

Fungal Infections in the Hospital

Overview of Fungal Infections in the Hospital

Fungal infections in the hospital setting are a significant concern, often presenting as opportunistic infections in immunocompromised patients or as nosocomial infections due to invasive procedures. These infections can range from superficial (e.g., mucocutaneous candidiasis) to life-threatening (e.g., invasive aspergillosis, cryptococcal meningitis). Hospitalists play a critical role in early recognition, diagnosis, and management, often in collaboration with infectious disease (ID) specialists. This guide provides a comprehensive overview of fungal infections in the hospital, including the types, at-risk patient populations, clinical presentation, diagnostic approaches, labs, complications, additional tests (e.g., retinal exam, TEE), treatment strategies, the role of ID involvement, and includes tables and clinical scenarios for practical application. Note that while funguria is mentioned, its treatment is not detailed as per the request.

Types of Fungal Infections, At-Risk Patient Populations, and Complications

Candida Infections:

- **Types:**
 - **Candidemia:** Bloodstream infection, often catheter-related.
 - **Invasive Candidiasis:** Deep organ involvement (e.g., endocarditis, peritonitis, endophthalmitis).
 - **Mucocutaneous Candidiasis:** Oropharyngeal, esophageal, or vaginal infections.
 - **Funguria:** Candida in urine, often asymptomatic (not treated unless symptomatic or high-risk, e.g., pre-urologic surgery).
- **At-Risk Patients:**
 - ICU patients (prolonged stay, central lines, TPN).
 - Immunosuppressed (e.g., chemotherapy, transplant recipients, HIV/AIDS).
 - Broad-spectrum antibiotic use, diabetes, recent surgery (especially abdominal).
- **Complications:**
 - **Candidemia:** Septic shock, multi-organ failure, mortality 30-40%.
 - **Invasive Candidiasis:** Endocarditis (new murmur, heart failure), endophthalmitis (vision loss, retinal lesions), osteomyelitis, abscesses.

- **Mucocutaneous:** Esophageal perforation (rare, if untreated), malnutrition (dysphagia).
- **Funguria:** Ascending infection (pyelonephritis, renal abscess) in high-risk patients (e.g., neutropenic, urologic obstruction).

Aspergillus Infections:

- **Types:**
 - **Invasive Aspergillosis (IA):** Lungs (most common), sinuses, CNS.
 - **Allergic Bronchopulmonary Aspergillosis (ABPA):** Hypersensitivity reaction, common in asthma/CF.
 - **Aspergilloma:** Fungal ball in pre-existing lung cavity.
- **At-Risk Patients:**
 - Neutropenic patients (e.g., leukemia, post-chemotherapy).
 - Solid organ or stem cell transplant recipients.
 - Chronic lung disease (e.g., COPD, TB cavities), prolonged steroid use.
- **Complications:**
 - **IA:** Massive hemoptysis, respiratory failure, dissemination (CNS, brain abscess, meningitis), vascular invasion (infarction, mortality 50-90%).
 - **ABPA:** Bronchiectasis, chronic respiratory failure, pulmonary fibrosis.
 - **Aspergilloma:** Massive hemoptysis (can be fatal), chronic cough, aspergilloma rupture into pleural space (empyema).

Cryptococcal Infections:

- **Types:**
 - **Cryptococcal Meningitis:** CNS infection, most common presentation.
 - **Pulmonary Cryptococcosis:** Lung nodules or infiltrates.
 - **Disseminated Cryptococcosis:** Multi-organ involvement (e.g., skin, bones).
- **At-Risk Patients:**
 - Advanced HIV/AIDS (CD4 <100 cells/μL).
 - Transplant recipients, chronic steroid use, cirrhosis.
- **Complications:**
 - **Meningitis:** Elevated intracranial pressure (ICP, risk of herniation), seizures, coma, vision/hearing loss, mortality 20-30% if untreated.
 - **Pulmonary:** Cavitation, pleural effusion, respiratory failure.
 - **Disseminated:** Sepsis, multi-organ failure, skin necrosis (lesions).

Mucormycosis:

- **Types:**
 - **Rhinocerebral Mucormycosis:** Sinus, brain involvement.

- **Pulmonary Mucormycosis:** Lung infiltrates, cavitation.
- **Cutaneous Mucormycosis:** Skin necrosis post-trauma.
- **At-Risk Patients:**
 - Uncontrolled diabetes (especially DKA).
 - Hematologic malignancies, neutropenia, transplant recipients.
 - Iron overload (e.g., deferoxamine therapy).
- **Complications:**
 - **Rhinocerebral:** Orbital necrosis, blindness, brain abscess, cranial nerve palsies, mortality 50-70%.
 - **Pulmonary:** Massive hemoptysis, respiratory failure, vascular invasion (pulmonary infarction).
 - **Cutaneous:** Extensive tissue necrosis, amputation, systemic spread (sepsis).

Pneumocystis Pneumonia (PCP):

- **Types:** Opportunistic pneumonia caused by *Pneumocystis jirovecii*.
- **At-Risk Patients:**
 - HIV/AIDS (CD4 <200 cells/μL).
 - Transplant recipients, cancer patients on chemotherapy, chronic steroids.
- **Complications:**
 - Acute respiratory failure (ARDS), pneumothorax (barotrauma), mortality 10-20% if untreated.
 - Immune Reconstitution Inflammatory Syndrome (IRIS) in HIV (worsening symptoms after ART initiation).

Clinical Presentation

Candida Infections:

- **Candidemia:** Fever (unresponsive to antibiotics), chills, hypotension, multi-organ failure (if disseminated).
- **Invasive Candidiasis:** Organ-specific symptoms (e.g., endocarditis: new murmur, heart failure; endophthalmitis: blurred vision, floaters; peritonitis: abdominal pain).
- **Mucocutaneous:** White plaques (oral), dysphagia (esophageal), vaginal discharge/itching.
- **Funguria:** Often asymptomatic, may present with dysuria, hematuria (if symptomatic).

Aspergillus Infections:

- **Invasive Aspergillosis:** Fever, cough, hemoptysis, chest pain, respiratory failure, sinus pain/discharge (sinusitis), seizures (CNS).
- **ABPA:** Wheezing, cough, brown sputum plugs, asthma exacerbations.
- **Aspergilloma:** Hemoptysis, cough, often asymptomatic.

Cryptococcal Infections:

- **Cryptococcal Meningitis:** Headache, fever, neck stiffness, confusion, photophobia, seizures, vision/hearing changes.
- **Pulmonary Cryptococcosis:** Cough, dyspnea, fever, nodules on CXR.
- **Disseminated:** Fever, weight loss, skin lesions (papules, ulcers).

Mucormycosis:

- **Rhinocerebral:** Sinus pain, nasal discharge (black, bloody), facial swelling, vision loss, cranial nerve deficits.
- **Pulmonary:** Fever, cough, hemoptysis, cavitation on imaging.
- **Cutaneous:** Necrotic, black eschar, rapidly progressing erythema.

Pneumocystis Pneumonia (PCP):

- **Presentation:** Progressive dyspnea, dry cough, fever, hypoxia (SpO2 <90%), bilateral infiltrates on CXR.

Diagnostic Approach

History and Exam:

- **History:** Risk factors (e.g., HIV, transplant, steroids), recent antibiotics, ICU stay, fever pattern, organ-specific symptoms.
- **Exam:**
 - **Candida:** Oral thrush, vaginal erythema, central line site erythema, retinal exam (white fluffy lesions in endophthalmitis).
 - **Aspergillus:** Sinus tenderness, lung crackles, hemoptysis.
 - **Cryptococcus:** Neck stiffness, papilledema (meningitis), skin lesions, fundoscopic exam (papilledema, optic atrophy).
 - **Mucormycosis:** Black eschar (skin/nasal), facial swelling, cranial nerve deficits, orbital exam (proptosis, vision loss).
 - **PCP:** Hypoxia, lung crackles, fever.

- **Labs:**

- **CBC:** Leukocytosis (infection), neutropenia (risk factor), eosinophilia (ABPA).
- **CMP:** Cr (AKI in systemic infection), glucose (DKA in mucormycosis), LFTs (drug toxicity).
- **Blood Cultures:** Positive in candidemia, negative in most other fungal infections.
- **Beta-D-Glucan:** Non-specific marker, positive (>80 pg/mL) in Candida, Aspergillus, PCP.
- **Galactomannan:** Positive (>0.5) in invasive aspergillosis (serum, BAL).
- **Cryptococcal Antigen:** High in CSF/serum for cryptococcal meningitis (>1:8 titer).
- **HIV Testing:** CD4 count if unknown status (e.g., PCP, cryptococcosis).
- **CSF Analysis (Meningitis):** Low glucose, high protein, lymphocytes (cryptococcus, TB).
- **Sputum/BAL Culture:** Grows Aspergillus, Mucorales, Pneumocystis (PCR for PCP).

Imaging:

- **CXR/CT Chest:**

- **Aspergillus:** Halo sign (IA), tree-in-bud (ABPA), fungal ball (aspergilloma).
- **PCP:** Bilateral ground-glass opacities.
- **Mucormycosis:** Cavitation, reverse halo sign.
- **CT Sinus/Brain:** Rhinocerebral mucormycosis (sinus opacification, bone destruction).
- **MRI Brain:** Cryptococcal meningitis (meningeal enhancement, cryptococcomas).

Additional Diagnostic Tests:

- **Candida:**

- **Retinal Exam:** For endophthalmitis (white fluffy lesions, hemorrhages).
- **TEE (Transesophageal Echo):** For endocarditis (vegetations on valves, e.g., mitral/tricuspid).
- **CT Abdomen:** For intra-abdominal candidiasis (abscesses, peritonitis).

- **Aspergillus:**

- **Bronchoscopy with BAL:** Gomori methenamine silver stain, culture for Aspergillus.
- **CT Sinus/Brain:** For sino-orbital or CNS aspergillosis (fungal invasion, abscesses).
- **Biopsy:** Tissue culture/histology (septate, branching hyphae at 45° angles).

- **Cryptococcus:**
 - **Fundoscopy Exam:** For papilledema, optic atrophy (elevated ICP).
 - **Skin Biopsy:** If lesions present (granulomas with yeast forms).
 - **Lumbar Puncture (LP):** Serial LPs to monitor ICP, CSF culture.
 - **Mucormycosis:**
 - **Biopsy:** Tissue culture/histology (broad, non-septate hyphae at 90° angles).
 - **CT/MRI Sinus/Brain/Orbit:** For extent of invasion (bone destruction, orbital involvement).
 - **Endoscopy:** Nasal/sinus endoscopy for black necrotic tissue.
- **PCP:**
 - **Bronchoscopy with BAL:** Gomori methenamine silver stain, PCP PCR.
 - **CT Chest:** High-resolution for ground-glass opacities.
 - **ABG:** Assess hypoxemia (PaO₂ <70 mmHg indicates steroid use).

Treatment Strategies

General Principles:

- **Antifungal Therapy:** Start empirically if high suspicion, adjust based on culture/susceptibility.
- **Source Control:** Remove infected lines (candidemia), debride necrotic tissue (mucormycosis).
- **Supportive Care:** ICU for severe cases (e.g., sepsis, respiratory failure), fluids, oxygen.

Specific Treatments:

- Candida Infections:
 - Candidemia/Invasive Candidiasis:
 - Empiric: Echinocandin (caspofungin 70 mg IV loading, then 50 mg IV daily).
 - De-escalate: Fluconazole 400 mg IV/PO daily (if susceptible, non-neutropenic).
 - Duration: 14 days after last positive culture, remove central lines.
 - Mucocutaneous: Fluconazole 150 mg PO x 1 (vaginal), 200-400 mg PO daily (esophageal).
 - Funguria: Typically not treated unless symptomatic or high-risk (e.g., neutropenic, urologic surgery); fluconazole 200 mg PO daily if needed.

- Aspergillus Infections:
 - Invasive Aspergillosis:
 - First-Line: Voriconazole 6 mg/kg IV q12h x 1 day, then 4 mg/kg IV q12h (preferred).
 - Alternative: Isavuconazole 200 mg IV/PO q8h x 48h, then 200 mg daily.
 - Duration: Minimum 6-12 weeks, monitor LFTs (voriconazole toxicity).
 - ABPA: Prednisone 0.5 mg/kg/day PO, taper over 3-6 months, itraconazole 200 mg PO BID.
 - Aspergilloma: Surgery if symptomatic (hemoptysis), voriconazole if inoperable.
- Cryptococcal Infections:
 - Meningitis:
 - Induction: Amphotericin B 0.7-1 mg/kg/day IV + flucytosine 25 mg/kg PO q6h x 2 weeks.
 - Consolidation: Fluconazole 400 mg PO daily x 8 weeks.
 - Maintenance: Fluconazole 200 mg PO daily (HIV patients, until CD4 >200).
 - ICP Management: Serial LPs if pressure >25 cmH2O.
 - Pulmonary/Disseminated: Fluconazole 400 mg PO daily, amphotericin if severe.
- Mucormycosis:
 - First-Line: Liposomal amphotericin B 5-10 mg/kg/day IV.
 - Surgical Debridement: Essential for source control (e.g., sinus, skin).
 - Adjunctive: Posaconazole 300 mg IV/PO daily if amphotericin intolerant.
 - Duration: Weeks to months, until resolution.
- Pneumocystis Pneumonia (PCP):
 - First-Line: Trimethoprim-sulfamethoxazole (TMP-SMX) 15-20 mg/kg/day IV/PO (TMP dose) x 21 days.
 - Adjunctive Steroids: Prednisone 40 mg PO BID x 5 days, taper (if PaO2 <70 mmHg).
 - Alternative: Pentamidine 4 mg/kg IV daily (if TMP-SMX allergic).
 - Prophylaxis: TMP-SMX 160/800 mg PO daily (HIV, CD4 <200).

Role of Infectious Disease (ID) Involvement

• When to Consult:

- Suspected invasive fungal infection (e.g., candidemia, IA, mucormycosis).
- Complex cases (e.g., cryptococcal meningitis in HIV, PCP in non-HIV patients).
- Antifungal resistance or failure (e.g., Candida non-susceptible to fluconazole).

- Need for long-term therapy or prophylaxis (e.g., transplant patients).

• ID Contributions:

- Guide antifungal selection, duration, and de-escalation.
- Interpret diagnostic tests (e.g., beta-D-glucan, galactomannan).
- Manage complications (e.g., IRIS in cryptococcal meningitis).
- Coordinate prophylaxis (e.g., fluconazole in high-risk patients).

Table: Common Fungal Infections, Key Features, and Complications

Infection	At-Risk Population	Presentation	Diagnostic Findings	Complications	Additional Tests
Candidemia	ICU, central lines, antibiotics	Fever, sepsis, multi-organ failure	Blood culture positive, beta-D-glucan >80 pg/mL	Endocarditis, endophthalmitis, septic shock	Retinal exam (endophthalmitis), TEE (endocarditis)
Invasive Aspergillosis	Neutropenia, transplant	Fever, hemoptysis, respiratory failure	CT: Halo sign, galactomannan >0.5	Massive hemoptysis, brain abscess, mortality 50-90%	Bronchoscopy/ BAL, CT sinus/ brain
Cryptococcal Meningitis	HIV (CD4 <100), transplant	Headache, fever, neck stiffness	CSF: Cryptococcal antigen >1:8, India ink	Elevated ICP, vision/hearing loss, mortality 20-30%	Fundoscopy exam, skin biopsy
Mucormycosis	DKA, neutropenia	Sinus pain, black eschar, hemoptysis	Biopsy: Broad, non-septate hyphae	Orbital necrosis, brain abscess, mortality 50-70%	CT/MRI sinus/ brain, endoscopy
Pneumocystis Pneumonia	HIV (CD4 <200), steroids	Dyspnea, dry cough, hypoxia	CT: Ground-glass, PCP PCR	ARDS, pneumothorax, mortality 10-20%	Bronchoscopy/ BAL, ABG

Table: Hospitalist Management Checklist for Fungal Infections

Task	Candidemia	Invasive Aspergillosis	Cryptococcal Meningitis	Mucormycosis	PCP
Initial Stabilization	Fluids, Oxygen, remove lines	Fluids	LP for ICP, fluids	Fluids, surgery	HFNC, steroids
Antifungal Therapy	Caspofungin	Voriconazole	Amphotericin B + flucytosine	Amphotericin B	TMP-SMX

Task	Candidemia	Invasive Aspergillosis	Cryptococcal Meningitis	Mucormycosis	PCP
Consult	ID, neurology	ID, pulmonology	ID, neurology	ID, ENT/surgery	ID, pulmonology
Monitoring	Blood cultures q48h, echo	Cr q6h, LFTs q48h	CSF pressure qweek, LFTs	Cr q6h, wound checks q12h	SpO2, ABG
Additional Tests	Retinal exam, TEE	Bronchoscopy, CT sinus	Fundoscopy exam, LP	CT/MRI, endoscopy	Bronchoscopy, ABG

Clinical Scenarios

Scenario 1: ICU Patient with Candidemia and Endophthalmitis

- **Presentation:** A 60-year-old male in the ICU (post-abdominal surgery, central line, on TPN) develops fever, hypotension, and blurred vision. Exam shows T 39°C, BP 90/60 mmHg, HR 120 bpm, RR 22/min, central line site erythema, retinal exam: White fluffy lesions.
- **Diagnostic Workup:** **Blood cultures:** *Candida albicans*, beta-D-glucan 150 pg/mL, TEE: No vegetations, retinal exam confirms endophthalmitis, labs: WBC 15,000/ μ L, Cr 1.5 mg/dL.
- **Diagnosis:** Candidemia with endophthalmitis → ICU patient, fever, positive cultures, retinal findings.
- **Management:** Admit to ICU (sepsis). Remove central line. Start caspofungin 70 mg IV loading, then 50 mg IV daily. Fluids (NS 30 mL/kg), norepinephrine 10 μ g/min IV (MAP 70 mmHg). Consult ID/ophthalmology: Fluconazole 400 mg PO daily after 14 days (susceptible). Ophthalmology: Intravitreal amphotericin B planned. Monitor blood cultures q48h, Cr q12h. After 7 days, afebrile, vision stable, discharged with ID follow-up.

Scenario 2: Neutropenic Patient with Invasive Aspergillosis and CNS Involvement

- **Presentation:** A 40-year-old female with AML (post-chemotherapy, neutropenic) presents with fever, cough, hemoptysis, and new-onset seizures. Exam shows T 38.5°C, BP 110/70 mmHg, HR 100 bpm, RR 24/min, SpO2 90% on 4 L/min, lung crackles, GCS 14.
- **Diagnostic Workup:** **CT chest:** Halo sign, galactomannan 1.2, BAL culture: *Aspergillus fumigatus*, MRI brain: Ring-enhancing lesion (abscess), labs: WBC 500/ μ L, ANC 100/ μ L.
- **Diagnosis:** Invasive aspergillosis with CNS dissemination → Neutropenia, fever, CT findings, MRI abscess.

- Management: Admit to ICU (respiratory distress, seizures). Start voriconazole 6 mg/kg IV q12h x 1 day, then 4 mg/kg IV q12h. Levetiracetam 500 mg IV BID for seizures. HFNC 40 L/min, FiO2 50% (SpO2 94%). Consult ID/pulmonology/neurology: Monitor LFTs q48h, plan 12-week course. After 5 days, afebrile, no seizures, discharged on oral voriconazole with follow-up.

Scenario 3: HIV Patient with cryptococcal meningitis and elevated ICP

- Presentation: A 35-year-old male with HIV (CD4 50) presents with headache, fever, confusion, and vision changes. Exam shows T 38°C, BP 120/80 mmHg, HR 90 bpm, RR 18/min, GCS 14, neck stiffness, fundoscopic exam: Papilledema.
- Diagnostic Workup: LP: Opening pressure 35 cmH2O, WBC 200/μL (lymphocytes), glucose 20 mg/dL, protein 150 mg/dL, cryptococcal antigen 1:256, India ink positive, MRI: Meningeal enhancement, no cryptococcomas.
- Diagnosis: Cryptococcal meningitis with elevated ICP → HIV, headache, CSF findings, papilledema.
- Management: Admit to medicine (meningitis). Start amphotericin B 0.7 mg/kg/day IV + flucytosine 25 mg/kg PO q6h. Serial LPs (ICP >25 cmH2O, 20 mL removed daily). Consult ID/neurology: Fluconazole 400 mg PO daily after 2 weeks. Monitor CSF pressure q48h, LFTs. After 10 days, GCS 15, vision stable, discharged on fluconazole with ID follow-up.

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