Fungal infections of Lungs

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Fungi, Yeasts, Molds
Introduction

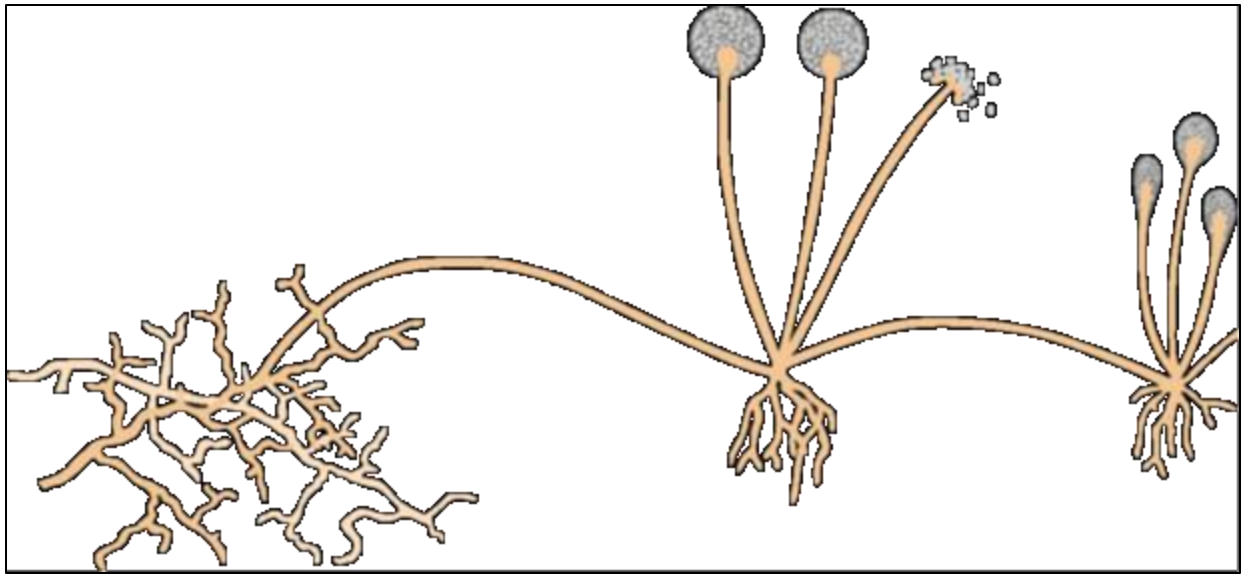
- **Eukaryotic Organisms:** Distinct nucleus and organelles.
- **Diversity:** Includes molds, yeasts, and mushrooms.

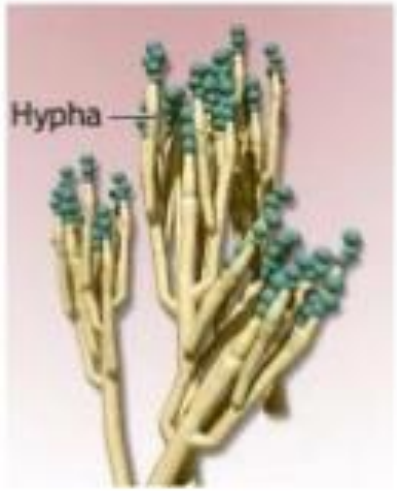
Fungi, Yeasts, Molds
Molds and Yeasts

- **Two main types relevant to medical mycology:**
  - **Molds:**
    - Multicellular fungi that grow as branching filaments called hyphae
  - **Yeasts:**
    - Unicellular fungi that reproduce by budding
  - Some fungi (like Candida albicans) can exist in both yeast and mold forms (**dimorphic**) based on the environment
    - Usually as a mold in the environment (25°C) and as yeast form in human tissues (37°C)

Fungi, Yeasts, Molds
Molds and Yeasts

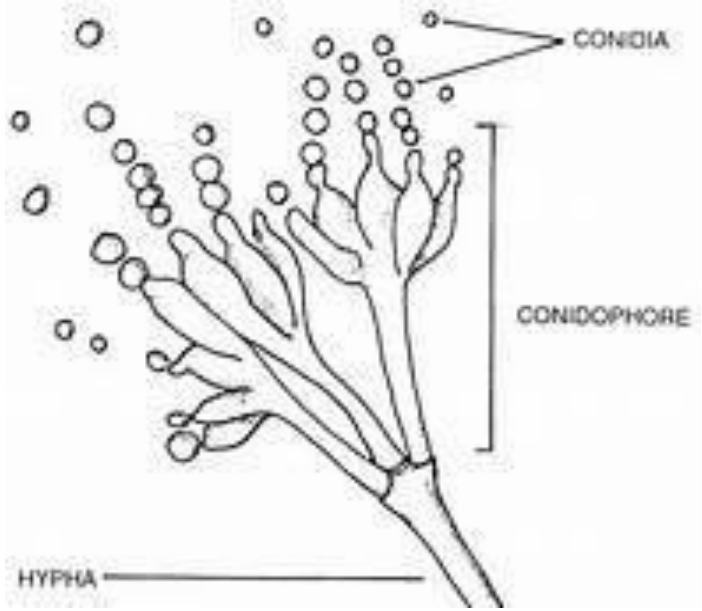
- **Molds:**
  - Multicellular fungi that grow as branching filaments called hyphae

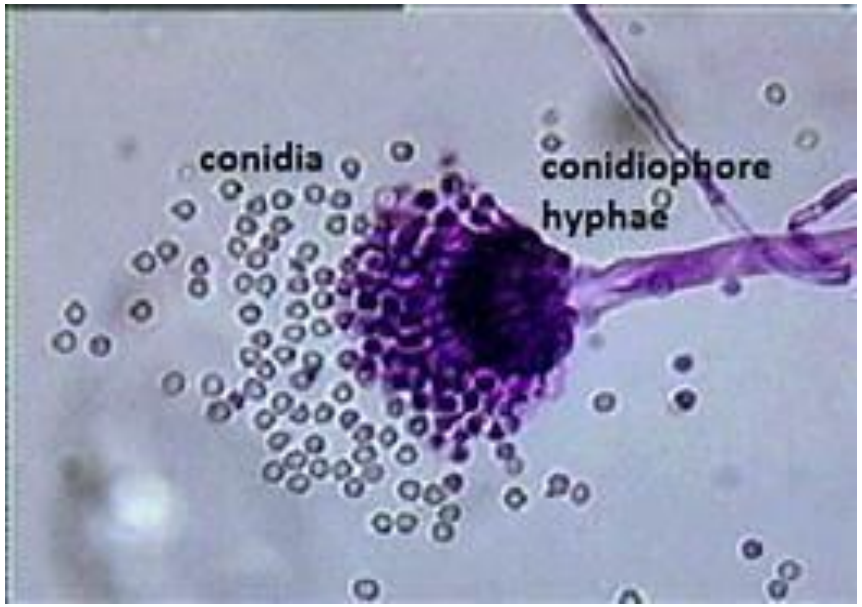




Fungi, Yeasts, Molds
Molds and Yeasts

Hyphae

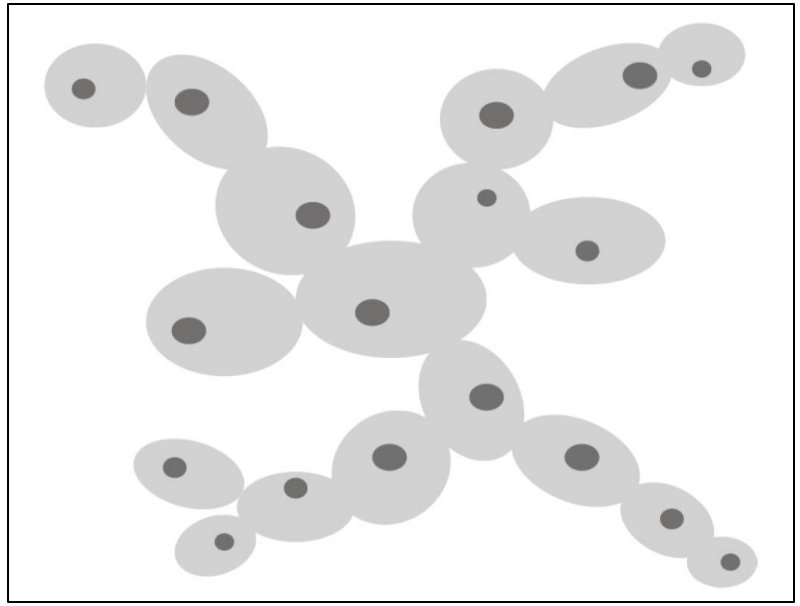


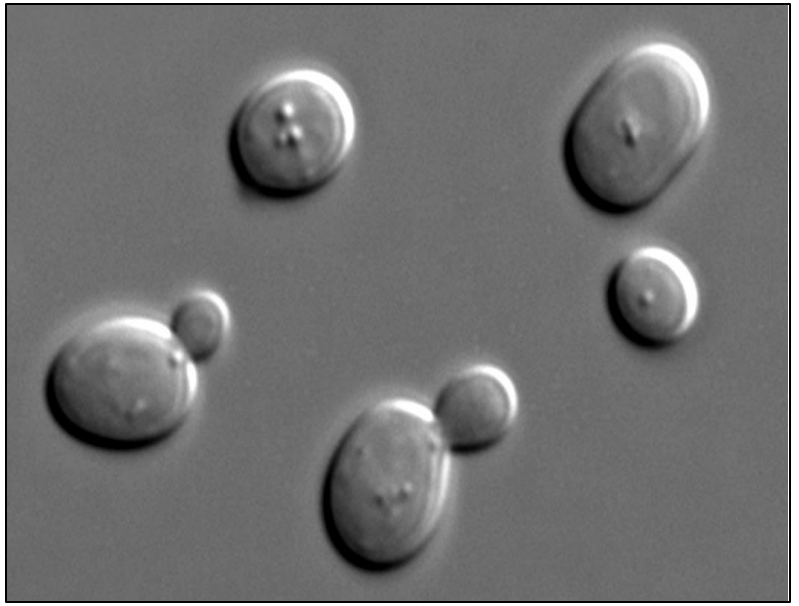


- **Hyphae (Hypha, singular):** is a long, branching filamentous structure of a fungus with fruiting body on the top that give conidia.
- Hyphae may be septate, having internal septa, or nonseptate.

Fungi, Yeasts, Molds
Molds and Yeasts

- **Yeasts:**
  - Unicellular fungi that reproduce by budding
  - Budding → Single yeast cell and a small new one start to form as a bud





Overview of Pulmonary Mycoses

- Pulmonary mycoses are categorized into two main groups:
  1. Infections due to primary pathogenic fungi:
     - Histoplasma capsulatum
     - Coccidioides immitis
  2. Infections due to opportunistic fungi:
     - Aspergillus fumigatus
     - Pneumocystis jirovecii

Overview of Pulmonary Mycoses
Characteristics of systemic pulmonary mycoses

- Infection typically acquired by inhalation of fungal spores (conidia)
- Most infections are asymptomatic and self-limiting
- In immunocompromised individuals, infection can disseminate to other organs
- Infected persons rarely transmit the disease to others

Predisposing Factors for Fungal Infections

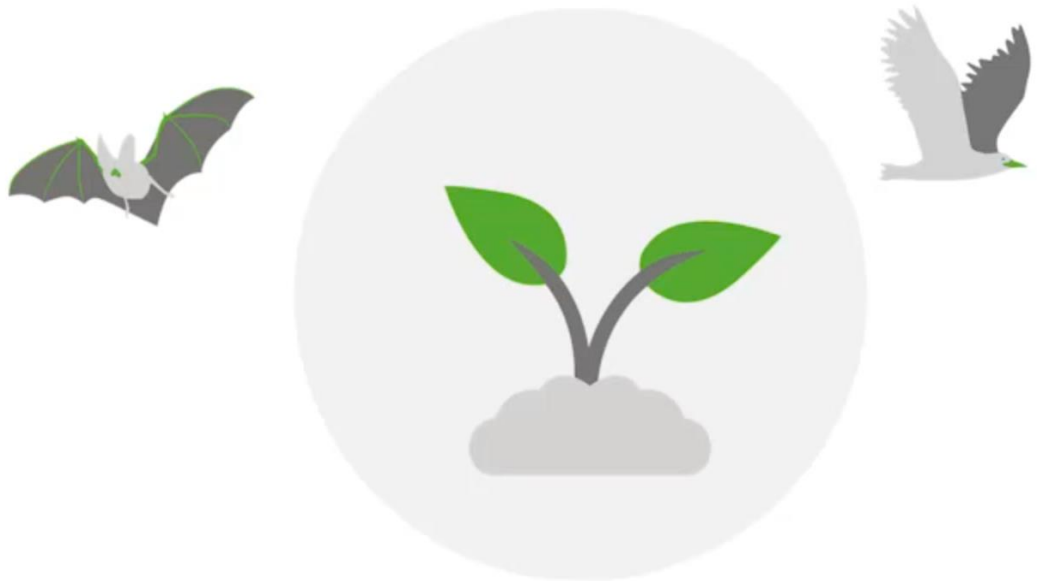
- Prolonged use of broad-spectrum antibiotics
  - Disrupts normal bacterial flora, allowing fungal overgrowth
- Immunosuppression:
  - Diseases: AIDS, diabetes mellitus
  - Medications: corticosteroids, chemotherapy drugs
- Age extremes:
  - Very young (immature immune system)
  - Very old (declining immune function)
- Underlying lung diseases:
  - Chronic obstructive pulmonary disease (COPD)
  - Cystic fibrosis
  - Pre-existing lung cavities (e.g., from tuberculosis)

Histoplasmosis

Primary Pathogenic Fungi - Histoplasmosis

- **Causative agent:** *Histoplasma capsulatum*
- **A dimorphic fungus:**
  - Grows as a mold in the environment (25°C)
  - Exists as yeast form in human tissues (37°C)
- **Epidemiology and habitat:**
  - Endemic in parts of the United States, particularly the Ohio and Mississippi River valleys
  - Found in soil enriched with bird or bat droppings
  - Caves explorers (exposure to bats) or cleaning bird cages
- Causing acute pneumonia or chronic cavitary lesions in the lungs (as T.B).

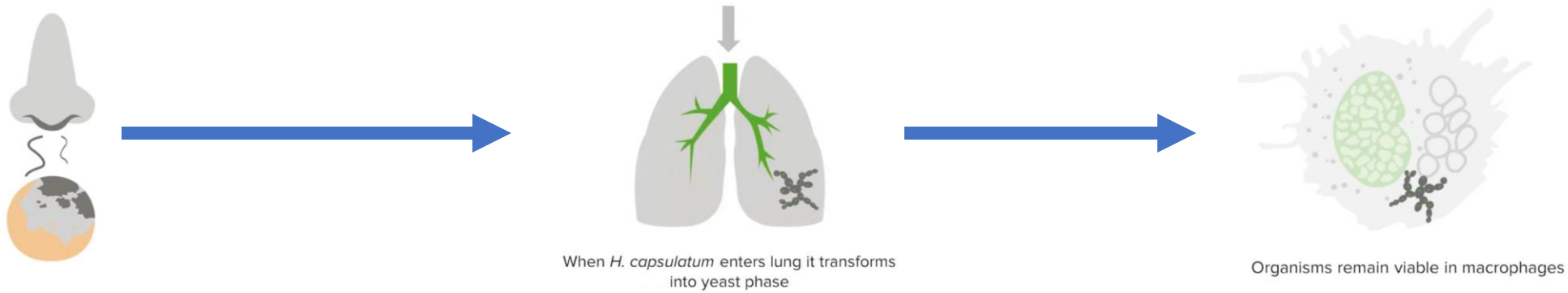
Primary Pathogenic Fungi - Histoplasmosis



Lives in soil, growth enhanced by high nitrogen content associated with bird or bat droppings

Primary Pathogenic Fungi – Histoplasmosis
Mode of infection

- Inhaling fungal spores from environmental mold form
- Spores are phagocytosed by alveolar macrophages
- Within macrophages, spores transform into yeast form and multiply



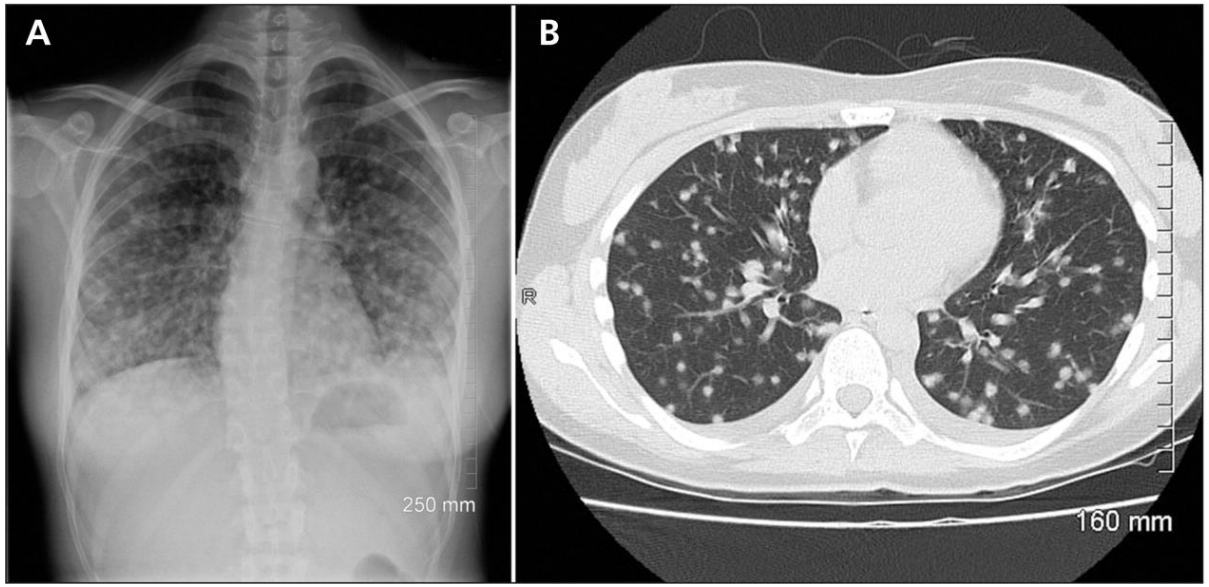
Primary Pathogenic Fungi – Histoplasmosis Characteristics

- **Not Encapsulated:** Despite the name (Misnomer).
- **Virulence Factor:**
  - Survives inside macrophages.
  - Modulates phagolysosome pH.

Primary Pathogenic Fungi – Histoplasmosis Clinical Presentation

1. Most of infected people are asymptomatic (95%).
2. 5% may have acute pneumonia with flue-like symptoms (ex. fever, chills, headache, cough, chest pain, fatigue, body aches, mouth sores) & red skin bumps called erythema nodosum, most often on the lower limbs.
3. Sometimes the infection progress to become chronic (in immunocompromised).
4. In immunocompromised patients, the infection disseminates to different organs via reticuloendothelial cells to the liver, spleen & Lymph Nodes and to CNS (headache & neck stiffness due to high fever).
5. Enlarged mediastinal and hilar lymph nodes

Primary Pathogenic Fungi – Histoplasmosis
Clinical Presentation



Acute pulmonary histoplasmosis

diffuse pulmonary infiltrates (reticulonodular)

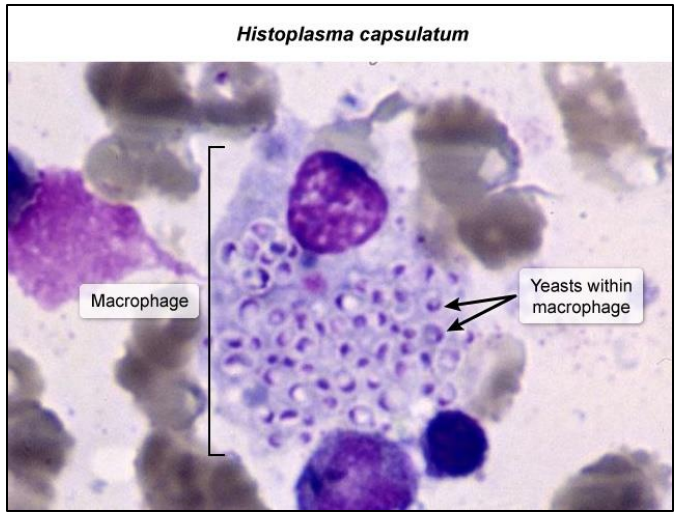
In Chronic → cavitation

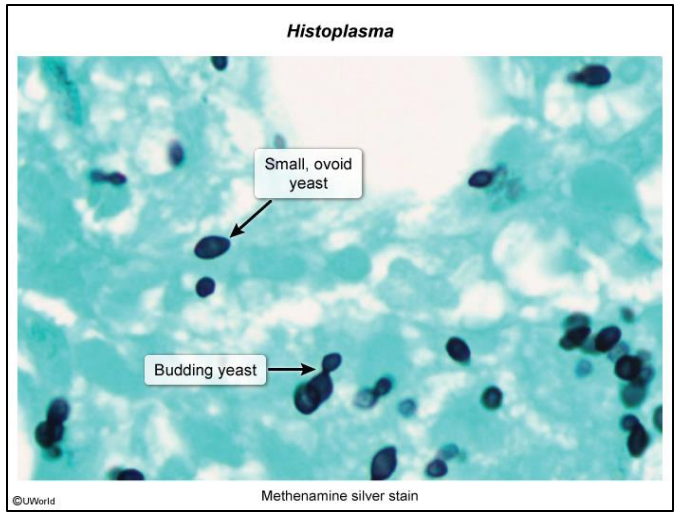
Erythema nodosum
(red, tender nodules on shins)

Primary Pathogenic Fungi – Histoplasmosis

Diagnosis

1. Direct methods:
   - Microscopic examination of sputum, histopathology (macrophages with intracellular ovoid/round yeast), or body fluids
   - Special stains: Periodic Acid-Schiff (PAS), Giemsa stain, Methenamine silver stain
   - Culture on Sabouraud's agar at 25 C (takes up to 3 weeks)
2. Indirect methods:
   - Histoplasmin skin test (not for acute diagnosis)
   - Serological tests for antibodies or fungal antigens
   - Histoplasma antigen testing of the urine or blood
   - Polymerase Chain Reaction (PCR)
3. Imaging:
   - Chest X-ray and CT scan to visualize lung lesions





Primary Pathogenic Fungi – Histoplasmosis Treatment

1. Mild to moderate cases:
   - Oral itraconazole for 6-12 weeks
2. Severe or disseminated cases:
   - Intravenous amphotericin B followed by oral itraconazole
   - Treatment duration: 3 months to 1 year depending on severity

➢ Amphotericin B:
- Binds to ergosterol, disrupting cell membrane integrity.
- Nephrotoxic; requires monitoring of kidney function.

➢ Itraconazole (Oral):
- Inhibits ergosterol synthesis.

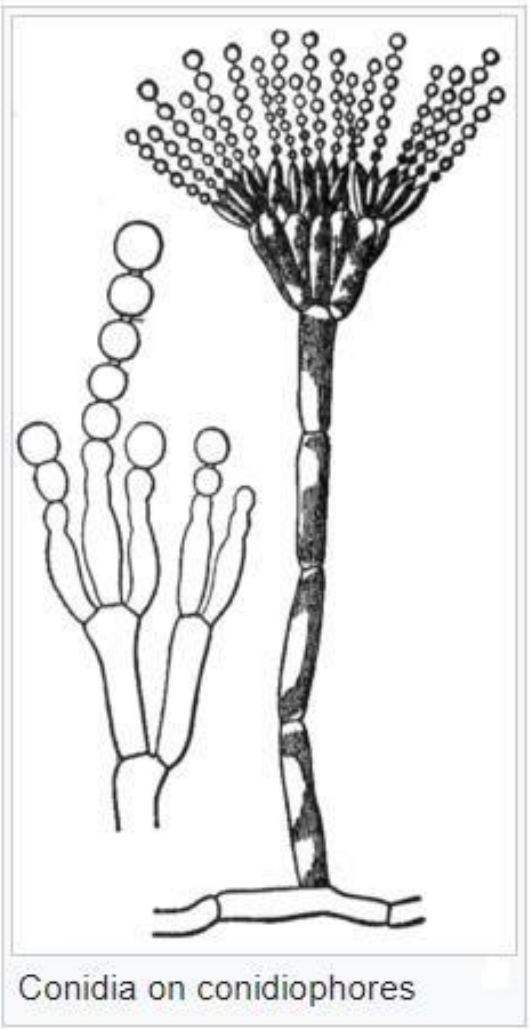
Primary Pathogenic Fungi – Histoplasmosis Summary

Histoplasma capsulatum	
Epidemiology	• Dimorphic fungus - mold in environment, yeast at body temperature • Endemic to Ohio & Mississippi River Valleys • Soil contaminated by bird or bat droppings
Pathophysiology	• Inhaled → phagocytosed by alveolar macrophages → escapes lysosome destruction → spreads to hilar/mediastinal lymph nodes
Disease course	• Immunocompetent: Asymptomatic (primarily) or self-limited pneumonia with mediastinal/hilar lymphadenopathy • **Immunocompromised**: Disseminated disease through liver, spleen, or bone marrow
Diagnosis	• Urine antigen testing • Biopsy with histopathology → granulomas & macrophages with **intracellular ovoid/round yeast**

Aspergillosis

Opportunistic Fungi - Aspergillosis Introduction

- **Causative Agents:**
  - *Aspergillus fumigatus* → causing pulmonary aspergillosis
  - *Aspergillus flavus* → causes sinus and cutaneous infections
  - *Aspergillus niger* → causing invasive infections and otitis
- **Habitat:**
  - Soil, decaying vegetation, air, contaminated food, bedding, and air conditions.
- **Transmission:** Airborne
- **Morphology:**
  - Filamentous fungus with Septate hyphae.
  - Conidial heads.



Conidia on conidiophores

Opportunistic Fungi - Aspergillosis
Pulmonary aspergillosis

- It is a disease affecting the lung caused by **A. fumigatus** fungus.
- Portal of entry: nasal passage & respiratory tract (inhalation of spores).
- The disease my occurs in 3 forms:
    1. Allergic pulmonary aspergillosis.
    2. Aspergilloma or fungal ball.
    3. Invasive aspergillosis.

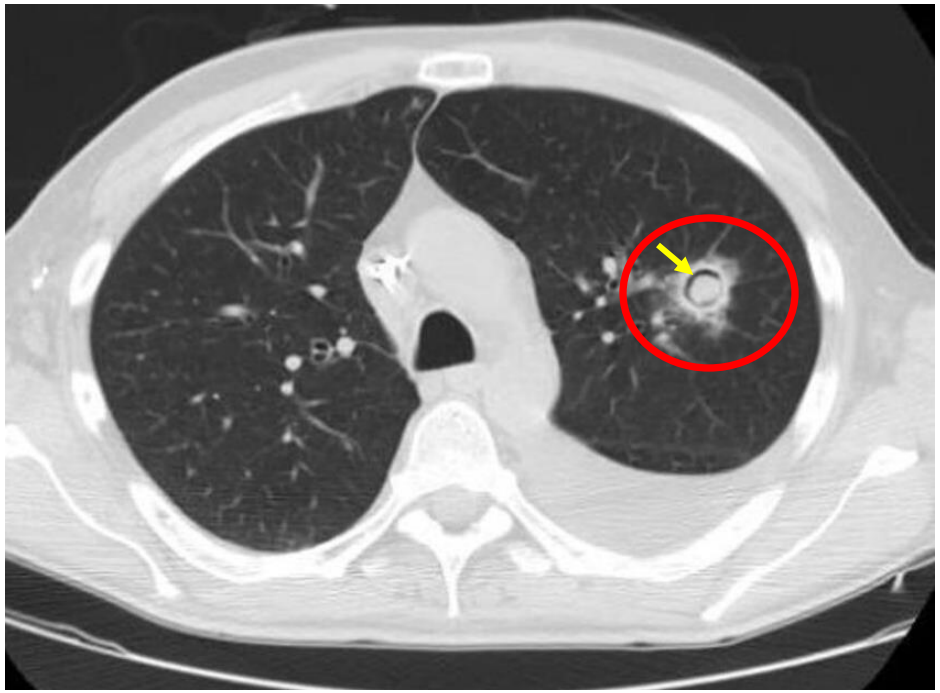
Opportunistic Fungi - Aspergillosis
Types of Pulmonary Aspergillosis (3 forms)

1. **Allergic bronchopulmonary aspergillosis (ABPA):**
   - Occurs due to Hypersensitivity (IgE) reaction to *A. fumigatus* in airways
   - Occurs in patients with asthma or cystic fibrosis
   - Presentation: recurrent attack of wheeze, cough & expectoration.
2. **Aspergilloma (fungal ball):**
   - Fungal colonization of pre-existing lung cavities
   - Most common in patients with prior tuberculosis
3. **Invasive pulmonary aspergillosis:**
   - Occurs in severely immunocompromised patients **(especially in neutropenic patients)**
   - Causing acute pneumonia & haemoptysis
   - Fungus invades lung tissue and may disseminate

Chest CT demonstrating an aspergilloma within a prior lung cavity – note minimal surrounding tissue inflammation

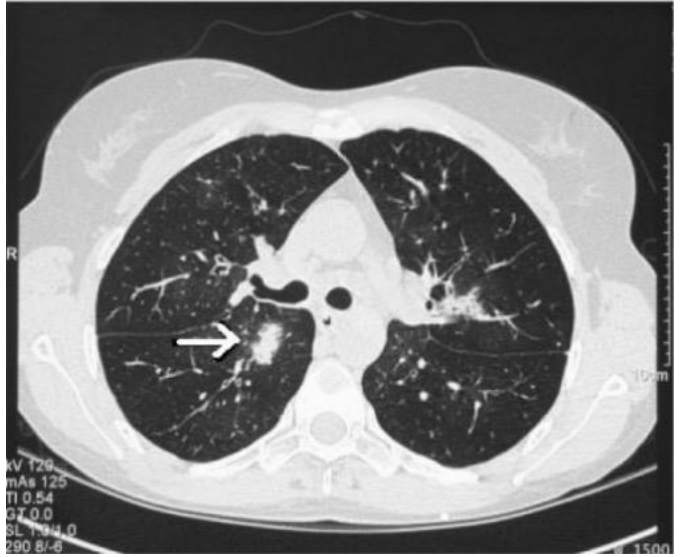
Opportunistic Fungi - Aspergillosis
Clinical Presentation

- **Allergic bronchopulmonary aspergillosis (ABPA):**
  - Recurrent episodes of wheezing and coughing
  - Expectoration of brown mucus plugs
  - Fever, malaise
  - Can lead to bronchiectasis if untreated
- **Aspergilloma (fungal ball):**
  - Often asymptomatic
  - May cause hemoptysis (can be severe)
  - Chronic cough
- **Invasive pulmonary aspergillosis:**
  - Fever unresponsive to antibiotics
  - Cough, chest pain, dyspnea
  - Hemoptysis
  - May progress to respiratory failure
  - May disseminate to brain, causing stroke-like symptoms

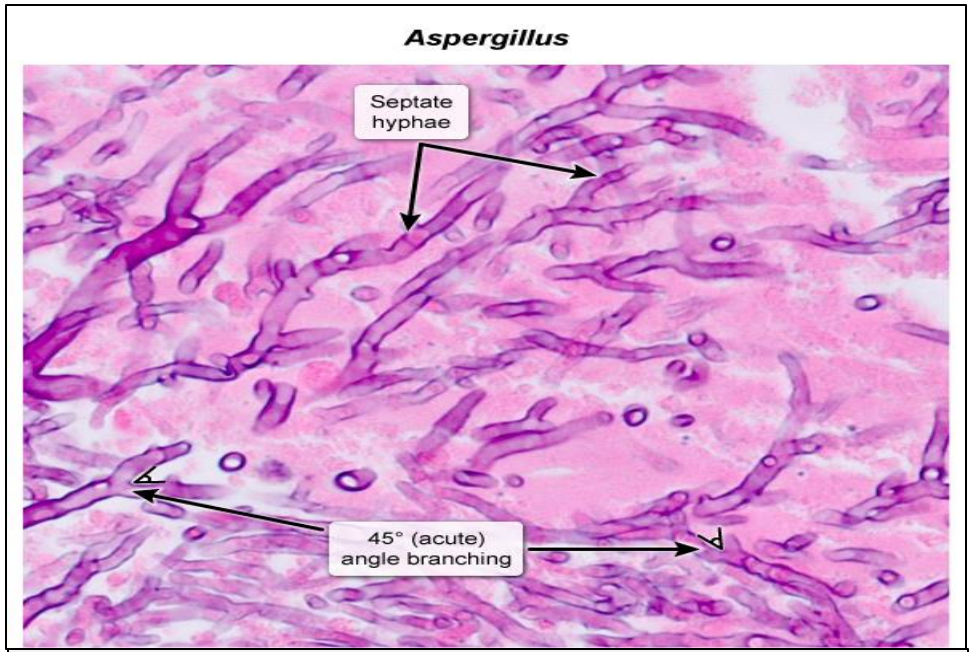


Opportunistic Fungi - Aspergillosis Diagnosis

- **Microscopy and culture:**
  - Direct microscopy of respiratory samples
  - Culture on Sabouraud's agar
    - A. fumigatus grows as white filaments with green spores
    - A. flavus : gives white filaments with yellowish green spores.
    - A. niger : gives white filaments with black spores.
- **Serology:**
  - Galactomannan antigen test for invasive aspergillosis
  - Aspergillus-specific IgE and IgG for ABPA
- **Molecular techniques:** PCR for detection of Aspergillus DNA
- **Imaging:**
  - Chest X-ray and CT scan
  - "Halo sign" on CT is characteristic of early invasive disease



A CT demonstrating a 'halo sign' indicative of hemorrhage due to angioinvasion of aspergillosis

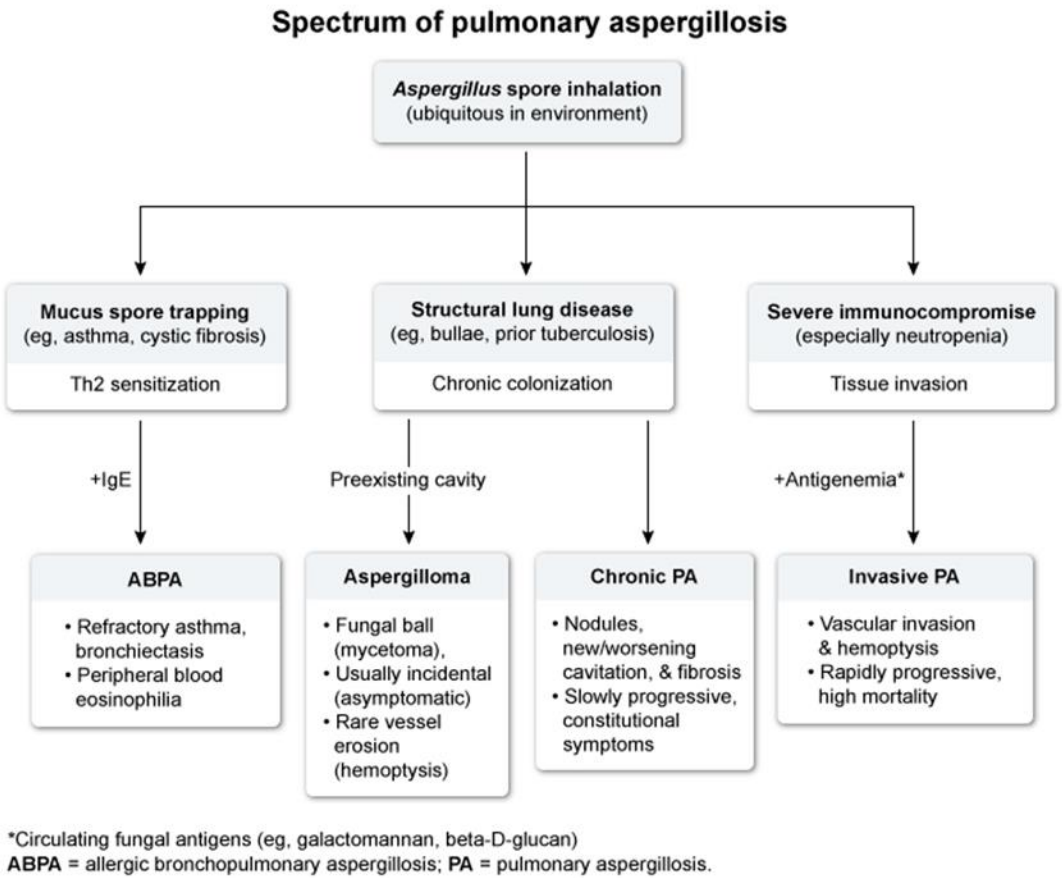


biopsy shows fungal **hyphae** branching at **acute angles** with **septations**, findings characteristic of ***Aspergillus fumigatus***. → (monomorphic, existing only in mold form (ie, multicellular hyphae))

Opportunistic Fungi - Aspergillosis Treatment

- **ABPA:**
  - Corticosteroids to reduce inflammation
  - Antifungal therapy (itraconazole) in some cases
- **Aspergilloma:**
  - Observation for asymptomatic cases
  - Antifungal therapy for symptomatic cases
  - Surgical resection for recurrent hemoptysis
- **Invasive aspergillosis:**
  - Voriconazole as first-line therapy
  - Alternatives: Amphotericin B, isavuconazole, or posaconazole. Duration: at least 6-12 weeks, often longer

Opportunistic Fungi - Aspergillosis Summary



Other Fungal Lung Infections

- **Coccidioidomycosis:**
  - Caused by Coccidioides immitis
  - Endemic in southwestern United States
  - Most infections are asymptomatic
  - Can cause acute pneumonia or disseminated disease
- **Pneumocystis pneumonia (PCP):**
  - Caused by Pneumocystis jirovecii (formerly P. carinii)
  - Major opportunistic infection in AIDS patients
  - Presents with fever, dry cough, and progressive dyspnea
  - Diagnosis: Characteristic chest X-ray, demonstration of cysts in bronchial washings
  - Treatment: Trimethoprim-sulfamethoxazole, pentamidine as alternative

Thank You