease Epidemiology
Arizona Department of Health Services

Valley Fever at UA Campus Health 1998-2006

Patient group	Cases per 100,000 Incidence	95% CI
Scholarship Athletes:		
475 per yr	374	192-639
Non-Athletes:		
35,525 per yr	90	79-103

Chi square, $p < 0.00001$

N Stern Emerg. Inf. Dis. 2010

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Valley Fever at UA Campus Health 1998-2006

Patient group	Percent Tested: Tested	Percent Tested: 95% CI
Athletes:		
197 tests	4.6%	3.9%-5.4%
Non-Athletes:		
2,558 tests	0.8%	.77%-.84%

Chi square, $p < 0.000001$

N Stern Emerg. Inf. Dis. 2010

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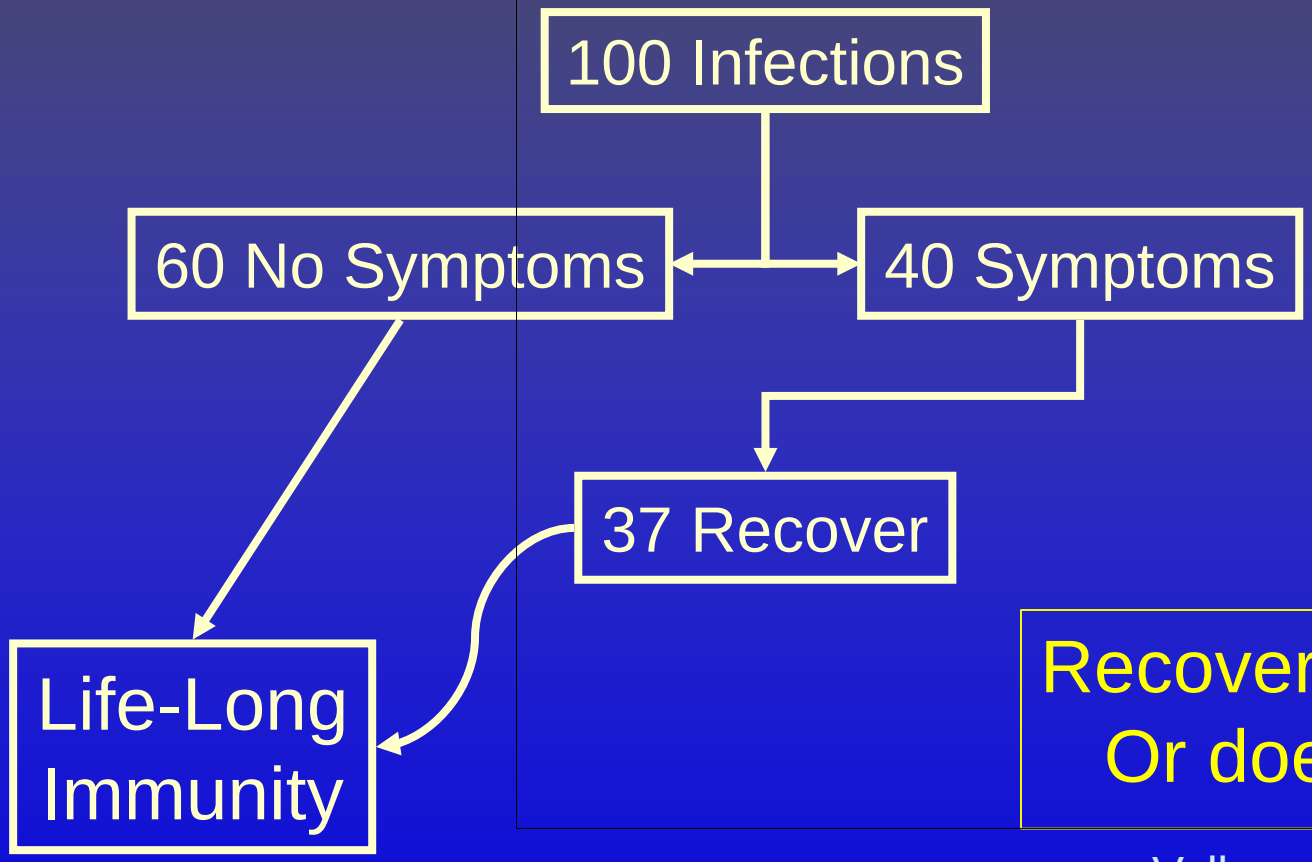
Coccidioidomycosis Spectrum of Disease



Recover=Mild
Or does it?

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Common “Mild” Valley Fever

- Manifestations:
  - Cough, chest pain, fever, weight loss
  - Fatigue
  - Bone and joint pains (a.k.a. Desert Rheumatism)
  - Skin rashes (painful or intense itching)
- Course of illness:
  - Weeks to months
  - 1 of 4 college students are sick for > 4 months
  - 4-fold more drop a semester for Valley Fever than for Mononucleosis

Coccidioidomycosis as Community-Acquired Pneumonia

In Southern Arizona
29% (CI: 16% - 44%) of all CAP
is Valley Fever

Tourists to Arizona: average risk is <1:15,000
But
CAP weeks after trip to Arizona,
Risk same as if you live in Arizona

Valdivia et al, Emerg. Inf. Dis, 2006

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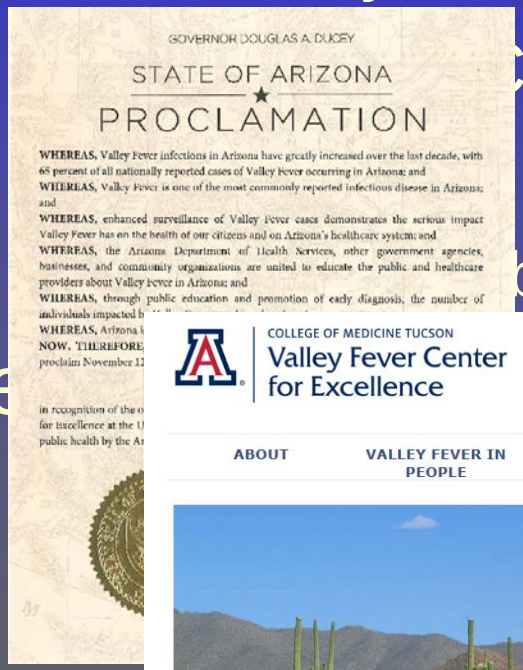
22nd Anniversary of the UA VFCE

- Education
  - 2002 Valley Fever Awareness Program
  - [illegible] Care Tutorial, 2nd Edition
  - [illegible]
  - [illegible] pe
- Re[illegible]
  - [illegible] mmunol., [illegible] accines
- Clinica[illegible]


GOVERNOR DOUGLAS A. DUCEY

STATE OF ARIZONA

PROCLAMATION

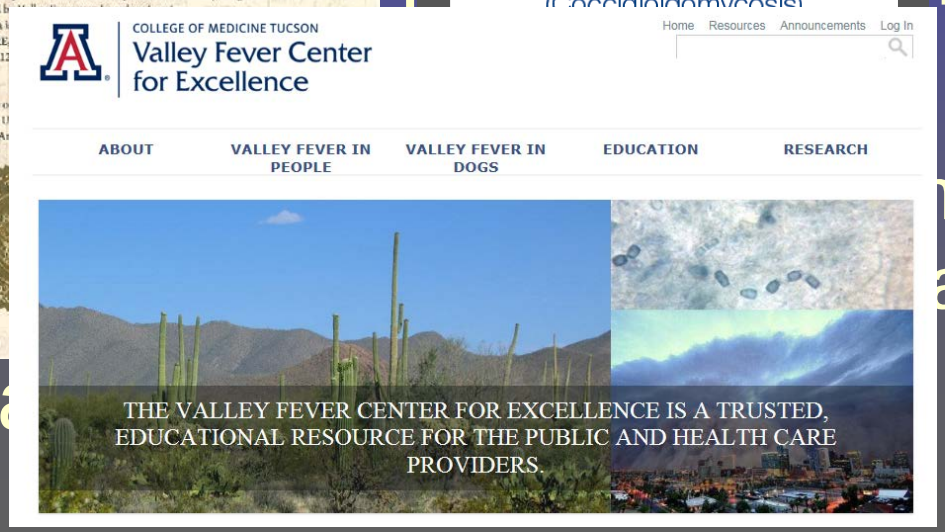
WHEREAS, Valley Fever infections in Arizona have greatly increased over the last decade, with 65 percent of all nationally reported cases of Valley Fever occurring in Arizona; and

WHEREAS, Valley Fever is one of the most commonly reported infectious disease in Arizona; and

WHEREAS, enhanced surveillance of Valley Fever cases demonstrates the serious impact Valley Fever has on the health of our citizens and on Arizona's healthcare system; and

WHEREAS, the Arizona Department of Health Services, other government agencies, businesses, and community organizations are united to educate the public and healthcare providers about Valley Fever in Arizona; and

WHEREAS, through public education and promotion of early diagnosis, the number of



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How bad is it?

Ariz CAP

- ~25%-30% due to *Coccidioides* BUT
- <15% are tested for *Coccidioides*.

~1,000 new Az medical licenses/yr

- 12% received MD in Az; 40% no Az GME

80% didn't know: VF is reportable;
Vaccine does not exist

40% of clinicians not confident to treat VF

•**Chang, 2008; Chen, 2011**

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Consequences of Current Standard Practices

- Delays in diagnosis of early coccidioidal infections: In BUMC-T, 30% > 1 month*
  - Unnecessary anti-bacterial drug use
  - Protracted patient anxiety and fear
  - Over-utilization CT scans and bronchoscopies, even thoracotomies
- Hypothesis: Earlier diagnosis would improve outcomes and reduce cost.

*Donovan et al, unpublished 2018

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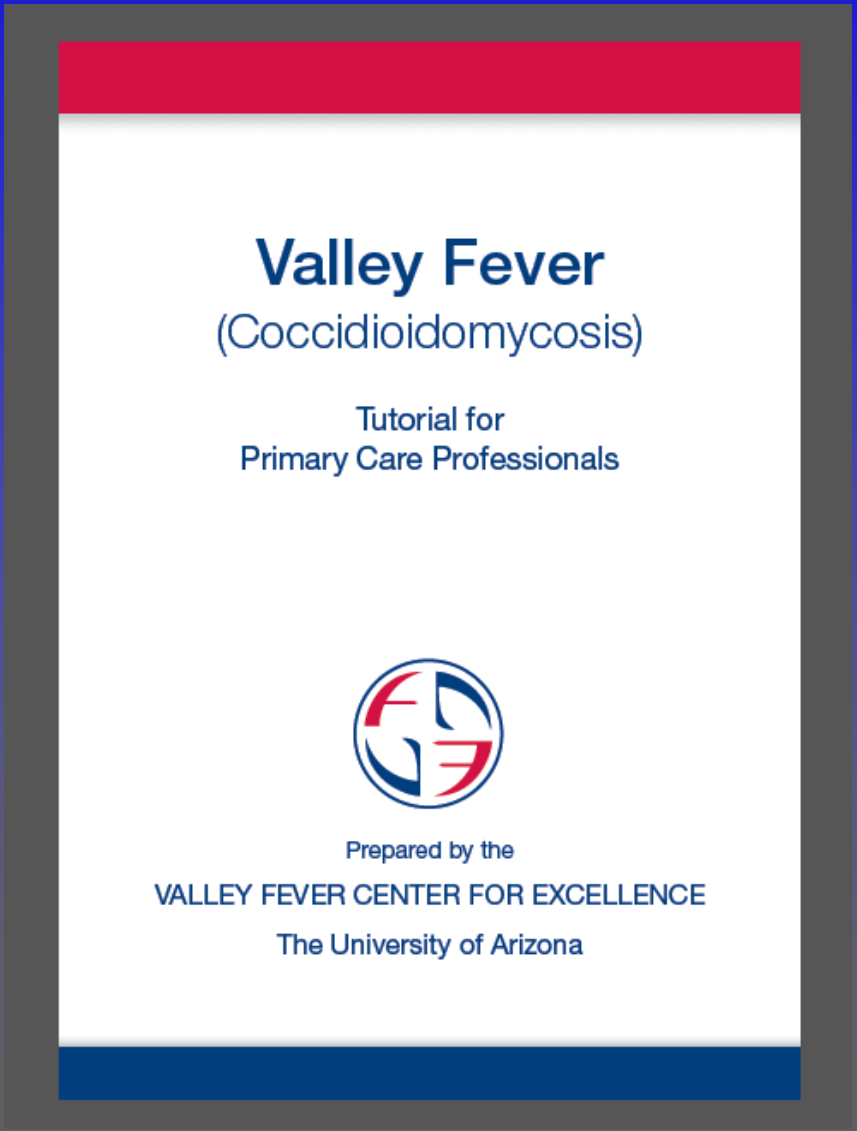
This syllabus is available at htpp://www.vfce.arizona.edu



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Primary Care of Coccidioidomycosis

C onsider	**the diagnosis**
O rder	**the right tests**
C heck	**for risk factors**
C heck	**for complications**
I nitiate	**management**

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When to think of Valley Fever

Symptoms

- Pulmonary
  - Cough
  - Chest pain
  - Dyspnea
  - Hemoptysis
- Arthralgias/Myalgias
- Headache (20%)
- Systemic
  - Fatigue
  - Night sweats

Signs

- Fever
- Weight loss
- Skin rashes
  - Maculopapular rash
  - *Erythema nodosum*
  - *Erythema multiforme*

Pulmonary symptoms may not be prominent

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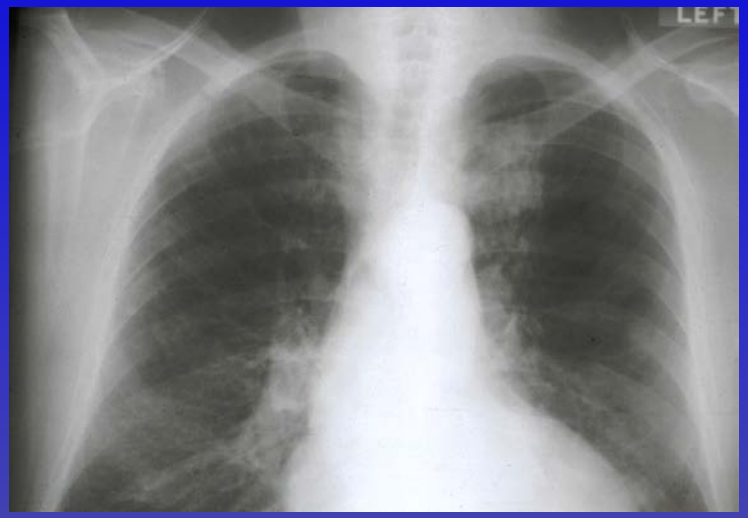
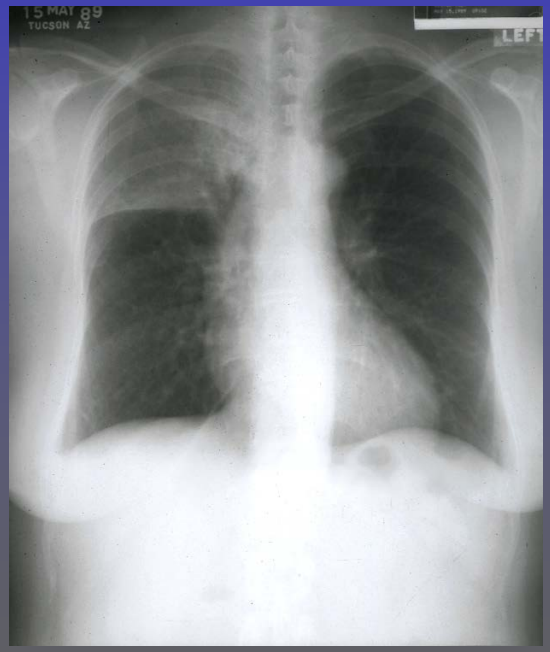


What's causing this Pneumonia?



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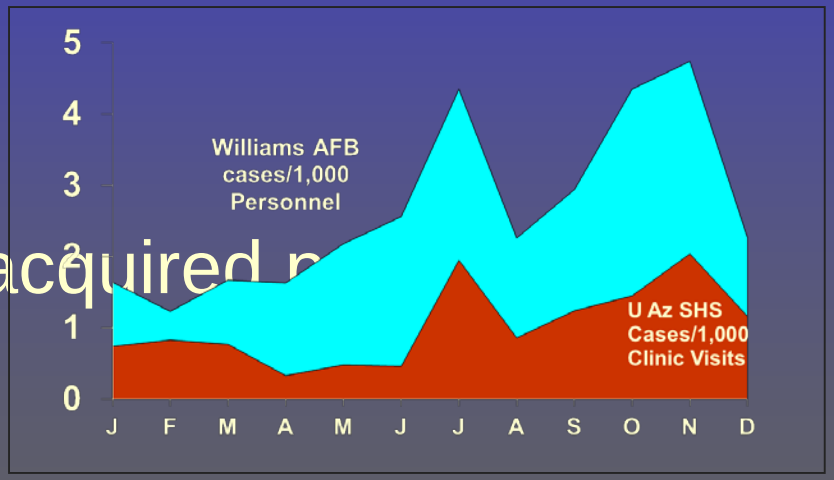
Consider the diagnosis

- In Arizona, Valley Fever is very common. It should be in the differential often.
- More frequent between the monsoons and the winter rains.
- Syndromes:

  <u>Always</u> in community acquired p

  Rheumatism.

  Rashes.



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Coccidioidomycosis is a Laboratory Diagnosis

- Detection of anti-coccidioidal antibodies
- Histologic identification of spherules
- Culture of *Coccidioides* spp.
- Other tests
  - Detection of coccidioidal antigens
  - PCR detection of coccidioidal DNA

Order the Right Tests
Detecting Coccidioidal Antibodies

- **If coccidioidal antibodies are detected, this is a very specific result and usually important.**
- **A negative test does not eliminate the possibility of Valley Fever. Repeated testing improves diagnostic sensitivity.**

KOH Examination

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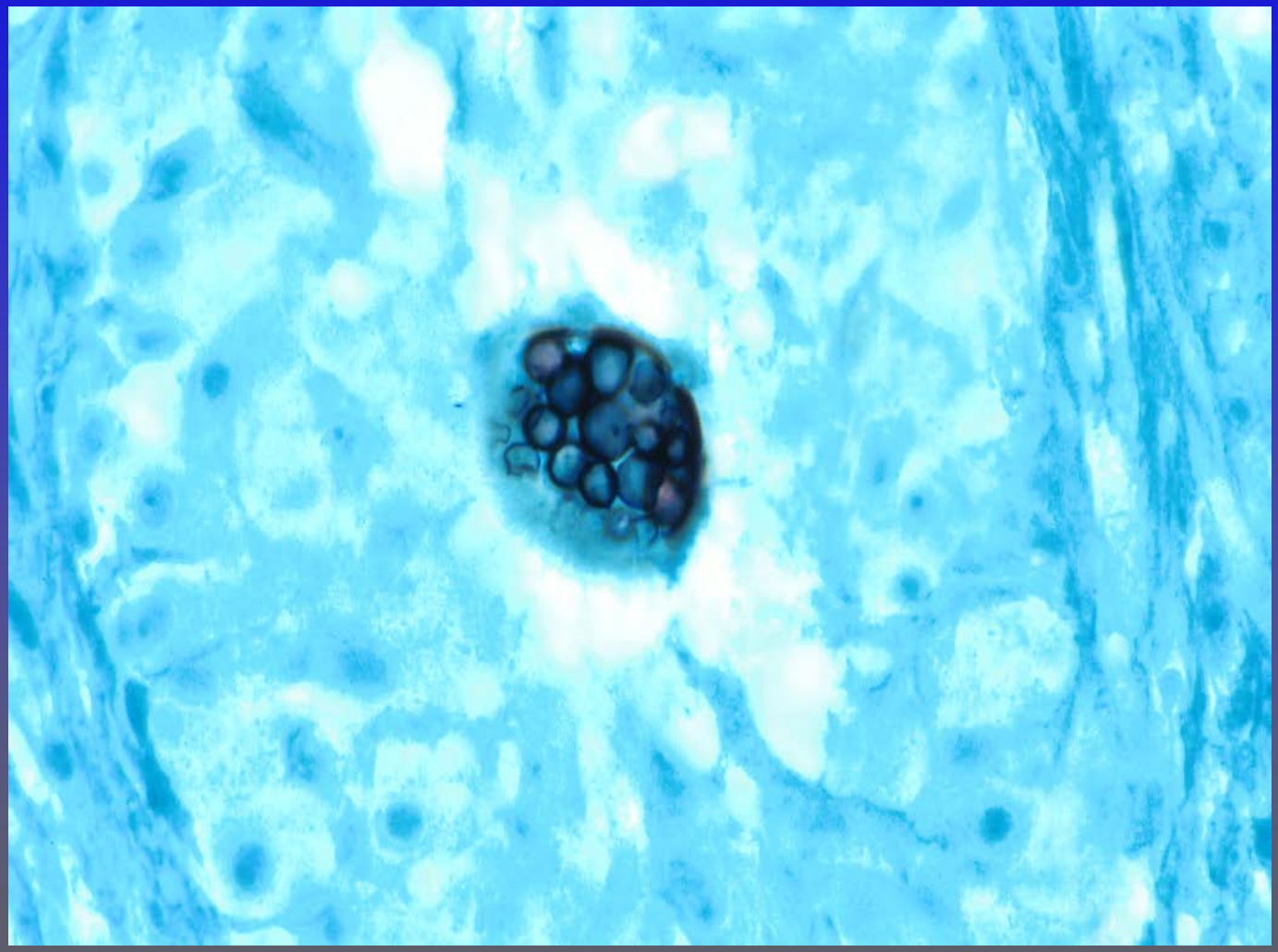
Spherule (Silver stain of BAL fluid)



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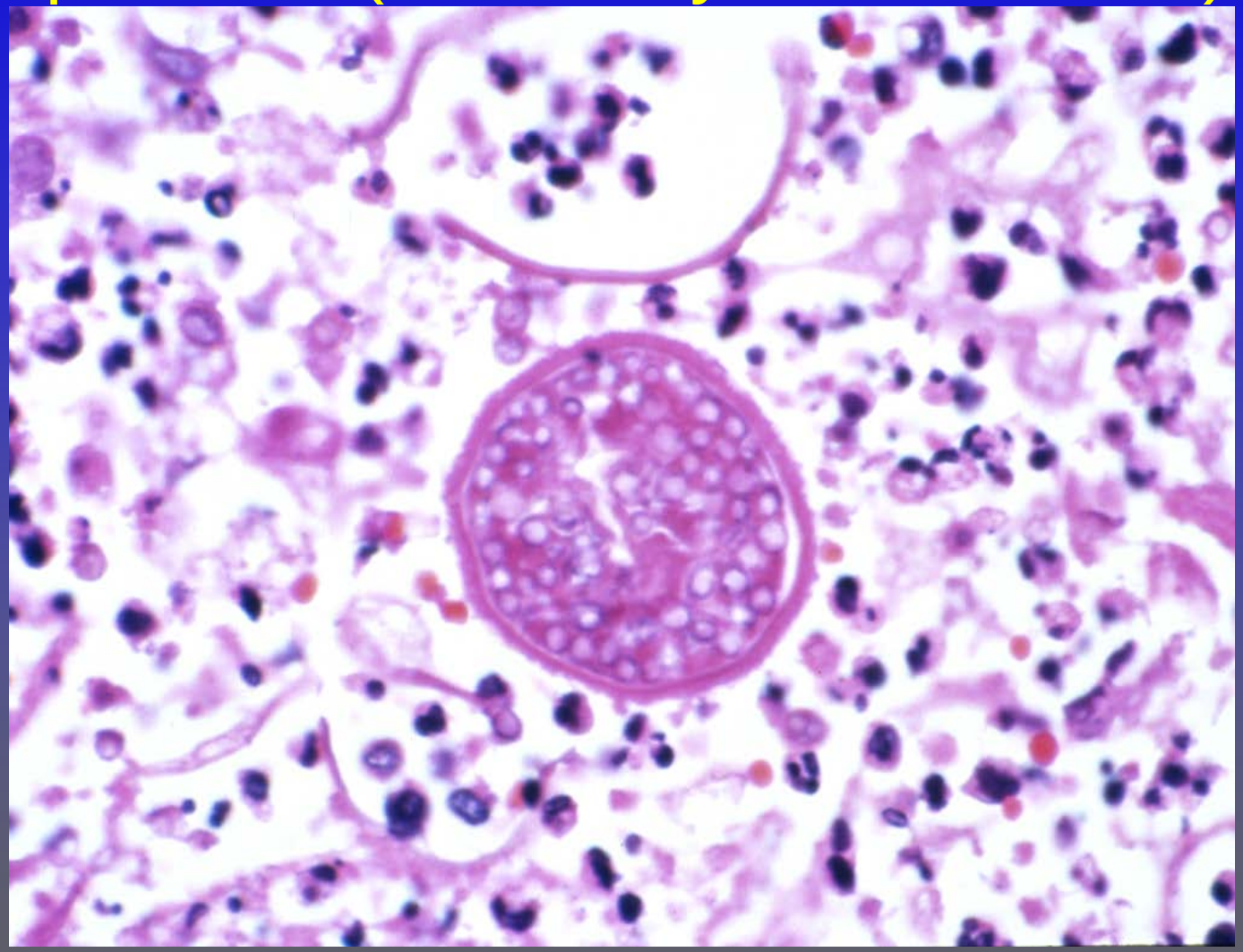
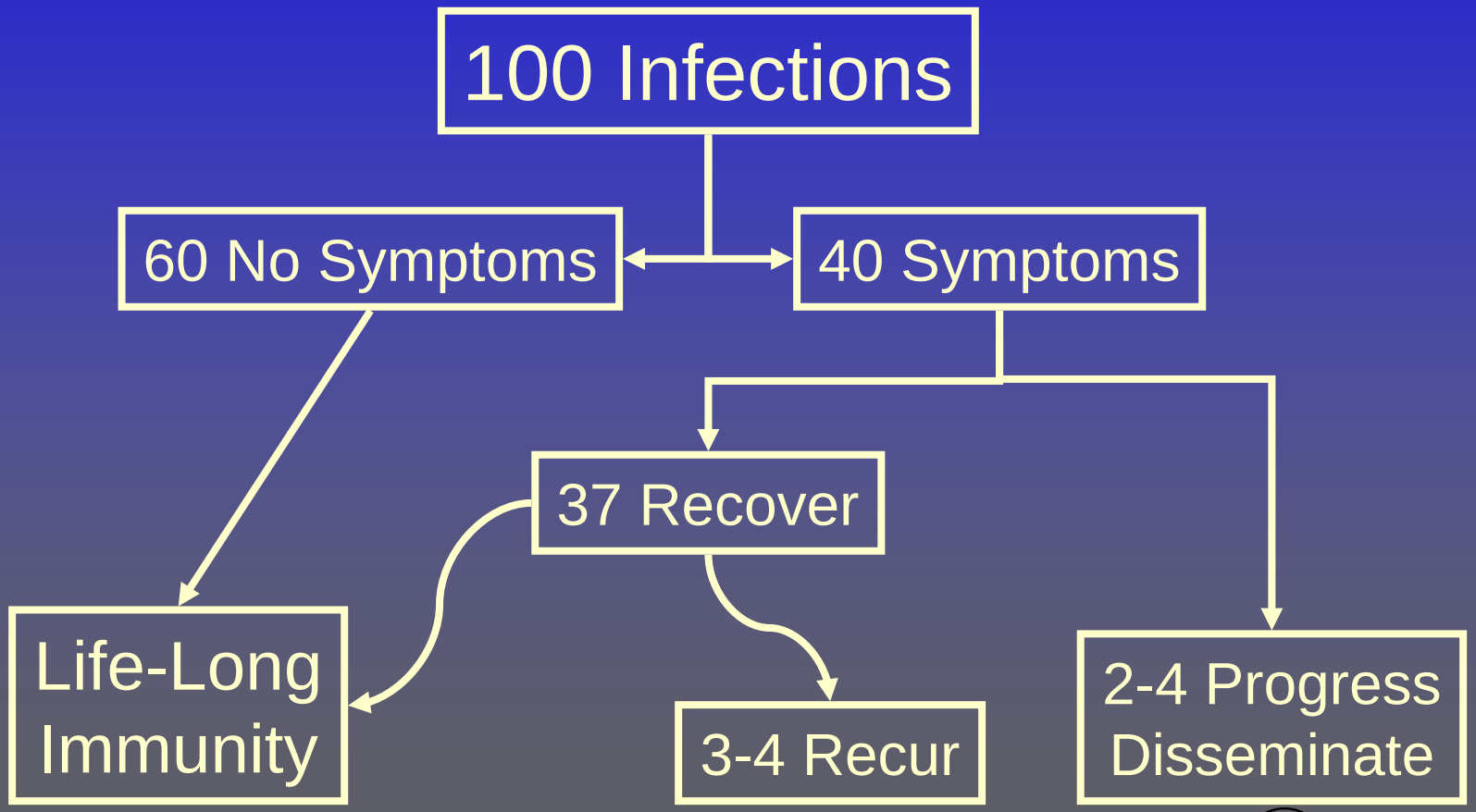
Spherules (Hematoxylin-Eosin stain)



Coccidioidomycosis Spectrum of Disease



Primary Care of Coccidioidomycosis

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I nitiate	**management**

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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

Primary Care of Coccidioidomycosis

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Detecting Focal Lesions in Coccidioidomycosis

- Review of Systems: Pain or discomfort
  - Headache
  - Back pain
  - Joint pain or loss of function
- Physical Examination:
  - Skin lesions
  - Subcutaneous fluctuation
  - Joint effusions

Widely disseminated Coccidioidomycosis

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•**Disseminated Coccidioidomycosis**

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Disseminated Coccidioidomycosis

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Check for Complications Summary

- Most complications are focal
- **A careful review of systems and physical examination will usually detect or exclude the possibility of complications**.
- If new focal findings are present, further imaging and laboratory studies can determine if they are related to infection.

Primary Care of Coccidioidomycosis

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Management
Low Risk, Simple Early Infection

- Follow-up office visits
- Serial body weights
- Check for new symptoms or signs
- Repeat coccidioidal antibody testing
- Repeat Chest PA and Lateral X-rays
- Most patients do not need therapy

Management
Low Risk, Simple Early Infection

- Follow-up office visits for one year

2-4 weeks	ROS; Exam; Chest X-ray
2-3 months	ROS; Exam; serology
3-6 months	ROS; Exam;
12 months	ROS; Exam; Chest X-ray

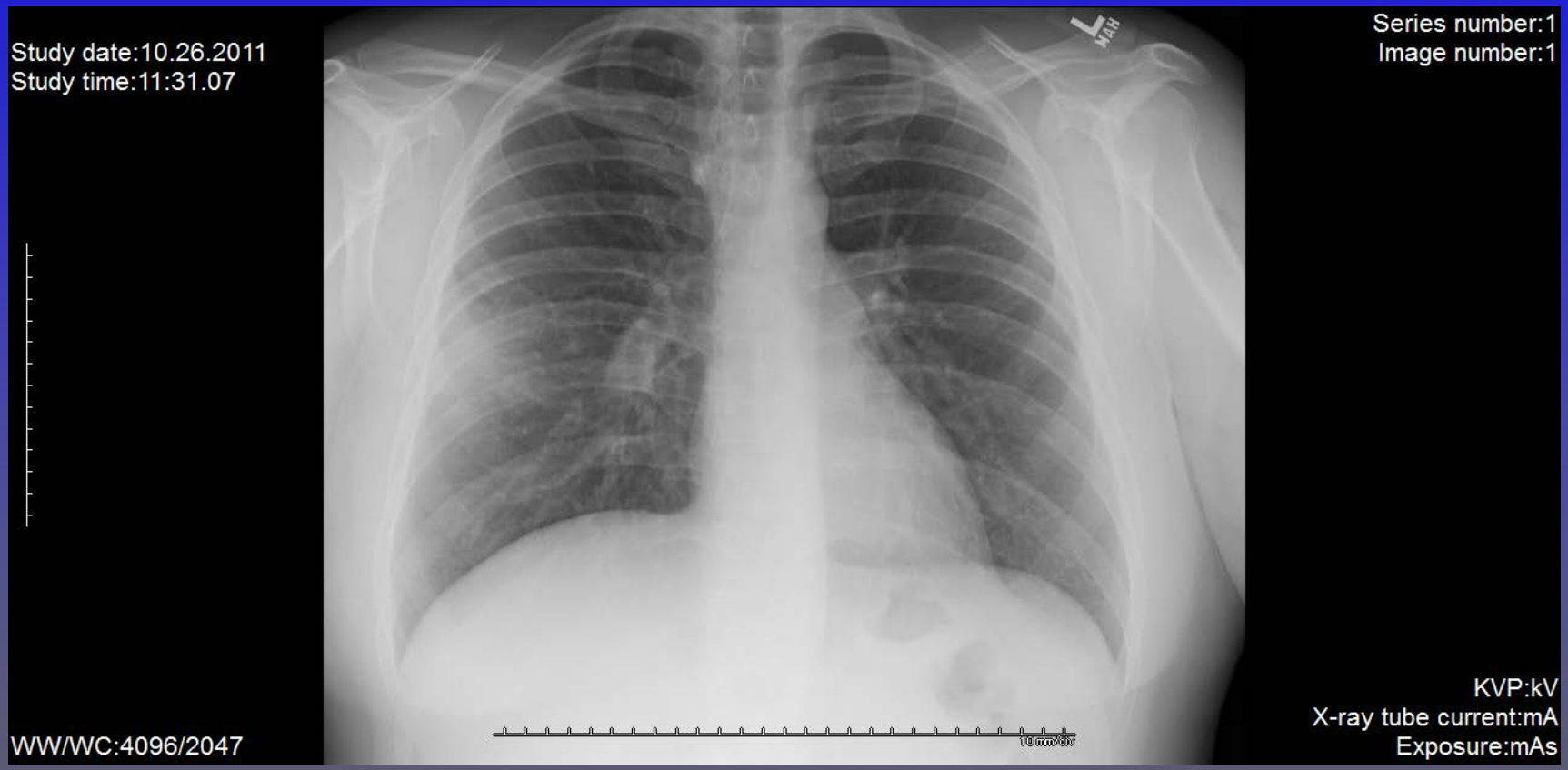
Follow-up Chest X-rays
What to order?

Purposes:

- Identify if infiltrate cavitates.
- Determine if there is a residual nodule (could be confused with cancer in later years)

In most patients, these objectives can be accomplished with simple PA and lateral X-rays; CT scans are usually not needed.

Primary Coccidioidal Pneumonia



October 26

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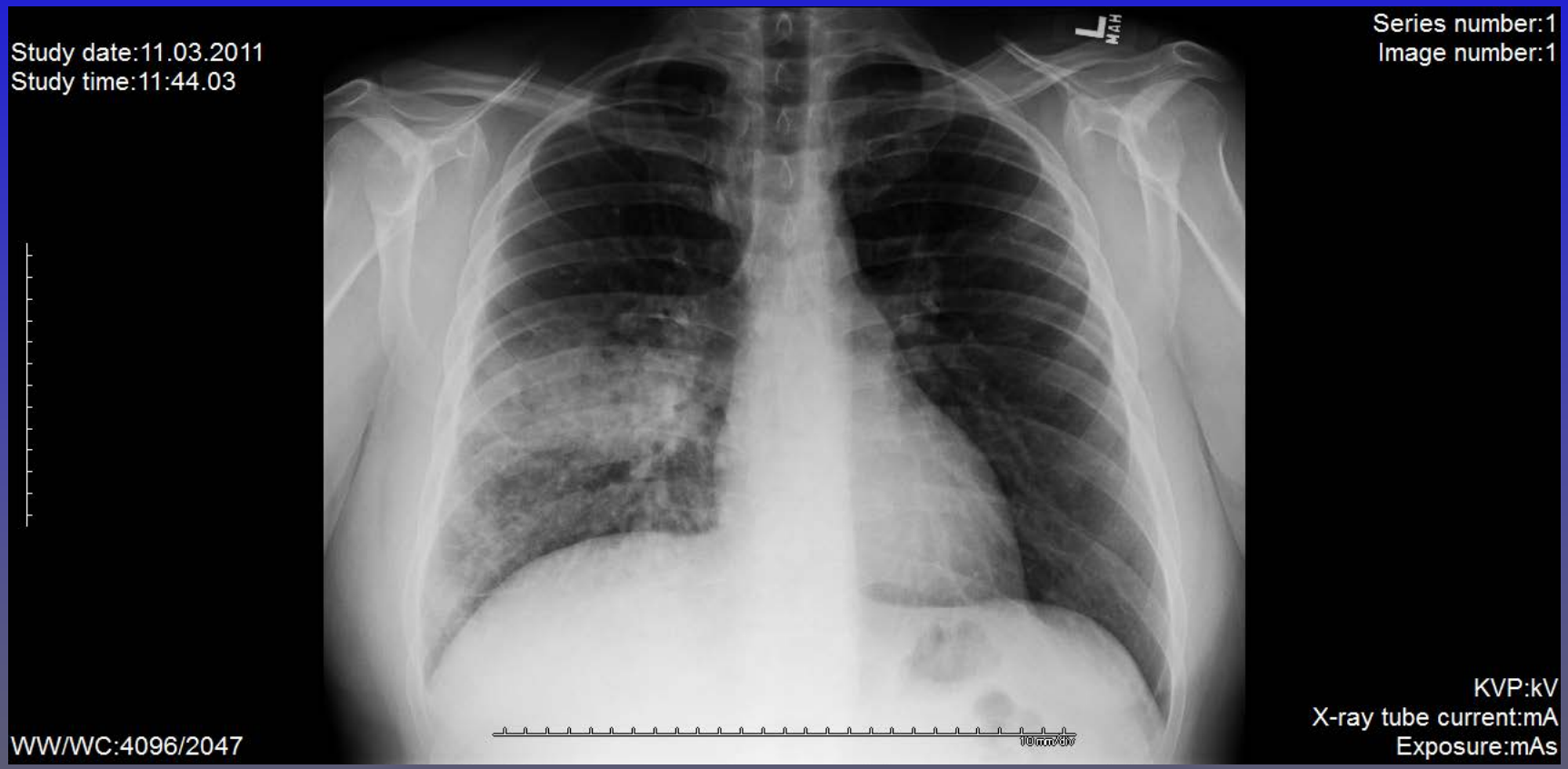
Primary Coccidioidal Pneumonia



November 3

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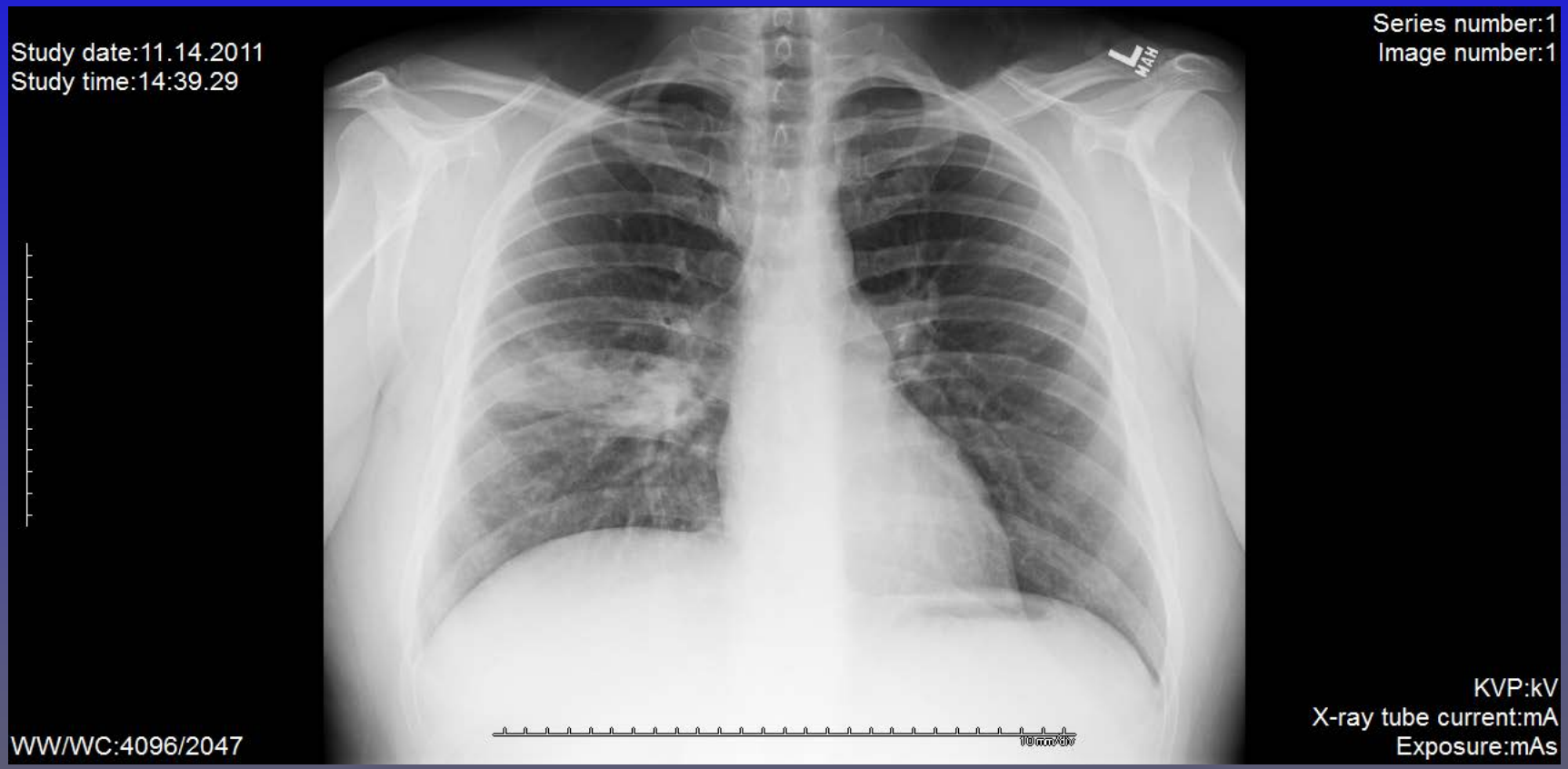
Primary Coccidioidal Pneumonia



November 14

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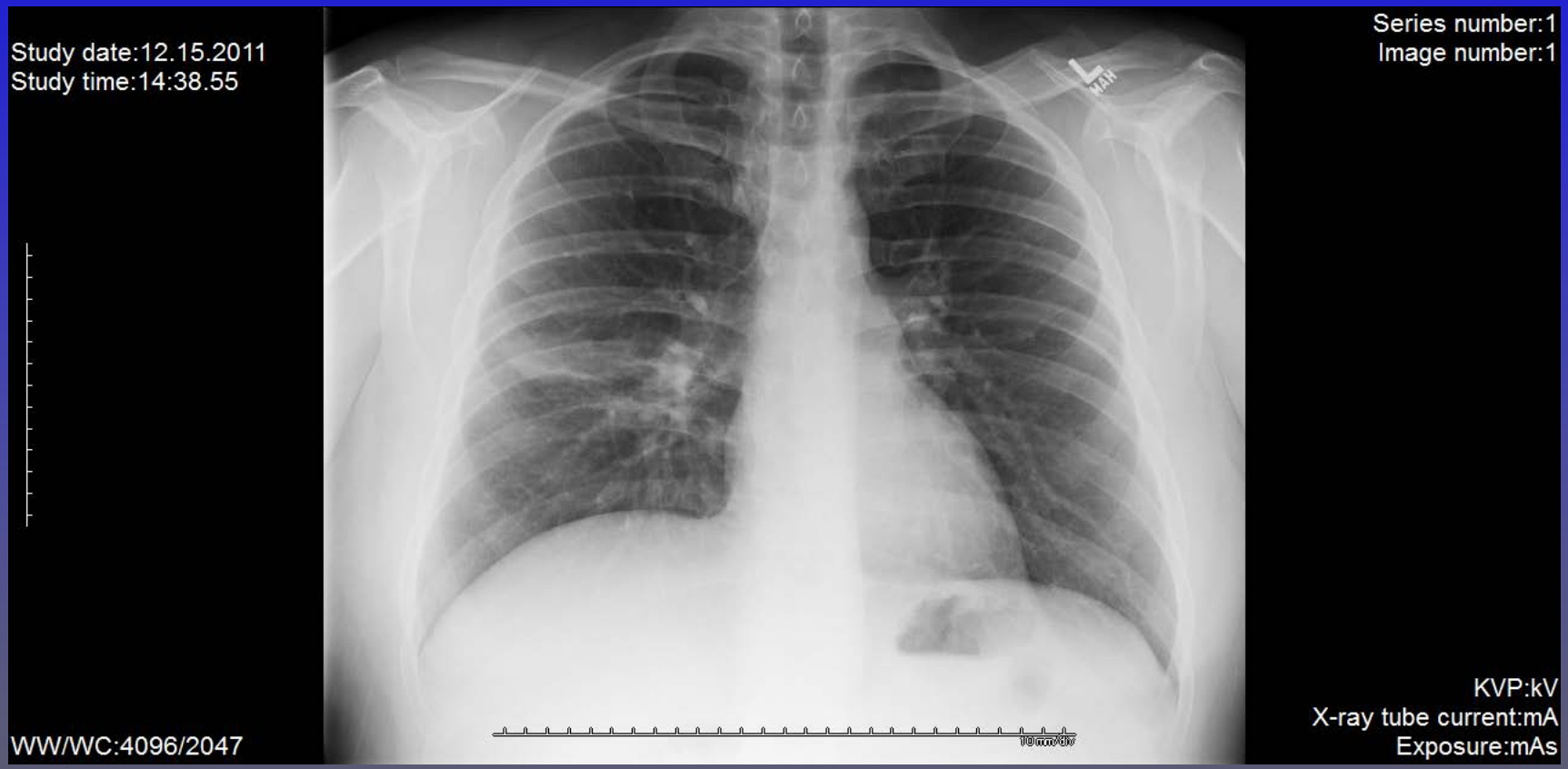
Primary Coccidioidal Pneumonia



December 15

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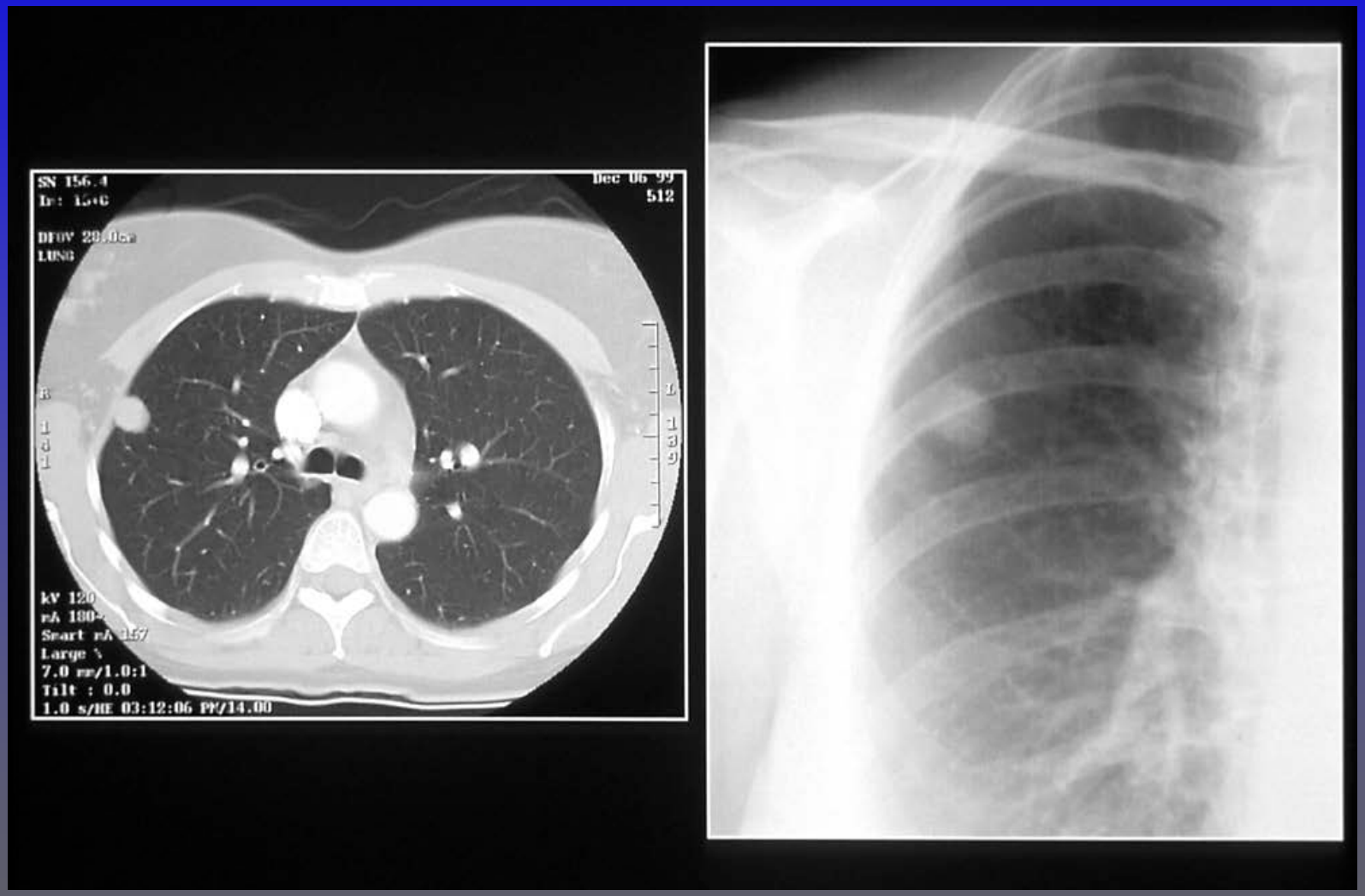
Peripheral Coccidioidal nodule



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Follow-up Coccidioidal Serology How do they help?

- As patients improve, titers generally decrease
- The decrease typically occurs over several months, occasionally even slower.
- If titers increase, re-evaluate for possible complications.
- Titers are a marker, not a disease

Fatigue: Often the Last Symptom Typical Problem

- Primary coccidioidal pneumonia diagnosed serologically in an otherwise healthy active person.
- Over several weeks, weight returns to normal, fever resolves and pulmonary symptoms gone. ESR becomes normal. CF low or neg.
- However, patient complains of profound inability to carry out normal activities.
- How should this be managed?

Potential Causes of Fatigue

- In some, striking deficit in O_2 utilization (VO_2 peak <10% of predicted)*
- Physical deconditioning because of decreased activity.
- Lack of experience by the patient with subacute or chronic disability.
- Patient with excessive expectations of own performance.

*Ganley, Open Forum Infectious Diseases 2017

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Management Strategies

- **Exclude objective evidence of tissue destruction or focal lesions.**
- **Patient Education**
  - Prolonged fatigue common and resolves
  - No evidence of permanent damage
  - Deconditioning and unrealistic expectations
- **Patient Actions**
  - Keep a journal
  - Refer patient to Physical Therapist for reconditioning
- **Antifungal drugs? Usually not helpful**

Clinical Infectious Diseases

IDSA GUIDELINE

IDSA Infectious Diseases Society of America

hivma hiv medicine association

OXFORD

2016 Infectious Diseases Society of America (IDSA) Clinical Practice Guideline for the Treatment of Coccidioidomycosis

John N. Galgiani,[1] Neil M. Ampel,[2] Janis E. Blair,[3] Antonino Catanzaro,[4] Francesca Geertsma,[5] Susan E. Hoover,[6] Royce H. Johnson,[7] Shimon Kusne,[3] Jeffrey Lisse,[8] Joel D. MacDonald,[9] Shari L. Meyerson,[10] Patricia B. Raksin,[11] John Siever,[12] David A. Stevens,[13] Rebecca Sunenshine,[14,15] and Nicholas Theodore[16]

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IDSociety.org Downloads thru Sept 2017

Full-text, Exec. summary, Online flipbook, Pocket card

>21,000 total

Clin Infect Dis, Sept 15th, 2016

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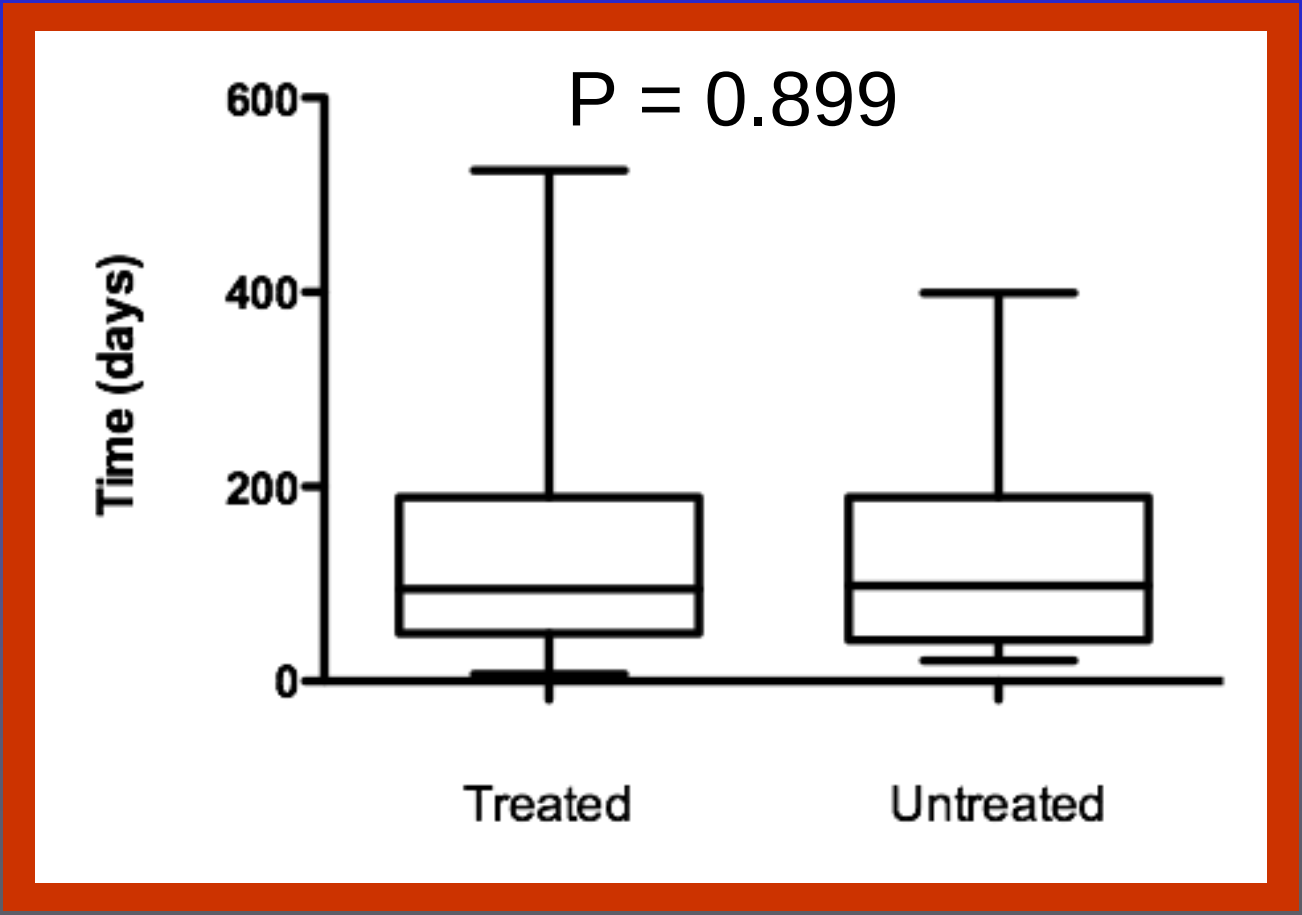
2016 IDSA Guidelines Treatment of Coccidioidomycosis

"It should be emphasized that no randomized trials exist to assess whether antifungal treatment either shortens the illness of early uncomplicated coccidioidal infections or prevents later complications."

Median days to ≥50% decline in total clinical score



Ampel et al. CID 2009

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Outcome of Subjects
(> 1 month follow-up)

- 50 not treated
  - Median follow-up: 3.1 years
  - All without complications
- 51 treated
  - Median follow-up: 2.9 years
  - 38 off-therapy and without complications
  - 5 remained on treatment
  - 8 had relapses
    - 5 with pulmonary disease
    - 3 with extrapulmonary dissemination
    - Relapses occurred up to 2 years after stopping treatment

Ampel et al. CID 2009

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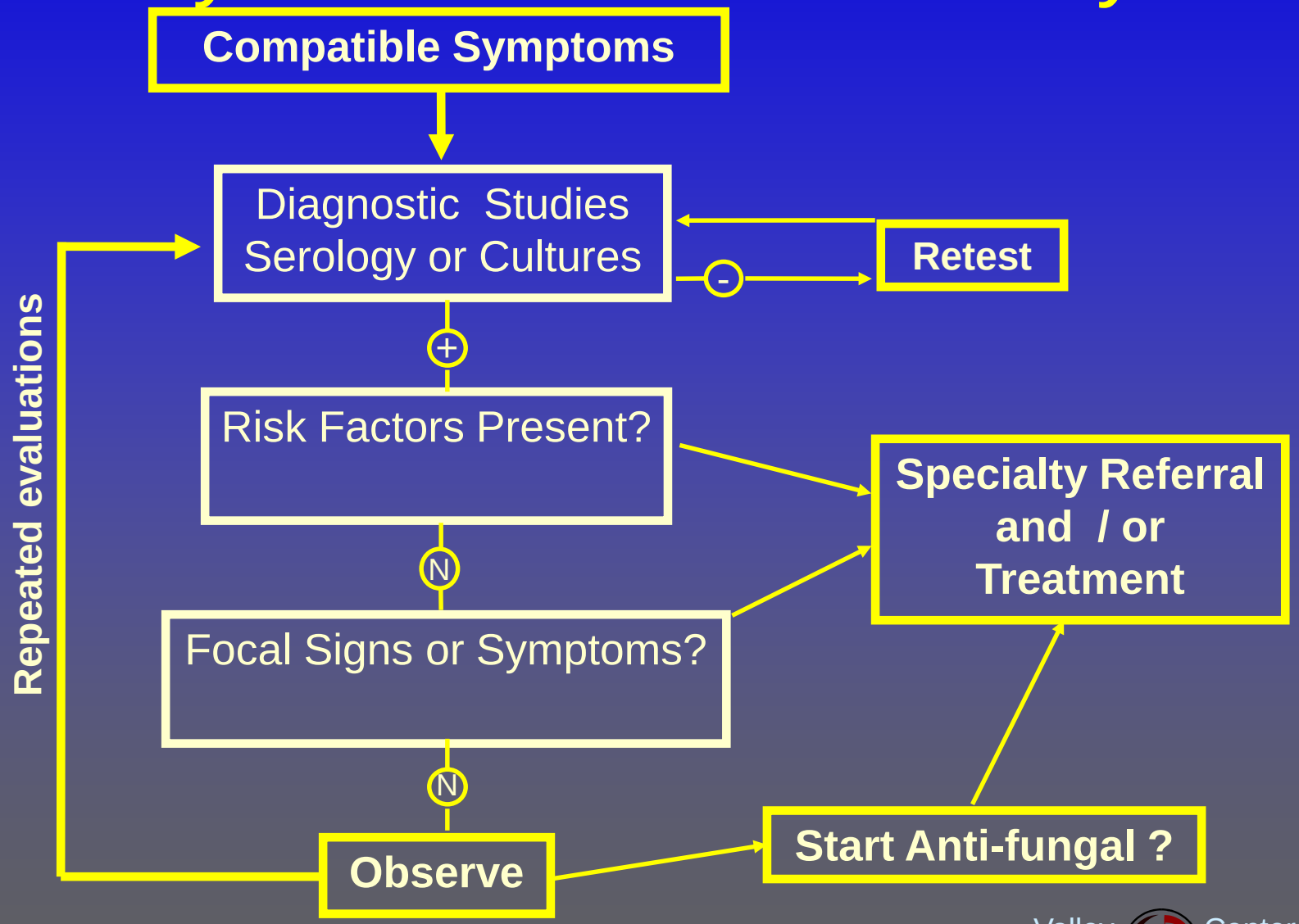
Primary Care of Coccidioidomycosis



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Questions?

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