Systemic Mycosis

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Course: Medical Mycology

Summer School

W. 3

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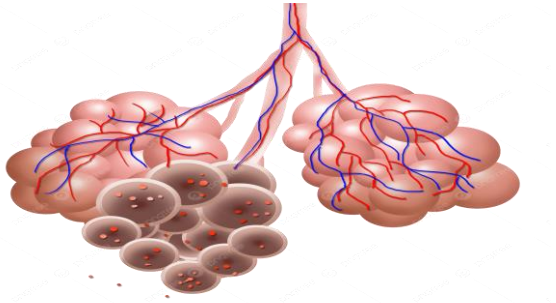
Systemic Fungal Infection?

- **Definition:** Infections that do not remain superficial (like ringworm) but invade deep tissue, enter the vascular system, and spread throughout the body.
- **The Common Entrance:** Inhalation of airborne fungal spores/conidia into the pulmonary alveoli.
- **The Host Factor:** Why immunity matters—normal hosts contain the infection (granulomas or mild symptoms), while immunocompromised hosts suffer severe dissemination (meningitis, invasive pulmonary disease).



pulmonary alveoli

ringworm

Target Organs of Systemic Mycoses

- **Pulmonary System:** Primary site for all three (cough, pneumonia, lung balls/cavities).
- **Central Nervous System (CNS):** Major target for *Cryptococcus* (Meningitis).
- **Reticuloendothelial System (e.g. Macrophage):** Major target for *Histoplasma* (Liver, Spleen, Lymph nodes).
- **Vascular System / Angioinvasion:** Major feature of *Aspergillus* (Thrombosis, Tissue Infarction).

Angioinvasion: Are aggressive molds and yeasts that grow into and destroy blood vessel walls,

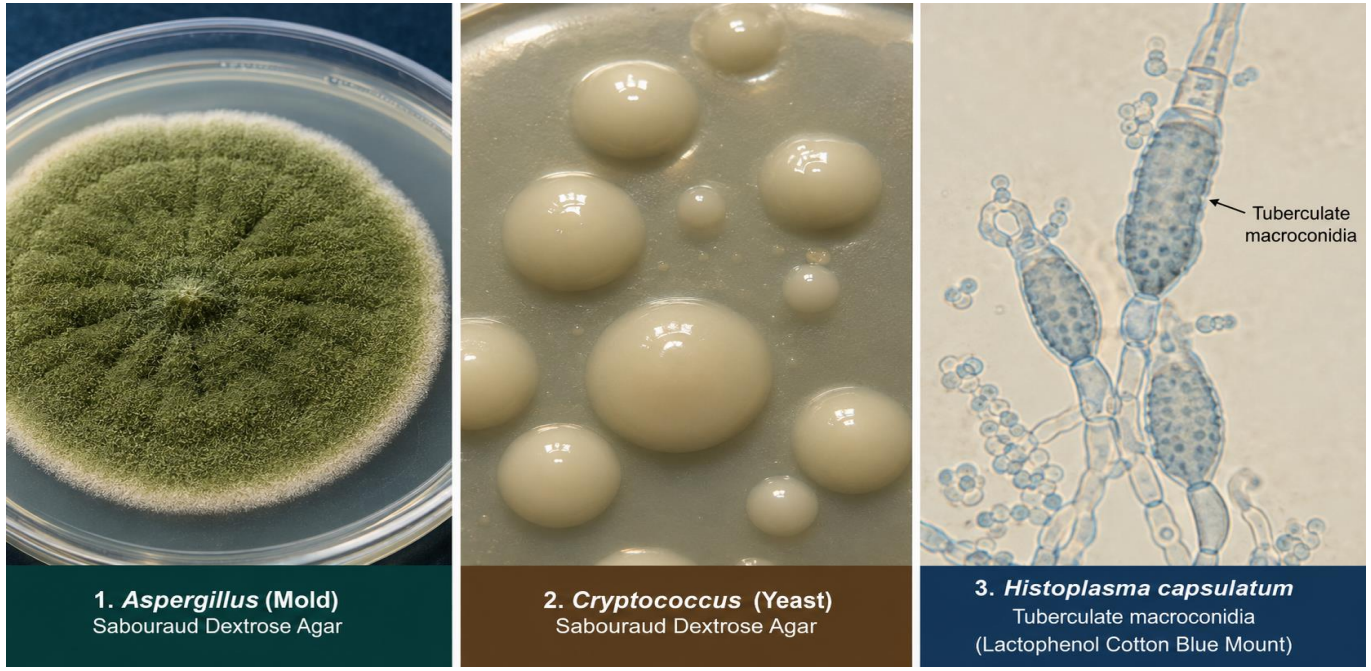
What is the deference between monomorphic and dimorphic fungi?

The Three Fungal Categories

Monomorphic Mold: *Aspergillus* spp. (Grows only as a mold in nature and in tissue).

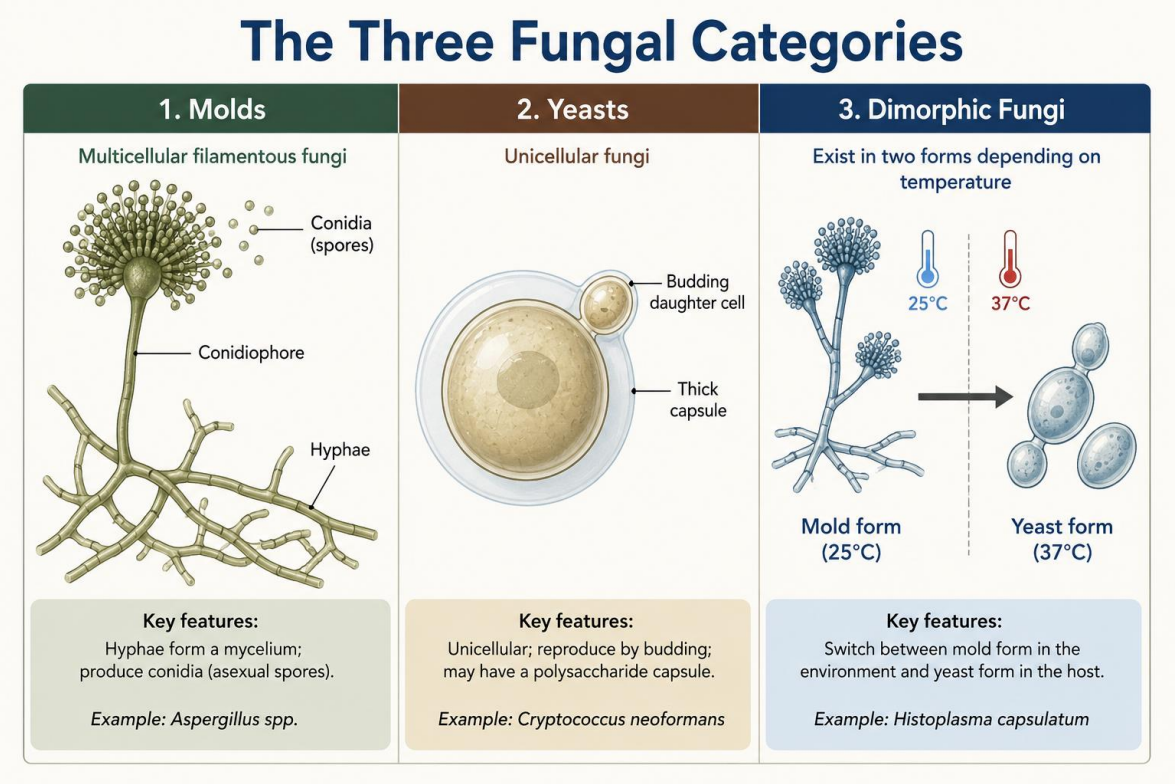
Encapsulated Yeast: *Cryptococcus neoformans* (Grows only as a budding yeast surrounded by a thick capsule).

Thermal Dimorphic Fungus: *Histoplasma capsulatum* ("Mold in the cold, Yeast in the heat").



Where Do Patients Catch Them? (Environmental Sources)

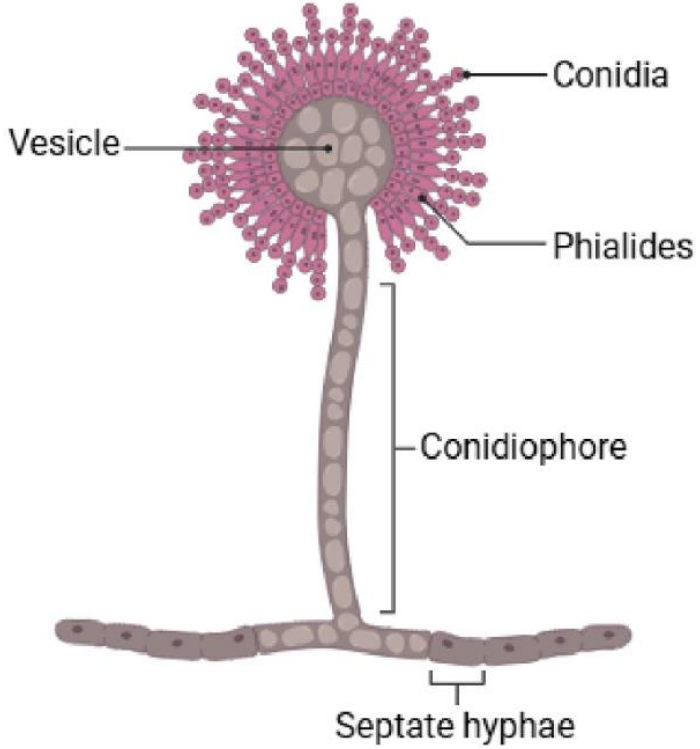
- ***Aspergillus*:** Ubiquitous in soil, air, dust, and decaying vegetation.
- ***Cryptococcus*:** Soil enriched with **pigeon excreta** (birds host the yeast but do not get sick).
- ***Histoplasma*:** Bird and bat droppings



Organism	Form in Tissue	Key Virulence Factor	Primary Clinical Presentation
Aspergillus spp.	Septate hyphae (45° branching)	Proteases, Toxins (Aflatoxin)	ABPA, Aspergilloma, Invasive Disease
C. neoformans	Encapsulated yeast	Thick Polysaccharide Capsule	Cryptococcal Meningitis (CNS)
H. capsulatum	Small intracellular yeast	Intracellular survival in macrophages	Granulomatous lung disease (TB mimic)

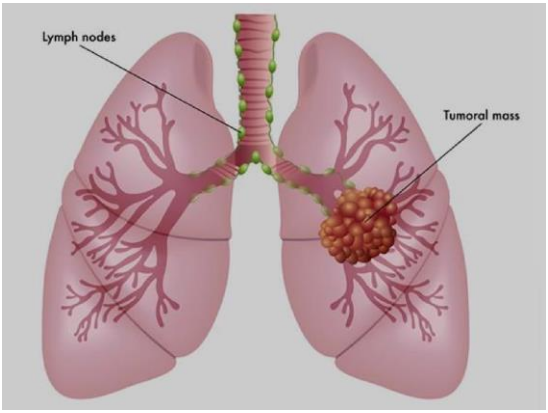
1- Aspergillus Morphology & Microscopic

- **Hyphae: Septate hyphae**.
- **Conidiophores:** Flask-shaped vesicles producing chains of conidia (spores).
- **Key Concept:** Inhalation of airborne conidia is the main route of exposure.



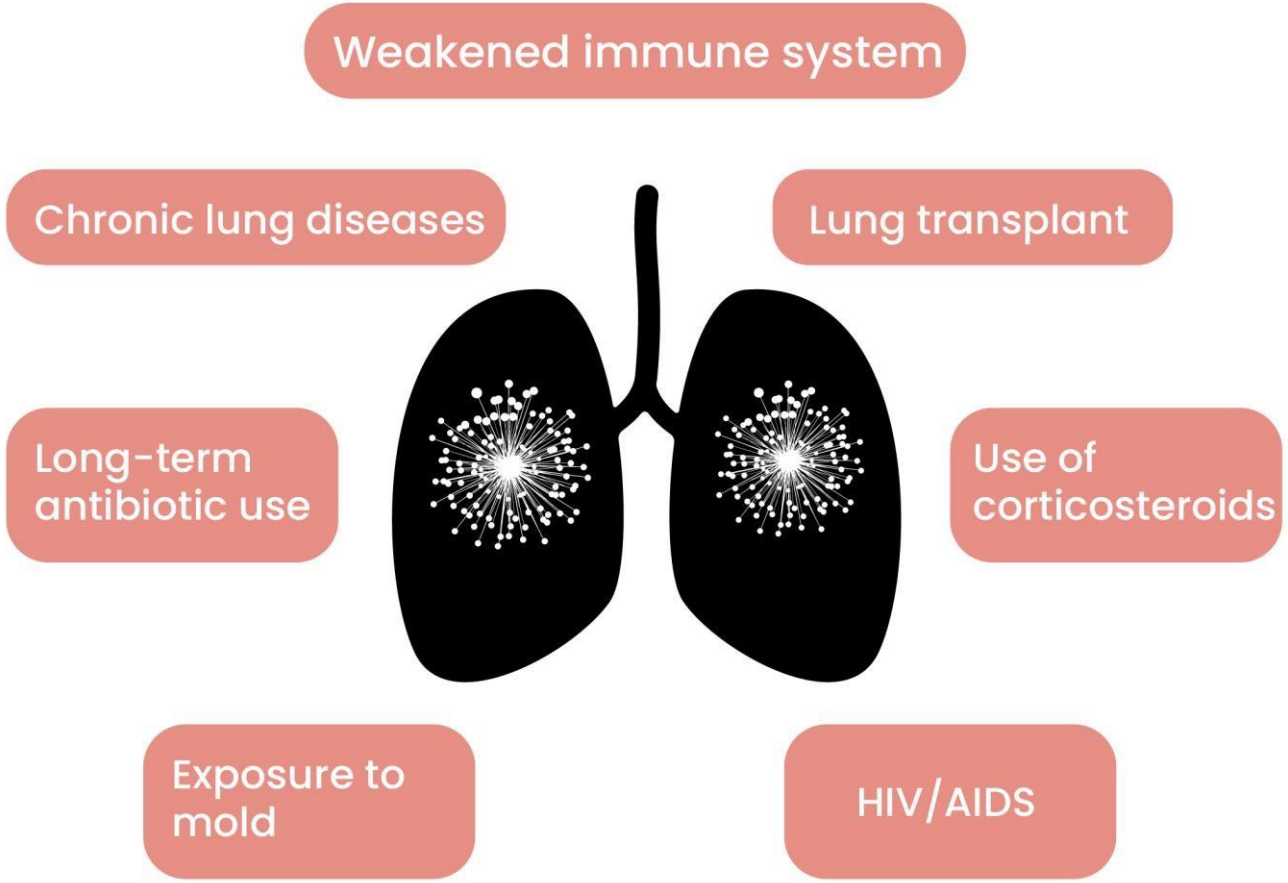
The Clinical Spectrum of Aspergillosis (Disease)

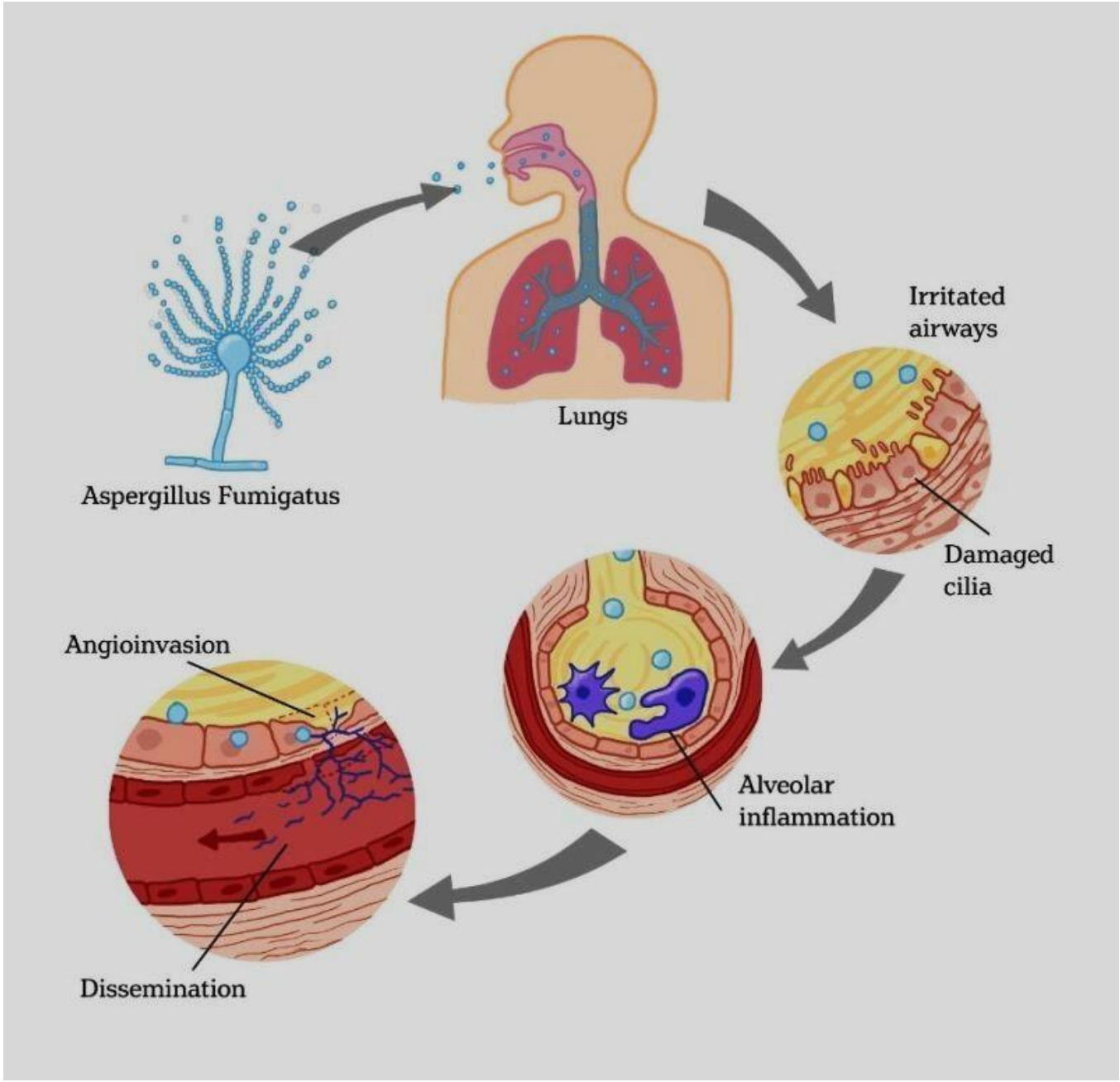
- **Allergic Bronchopulmonary Aspergillosis (ABPA):** Hypersensitivity response in patients with asthma or cystic fibrosis.
- **Aspergilloma (Fungal Ball):** Non-invasive fungal mass colonizing a pre-existing lung cavity
- **Invasive Aspergillosis:** Severe angioinvasive infection in severely



Fungal Ball

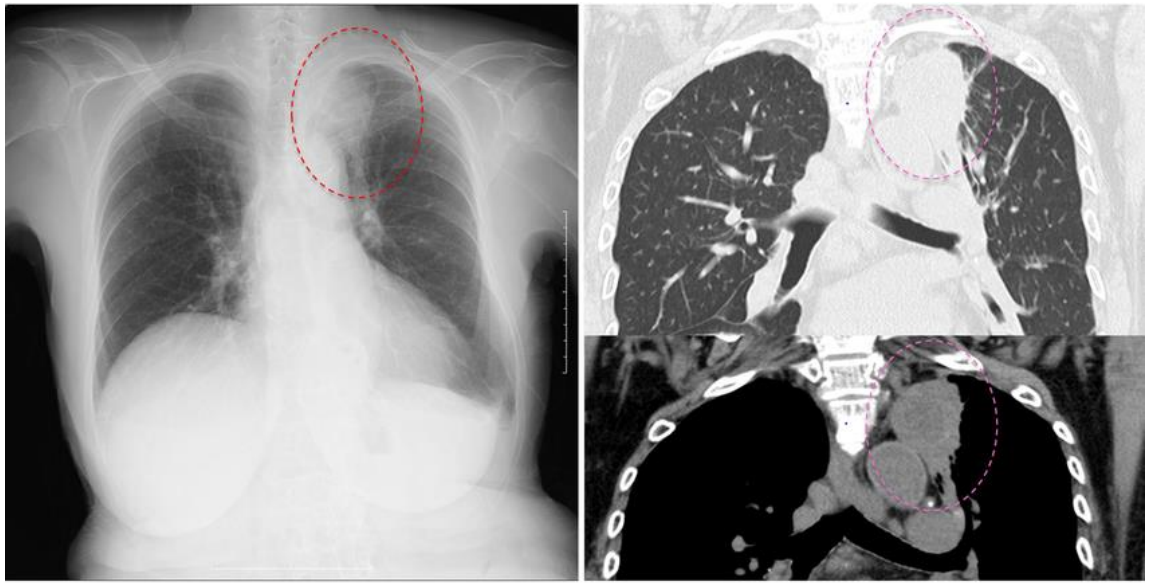
Aspergillosis risk factors




Aspergillus Fumigatus
Lungs
Irritated airways
Damaged cilia
Alveolar inflammation
Angioinvasion
Dissemination

Visualizing Aspergillosis (Chest X-Rays & CT)

- **Aspergilloma:** Shows a round mass inside a cavity with a crescent of air around it.
- **Invasive Aspergillosis:** Shows lung nodules surrounded by ground-glass opacity indicating tissue infarction and hemorrhage.



Chest X-ray

Chest CT

Main Aspergillus species

A- Aspergillus fumigatus

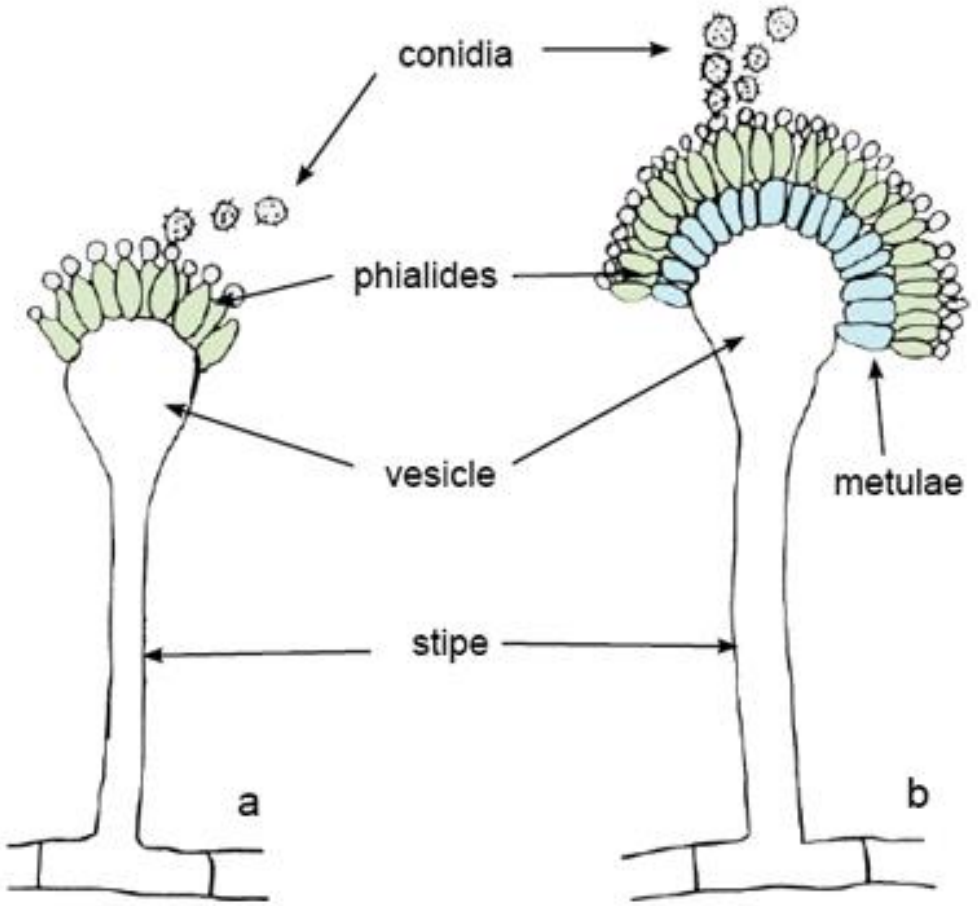
- Most common species causing clinical infections.
- Responsible for the vast majority of invasive aspergillosis cases in hospital settings.
- Colony morphology: Greenish-gray or blue-green velvety growth on agar.

B- Aspergillus flavus

- Notorious for contaminating stored grains, corn, and peanuts.
- Produces **Aflatoxin B1**: A potent toxin and natural carcinogen linked to hepatocellular carcinoma (liver cancer).

C-Aspergillus niger

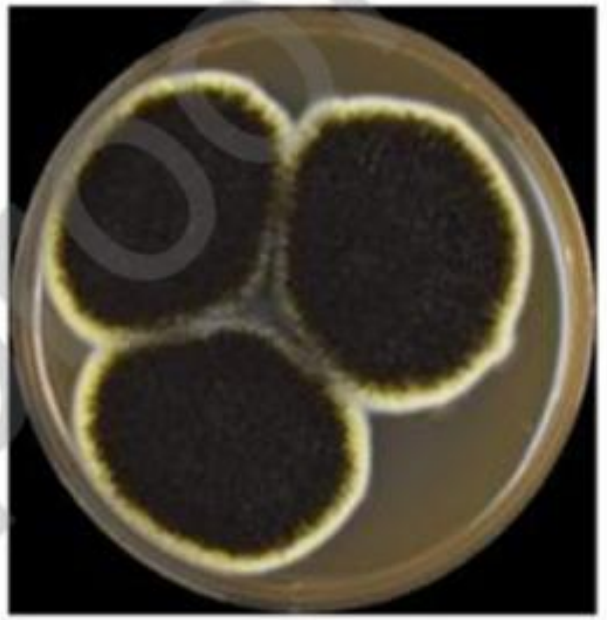
- Causes **Otomycosis**: Fungal ear infection causing intense itching, pain, and black debris/discharge.



Conidial head morphology in *Aspergillus* (a) uniseriate, (b) biseriate.

Aspergillus fumigatus

Aspergillus flavus



Aspergillus niger

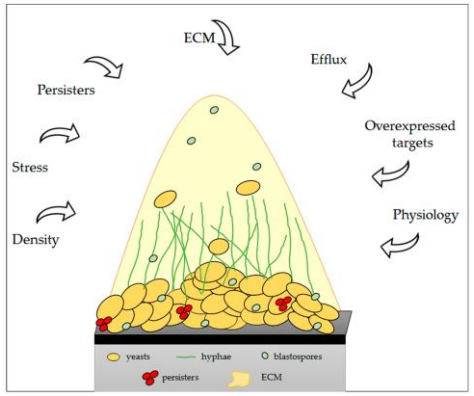
Cryptococcus neoformans

Morphological Features of *Cryptococcus*

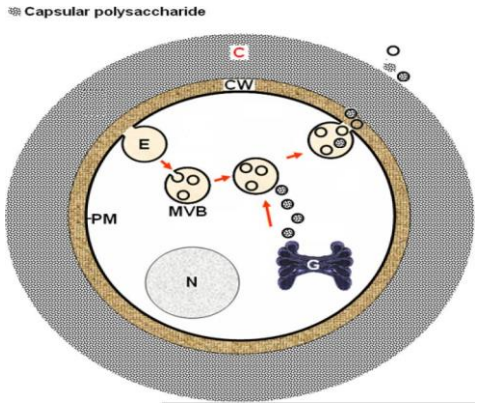
- Encapsulated, oval-to-round yeast.
- Displays **narrow-based budding** (Unlike *Blastomyces*, which forms broad-based buds).
- **Non-dimorphic:** Remains a yeast at both room temperature (25°C) and body temperature (37°C).

Virulence Factors of *Cryptococcus*

1. **Polysaccharide Capsule:** Blocks phagocytosis and hides the yeast from immune surveillance.
2. **Melanin Production:** Protects the organism against oxidative damage inside host tissues.
3. **Biofilm Formation:** Protects fungal colonies from antimicrobial penetration.



Biofilm



Capsule

Clinical Presentation

- **Pulmonary Cryptococcosis:** Mild cough or chest pain following spore inhalation.
- **Cryptococcal Meningitis:** Organism disseminates via the bloodstream to the central nervous system (CNS).
- **Symptoms:** Subacute headache, fever, neck stiffness, photophobia, and altered mental state.
- **High-Risk Patient:** Advanced HIV/AIDS.

Histoplasma capsulatum

Thermal Dimorphism Explained

- **At Environment (**25°C**):** Grows as a mold with tuberculate macroconidia (spiky wheel shape).
- **At Body Temp (**37°C**):** Transforms into a tiny, oval budding yeast (2—4 μm).

Pathogenesis & Intracellular Survival

- **Survival Strategy:** Prevents phagolysosome acidification and replicates *inside* macrophages, traveling throughout the lymphatic system.

Clinical Manifestations

- **Primary Pulmonary:** Asymptomatic or self-limiting flu-like illness; leaves calcified pulmonary nodules/granulomas on X-ray (frequently mimics Tuberculosis).
- **Severe Disseminated Histoplasmosis:** Occurs in immunocompromised patients; causes fever, weight loss, hepatosplenomegaly, and oral ulcers.

1. Enumerate three (3) major systemic fungal pathogens covered in this topic.
2. Enumerate four (4) distinct clinical manifestations caused by *Aspergillus* species.
3. Enumerate three (3) primary virulence factors of *Cryptococcus neoformans*.
4. Enumerate two (2) specific environmental reservoirs high in organic nitrogen associated with systemic fungi.
5. Enumerate three (3) hallmark diagnostic or microscopic features of *Histoplasma capsulatum*.

Which fungal pathogen is classified as a monomorphic mold that grows exclusively as hyphae in both environmental conditions and host tissue?
a) *Histoplasma capsulatum*
b) *Cryptococcus neoformans*
c) *Aspergillus spp.*
d) *Candida albicans*

A patient presenting with intense ear itching, pain, and black discharge in the external auditory canal is most likely infected with which organism?
a) *Aspergillus niger*
b) *Aspergillus fumigatus*
c) *Cryptococcus neoformans*
d) *Histoplasma capsulatum*

What is the primary route of entry for systemic fungal pathogens into the human body?
a) Direct skin inoculation
b) Ingestion of contaminated food
c) Inhalation of airborne fungal spores into pulmonary alveoli
d) Person-to-person respiratory droplets

Which species of *Aspergillus* produces Aflatoxin B1, a potent toxin strongly associated with hepatocellular carcinoma?
a) *Aspergillus fumigatus*
b) *Aspergillus niger*
c) *Aspergillus flavus*
d) *Aspergillus terreus*

What is the main environmental source specifically associated with *Cryptococcus neoformans*?
a) Contaminated municipal water supplies
b) Decaying hardwood trees only
c) Stagnant agricultural drainage
d) Soil enriched with pigeon excreta

What is the characteristic microscopic appearance of *Aspergillus spp.* hyphae in infected host tissue?
a) Broad, non-septate, ribbon-like hyphae
b) Short, unbranched pseudohyphae with blastoconidia
c) Septate hyphae with acute-angle (45°) dichotomous branching
d) Encapsulated round yeast cells with narrow-based budding

Which virulence factor allows *Cryptococcus neoformans* to directly inhibit host cell phagocytosis?
a) Thick polysaccharide capsule
b) Tuberculate macroconidia
c) Elastase and protease enzymes
d) Aflatoxin B1 production

Histoplasma capsulatum exhibits thermal dimorphism. What is its predominant structural form inside host tissue at body temperature ($37^{\circ}C$)?
a) Multicellular septate hyphae
b) Small intracellular yeast residing inside macrophages
c) Thick-walled encapsulated extracellular yeast
d) Spiky wheel-shaped macroconidia

Which species is recognized as the leading cause of invasive hospital-acquired aspergillosis in immunocompromised hosts?
a) *Aspergillus flavus*
b) *Aspergillus niger*
c) *Aspergillus terreus*
d) *Aspergillus fumigatus*

What is the primary mechanism by which *Histoplasma capsulatum* survives and multiplies inside host immune cells?
a) Preventing phagolysosome acidification inside macrophages
b) Penetrating host red blood cells directly
c) Forming thick mucinous biofilms on alveolar walls
d) Replicating extracellularly in host blood plasma

The term **angioinvasion** describes which dangerous pathogenic event caused by aggressive fungal molds?
a) Colonization of superficial skin structures
b) Fungal growth into blood vessel walls, causing thrombosis and tissue necrosis
c) Fungal penetration into peripheral nerve sheaths
d) Invasion of alveolar lumen without vascular destruction

What diagnostic feature is produced by *Histoplasma capsulatum* when cultured at room temperature ($25^{\circ}C$)?
a) Encapsulated budding yeasts
b) Tuberculate macroconidia with spiky/wheel-like projections
c) Flask-shaped phialides with long chains of conidia
d) Pseudohyphae with terminal chlamydospores

What role does the pigment **melanin** play in the pathogenesis of *Cryptococcus neoformans*?
a) It degrades host extracellular collagen
b) It triggers allergic airway hyperresponsiveness
c) It protects the yeast from host oxidative damage
d) It allows the organism to adhere to environmental surfaces

Which environmental reservoir is classic for *Histoplasma capsulatum*?
a) Soil contaminated with bird and bat droppings
b) Stagnant standing water in air cooling units
c) Unpasteurized dairy products
d) Fresh water reservoirs and rivers

- **Explain how *Histoplasma capsulatum* evades destruction by host immune cells after phagocytosis.**
- **Identify the main virulence factor of *Cryptococcus neoformans* and list two ways it aids fungal survival.**
- **What is Aflatoxin B1, which organism produces it, and what is its primary clinical concern?**

Define

- **Systemic Mycosis**
- **Thermal Dimorphism**
- **Angioinvasion**
- **Aspergilloma (Fungal Ball)**
- **Tuberculate Macroconidia**