

# "Fungal Respiratory Infections"

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## General Characteristics of Fungi

- Non-motile heterotrophs: Obtain nutrients from other organisms.
  - Aerobic → facultative anaerobes: Grow best on Sabouraud Dextrose Agar (SDA) .
  - Saprophytic & decomposers: Feed on dead/decaying tissue → food spoilage.
  - Some parasitic: Extract nutrients from living hosts.
  - Medically important fungi: 100-150 species out of ~50,000 known species.
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## Fungal Cellular Features

- Mostly haploid; diploid only during meiosis.
- Non-vascular: No internal nutrient transport.

- Cell wall: Chitin (vs. peptidoglycan in bacteria).
- Cell membrane: Contains ergosterol → antifungal target.
- Closer to animals than plants (DNA evidence).

## Comparison: Fungi vs Bacteria

| Feature            | Fungi                                    | Bacteria                                   |
|--------------------|------------------------------------------|--------------------------------------------|
| Diameter           | ~4 $\mu\text{m}$ (e.g., <i>Candida</i> ) | ~1 $\mu\text{m}$ ( <i>Staphylococcus</i> ) |
| Nucleus            | Eukaryotic                               | Prokaryotic                                |
| Cytoplasm          | Mitochondria & ER present                | Absent                                     |
| Cell membrane      | Sterols present                          | Sterols absent (except <i>Mycoplasma</i> ) |
| Cell wall          | Chitin                                   | Peptidoglycan                              |
| Spores             | Sexual & asexual                         | Endospores (survival only)                 |
| Thermal dimorphism | Present (some)                           | Absent                                     |

|            |                        |                                                         |
|------------|------------------------|---------------------------------------------------------|
| Metabolism | Require organic carbon | Many obligate anaerobes; may not require organic carbon |
|------------|------------------------|---------------------------------------------------------|

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## Morphological Classification of Fungi

### 1. Yeasts

- Single-celled: spherical, oval, or cylindrical.
- Reproduce via budding or binary fission.

### 2. Molds

- Filamentous → hyphae → mycelium.
- Hyphae: septate (cross-walls) or non-septate.
- Spores germinate → hyphal growth.

### 3. Dimorphic Fungi

- Two forms based on temperature:
  - 37°C → Yeast
  - 25°C → Mold

Examples by Type:

| Type      | Examples                                                                                                                                           |
|-----------|----------------------------------------------------------------------------------------------------------------------------------------------------|
| Molds     | <i>Aspergillus fumigatus</i> , <i>Mucor</i> , <i>Rhizopus</i> , Dermatophytes ( <i>Trichophyton</i> , <i>Microsporum</i> , <i>Epidermophyton</i> ) |
| Yeasts    | <i>Candida albicans</i> , <i>Cryptococcus neoformans</i> / <i>gattii</i> , <i>Malassezia furfur</i> / <i>globosa</i>                               |
| Dimorphic | <i>Histoplasma capsulatum</i> , <i>Coccidioides immitis</i> , <i>Blastomyces dermatitidis</i> , <i>Sporothrix schenckii</i>                        |

## Clinical Classification of Mycoses

| Type                      | Site Affected      | Examples                                                  |
|---------------------------|--------------------|-----------------------------------------------------------|
| Superficial / Cutaneous   | Skin, hair, nails  | Dermatophytes ( <i>Tinea</i> )                            |
| Subcutaneous              | Below dermis       | Mycetoma                                                  |
| Systemic / True pathogens | Deep organs, blood | <i>Histoplasma</i>                                        |
| Opportunistic             | Immunocompromised  | <i>Candida</i> , <i>Cryptococcus</i> , <i>Aspergillus</i> |

# Important Respiratory Fungal Pathogens 🌍

## 1. True Pathogens

- Characteristics:
  - Dimorphic, geographically restricted.
  - Infection via inhalation of spores.
  - Cause granulomatous response (TB-like).
  - Can infect immunocompetent hosts.
- Examples:
  - *Histoplasma capsulatum*
  - *Coccidioides immitis*
  - *Blastomyces dermatitidis*
- Flowchart – True Pathogen Infection:

Inhalation of spores → Lung colonization →  
Granulomatous / pyogenic response → TB-like infection

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## 2. Opportunistic Pathogens

- Characteristics:

- Yeasts or molds
- Multiple routes of infection
- Mainly in immunocompromised hosts
- Variable host response; no lasting immunity
- Examples:
  - *Aspergillus*
  - Mucorales (*Mucor*, *Rhizopus*)
  - *Candida*
  - *Cryptococcus*

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## Systemic Fungal Diseases – True Pathogens

| Genus               | Form in Tissue | Geographic Location             | Clinical Findings                                                                                                  |
|---------------------|----------------|---------------------------------|--------------------------------------------------------------------------------------------------------------------|
| <i>Coccidioides</i> | Spherules      | Southwestern USA, Latin America | "Valley fever"; may disseminate → bones, meninges (esp. immunocompromised, pregnant, African Americans, Filipinos) |

|                         |                                            |                                                              |                                                                        |
|-------------------------|--------------------------------------------|--------------------------------------------------------------|------------------------------------------------------------------------|
| <i>Histoplasma</i>      | Yeasts inside macrophages 🧑                | Ohio & Mississippi River valleys; worldwide (bird/bat guano) | Cavitary lung lesions, hepatosplenomegaly, pancytopenia, tongue ulcers |
| <i>Blastomyces</i>      | Yeast with broad-based bud 🍈               | Central/Southeastern USA; Africa                             | Lung lesions, granulomas, ulcerated skin lesions                       |
| <i>Paracoccidioides</i> | Yeast with multiple buds ("pilot's wheel") | Latin America (esp. Brazil)                                  | Ulcerated facial/mouth lesions                                         |

## Histoplasmosis 🧪

- Agent: *Histoplasma capsulatum* (dimorphic)
- Transmission: Inhalation of dust contaminated with bird/bat droppings → spores (microconidia)
- Pathogenesis: Intracellular → survives in macrophages
- Histology: Non-caseating granulomas, Langhans giant cells
- Clinical Spectrum:

- Primary → self-limited pulmonary infection (often latent)
- Secondary → chronic progressive (cough, fever, night sweats)
- Disseminated → infants & immunocompromised → liver, spleen, adrenals, meninges

### Flowchart - Histoplasma Disease Progression:

Inhalation of spores (soil) → Lungs → Phagocytosis by macrophages → Intracellular multiplication → Granuloma formation → Latent / Chronic / Disseminated disease

Exam Point: True pathogens = dimorphic, infect healthy hosts, geographically restricted.

Opportunistic fungi = ubiquitous, attack immunocompromised, no lasting immunity.

# Coccidioidomycosis ("Valley Fever")

- Agent: *Coccidioides immitis* (dimorphic soil fungus)
- Transmission: Inhalation of arthrospores
- Pathogenesis:
  - Arthrospores → lungs → transform into spherules with endospores
  - Spherules rupture → release endospores → new spherules form
  - Blocks phagolysosome fusion → resists intracellular killing
  - Elicits Type IV hypersensitivity (TB-like)

Flowchart - Life Cycle & Pathogenesis:

Soil (arthrospores) → Inhalation → Lungs → Transform into spherules → Contain endospores → Rupture → Local spread / hematogenous dissemination

## Clinical Features:

- Most: asymptomatic
- 10%: Pulmonary disease → lung lesions, fever, cough, pleuritic pain ± erythema nodosum/multiforme
- <1%: Disseminated (pregnancy, dark-skinned, immunocompromised) → skin, bone, CNS

## Epidemiology:

- Endemic: Lower Sonoran life zone (arid)
- Geographic: Southwestern USA, Mexico, Central & South America

## Diagnostics:

- Histology: Large, thick-walled spherules with endospores
- Skin test: Coccidioidin (Type IV hypersensitivity)
- Stains: PAS highlights spherules

Exam Tip: "Farmer in Arizona with flu-like illness + erythema nodosum → Coccidioidomycosis" 🌵

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## Blastomycosis 🌳

Agent: *Blastomyces dermatitidis* (dimorphic soil fungus)

Transmission: Inhalation of spores

### Clinical Forms 🧪

#### 1. Pulmonary blastomycosis

- Acute, abrupt onset: productive cough, chest pain, fever, night sweats, weight loss
- Lung lesions: suppurative granulomas

#### 2. Disseminated blastomycosis

- Hematogenous spread → skin, bone, genitourinary tract

#### 3. Primary cutaneous blastomycosis (rare)

- Acquired via trauma / inoculation

### Morphology 📄

- Tissue form: round, thick-walled yeast (5-15  $\mu\text{m}$ )
- Broad-based budding → diagnostic hallmark 🧐

- Double-contoured cell wall, visible nucleus
- Habitat: humid woodlands, mid-Atlantic countryside, beaver dams, peanut farms, organic debris

Flowchart – Clinical Course:

Inhalation of spores → Pulmonary infection  
 (suppurative granulomas) → Hematogenous spread  
 → Skin / Bone / Other organs

Exam Point: "Patient from Mississippi river basin + ulcerated skin lesion + broad-based budding yeast  
 → Blastomycosis."

## Key Differentiation Table

| Feature | Coccidioidomycosis          | Blastomycosis                   |
|---------|-----------------------------|---------------------------------|
| Agent   | <i>Coccidioides immitis</i> | <i>Blastomyces dermatitidis</i> |

|                |                                                      |                                                             |
|----------------|------------------------------------------------------|-------------------------------------------------------------|
| Tissue form    | Spherules with endospores                            | Yeast with broad-based budding                              |
| Habitat        | Arid regions (SW USA, Mexico, Central/South America) | Moist soil, decaying wood (Ohio & Mississippi River basins) |
| Host reaction  | Delayed hypersensitivity; erythema nodosum           | Suppurative granulomas                                      |
| Dissemination  | Skin, bone, CNS                                      | Skin, bone, GU tract                                        |
| Risk groups    | Pregnancy, dark-skinned, immunocompromised           | Immunocompromised, outdoor exposure                         |
| Exam buzz word | "Valley fever"                                       | "Broad-based budding yeast"                                 |

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## Opportunistic Fungal Infections

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## 1. Aspergillosis

Agents: *Aspergillus fumigatus*, *A. flavus*, *A. niger* (~184 species)

Transmission: Inhalation of airborne conidia

Diseases: Pulmonary, ear, eyes, skin, meninges, sinuses, bloodstream

Special: *A. flavus* → aflatoxins → liver carcinogen

Morphology:

- Septate hyphae, acute angle (dichotomous) branching
- Colonies: black (*A. niger*)

### Pulmonary Aspergillosis – Clinical Forms

1. Allergic bronchopulmonary aspergillosis (ABPA)
  - Asthmatics / CF patients
  - IgE-mediated hypersensitivity
2. Aspergilloma (fungus ball)
  - Colonizes pre-existing lung cavities (e.g., post-TB)

- Ball-like mass on imaging
- May cause hemoptysis

### 3. Farmer's lung 🌾

- Hypersensitivity pneumonitis from inhaled spores

### 4. Invasive Aspergillosis

- Immunocompromised (bone marrow transplant)
- Rapidly progressive, often fatal
- Lung → brain, kidney, heart dissemination

### ● Flowchart – Aspergillus Infections:

Inhaled spores →

- Hypersensitivity → ABPA / Farmer's lung
- Colonization → Aspergilloma
- Invasion (immunocompromised) → Invasive aspergillosis → Dissemination

Exam Point: "Acute angle branching septate hyphae  
→ Aspergillus"

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## 2. Mucormycosis (Zygomycosis) 🧟

Agents: *Mucor*, *Rhizopus*, *Lichtheimia*, *Cunninghamella*, *Absidia*

- No yeast phase
- Transmission: inhalation of spores

Predisposing factors:

- Diabetes mellitus (ketoacidosis)
- Neutropenia
- Corticosteroid therapy
- Iron overload
- Trauma / burns

Clinical Forms:

1. Rhinocerebral mucormycosis (classic)

- Spores → paranasal sinuses → palate, orbit, sphenoid, cavernous sinus, brain
- Rapid progression → necrosis, neurological deficits

2. Pulmonary mucormycosis → pneumonia → infarction

3. Sinusitis → brain abscess

Exam Point: "Broad, non-septate hyphae with right-angle branching → Mucorales"

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### 3. Candidiasis 🍞

Agent: *Candida albicans* (most common)

Normal flora: Oral cavity (25–30%), GI tract (50%), vagina (30%)

Morphology:

- Oval yeast (2–4  $\mu\text{m}$ ), Gram-positive
- Forms pseudohyphae
- Creamy colonies, yeast smell
- Diagnostic: Germ tube test (in plasma)

Clinical Manifestations:

- Mucosal: Oral thrush, esophagitis, vulvovaginitis, GI candidiasis, peritonitis
- Cutaneous: Diaper rash, onychomycosis, folliculitis, chronic mucocutaneous candidiasis

- Disseminated: Endocarditis, septicemia, hepatosplenic candidiasis

Exam Point: "Germ tube positivity = *Candida albicans*"

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## 4. Cryptococcosis

Agents: *Cryptococcus neoformans*, *C. gattii*

Morphology: Encapsulated yeast (polysaccharide capsule)

Transmission: Inhalation from soil (bird droppings)

Clinical Features:

1. Pulmonary → often asymptomatic; may progress
2. CNS (most important) → meningitis / meningoencephalitis, cryptococcoma
3. Others → cutaneous, bone/joint, ocular, genitourinary

Laboratory Diagnosis:

- India ink → encapsulated yeast

- Latex agglutination → capsular antigen

Exam Point: "Encapsulated yeast seen with India ink → *Cryptococcus*"

## Comparison Table – Opportunistic Mycoses

| Feature         | <i>Aspergillus</i>                    | Mucorales                                 | <i>Candida</i>                    | <i>Cryptococcus</i> |
|-----------------|---------------------------------------|-------------------------------------------|-----------------------------------|---------------------|
| Morphology      | Septate hyphae, acute angle branching | Broad, non-septate, right-angle branching | Yeast + pseudohyphae, germ tube + | Encapsulated yeast  |
| Major risk      | Neutropenia, steroids                 | Diabetes ketoacidosis                     | Antibiotics, immunosuppression    | AIDS                |
| Hallmark lesion | Aspergilloma (fungus ball)            | Rhino cerebral invasion                   | Thrush, vulvovaginitis            | Meningitis          |

|                 |                         |                         |                      |                              |
|-----------------|-------------------------|-------------------------|----------------------|------------------------------|
| Diagnostic test | Histology, culture      | Histology, culture      | Germ tube test       | India ink, antigen detection |
| Exam buzzword   | "Acute angle branching" | "Right-angle branching" | "Germ tube positive" | "Encapsulated yeast"         |