A man with multiple skin nodules

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Part I

Bug from afar

January 2009

- M 42
- Married
- No children no pet
- Ex-smoker social drinker
- Truck driver
- Left renal stone with ESWL
  in 2000, 01, 05

History

- On and off fever from Dec 2008
- Non-productive cough
- Generalized malaise
- Weight loss of 8 kg
- Recent right eyebrow and LUL growth

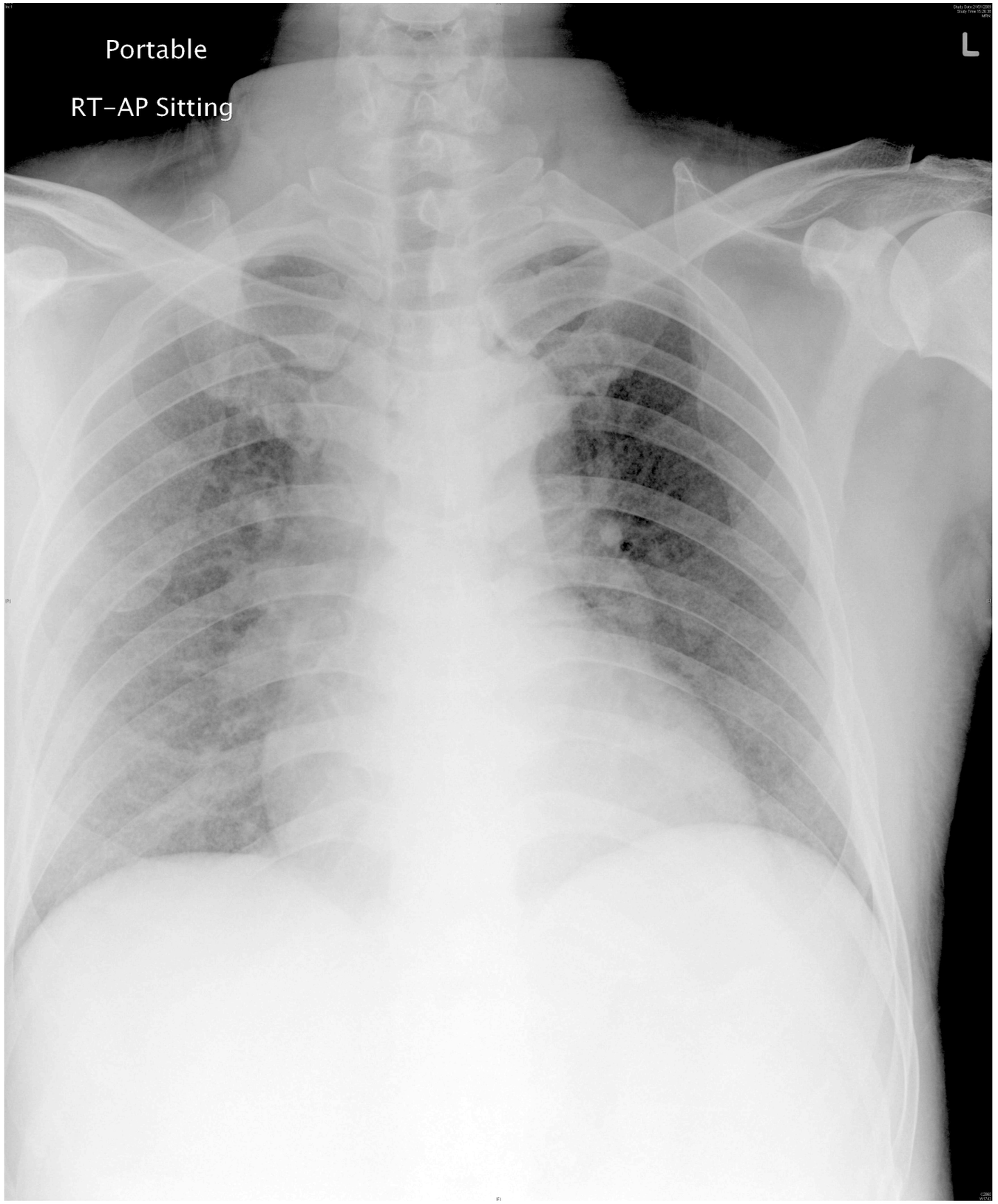
History

- Travelled Shenzhen in Dec 2009 for 1 day
- Travelled South Korea and Phuket few years ago
- Never travelled outside Asia
- Denied venereal exposure

Physical exam

- No palpable LN
- Chest clear
- HS normal no murmur
- Abdomen soft
- Verrucated growth over right eyebrow and LUL

- Sought medical attention in private doctor:
  - CXR (25 Dec 2008)
    - Miliary soft tissue nodules throughout both lungs
  - PET/CT (16 Jan 2009)
    - Multiple hypermetabolic LNs at left neck, bilateral SCF, mediastinum, bilateral hila and axilla
    - Splenomegaly
    - Findings highly suggestive of haematological malignancy such as lymphoma
    - Focal bony involvement
    - Diffuse increased activity is also seen in both lungs, may represent pneumonitis or lymphomatous involvement



CXR

Investigations

- Hb 7.3/ WBC 8.2/ Plt 335
- Na 134/ K 3.4/ Ur 4.9/ Cr 122
- Alb 19/ ALP 144/ ALT 17
- HBsAg positive, HBeAg negative
- Anti-HIV negative

- Bone marrow aspirate
  - Hypocellular marrow with plasmacytosis
  - Eosinophilla
- Bone marrow trephine
  - Presence of trilineage haemopoiesis with mild plasmacytosis

What is that?

- Left SCF LN biopsy and skin biopsy
  - Evidence of fungal infection
  - Similar to blastomycosis
  - No evidence of lymphoma or TB
- 1,3 beta-D-glucan >500pg/ml

Some histopathology

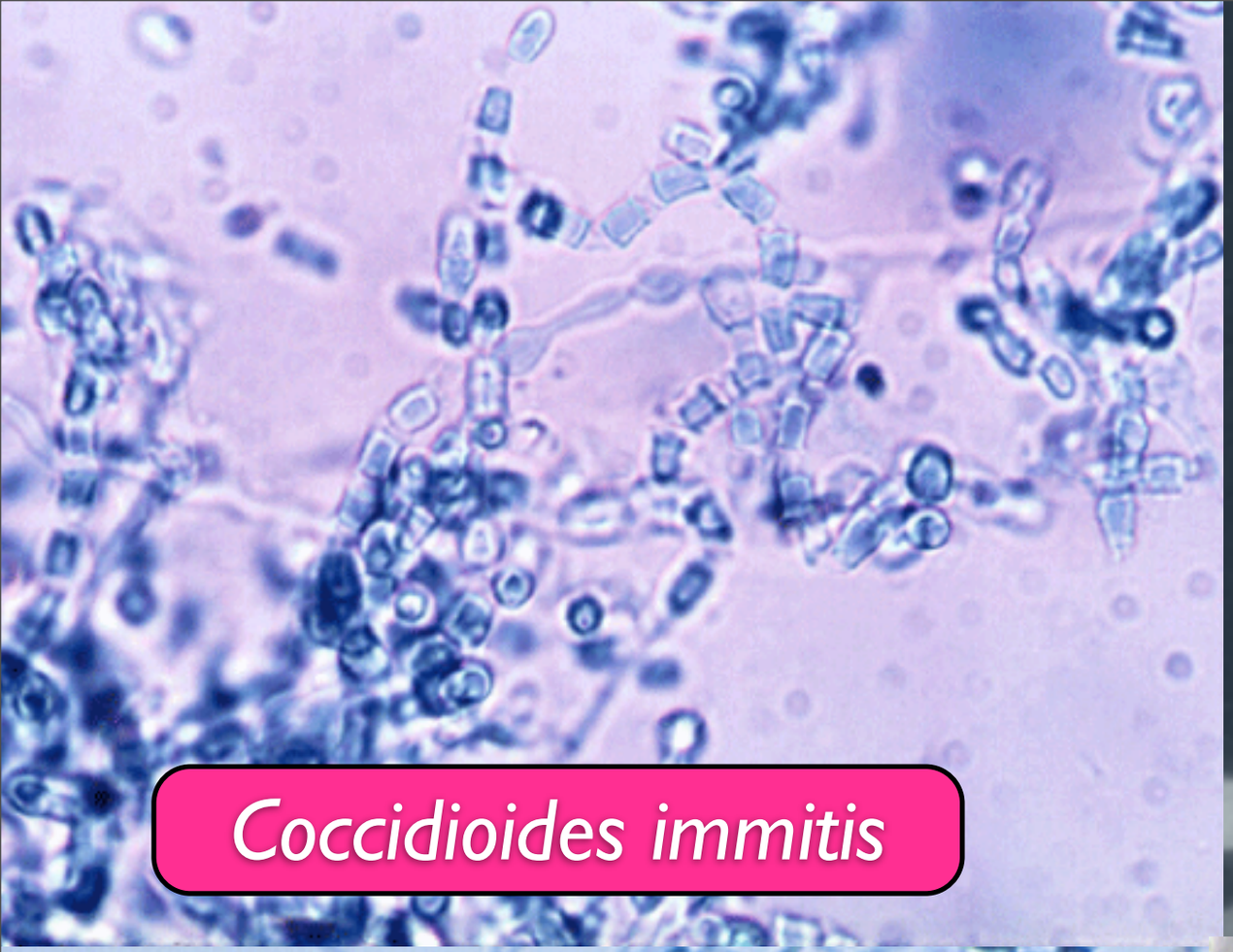
Coccidioides immitis

20 µm

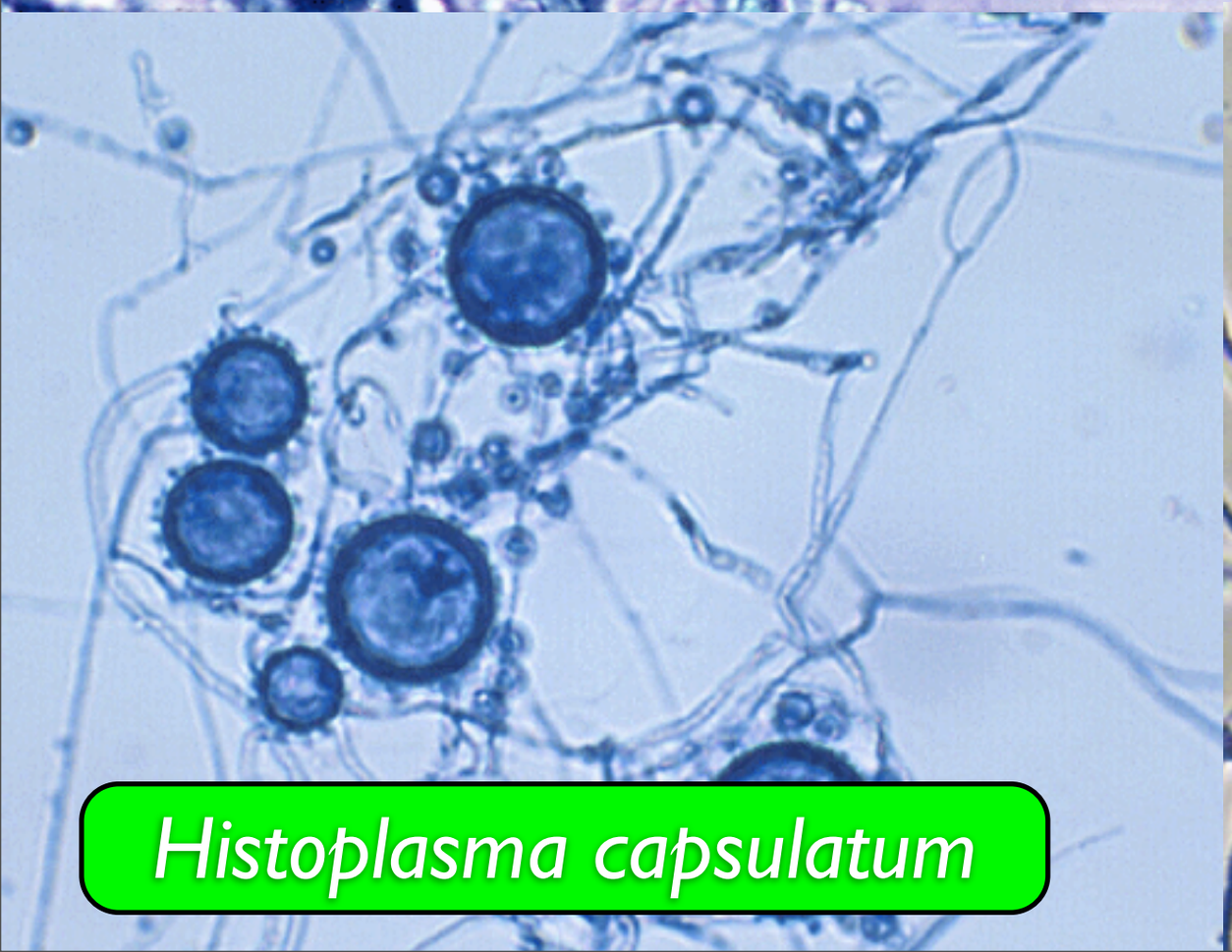
Blastomyces dermatiditis

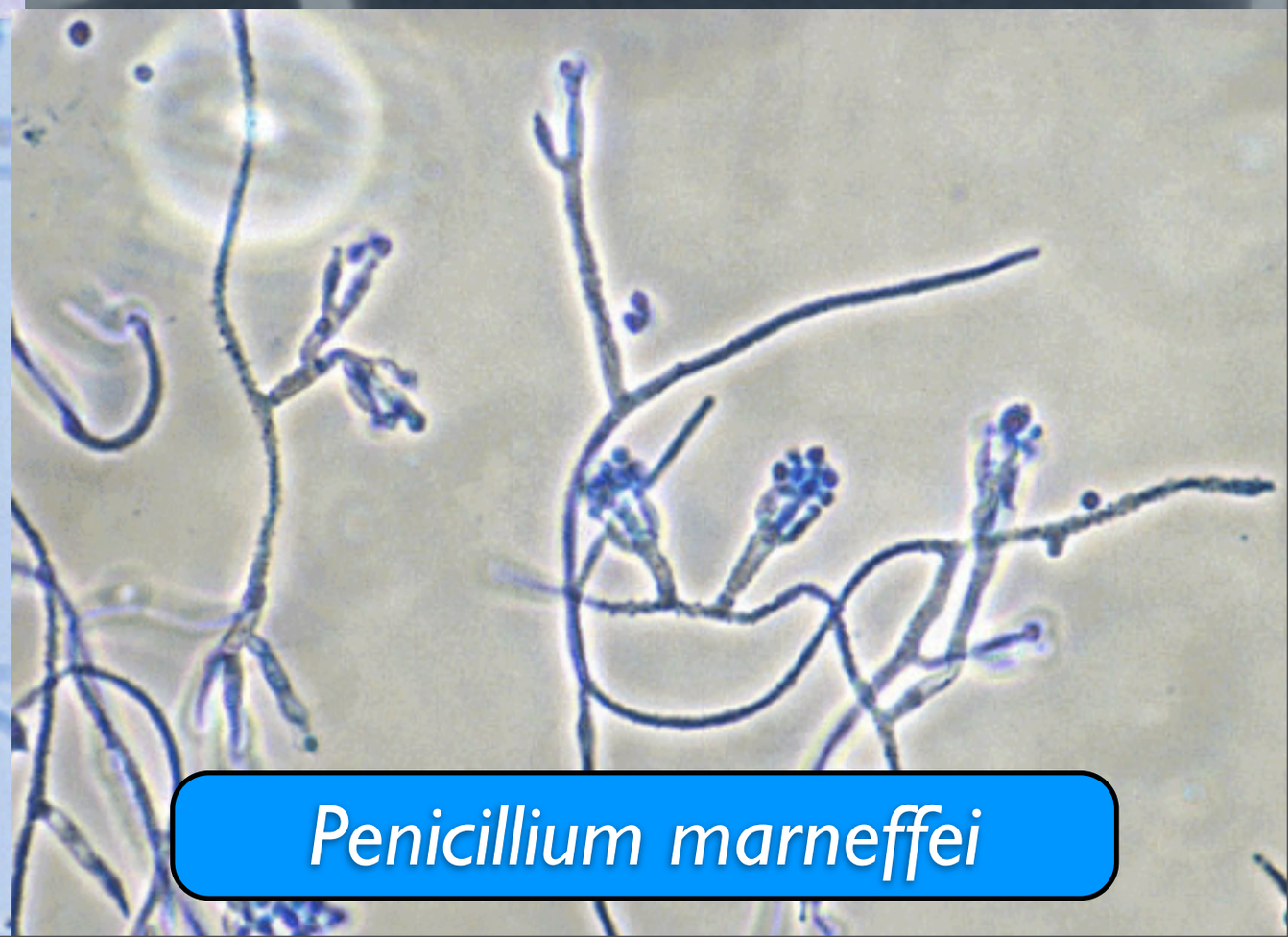
Histoplasma capsulatum

Penicillium marneffei


Coccidioides immitis


Blastomyces dermatiditis


Histoplasma capsulatum


Penicillium marneffei

What is your diagnosis?

A. *Coccidioides immitis*

B. *Blastomycosis dermatitidis*

C. *Histoplasma capsulatum*

D. *Penicillium marneffei*

E. None of the above

- Features of skin biopsy compatible with coccidioidomycosis
- Serum *Coccidioides immitis* antibody positive
- Perpherial and bone marrow fungal culture negative

Part II

Coccidoidomycosis

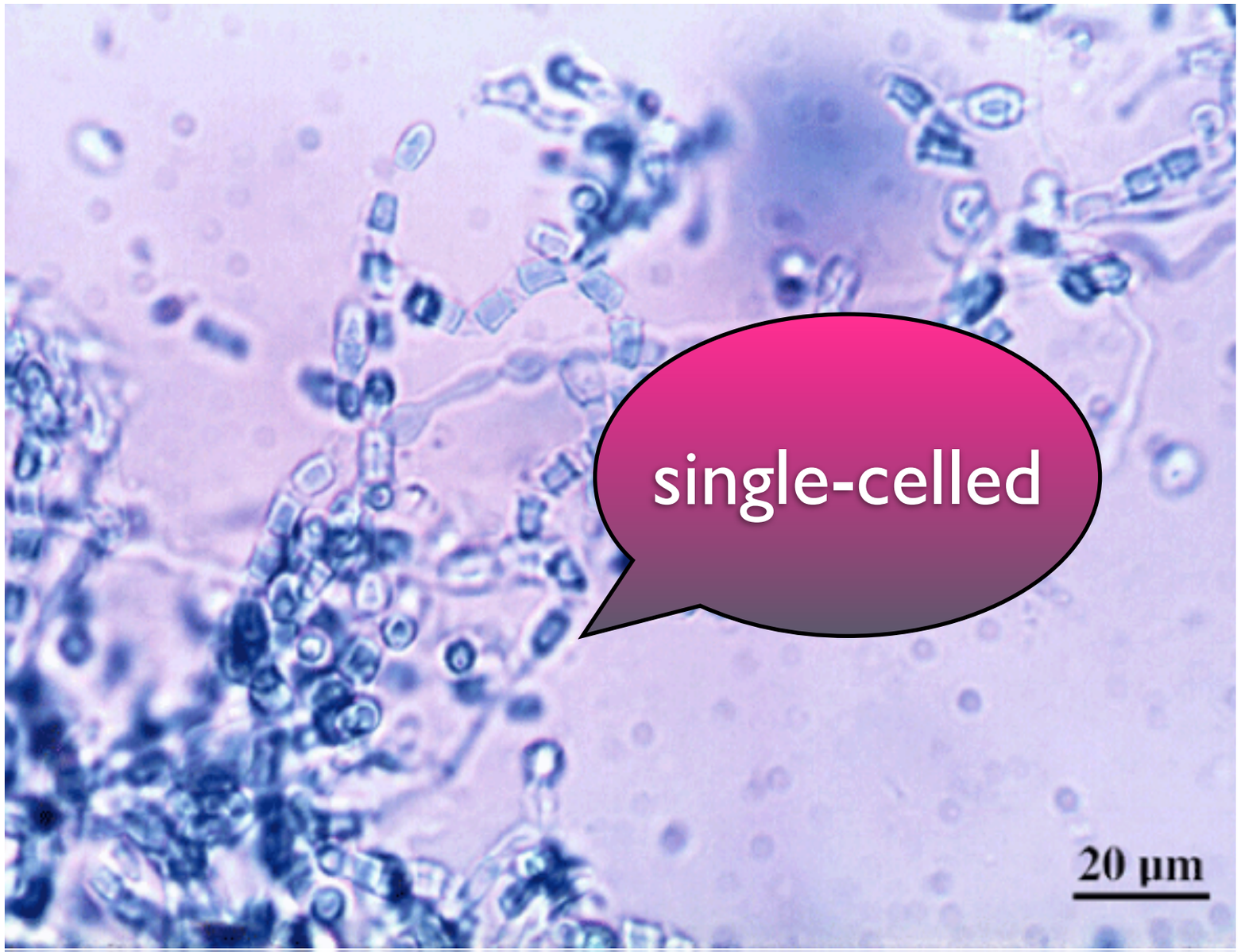
Coccidioides spp.

- Endemic fungus
    - USA - Arizona, California, New Mexico, Texas
    - Mexico
    - Central and South America

Coccidioides spp.

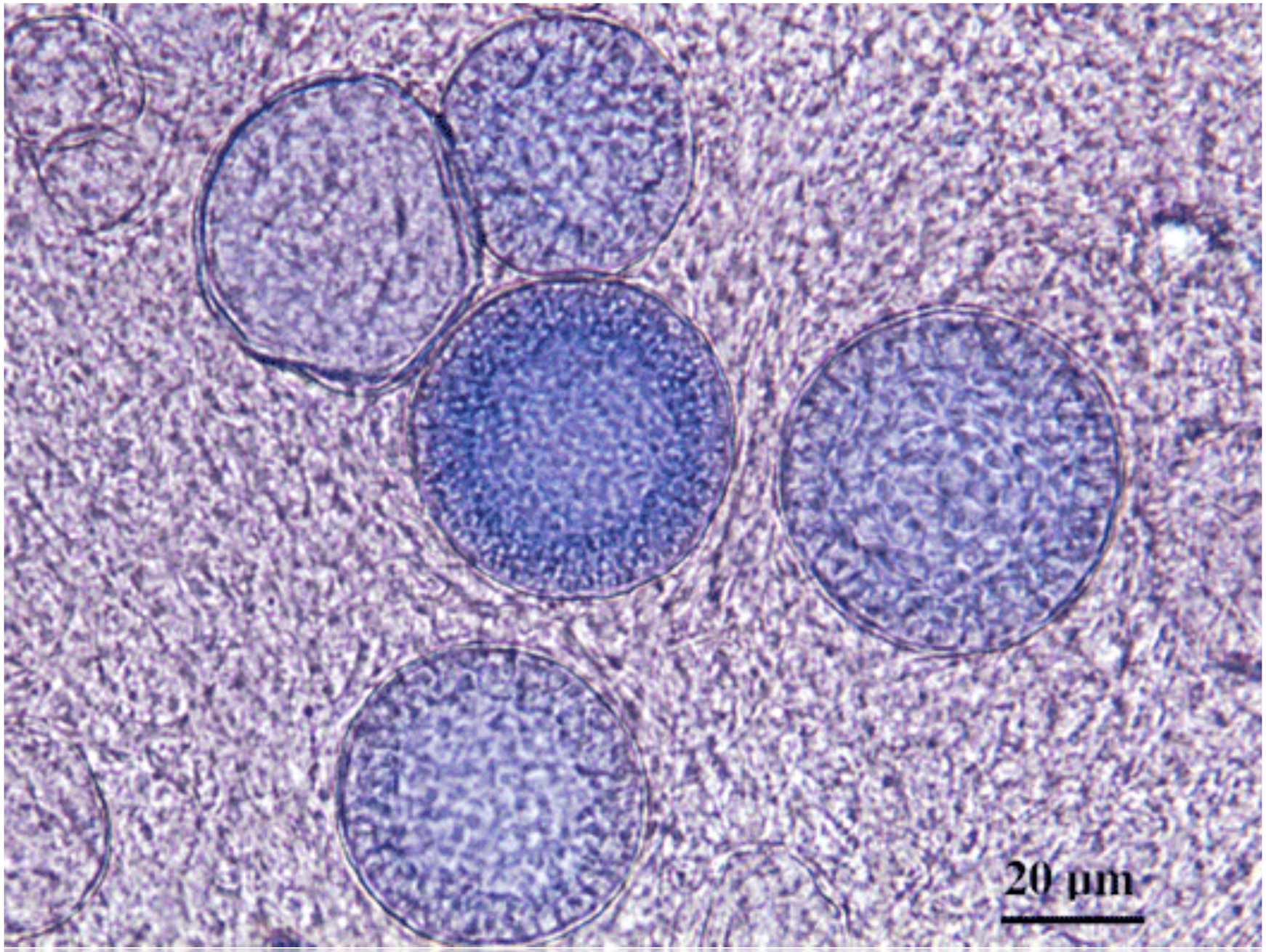
- Dimorphic fungus
  - Grow as mould in soil
  - Grow as *spherule* in host
- Two species have the same spectrum of diseases
  - *Coccidioidoes immitis* (predominately in California)
  - *Coccidioidoes posadasii* (other regions)

- *Arthroconidia*
  - Reproductive structure
  - Released into atmosphere when hyphae rupture
  - Humans and animals are infected as inhaled arhroconidia
  - Develops into *spherules* inside the lungs
  - Spherules release endospores on maturation



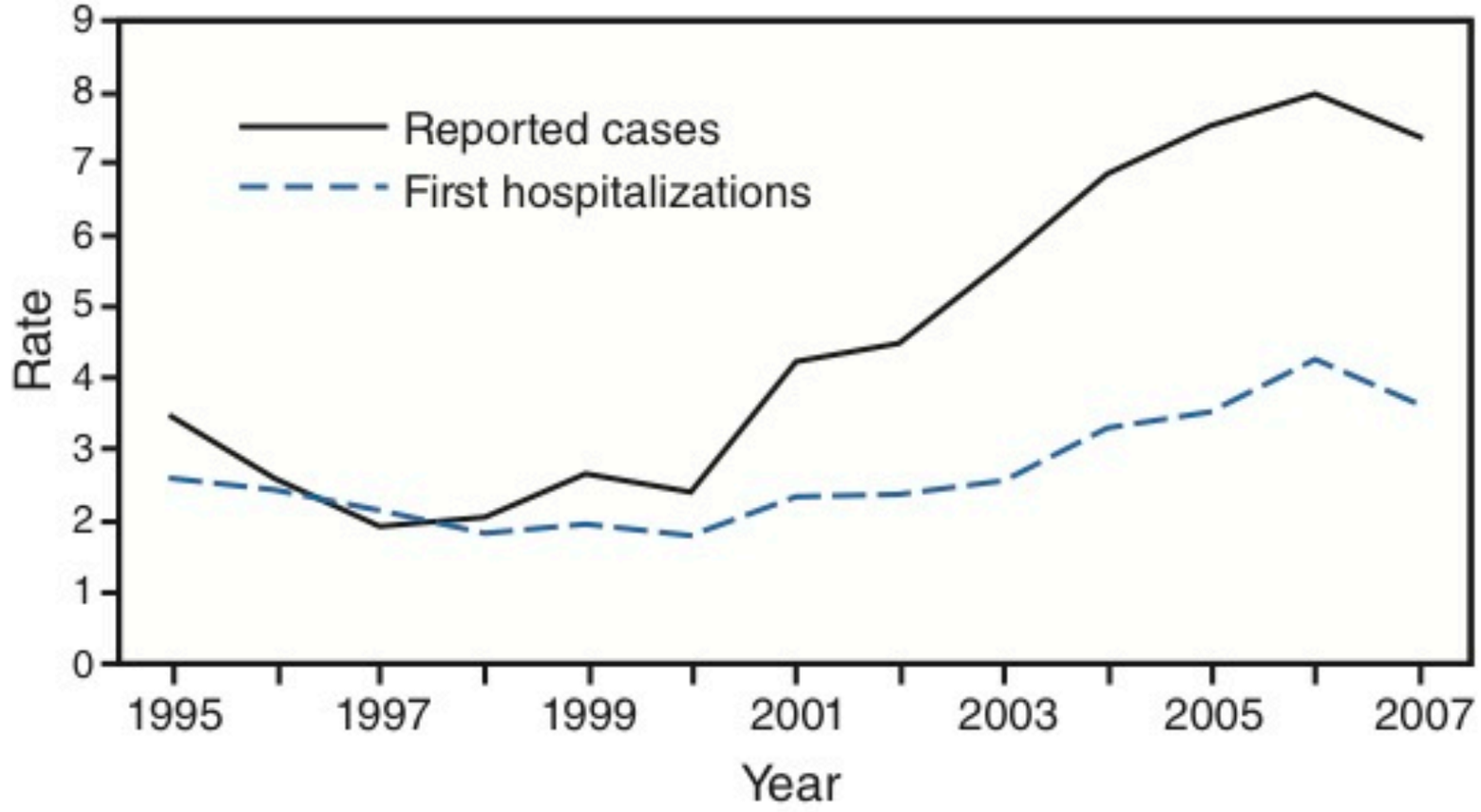
Coccidoides immitis

- Risk of endemic exposure
  - ~3% per year
  - Seasonal, typically in dry periods following a rainy season
- Dramatic increase of incidence after dust stroms and earthquakes



Direct microscopy of skin scrappings: endosporulating spherules (sporangia) of *Coccidioides immitis*

FIGURE 1. Rates* of reported cases of coccidioidomycosis and first hospitalizations among persons with coccidioidomycosis diagnosed — California, 1995–2007†

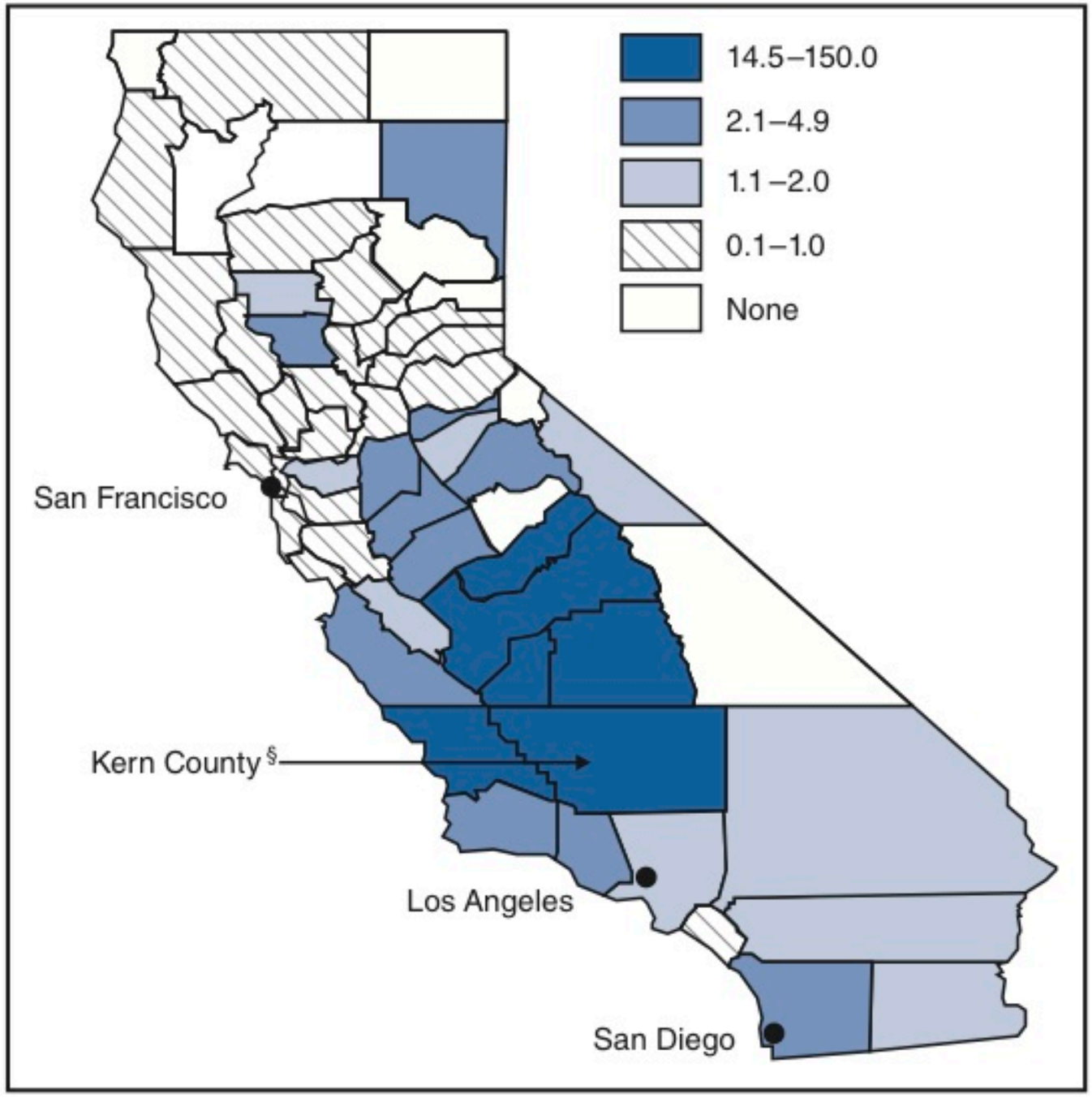


* Per 100,000 population.

† Data on reported cases of coccidioidomycosis are from California Department of Public Health Confidential Morbidity Reports. Data on first hospitalizations of persons with coccidioidomycosis diagnosed are from the California Patient Discharge Data Set. Population data are from California Department of Finance population projections.

MMWR Increase in Coccidioidomycosis - California, 2000-2007
CDC Feb 13 2009

FIGURE 2. Average annual rate* of reported cases of coccidioidomycosis, by county — California, 2000–2007†



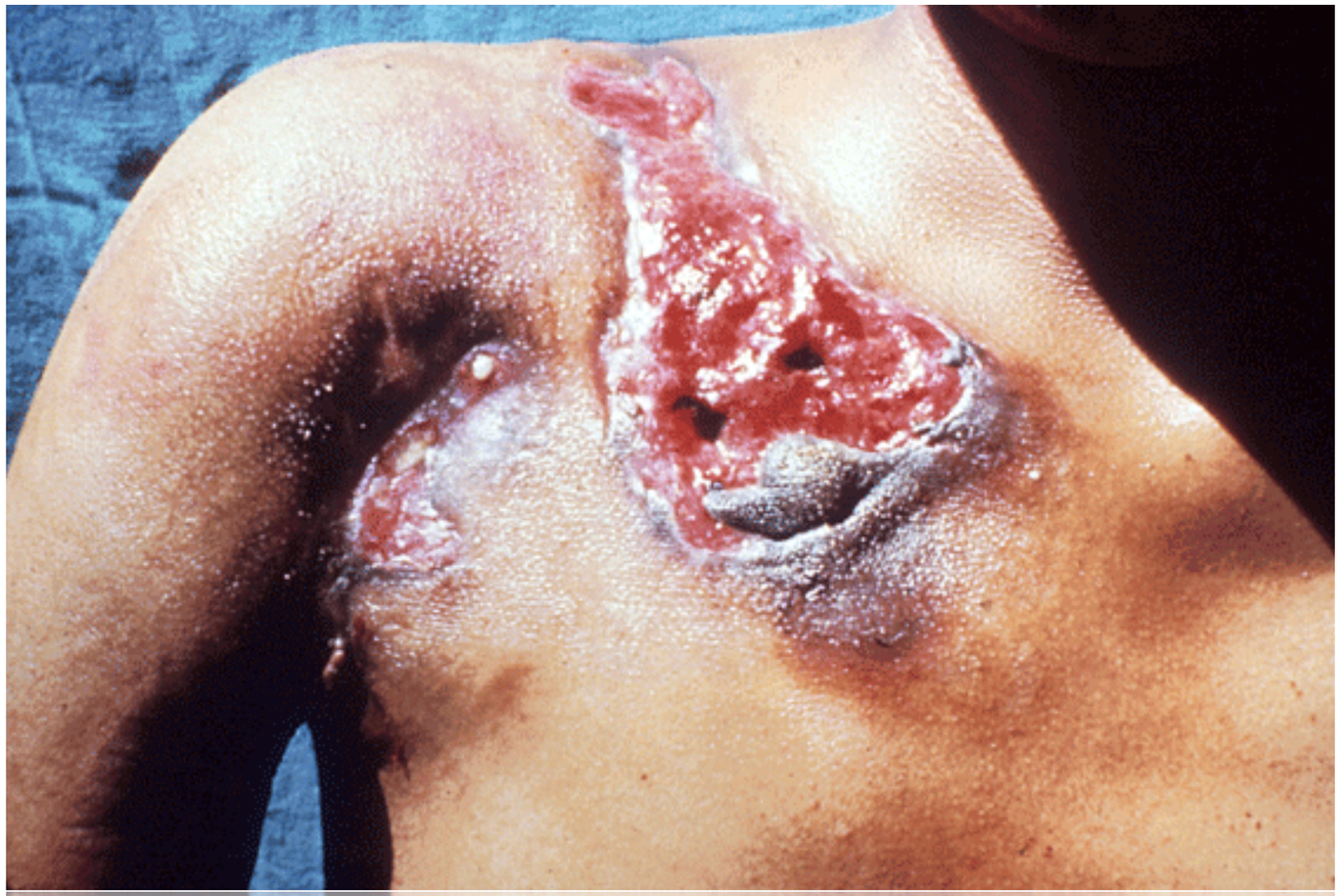
* Per 100,000 population.

† Data on reported cases are from California Department of Public Health Confidential Morbidity Reports. County population data are from California Department of Finance population projections.

§ Kern County, located in the San Joaquin Valley region, where coccidioidomycosis is endemic, had the highest rate among counties (150.0 cases per 100,000 population).

Clinical manifestations

- Infection virtually always acquired by inhalation of spores
- Primary pulmonary infection
  - Often subclinical
    - <50% infections come to medical attention
    - Increases with more higher spore exposure
  - Resembles CAP
    - IP: 7-21 days after exposure
    - Fever, cough and chest pain

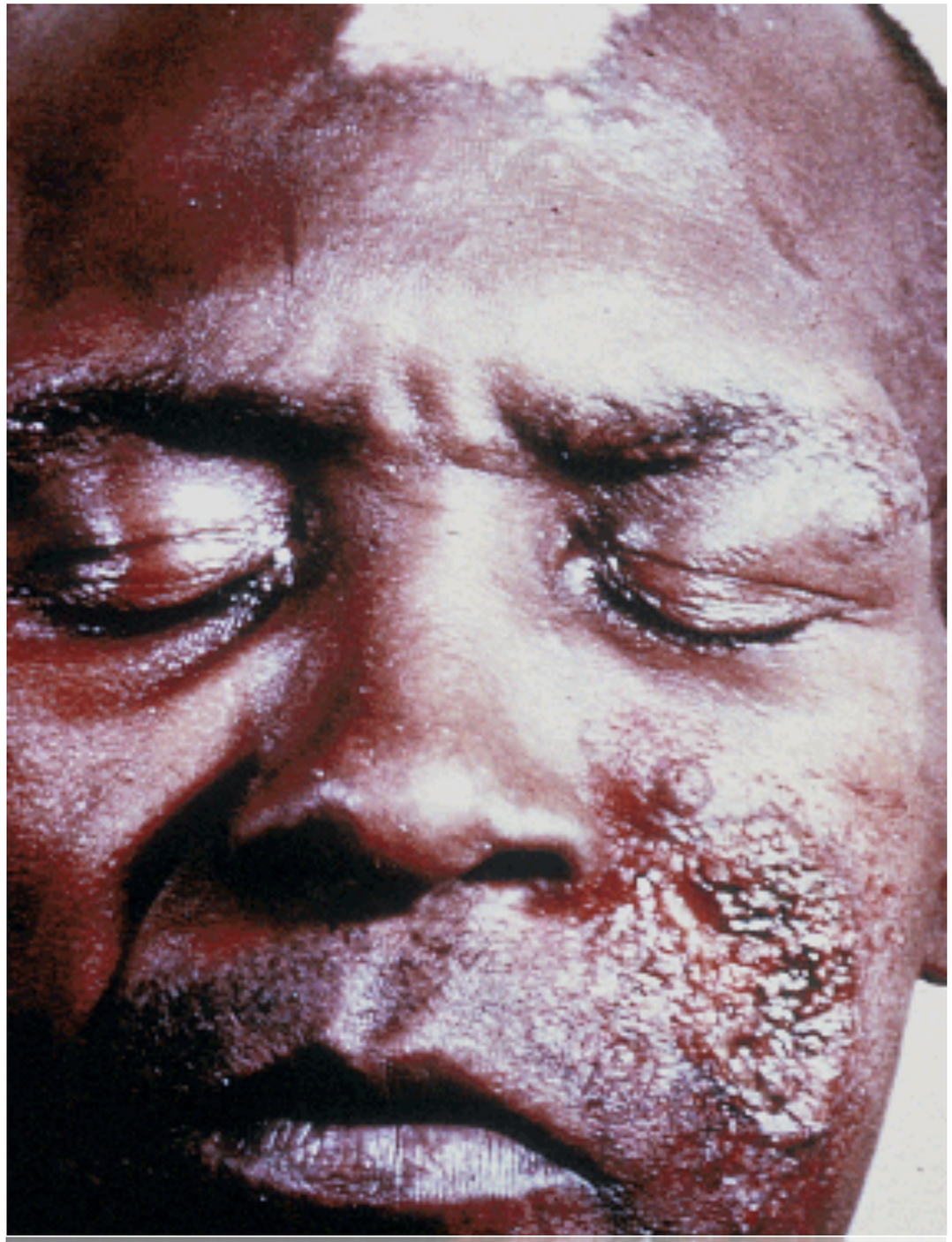


Extension of pulmonary coccidioidomycosis showing a large superficial, ulcerated plaque

Mycology Online, The University of Adelaide

Extrapulmonary manifestations

- Skin
  - Erythema nodosum
  - Erythema multiforme
- Bone and joints
- CNS
- “Desert rheumatism”
  - Triad of fever, erythema nodosum and arthralgia



Chronic lesions of the face
Active lesions in the cheek
Atrophic depigmented scar at forehead

Risk factors for disseminated infection

- Suppressed cellular immunity
  - HIV infection
  - Organ transplant recipents
  - High dose steroid administration
  - Anti-TNF therapy
- Pregnancy (especially in 3rd trimester)
- DM
- Lymphoma
- Chemotherapy for solid tumors
- African and Philippine descents (x7)

Investigation

Mostly nonspecific

- ESR (x1-2 >ULN)
- Eosinophilla (>5%) in 25%
- CXR (normal in 25%)
  - Unilateral infltrate and ipsilateral hilar adenopathy
  - Cavities or nodules

More specific

- Fungal culture
- Serology
- Histopathology
  - Identification of spherules in tissue
  - Sliver stain, H&E, PAS
- PCR

Management

- Uncomplicated infections
  - Healthy patients without evidence or risk factors of dissemination do NOT need antifungal
- Periodic reassessment to demonstrate resolution

- Treatment in:
  - With evidence and risk factors of dissemination
  - Indicators
    - >10% weight loss
    - Night sweats >3/52
    - Infiltrates >1/4 of lung fields
    - Symptomatic >2/12

Treatment

Uncomplicated

- Azoles
  - Fluconazole (400-800mg/d)
  - Itraconazole (200mg/BD)
- Amphoteracin B
  - Respiratory failure
  - Rapidly progressive infections
  - Pregnancy

Disseminated

Antifungal
- Fluconazole (A-II)
- Itraconazole (A-II)

Surgical debridement
- Abscess
- Spine instability
- Shunt

CNS involvement
- Lifelong antifungal
- Shunt

IDSA guideline 2005

Dx: Disseminated coccidioidomycosis

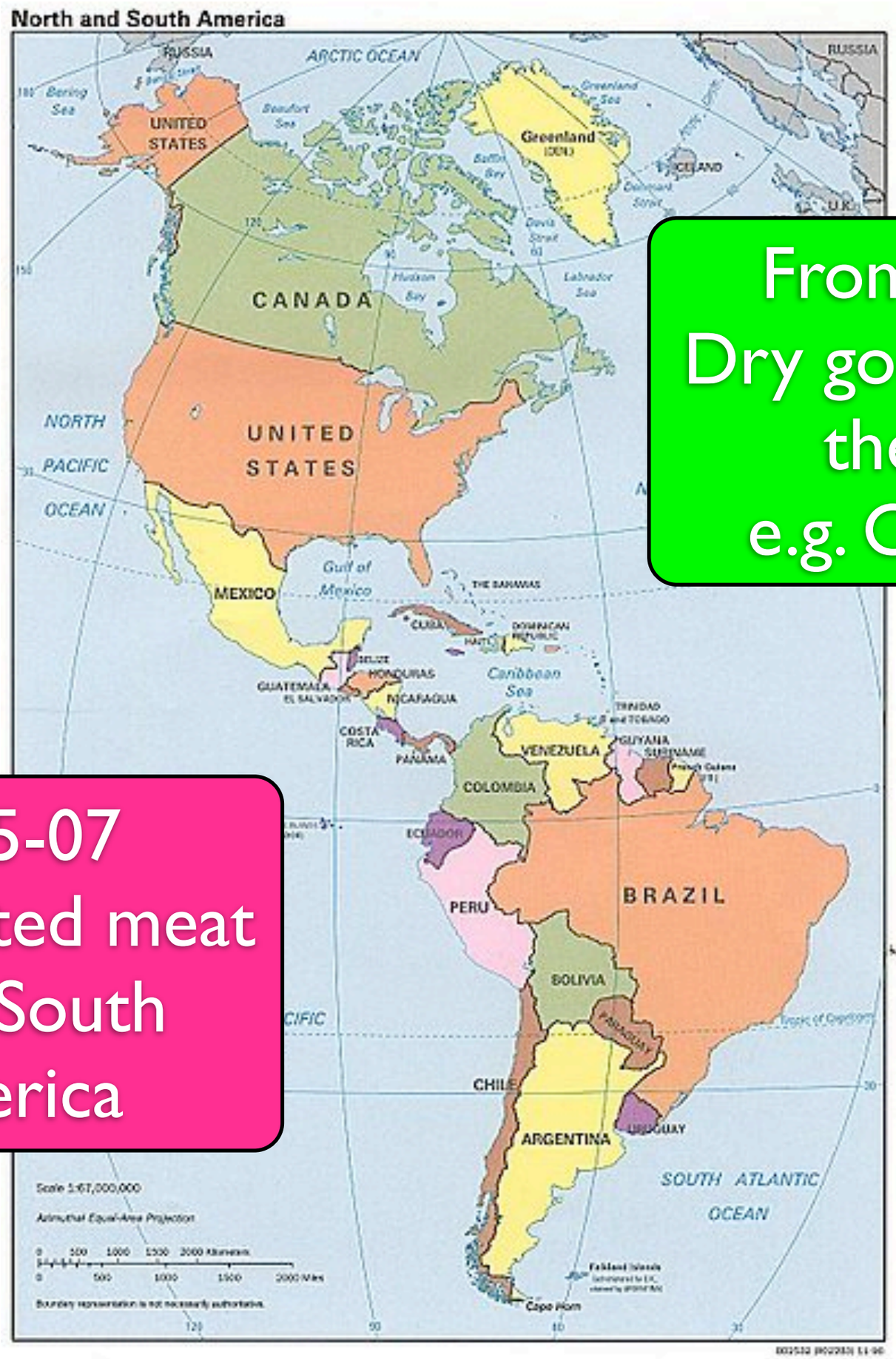
- High swinging fever from admission
- Started Amphoteracin B
  - 0.7mg/kg/day (from 22 Jan)
  - 1mg/kg/day (from 25 Jan)
- Fever responded initially
- Phebilitis managed with Augmentin
- Stepped down to
  - Fluconazole 400mg daily PO
- Plain CT brain NAD
- Serial CXR no improvement

Does he really have coccidioidomycosis?

- Pure Chinese (籍貫：廣東 大鵬)
- Never travels to the Americas
- No human or animal visit from endemic areas
- No family history of immunodeficiency
- HIV negative

Part III

What happen to this man?



From 2007
Dry goods from the US
e.g. CD box

2005-07
Refigerated meat from South America

Room temperature, 4 openings in a single container

Clean and return the container at the container

Did NOT use water for

Clean mostly in the morning 11am No bath till

"Sometimes I noticed some dust on

Did not wear a mask

Progress

- Continued Fluconazole 400mg daily PO
- Skin lesions resolved
- Noted HT and put on ACEI
- Noted DM on diet control
- PET (20 Oct 2009)
  - Improvement of signals
  - Spleen and bilateral axilla signals smaller
  - Both lungs changes resolved
  - Hilar lesions improved
- Continue follow up in clinic

End

Special thanks

Medical Infectious Diseases Team

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Dr Lai ST