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Human Fungal Pathogen Identification

Methods and Protocols

Edited by

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Preface

Fungal infections constitute an ever-growing healthcare problem worldwide. Invasive fungal disease (IFD) is a leading cause of morbidity and mortality in severely immunocompromised individuals, including a variety of critically ill patients. High-risk conditions for IFD include hematologic malignancies, hematopoietic stem cell or solid organ transplantations, primary or acquired immunodeficiencies such as AIDS, long-term treatment at intensive care units, preterm birth, long-term immunosuppressive therapy, broad-spectrum antibiotic therapy, and long presence of central indwelling catheters. Despite the availability of a number of potent antifungal drugs, successful treatment of IFD is often hampered by the limited diagnostic options which neither permit rapid and reliable identification of systemic, acute, or latent fungal infections nor facilitate assessment of host susceptibility. The resulting delay in the onset of antifungal therapy is an important factor contributing to the poor overall clinical outcome of IFD. Moreover, the widespread use of prophylactic or empirical treatment without firm evidence of IFD leads to a high rate of overtreatment associated with considerable toxic side effects, and broad-spectrum antimycotic therapy administered against unidentified fungal pathogens can promote the evolution of clinical drug resistance.

The vast majority of IFDs are caused by *Candida* and *Aspergillus* species. However, changes in the epidemiology have occurred over the last decades, with a number of newly emerging fungal pathogens affecting even immunocompetent patients. Additionally, rare but pronounced antifungal drug resistance of some major fungal pathogens (e.g., *C. glabrata, C. krusei, A. terreus*) poses a serious challenge for treatment. Despite current evidence that the innate immune surveillance is critical for defence against invasive fungal infections, host predisposition to IFD, which would permit targeted preventive treatment, is barely considered in diagnostic procedures. Microbiological diagnostic criteria of IFD provided by the EORTC/MSG (European Organization for Research and Treatment of Cancer/Mycoses Study Group) include the detection of fungal pathogens by cytology, direct microscopy, or culture and serological detection of antigens or cell wall constituents, such as galactomannan or ß-d-glucan. By contrast, molecular detection of fungal nucleic acids is currently not accepted as microbiological evidence of IFD due to insufficient clinical evidence and lack of standardized and validated assays.

Rapid, reliable, and species-specific diagnosis of fungal pathogens causing IFD is a prerequisite for cost-effective and successful therapy but remains one of the great challenges. The changing epidemiology, the increasing variety of fungal pathogens, and the rising number of affected patients create a growing demand for broad-range and cost-effective clinical diagnostic tests, also permitting the prediction of pathogenicity and resistance to antifungal agents. The knowledge of host-related predisposing factors and stratified treatment options facilitating timely onset of adequate antifungal therapy are critical for successful clinical management and outcome of IFD. This requires not only rapid diagnosis of a fungal infection and identification of the causative species but also

assessment of pathogen/host factors related to pathogenicity, susceptibility, and response to treatment. The present book responds to the great need for timely and authoritative information offering a comprehensive overview of the current state of the art in fungal diagnostics. Moreover, it addresses ongoing developments expected to provide a basis for targeted treatment strategies resulting in improved outcome of invasive mycoses.

Vienna, Austria *Thomas Lion*

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