Pulmonary infection – Is this tuberculosis?

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- The speaker declares no conflict of interest.

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Case Scenario

A 45-year-old woman

- Previously healthy and no-known underlying disease

Chief complaint: Non-productive cough for 2 weeks

Present illness:

- She developed non-productive cough 2 weeks after returning from a vacation. The symptom persisted for 2 weeks without improvement.
- She had malaise, difficulty in breathing, anorexia and weight loss for 2 kg during 2 weeks of illness.
- She had no fever, no headache, no orthopnea, no dyspnea on exertion, no rash.

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Case Scenario

Past history:

- She had no underlying disease and no previous hospitalization.

Personal history:

- She refuses alcohol drinking and smoking.

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Question 1:

What is (are) additional history you would like to ask for getting to the diagnosis?

A. Tuberculosis in her family
B. Sexual history and partners
C. Travel history
D. Animal exposure
E. All of the above

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What is (are) additional history you would like to ask for getting to the diagnosis?

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Case Scenario: Additional history

- She had no history of tuberculosis in her family'
- She is single and refuses multiple sexual partners.
- She is not taking any drug.
- She has 2 cats at home.
- She hiked in a forest in Southern Thailand 2 weeks prior to developing symptoms.

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Physical Examination

Vital signs: T 37.7 C, RR 22/min, PR 98/min, BP 126/78 mmHg

General appearance: conscious, not pale, no jaundice, no edema, no lymph node enlargement

CVS: unremarkable

RS: crackles both lungs

Abdomen: liver and spleen- not palpable

Neuro: normal

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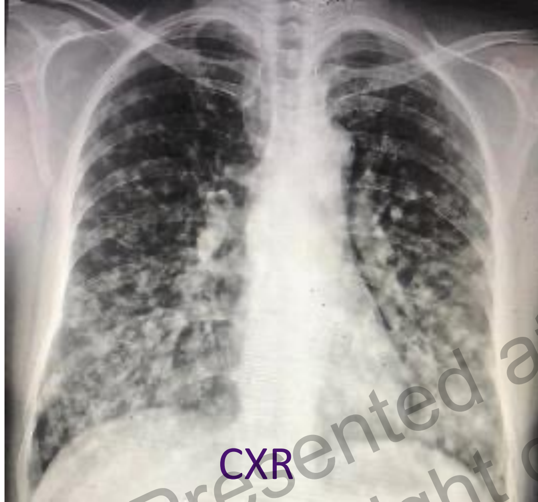
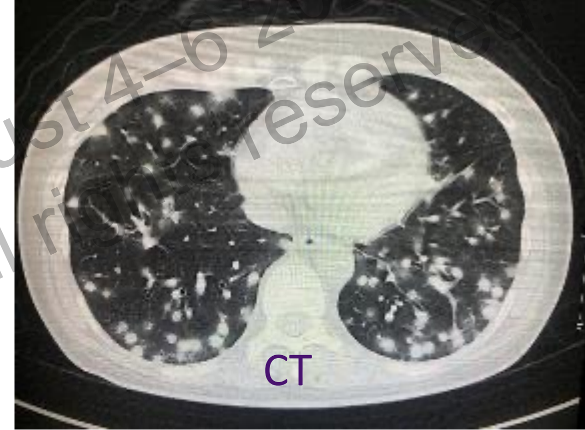
Chest X-rays and Chest CT





Left adrenal gland 0.5 x1.1 cm
Mild splenomegaly

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Question 2:

What is most likely diagnosis ?

A. Tuberculosis
B. Histoplasmosis
C. Cryptococcosis
D. Talaromycosis
E. Metastatic cancer

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What is most likely diagnosis ?

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Question 3:

What is (are) are the laboratory test should be sent for diagnosis?

A. Sputum acid fast stain and culture for mycobacteria
B. Sputum culture for fungus
C. Serum cryptococcal antigen
D. Urine histoplasma antigen
E. Serum galactomannan

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What is (are) are the laboratory test should be sent for diagnosis?

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Case Scenario: Additional history

- Anti-HIV – non-reactive
- Sputum acid fast stain – negative
- Sputum culture for mycobacteria and fungus - pending
- Serum cryptococcal antigen - negative
- Serum galactomannan - negative
- She underwent bronchoscopy with bronchoalveolar lavage and transbronchial biopsy

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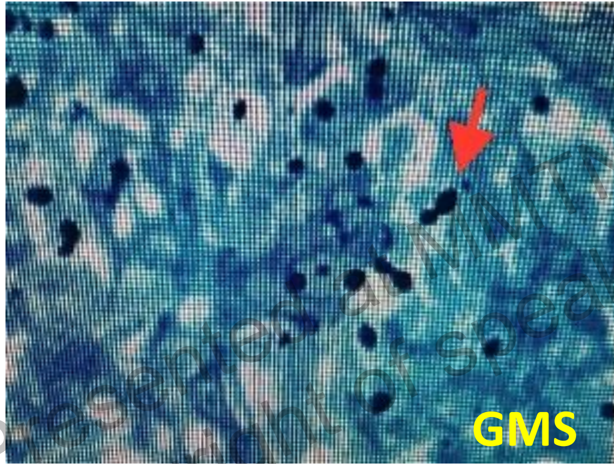
Histopathology of lung tissue



- Necrotizing granulomatous inflammation
- No AFB detected
- No malignancy

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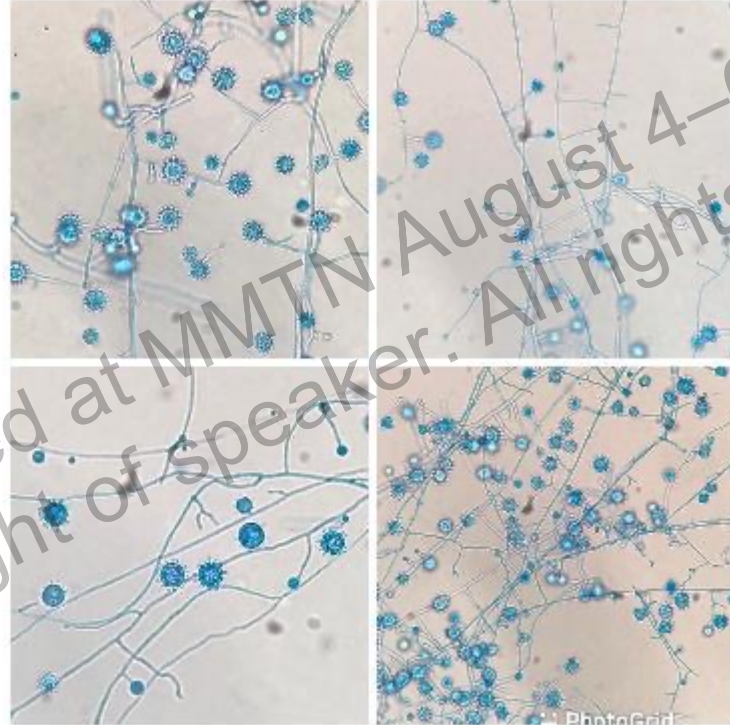
BAL Culture



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Question 4:

What is the diagnosis ?

A. Tuberculosis
B. Histoplasmosis
C. Cryptococcosis
D. Talaromycosis
E. Metastatic cancer

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What is the diagnosis?

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Urine histoplasma antigen test

Positive

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Question 5:

What is the most appropriate treatment?

A. Amphotericin B
B. Amphotericin B plus flucytosine
C. Fluconazole
D. Itraconazole
E. Voriconazole

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What is the most appropriate treatment?

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Travel history: 2 weeks before symptoms

Lesser false vampire bat
(*Megaderma spasma*)

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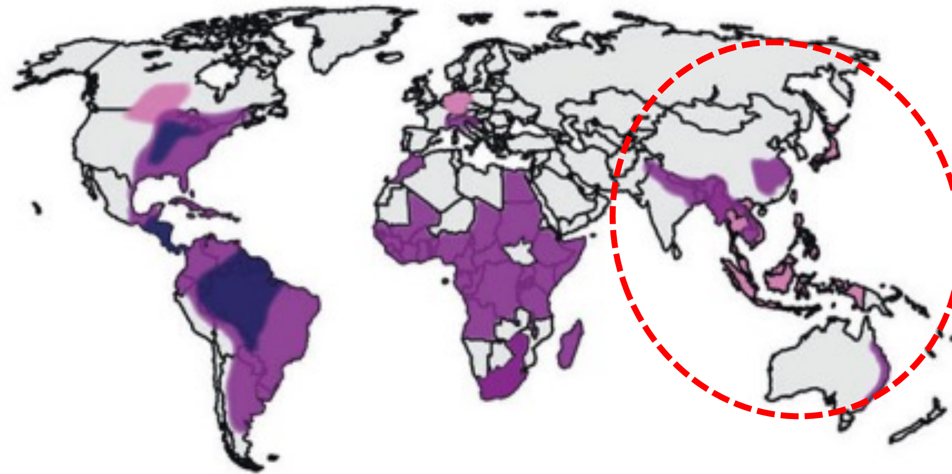
Geographic Region of Histoplasmosis



Thompson GR 3rd, et al. Lancet Infect Dis. 2021 ;21(12):e364-e374.

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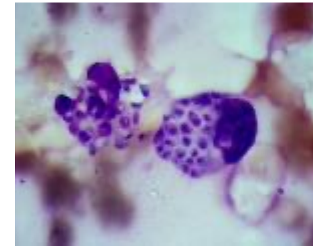
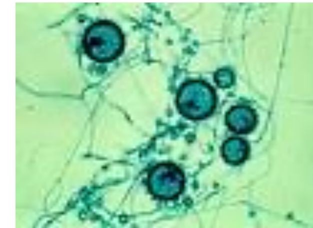
Histoplasma capsulatum

- Found in soil, bird and bat droppings
- Thermally dimorphic
- Heterothallic form [(+) and (-)]
  - *Histoplasma capsulatum* vs. *Ajellomyces capsulata(us)*
- 5 clades
  - Class 1 and Class 2 North Americans (class 1-less virulent)
  - South American Group A and Group B (more skin lesions)
    - *H. capsultum* var. *farciminosum* (Group A)
  - Central American
  - *H. capsulatum* var. *duboisii*
    (African histoplasmosis)



37°C

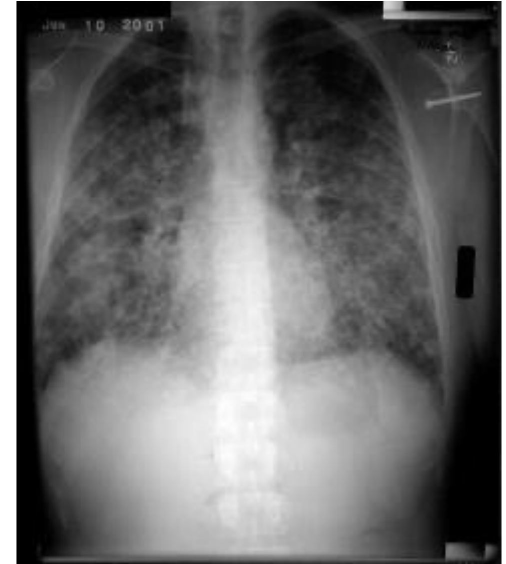


25°C

Med Mycol May 2011, 49, 337–344

Acute pulmonary histoplasmosis

- Incubation period 14 days (7-21 days)
- Asymptomatic or flu-like illness
  - Fever, headache, non-productive cough, chest pain
  - Extrapulmonary S&S: arthralgia, erythema nodosum, erythema multiforme
- Resolve within 10 days (>90% unrecognized)
- Chest radiograph
  - Mediastinal or nodes enlargement
  - Patchy infiltrates
  - Calcifications



Infect Dis Clin N Am 30 (2016) 207–227

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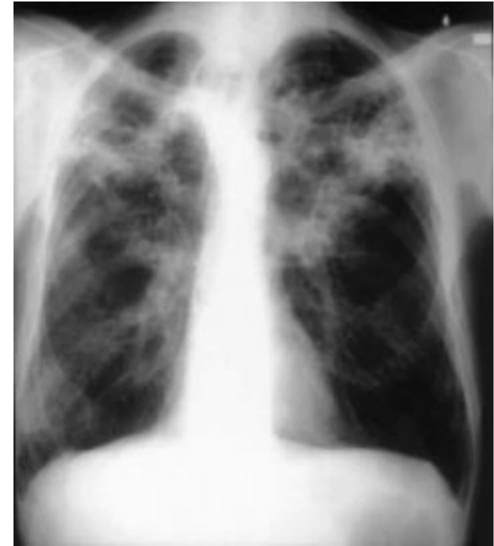
Chronic pulmonary histoplasmosis

- **Cavitary**
  - Low-grade fever, weight loss
  - Productive cough
  - Dyspnea, chest pain (early)
  - Hemoptysis (late)
  - **CXR**: patchy infiltrates,consolidation and cavitation
- **Noncavitary**
  - Cough
  - Weight loss
  - Fever and chill
  - **CXR**: nodules, infiltrates, lymphadenopathy



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Progressive Disseminated Histoplasmosis

- Immunocompromised hosts: HIV, hematologic malignancies, immunosuppessive therapy
- Multiple organ involvement
  - Lungs: cough, patchy pneumonitis, hilar/mediastinal lymphadenopathy
  - GI: uropharyngeal ulcer, diarrhea, hepatosplenomegaly
  - Blood: cytopenia
  - CNS: meningitis, cerebritis, mass lesions
  - Endovascular: endocarditis
  - Adrenal glands

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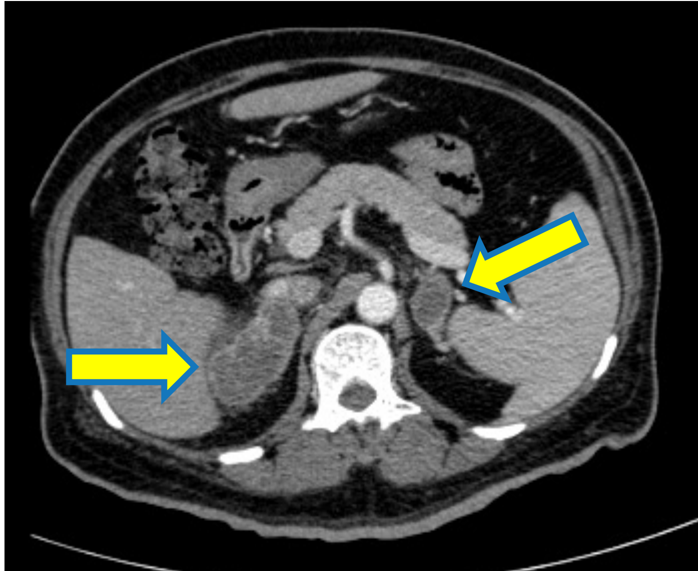
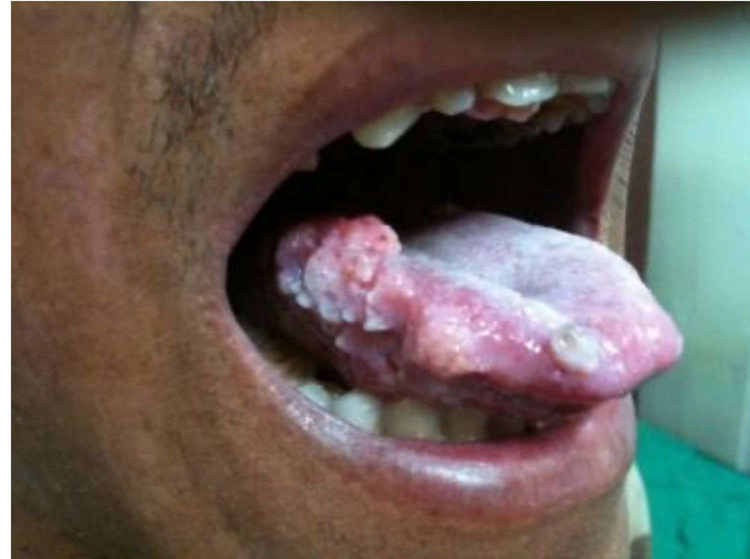
Adrenal Histoplasmosis and Oral Lesions





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Treatment of Disseminated Histoplasmosis

- L-AmB at 3 mg/kg daily was superior to AmB-deoxycholate (AmB-d), in patients with advanced HIV and disseminated histoplasmosis
- After successful induction therapy (1-2 weeks), itraconazole (200 mg twice daily) is given for at least 1 year
- For less severe disease, itraconazole can be initiated
  - Fluconazole has a lower success rate than itraconazole
  - Voriconazole is not routinely recommended
- Histoplasmosis secondary to tumour necrosis factor-α inhibitor therapy requires discontinuation of the TNF-α blocker during antifungal therapy
- Antifungal treatment is administered for around 12 months and the test results for the individuals are negative for *Histoplasma* spp antigen

Thompson GR 3rd, et al. Lancet Infect Dis. 2021 ;21(12):e364-e374.

Take home messages

- Pulmonary histoplasmosis may mimic pulmonary tuberculosis and it can occur in non-HIV patients
- History related to exposure is helpful for diagnosis (bat, bird, forest)
- The fungus is slow growing and can be missed if a fungal culture is not requested

Acknowledgement

- Dr. Manoon Leechawengvongse
  - Vichiyuth Hospital
  - The President of Thai Medical Mycology Forum (TMMF)

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Thank you