Aspergillosis

Prevention, diagnosis, antifungal agents/TDM, invasive syndrome treatment by site, prophylaxis, empiric/preemptive therapy, and chronic/allergic aspergillosis.

2016 IDSA Clinical Practice Guideline
Diagnosis and Management of Aspergillosis
Patterson, Thompson, Denning et al. · Clin Infect Dis
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FORMAT *98 recommendations across invasive, chronic/saprophytic, and allergic aspergillosis condensed by clinical theme; strength/quality vary by item — consult full text for GRADE ratings.*

1 Prevention & Environmental Precautions

–	RECOMMENDATION
HSCT/leukemia induction	Protected environment (HEPA filtration) to reduce mold exposure in hospitalized allogeneic HSCT recipients and other highly immunocompromised patients.
No protected env.	Private room, no construction-site connection, no plants/cut flowers in room.
Outpatients	Avoid gardening, mulch/compost, and close exposure to construction/renovation.
Surveillance	Transplant/leukemia centers should track mold infection incidence; investigate hospital source if increased above baseline.

2 Diagnosis

–	RECOMMENDATION
Specimens	Submit tissue/fluid for simultaneous histopathology/cytology + culture; molecular ID for atypical growth or resistance concern.
PCR	No consensus for routine use; if used, interpret case-by-case alongside other tests and clinical context.
Galactomannan (GM)	Serum + BAL GM accurate in heme malignancy/HSCT; NOT for routine blood screening on mold-active prophylaxis (BAL still useful); NOT for SOT or CGD screening.
β-D-glucan	Serum assay useful in high-risk (heme malignancy, allo-HSCT) but not Aspergillus-specific.
Chest CT	Obtain whenever IPA is suspected regardless of chest X-ray; contrast only if nodule/mass near a large vessel; follow-up CT after ≥2 wk of treatment (or sooner if deteriorating).
Bronchoscopy	BAL recommended if IPA suspected (unless precluded by hypoxemia/bleeding/thrombocytopenia); send for culture, cytology, and GM. Low yield for peripheral nodules — consider biopsy.
Response monitoring	Serial serum GM useful if baseline elevated (heme malignancy/HSCT) to track progression/response; β-D-glucan not well studied for this purpose.

3 Antifungal Agents & TDM

–	RECOMMENDATION
Triazoles	Preferred agents for treatment/prevention in most patients. TDM at steady-state for itraconazole, voriconazole, posaconazole suspension (and interacting drugs: cyclosporine, tacrolimus, sirolimus, TKIs).
AmB	Deoxycholate/lipid formulations appropriate when voriconazole cannot be used; deoxycholate reserved for resource-limited settings; aerosolized AmB may be prophylaxis option in prolonged neutropenia/lung transplant.
Echinocandins	Effective salvage (alone or combo); NOT recommended as primary monotherapy.
Combination Rx	Voriconazole + echinocandin may be considered in select documented IPA cases (preclinical synergy data inconsistent).
Susceptibility testing	Not routine — reserve for suspected azole resistance, treatment failure, or epidemiologic purposes.

4 Invasive Pulmonary Aspergillosis (IPA)

–	RECOMMENDATION
Primary	Voriconazole — start early while diagnostic workup proceeds.
Alternatives	Liposomal AmB, isavuconazole, or other lipid AmB formulations.
Combination	Voriconazole + echinocandin may be considered in select patients.
Duration	Minimum 6–12 wk, guided by immunosuppression degree/duration, site, and clinical response.
Secondary ppx	Initiate if further immunosuppression required after successful treatment.

5 Adjunctive Measures & Salvage Therapy

–	RECOMMENDATION
Immunosuppression	Reduce/eliminate when feasible as part of anti-Aspergillus therapy.
G-CSF/transfusion	Colony-stimulating factors may help in neutropenic IA; granulocyte transfusion for refractory IA with anticipated neutropenia >1 wk.
IFN-γ	Recommended prophylaxis in CGD patients; benefit as IA adjunct unknown.
Surgery	Consider for accessible localized disease (sinusitis, cutaneous); rational for endocarditis, osteomyelitis, focal CNS disease.
Chemo/HSCT timing	IA is NOT an absolute contraindication — joint ID + heme/onc decision weighing progression risk vs. malignancy risk.
Salvage strategy	Individualized: change antifungal class, taper immunosuppression, resect necrotic lesions. Options: lipid AmB, micafungin, caspofungin, posaconazole, itraconazole.

6 Extrapulmonary / Single-Organ IA

SITE	REGIMEN/PEARL
CNS	Voriconazole primary; lipid AmB if intolerant/refractory — highest mortality of all IA patterns; watch anticonvulsant interactions.
Sinus	Surgery + voriconazole or lipid AmB for invasive disease; surgery alone for fungal ball.
Tracheobronchial	Saprophytic form: no antifungal unless symptomatic/immunosuppressed — bronchoscopic mucoid clearance. Invasive: mold-active triazole or IV lipid AmB ± bronchoscopic debridement; lung transplant: add inhaled AmB for anastomotic/ischemic TBA.
Endocarditis	Early surgery + voriconazole/lipid AmB; lifelong antifungal after valve replacement.
Osteomyelitis/arthritis	Surgical debridement + voriconazole.
Eye	Endophthalmitis: systemic voriconazole + intravitreal voriconazole or AmB deoxycholate. Keratitis: topical natamycin 5% or topical voriconazole.
Skin	Voriconazole + search for primary focus (may reflect dissemination); debridement for burns/soft-tissue wounds.
Peritonitis	Prompt PD catheter removal + systemic voriconazole.
GI/hepatic	Voriconazole ± surgery to prevent hemorrhage/perforation/obstruction; hepatic: voriconazole or lipid AmB, surgery for refractory biliary obstruction.
Renal	Combined medical + urologic management; ureteral obstruction → decompression + local AmB deoxycholate instillation; parenchymal disease → voriconazole.
Ear	Otomycosis: mechanical cleansing + topical antifungal/boric acid. Invasive: prolonged systemic voriconazole + surgery.
Pediatric	Same regimens as adults — dosing differs and is unknown for some agents.

7 Prophylaxis & Empiric/Preemptive Therapy

–	RECOMMENDATION
High-risk neutropenia	Posaconazole, voriconazole, and/or micafungin during prolonged neutropenia; caspofungin probably effective; itraconazole effective but limited by absorption/tolerability.
GVHD	Posaconazole for allo-HSCT with GVHD at high risk; continue throughout chronic immunosuppression (prednisone-equivalent >1 mg/kg/d >2 wk or other anti-GVHD therapy).
Lung transplant	Systemic triazole or inhaled AmB × 3–4 mo post-transplant; reinitiate with immunosuppression augmentation (thymoglobulin, alemtuzumab, high-dose steroids).
Nonlung SOT	Base prophylaxis on institutional epidemiology + individual risk factors — no routine prophylaxis established outside lung transplant.
Breakthrough IA	Individualized approach; aggressive workup (bronchoscopy/CT-biopsy); check azole levels; switch antifungal class; consider susceptibility testing.
Empiric therapy	For high-risk, persistently febrile neutropenic patients despite antibiotics: lipid AmB, echinocandin, or voriconazole. NOT needed if neutropenia <10 d expected.
Preemptive (biomarker)	GM/β-D-glucan-guided therapy reduces unnecessary antifungal use without survival compromise — alternative to empiric approach.
Lung transplant IPA	Preemptive antimold therapy if airway colonization within 6 mo of transplant or 3 mo of rejection-immunosuppression; may withhold beyond 6 mo without recent augmentation if asymptomatic.

8 Chronic & Allergic Aspergillosis

–	RECOMMENDATION
CCPA diagnosis	≥3 mo symptoms/progressive imaging (cavitation, pleural thickening) + elevated Aspergillus IgG (most sensitive test) or other microbiologic data + minimal immunocompromise.
CCPA treatment	Asymptomatic/stable: observe q3–6mo. Symptomatic/progressive: ≥6 mo itraconazole or voriconazole (posaconazole 3rd-line); hemoptysis: tranexamic acid, embolization, or antifungal; refractory: IV micafungin/caspofungin/AmB or surgery.
Aspergilloma	Asymptomatic + stable size: observe. Symptomatic (esp. hemoptysis): resect ± periop antifungal if spillage risk.
ABPA (asthma/CF)	Elevated Aspergillus IgE + total IgE for diagnosis; itraconazole with TDM for symptomatic bronchiectasis/mucoid impaction or CF exacerbations to reduce corticosteroid need; corticosteroids remain cornerstone for exacerbations.
Allergic fungal rhinosinusitis	Diagnose via hyphae in eosinophilic mucin + anti-Aspergillus IgE/skin-prick. Polypectomy + sinus washout + topical nasal steroids first-line; oral triazole for refractory/relapsing disease only.

Patterson TF, Thompson GR 3rd, Denning DW, et al. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2016;63(4):e1-e60.