INVITED REVIEW SERIES:
TRANSLATING RESEARCH INTO PRACTICE
SERIES EDITORS: JOHN E HEFFNER AND DAVID CL LAM

Pulmonary fungal infections

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ABSTRACT
This review details some of the advances that have been made in the recent decade in the diagnosis, treatment and epidemiology of pulmonary fungal infections. These advances have occurred because of increasing knowledge regarding the fungal genome, better understanding of the structures of the fungal cell wall and cell membrane and the use of molecular epidemiological techniques. The clinical implications of these advances are more rapid diagnosis and more effective and less toxic antifungal agents. For example, the diagnosis of invasive pulmonary aspergillosis, as well as histoplasmosis and blastomycosis, has improved with the use of easily performed antigen detection systems in serum and bronchoalveolar lavage fluid. Treatment of angioinvasive moulds has improved with the introduction of the new azoles, voriconazole and posaconazole that have broad antifungal activity. Amphotericin B is less frequently used, and when used is often given as lipid formulation to decrease toxicity. The newest agents, the echinocandins, are especially safe as they interfere with the metabolism of the fungal cell wall, a structure not shared with human cells. Epidemiological advances include the description of the emergence of Cryptococcus gattii in North America and the increase in pulmonary mucormycosis and pneumonia due to Fusarium and Scedosporium species in transplant recipients and patients with haematological malignancies. The emergence of azole resistance among Aspergillus species is especially worrisome and is likely related to increased azole use for treatment of patients, but also to agricultural use of azoles as fungicides in certain countries.

Key words: aspergillosis, endemic mycosis, fungal pneumonia, galactomannan test, opportunistic mycosis.

INTRODUCTION
There have been important advances in the diagnosis and treatment of both the endemic and the opportunistic mycoses, in the delineation of the epidemiology of invasive pulmonary mould infections in immunocompromised patients and in the taxonomy of both yeasts and moulds that cause pulmonary infection. In the last decade, less well-known moulds, such as members of the Fusarium and Scedosporium genera, are increasingly found to cause invasive pulmonary infection. Newly described Aspergillus species that are pathogenic for humans are inherently more drug resistant, and acquired resistance is increasing among the usual species that cause human infection. Cryptococcus gattii has emerged in North America as a cause of pulmonary and central nervous system (CNS) infections. Understanding of many of these phenomena had to await the development of molecular methods that could be applied to fungal genomes.

Building on knowledge accrued in the last several decades regarding the cell wall composition of Aspergillus and the endemic fungi, Histoplasma capsulatum and Blastomyces dermatitidis, diagnostic tests for detecting these fungi have become a routine part of the approach to diagnosis. Antigen detection can be accomplished in urine, serum and body fluids, including respiratory samples obtained by bronchoalveolar lavage (BAL). Especially in immunocompromised patients, in whom antibody responses are notoriously poor, antigen detection has led to earlier diagnosis and improved outcomes.

In addition to improved diagnostic techniques, the introduction of new antifungal agents in the last decade has occurred because of studies detailing the synthesis of cell membranes and cell walls in yeasts and moulds. Armed with the knowledge of the action of fluconazole, voriconazole was synthesized specifically to allow more avid binding to the cell membrane of moulds, allowing an increase in the antifungal