

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)

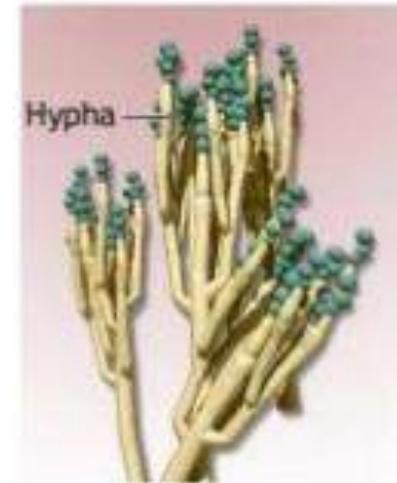
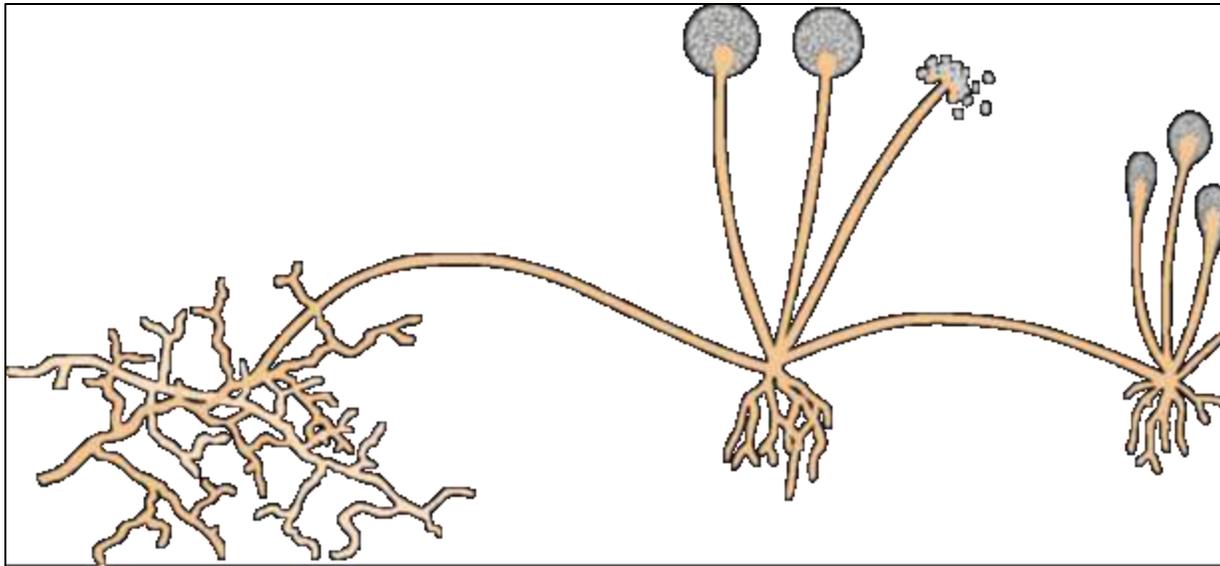


Fungi, Yeasts, Molds

Molds and Yeasts

- **Molds:**

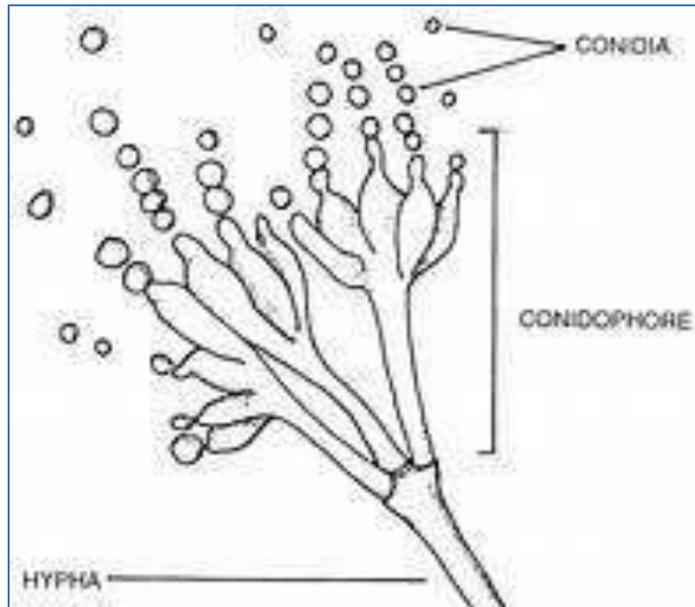
- Multicellular fungi that grow as **branching filaments** called **hyphae**



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 internal₅ septa, or nonseptate.

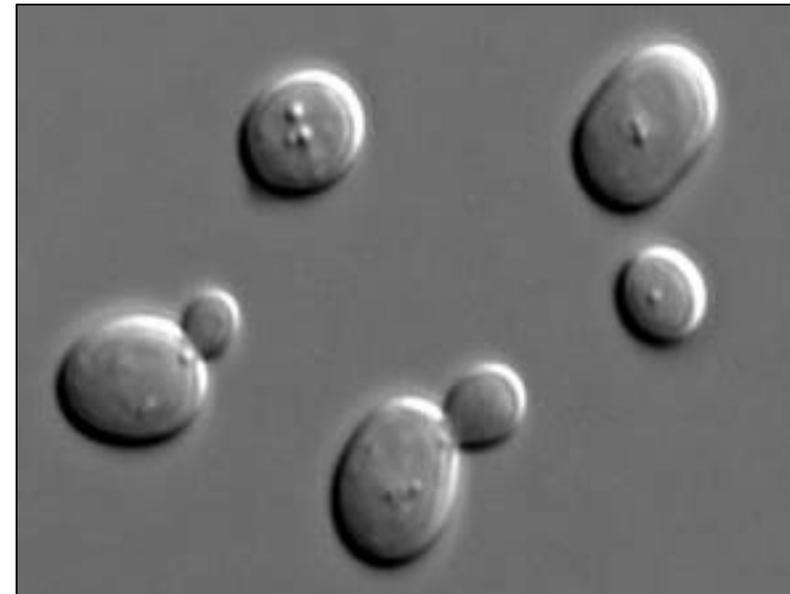
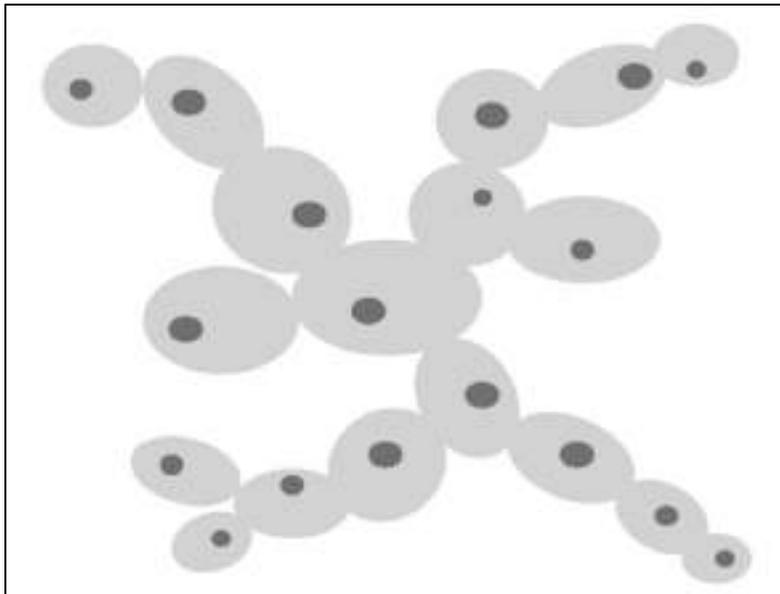


Fungi, Yeasts, Molds

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



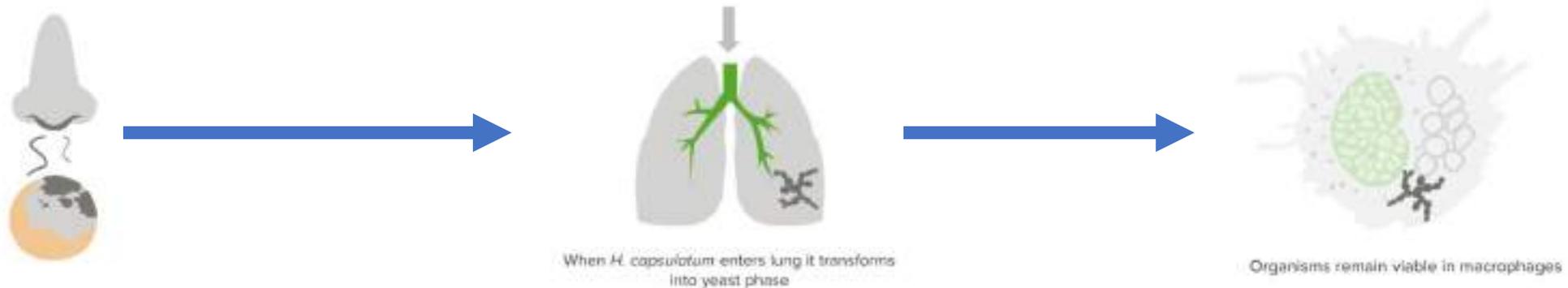
Lives in soil, growth enhanced by high nitrogen content associated with bird or bat droppings



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:

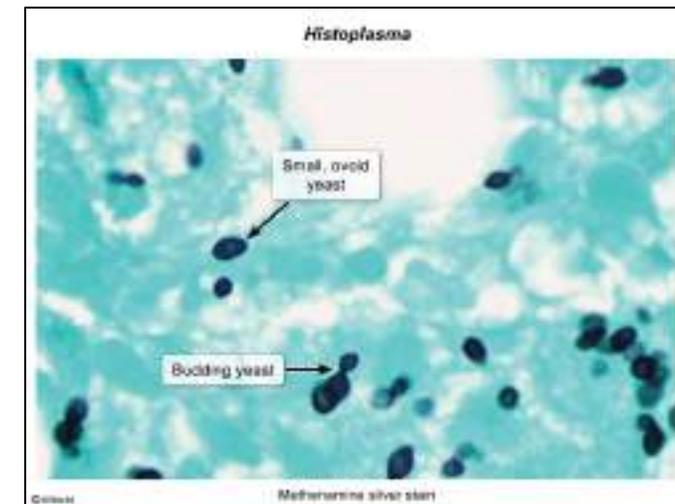
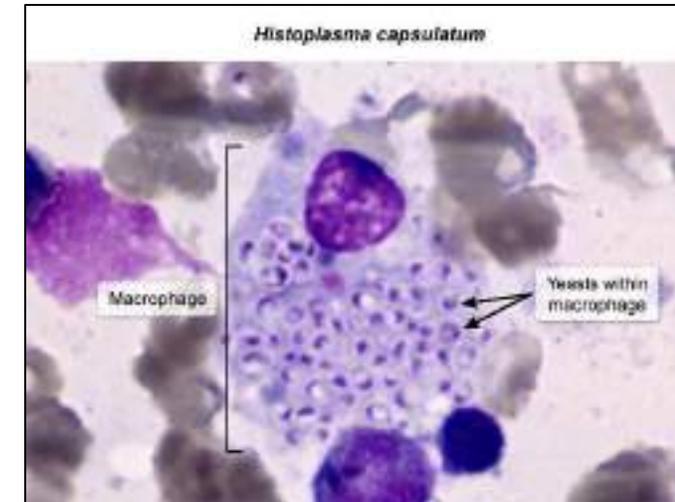
- Microscopic examination of sputum, histopathology (macrophages with intracellular ovoid/round yeast), or body fluids
- Special stains: Periodic Acid-Schiff (PAS), Giemsa stain, Methenamine silver stain
- Culture on Sabouraud's agar at 25 C (takes up to 3 weeks)

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

<i>Histoplasma capsulatum</i>	
Epidemiology	<ul style="list-style-type: none">• Dimorphic fungus - mold in environment, yeast at body temperature• Endemic to Ohio & Mississippi River Valleys• Soil contaminated by bird or bat droppings
Pathophysiology	<ul style="list-style-type: none">• Inhaled → phagocytosed by alveolar macrophages → escapes lysosome destruction → spreads to hilar/mediastinal lymph nodes
Disease course	<ul style="list-style-type: none">• Immunocompetent: Asymptomatic (primarily) or self-limited pneumonia with mediastinal/hilar lymphadenopathy• Immunocompromised: Disseminated disease through liver, spleen, or bone marrow
Diagnosis	<ul style="list-style-type: none">• 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

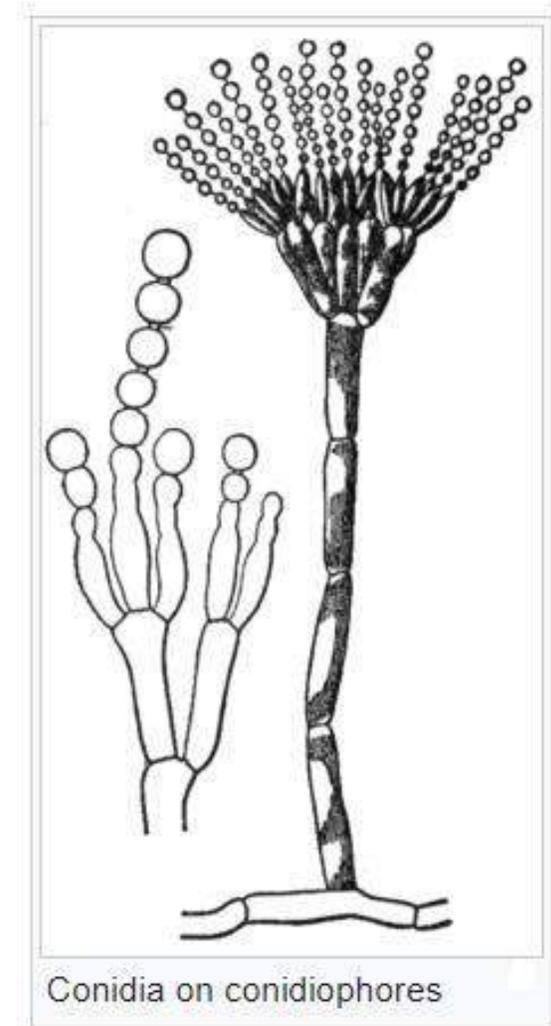
- **Habitat:**

- Soil, decaying vegetation, air, contaminated food, bedding, and air conditions.

- **Transmission:** Airborne

- **Morphology:**

- Filamentous fungus with Septate hyphae.
- Conidial heads.



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 may occur in **3 forms**:
 1. Allergic bronchopulmonary aspergillosis.
 2. Aspergilloma or fungal ball.
 3. Invasive aspergillosis.



Opportunistic Fungi - Aspergillosis

Types of Pulmonary Aspergillosis (3 forms)

1. Allergic bronchopulmonary aspergillosis (ABPA):

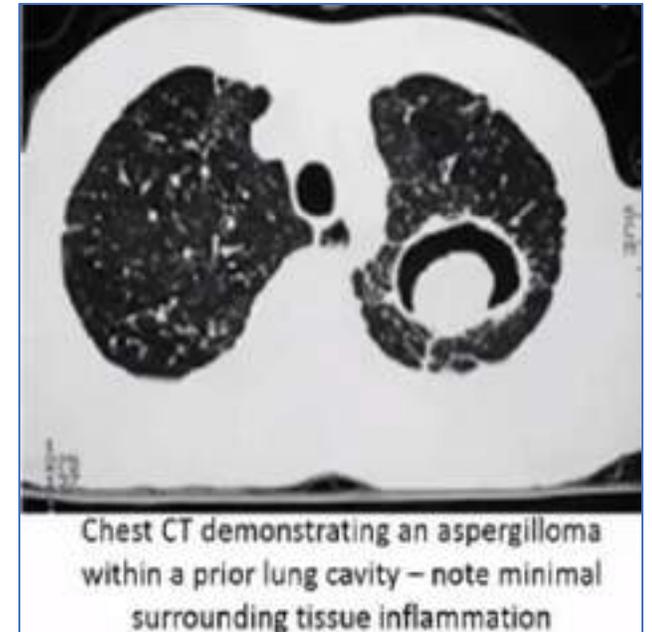
- Occurs due to **Hypersensitivity** (IgE) reaction to *A. fumigatus* in airways
- Occurs in patients with asthma or cystic fibrosis
- Presentation: recurrent attack of wheeze, cough & expectoration.

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



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



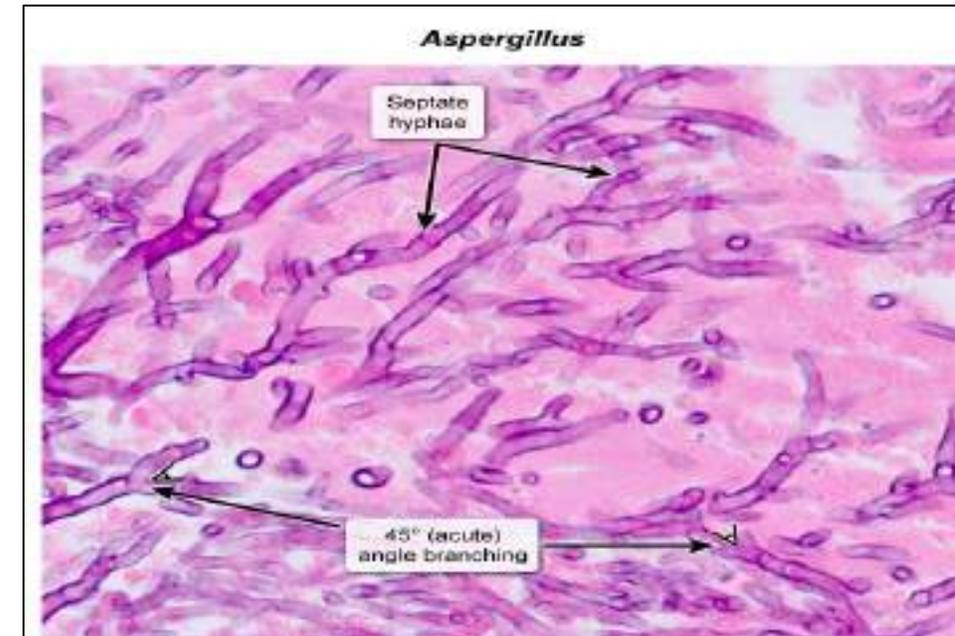
Opportunistic Fungi - Aspergillosis

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

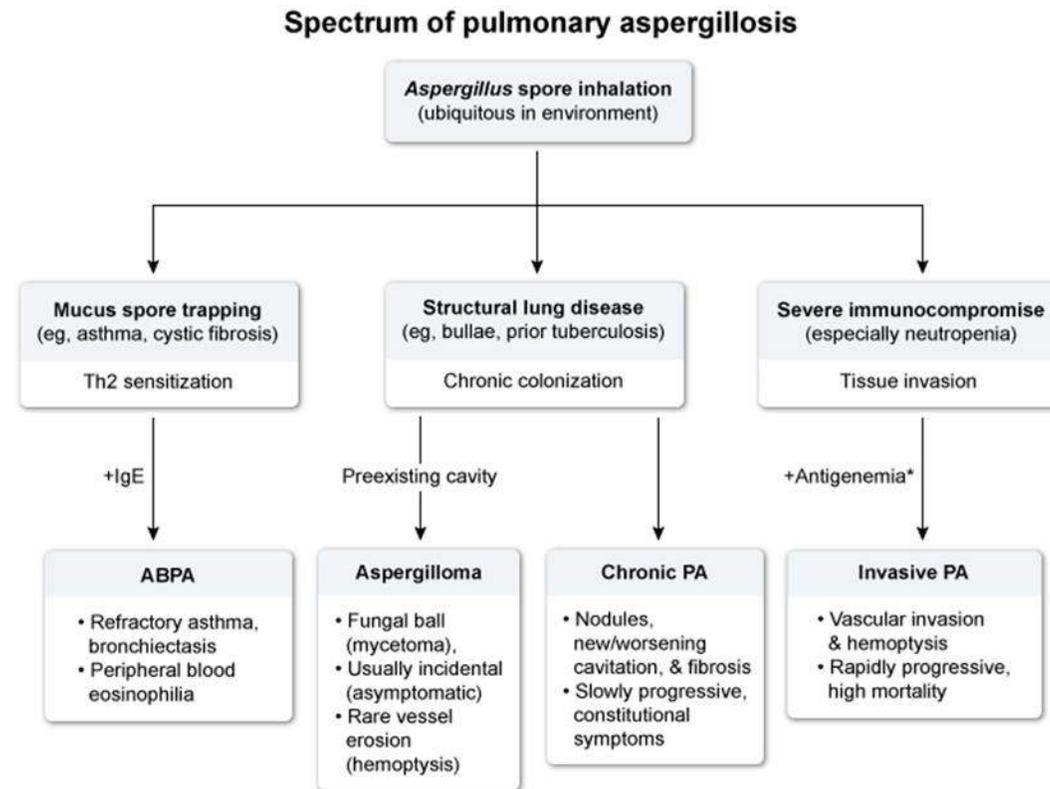
- **Invasive aspergillosis:**

- Voriconazole as first-line therapy
- Alternatives: Amphotericin B, isavuconazole, or posaconazole. Duration: at least 6-12 weeks, often longer



Opportunistic Fungi - Aspergillosis

Summary



*Circulating fungal antigens (eg, galactomannan, beta-D-glucan)
ABPA = allergic bronchopulmonary aspergillosis; PA = pulmonary aspergillosis.



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

