

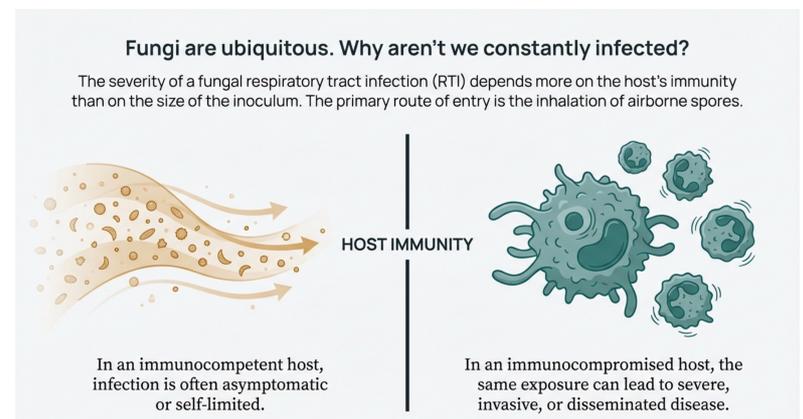
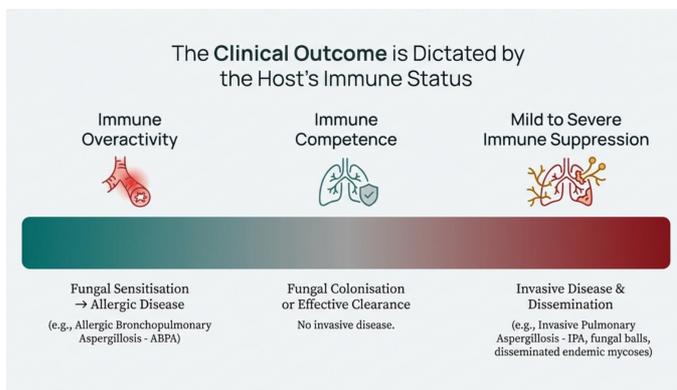
Microbiology lecture 6

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Fungal respiratory tract infections primarily occur through the inhalation of airborne spores. The severity of these infections is determined more by the immune status of the host than by the size of the initial inoculum.

Immunocompetent individuals often experience asymptomatic or self-limiting illness, while immunocompromised hosts are susceptible to severe, invasive, or disseminated diseases.

Clinically, these infections frequently mimic bacterial or tuberculosis pneumonia, presenting as subacute or chronic conditions that fail to respond to standard antibacterial therapies.



When to Suspect a Fungal Etiology

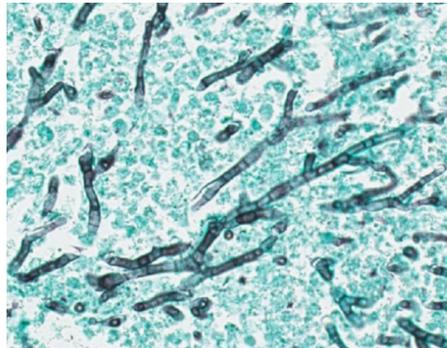
Healthcare providers should maintain a high index of suspicion in the following scenarios:

- **Host immunosuppression** such as HIV or AIDS, transplant recipients, or patients on prolonged corticosteroids or chemotherapy
- **Structural lung disease** including existing tuberculosis cavities, bronchiectasis, or COPD
- **Environmental or occupational exposure** such as contact with bird or bat droppings or work involving construction, soil, or caves
- **Clinical presentation of severe or atypical pneumonia** characterized by hypoxia out of proportion to imaging findings or diffuse interstitial patterns & poor response to antibiotics.

Aspergillus (Ubiquitous Environmental Mold)

Morphology

A filamentous mold with septate hyphae featuring acute angle 45 degree branching and a classic V-shaped appearance. It reproduces via airborne asexual spores called conidia.



Important Species

Aspergillus fumigatus is the most common and pathogenic species. Aspergillus flavus produces aflatoxin and is associated with invasive disease. Aspergillus niger is commonly linked to colonization and otomycosis.

Pathogenesis

In healthy individuals, alveolar macrophages and neutrophils kill inhaled conidia. In immunocompromised patients, such as those with neutropenia or on steroids, conidia germinate into hyphae that invade lung tissue and blood vessels. This angioinvasion causes thrombosis, infarction, hemorrhage, and dissemination to organs such as the brain, kidneys, and heart.

Disease Types

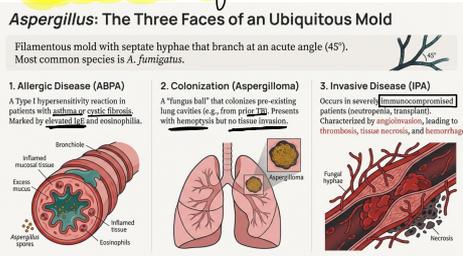
Allergic bronchopulmonary aspergillosis is a type I hypersensitivity reaction seen in patients with asthma or cystic fibrosis and is characterized by very high IgE levels and eosinophilia.

Aspergilloma, also known as a fungus ball, results from colonization of preexisting lung cavities caused by tuberculosis, sarcoidosis, or abscesses. It commonly presents with hemoptysis without tissue invasion.

Invasive pulmonary aspergillosis is a severe infection in profoundly immunosuppressed patients and involves tissue necrosis and hematogenous spread.



So important figure ↓



Diagnosis

Diagnosis includes detection of galactomannan antigen in serum or bronchoalveolar lavage, microscopy showing septate hyphae with 45 degree branching, and CT findings such as the halo sign in early disease or the air crescent sign in late disease.

Aspergillus

- Antigen Test:** Galactomannan antigen (serum or BAL).
- Microscopy:** 45° angle septate hyphae.
- Imaging:** CT scan showing a 'halo sign' (early) or 'air crescent sign' (late).

Treatment

Voriconazole is the first-line treatment. Alternatives include amphotericin B or echinocandins. Surgical resection may be required in resistant or localized cases.

Pathogen	First-Line Therapy	Maintenance / Severe Disease
Aspergillus	Voriconazole	Alternatives: Amphotericin B, echinocandins
Histoplasma	Mild: Itraconazole	Severe: Amphotericin B, followed by itraconazole
Cryptococcus	Induction: Amphotericin B + Flucytosine	Maintenance: Fluconazole
Pneumocystis	Trimethoprim-sulfamethoxazole (TMP-SMX)	Adjunctive steroids for severe hypoxemia

The Threat of Resistance

- Aspergillus: Increasing azole resistance due to environmental fungicide use.
- Cryptococcus: Emerging fluconazole resistance in some regions.
- Pneumocystis: TMP-SMX resistance is rare but documented.

Prevention

Prophylaxis with posaconazole or voriconazole is recommended for high-risk patients, along with avoidance of construction areas. Resistance to azole antifungals is increasing due to environmental fungicide use.

Histoplasma capsulatum (Endemic Dimorphic Fungus)

Nature

A dimorphic fungus that exists as mold in the environment and as yeast in the host. It is commonly associated with bird and bat droppings.

Pathogenesis

Histoplasma survives intracellularly within macrophages in a manner similar to tuberculosis, leading to granuloma formation and calcified nodules.

Clinical Forms

Most infections are asymptomatic or present as mild flu-like illness. Exposure to a high inoculum can cause acute pneumonia. Chronic cavitary pulmonary disease may develop in patients with COPD.

Diagnosis

Diagnosis relies on highly sensitive antigen detection tests in urine or serum and biopsy showing yeasts inside macrophages. Culture is slow but definitive.

↪ Histoplasma antigen

Treatment

Itraconazole is used for mild to moderate disease. (Severe) cases require amphotericin B followed by itraconazole maintenance therapy.

Prevention

Prevention involves reducing exposure to bird and bat droppings in endemic regions.

Histoplasma



• **Antigen Test:** *Histoplasma* antigen (urine or serum) is highly sensitive.

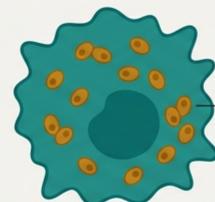


• **Microscopy:** Biopsy shows yeasts inside macrophages.

Histoplasma capsulatum: The Great Imitator

Key Characteristics

- **Classification:** Dimorphic, endemic fungus.
- **Source:** Associated with soil enriched with bird and bat droppings.
- **Pathogenesis:** Spores are inhaled and transform into yeast in the lungs. The yeast survives and replicates intracellularly within macrophages, leading to granuloma formation that can later calcify, mimicking TB.



Yeast cells within macrophage (pathogenic stage)

Clinical Spectrum

- Varies with inoculum size and host immunity, from asymptomatic/mild flu-like illness (most common) to acute pulmonary disease or chronic cavitary disease (in patients with COPD).



Endemic Regions



Histoplasma

The endemic, TB-mimicking fungus that evades destruction by hiding within the host's own macrophages.

Cryptococcus neoformans (Encapsulated Yeast)

Morphology

An encapsulated yeast with a thick polysaccharide capsule that provides strong anti phagocytic properties.

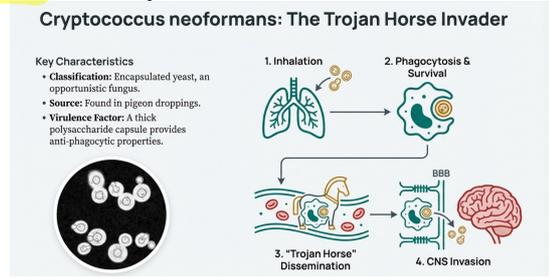
Exposure

It is commonly found in pigeon droppings.

Pathogenesis

Inhalation leads to pulmonary infection presenting as nodules or infiltrates.

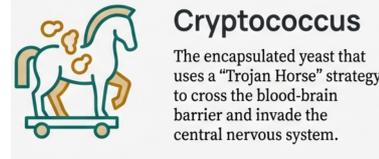
The organism frequently spreads hematogenously and has a strong tendency to involve the central nervous system, causing meningoencephalitis, especially in immunosuppressed patients.



Diagnosis

Diagnosis is made using India ink staining or cryptococcal antigen testing.

CSF: encapsulated yeast Very sensitive



Treatment

Initial induction therapy consists of amphotericin B combined with flucytosine, followed by maintenance therapy with fluconazole.

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Prevention

Prevention includes controlling pigeon exposure and performing antigen screening in high risk AIDS patients. Resistance to fluconazole has been reported in some regions.

Pneumocystis jirovecii (Atypical Fungus)

Nature

An atypical fungus that causes severe interstitial pneumonia.

Clinical Impact

It is a classic opportunistic infection in patients with AIDS and advanced immunosuppression.

↳ CD4 < 200

Diagnosis

+ PCR + BAL fluid

Diagnosis is made by microscopic identification using Grocott methenamine silver stain on bronchoalveolar lavage specimens.

↳ CXR: ground-glass opacities.

Pneumocystis jirovecii: The Quintessential Opportunistic Pneumonia

Key Characteristics

- **Classification:** Atypical fungus, previously classified as a protozoan. It cannot be cultured in the lab.
- **Target Population:** Primarily affects individuals with advanced immunosuppression, classic in AIDS patients with a CD4 count < 200.

Pathogenesis & Clinical Picture

- Inhaled ascospores attach to alveolar walls.
- Multiplication within the alveoli impairs gas exchange, leading to severe interstitial pneumonia.
- A key clinical sign is hypoxia that is often out of proportion to chest imaging findings.

Pneumocystis jirovecii in pulmonary alveoli

Alveolar wall, Type 2 pneumocyte, Gas exchange surface, Capillary, Grocott methenamine silver (GMS) stain

Pneumocystis

- **Microscopy:** Direct visualization in BAL fluid using Grocott methenamine silver (GMS) stain or direct fluorescent antibody (DFA).

Treatment

↳ TMP-SMX

Trimethoprim sulfamethoxazole is the first-line therapy. Corticosteroids are added in cases of severe hypoxemia. Alternatives include pentamidine or atovaquone.

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Prevention

Prophylaxis with trimethoprim sulfamethoxazole is required in AIDS patients when CD4 counts fall below 200.

Pneumocystis

The atypical fungus that causes life-threatening interstitial pneumonia when the host's T-cell defenses collapse.