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Fungus among us: A poster child for diagnostic stewardship

In this issue of *Cleveland Clinic Journal of Medicine*, El-Baba et al address the clinical significance of *Aspergillus* species isolated from respiratory cultures.¹ The authors elegantly and succinctly summarize the clinical classification and diagnostic approach to *Aspergillus*-related lung disease.

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Interpretation of diagnostic studies, including microbiologic tests, should always be predicated on the clinical indication for testing.² So before interpreting the clinical significance of isolation of *Aspergillus* species from respiratory cultures, we should first ask whether the culture was clinically indicated, or whether this was an incidental finding.

Aspergillus species are ubiquitous in the water environments of the home and of health-care facilities.³ Therefore, while *Aspergillus* species can cause several forms of lung disease, some of which are life-threatening, incidental growth of this organism should be expected due to contamination or colonization. Contamination refers to the transient presence of this organism in the airways without causing illness, or its accidental addition to inanimate objects in the process of collection, transport, or processing in the laboratory. Colonization refers to the persistent presence of the organism in the airways, again without causing illness, but it can be one step away from resulting in clinical disease. These concepts apply to other human organ systems, including the skin and the urinary tract.⁴

■ EVOLVING DEFINITIONS OF FUNGAL INFECTIONS

Clinicians have struggled to define fungal infections at the bedside for several decades. The first international consensus defining opportunistic invasive fungal infections in immunocompromised patients with cancer and hematopoietic stem cell transplants was published in 2002.⁵ Diagnostic and management approaches to invasive fungal infections evolved rapidly over the last 2 decades, necessitating consecutive updates in 2008⁶ and 2020.⁷

These consensus definitions were intended to harmonize research studies but nevertheless have been widely adopted for clinical practice. With each update, the definition of the “probable” category expanded, while the scope of the category “possible” was contracted. The International Society for Heart and Lung Transplantation published its own standardized definitions pertaining to lung and heart transplant recipients.⁸

■ NEEDED: DIAGNOSTIC STEWARDSHIP

El-Baba et al¹ describe the diagnostic accuracy of the available imaging and laboratory tests, their limitations, and the risks associated with invasive bronchoscopic and surgical procedures necessary for histopathologic confirmation.

Our antifungal drug options are limited, and most agents have significant adverse effects and drug interactions and are expensive, further complicating management decisions. Practice guidelines by the Infectious Diseases Society of America,⁹ the American Society of Transplantation,¹⁰ and the American Society of Transplantation and Cellular Therapy¹¹ provide excellent guidance in these patient populations.

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If all patients in whom *Aspergillus* species grow from respiratory cultures were to be treated, the risks would outweigh the benefits. In making these decisions, clinicians should apply the principles of diagnostic stewardship² before applying the principles of antimicrobial stewardship.¹²

El-Baba et al provide a clinically driven, systematic approach to applying these principles. ■

DISCLOSURES

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REFERENCES

1. El-Baba F, Watza D, Soubani AO. Is *Aspergillus* isolated from respiratory cultures clinically significant? *Cleve Clin J Med* 2021; 86(0):543–546. doi:10.3949/ccjm.88a.20188
2. Miller JM, Binnicker MJ, Campbell S, et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2018 Update by the Infectious Diseases Society of America and the American Society for Microbiology. *Clin Infect Dis* 2018; 67(6):e1–e94. doi:10.1093/cid/ciy381
3. Richardson M, Rautemaa-Richardson R. Exposure to *Aspergillus* in home and healthcare facilities' water environments: focus on biofilms. *Microorganisms* 2019; 7(1):7. doi:10.3390/microorganisms7010007
4. Dani A. Colonization and infection. *Cent European J Urol* 2014; 67(1):86–87. doi:10.5173/cej.2014.01.art19
5. Ascioglu S, Rex JH, de Pauw B, et al; Invasive Fungal Infections Cooperative Group of the European Organization for Research and Treatment of Cancer and Mycoses Study Group of the National Institute of Allergy and Infectious Diseases. Defining opportunistic invasive fungal infections in immunocompromised patients with cancer and hematopoietic stem cell transplants: an international consensus. *Clin Infect Dis* 2002; 34(1):7–14. doi:10.1086/323335
6. De Pauw B, Walsh TJ, Donnelly JP, et al; European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group; National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. *Clin Infect Dis* 2008; 46(12):1813–1821. doi:10.1086/588660
7. Donnelly JP, Chen SC, Kauffman CA, et al. Revision and update of the consensus definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium. *Clin Infect Dis* 2020; 71(6):1367–1376. doi:10.1093/cid/ciz1008
8. Husain S, Mooney ML, Danziger-Isakov L, et al; ISHLT Infectious Diseases Council Working Group on Definitions. A 2010 working formulation for the standardization of definitions of infections in cardiothoracic transplant recipients. *J Heart Lung Transplant* 2011; 30(4):361–374. doi:10.1016/j.healun.2011.01.701
9. Patterson TF, Thompson GR III, 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. doi:10.1093/cid/ciw326
10. Husain S, Camargo JF, on behalf of the AST Infectious Diseases Community of Practice. Invasive aspergillosis in solid-organ transplant recipients: guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant* 2019; 33:e13544. doi:10.1111/ctr.13544
11. Sanjeet S, Dadwal, Tobias M, et al. American Society of Transplantation and Cellular Therapy Series. 2: Management and prevention of aspergillosis in hematopoietic cell transplantation recipients. *Transplantation and Cellular Therapy* 2021; 27(3):201–211. doi:10.1016/j.jtct.2020.10.003
12. Dellit TH, Owens RC, McGowan JE, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007; 44(2):159–177. doi:10.1086/510393

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