

Invasive Aspergillosis

Current Strategies for Diagnosis and Management



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KEYWORDS

- Aspergillosis • Invasive pulmonary aspergillosis • Resistance
- Chronic cavitary aspergillosis • Aspergilloma

KEY POINTS

- Invasive aspergillosis remains a major cause of morbidity and mortality in immunosuppressed hosts.
- Laboratory confirmation of invasive aspergillosis remains a priority to help direct therapy and to evaluate for possible antifungal resistance.
- Voriconazole remains the recommended therapy for patients with invasive aspergillosis.
- New antifungal agents including new drugs like isavuconazole and new formulations of posaconazole offer the potential for improved outcome in patients with invasive aspergillosis.
- The role of combination therapy remains controversial but can be considered in high risk patients like those with hematological malignancy and severe disease.
- Prophylaxis may improve outcome in highest risk patients.

INTRODUCTION

The spectrum of aspergillosis encompasses a broad range of clinical entities, from noninvasive forms, such as allergic bronchopulmonary aspergillosis (ABPA) and chronic pulmonary aspergillosis syndromes, to invasive pulmonary aspergillosis (IPA) with possible widespread dissemination (**Fig. 1**).^{1,2}

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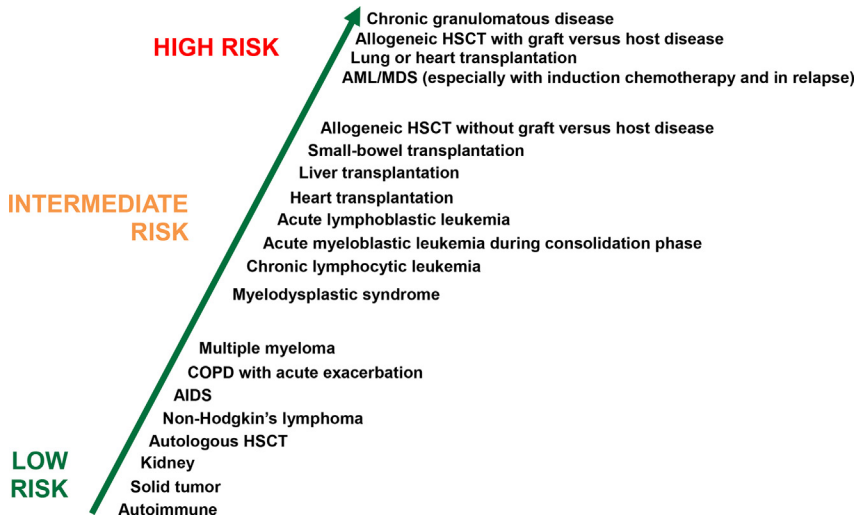


Fig. 1. Spectrum of risk for IA. (Data from Pagano L, Akova M, Dimopoulos G, et al. Risk assessment and prognostic factors for mould-related diseases in immunocompromised patients. *J Antimicrob Chemother* 2011;66(Suppl 1):i5–14.)

Although most frequently affecting the lungs, aspergillosis can develop within virtually any organ system and disseminated disease is particularly common among patients with prolonged granulocytopenia following chemotherapy.

Despite advances in the diagnosis and treatment of invasive aspergillosis (IA), mortality rates remain high, especially in the immunosuppressed host. During the past decade, triazole resistance has emerged in some regions of the world and is particularly concerning for management given the limited options to treat azole-resistant infections and the possibility that this may lead to failure of prophylaxis in immunocompromised hosts. Cryptic species of *Aspergillus*, strains that are difficult to identify morphologically, have also become increasingly important given the higher azole antifungal minimum inhibitory concentrations (MICs) of some of these species, the difficulty in differentiating these organisms on phenotypic appearance alone, and the uncertain clinical outcomes and therapeutic challenges they represent.

Despite these challenges, new diagnostic methods and antifungal agents have emerged in attempts to further reduce mortality from IPA. These newer agents possess potential advantages compared with existing agents, such as improved bioavailability (posaconazole tablets) and reduced toxicity (isavuconazole). These additions to the therapeutic armamentarium have been welcomed and provide clinicians with additional options during treatment.

MYCOLOGY AND EPIDEMIOLOGY

There are more than 250 species of *Aspergillus*, with several subgenera and multiple sections (previously known as groups).^{3,4} The most common species isolated in cases of invasive disease are *A fumigatus*, followed by *A flavus*, *A terreus*, and *A niger* (Table 1).⁵ Additional species have also been implicated in infection of severely immunocompromised patients. In most cases, identification to the genus level is not difficult; however, when poorly sporulating isolates are observed, identification even to the species complex level may be challenging.⁶ Most species of *Aspergillus* reproduce

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