

Table 1. Definitions of invasive fungal infections in patients with cancer and recipients of hematopoietic stem cell transplants.

Category, type of infection	Description
Proven invasive fungal infections	
Deep tissue infections	
Molds	Histopathologic or cytopathologic examination showing hyphae from needle aspiration or biopsy specimen with evidence of associated tissue damage (either microscopically or unequivocally by imaging); or positive culture result for a sample obtained by sterile procedure from normally sterile and clinically or radiologically abnormal site consistent with infection, excluding urine and mucous membranes
Yeasts	Histopathologic or cytopathologic examination showing yeast cells (<i>Candida</i> species may also show pseudohyphae or true hyphae) from specimens of needle aspiration or biopsy excluding mucous membranes; or positive culture result on sample obtained by sterile procedure from normally sterile and clinically or radiologically abnormal site consistent with infection, excluding urine, sinuses, and mucous membranes; or microscopy (India ink, mucicarmine stain) or antigen positivity (False-positive cryptococcal antigen reactions due to infection with <i>Trichosporon beigeli</i> , infection with <i>Stomatococcus mucilaginosus</i> , circulating rheumatoid factor, and concomitant malignancy may occur and should be eliminated if positive antigen test is only positive result in this category.) for <i>Cryptococcus</i> species in CSF
Fungemia	
Molds	Blood culture that yields fungi, excluding <i>Aspergillus</i> species and <i>Penicillium</i> species other than <i>Penicillium marneffei</i> , accompanied by temporally related clinical signs and symptoms compatible with relevant organism
Yeasts	Blood culture that yields <i>Candida</i> species and other yeasts in patients with temporally related clinical signs and symptoms compatible with relevant organism
Endemic fungal infections (Histoplasmosis, blastomycosis, coccidioidomycosis, and paracoccidioidomycosis.)	
Systemic or confined to lungs	Must be proven by culture from site affected, in host with symptoms attributed to fungal infection; if culture results are negative or unattainable, histopathologic or direct microscopic demonstration of appropriate morphological forms is considered adequate for dimorphic fungi (<i>Blastomyces</i> , <i>Coccidioides</i> and <i>Paracoccidioides</i> species) having truly distinctive appearance; <i>Histoplasma capsulatum</i> variant <i>capsulatum</i> may resemble <i>Candida glabrata</i>

Disseminated	May be established by positive blood culture result or positive result for urine or serum antigen by means of RIA
Probable invasive fungal infections	At least 1 host factor criterion (see table 2); and 1 microbiological criterion; and 1 major (or 2 minor) clinical criteria from abnormal site consistent with infection
Possible (This category is not recommended for use in clinical trials of antifungal agents but might be considered for studies of empirical treatment, epidemiological studies, and studies of health economics.) invasive fungal infections	At least 1 host factor criterion; and 1 microbiological or 1 major (or 2 minor) clinical criteria from abnormal site consistent with infection

Table 2. Host factor, microbiological, and clinical criteria for invasive fungal infections in patients with cancer and recipients of hematopoietic stem cell transplants.

Type of criteria	Criteria
Host factors	<p>Neutropenia (<500 neutrophils/μl for >10 days)</p> <p>Persistent fever for >96 h refractory to appropriate broad-spectrum antibacterial treatment in high-risk patients</p> <p>Body temperature either >38°C or >36°C and any of the following predisposing conditions: prolonged neutropenia (110 days) in previous 60 days, recent or current use of significant immunosuppressive agents in previous 30 days, proven or probable invasive fungal infection during previous episode of neutropenia, or coexistence of symptomatic AIDS</p> <p>Signs and symptoms indicating graft-versus-host disease, particularly severe (grade 2) or chronic extensive disease</p> <p>Prolonged (>3 weeks) use of corticosteroids in previous 60 days</p>
Microbiological	<p>Positive result of culture for mold (including <i>Aspergillus</i>, <i>Fusarium</i>, or <i>Scedosporium</i> species or Zygomycetes) or <i>Cryptococcus neoformans</i> or an endemic fungal pathogen (<i>H. capsulatum</i> variant <i>capsulatum</i>, <i>Blastomyces dermatitidis</i>, <i>Coccidioides immitis</i>, or <i>Paracoccidioides brasiliensis</i>) from sputum or bronchoalveolar lavage fluid samples</p> <p>Positive result of culture or findings of cytologic/direct microscopic evaluation for mold from sinus aspirate specimen</p> <p>Positive findings of cytologic/direct microscopic evaluation for mold or <i>Cryptococcus</i> species from sputum or bronchoalveolar lavage fluid samples</p> <p>Positive result for <i>Aspergillus</i> antigen in specimens of bronchoalveolar lavage fluid, CSF, or \geq2 blood samples</p> <p>Positive result for cryptococcal antigen in blood sample (See table 1 footnote <i>b</i> for causes of false-positive reactions that must be considered and eliminated from consideration.)</p> <p>Positive findings of cytologic or direct microscopic examination for fungal elements in sterile body fluid samples (e.g., <i>Cryptococcus</i> species in CSF)</p> <p>Positive result for <i>Histoplasma capsulatum</i> antigen in blood, urine, or CSF specimens</p> <p>Two positive results of culture of urine samples for yeasts in absence of urinary catheter</p> <p><i>Candida</i> casts in urine in absence of urinary catheter</p> <p>Positive result of blood culture for <i>Candida</i> species</p> <p>Lung infiltrate without microbiological evidence of bacterial infection from blood, sputum, broncho-alveolar lavage (comment: this criterium was part of the 1999 ICAAC presentation, but was eliminated for the 2001 CID full paper.)</p>
Clinical	<p>Must be related to site of microbiological criteria and temporally related to current episode</p>

Lower respiratory tract infection	
Major	Any of the following new infiltrates on CT imaging: halo sign, air-crescent sign, or cavity within area of consolidation (In absence of infection by organisms that may lead to similar radiological findings including cavitation, such as <i>Mycobacterium</i> , <i>Legionella</i> , and <i>Nocardia</i> species.)
Minor	Symptoms of lower respiratory tract infection (cough, chest pain, hemoptysis, dyspnea); physical finding of pleural rub; any new infiltrate not fulfilling major criterion; pleural effusion
Sinonasal infection	
Major	Suggestive radiological evidence of invasive infection in sinuses (i.e., erosion of sinus walls or extension of infection to neighboring structures, extensive skull base destruction)
Minor	Upper respiratory symptoms (e.g., nasal discharge, stuffiness); nose ulceration or eschar of nasal mucosa or epistaxis; periorbital swelling; maxillary tenderness; black necrotic lesions or perforation of hard palate
CNS infection	
Major	Radiological evidence suggesting CNS infection (e.g., mastoiditis or other parameningeal foci, extradural empyema, intraparenchymal brain or spinal cord mass lesion)
Minor	Focal neurological symptoms and signs (including focal seizures, hemiparesis, and cranial nerve palsies); mental changes; meningeal irritation findings; abnormalities in CSF biochemistry and cell count (provided that CSF is negative for other pathogens by culture or microscopy and negative for malignant cells)
Disseminated fungal infection	Papular or nodular skin lesions without any other explanation; intraocular findings suggestive of hematogenous fungal chorioretinitis or endophthalmitis
Chronic disseminated candidiasis	Small, peripheral, targetlike abscesses (bull's-eye lesions) in liver and/or spleen demonstrated by CT, MRI, or ultrasound, as well as elevated serum alkaline phosphatase level; supporting microbiological criteria are not required for probable category
Candidemia	Clinical criteria are not required for probable candidemia; there is no definition for possible candidemia

Adapted from: Ascoglu S, Rex JH, de Pauw B, et al. Defining Opportunistic Invasive Fungal Infections in Immunocompromised Patients with Cancer and Hematopoietic Stem Cell Transplants: An International Consensus. *Clinical Infectious Diseases* 2002; 34: 7–14.

and from: Ascoglu S, de Pauw B, Bennett JE, et al. Analysis of Definitions Used in Clinical Research on Invasive Fungal Infections (IFI): Consensus Proposal for New, Standardized Definitions. 39th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, USA, 1999.