New ATS Clinical Practice Guideline: Diagnosing fungal infections

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The American Thoracic Society has published an official clinical guideline on laboratory diagnosis of fungal infections in pulmonary and critical care medicine in the Society's Aug. 30 *American Journal of Respiratory and Critical Care Medicine*.

Though less common than bacterial and viral infections, fungal infections have surged in recent decades and present an important health care challenge to patients, particularly those whose immune systems are compromised because of illness or drugs they are taking. The guideline covers the diagnosis of invasive pulmonary aspergillosis, invasive candidiasis and the three most common endemic mycoses: blastomycosis, coccidioidomycosis and histoplasmosis.

Effective treatment of patients with these infections depends on rapid, accurate diagnosis of the infection and on timely treatment. Delays in diagnosis and treatment can be debilitating, leading to long hospital stays, high medical costs and even, death.

"Our goal was to produce a concise evidence-based clinical practice guideline that will help clinicians use newer laboratory methods in diagnosis of these important infections," said guideline co-chair Andrew H. Limper, MD, Robert D. and Patricia E. Kern Associate Dean of Practice Transformation, and the Walter and Leonore Annenberg Professor of Pulmonary Medicine at Mayo Clinic, in Rochester, Minn. "This guideline summarizes the best available evidence on the use of common laboratory tests to diagnose invasive pulmonary aspergillosis,

invasive candidiasis, as well as histoplasmosis, blastomycosis and coccidioidomycosis."

The 11-member panel that produced the guideline included experts in pulmonary and critical care, infectious disease and invasive procedures. The group conducted a systematic review of medical studies on diagnosing fungal infections published from 1980 to April 2016. Diagnostic methods for fungal infections include antigen testing in urine, blood and bronchoalveolar lavage fluid; serological testing to detect antibodies to fungal components; and nucleic acid-based assays using polymerase chain reaction approaches.

The panel asked four clinical questions that clinicians face when they care for patients with suspected fungal infections. Using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework, the panel made a series of recommendations based on those questions:

1) Is serum and/or bronchoalveolar lavage (BAL) galactomannan (GM) testing sufficiently accurate to guide therapeutic decisions in place of histopathology and/or fungal culture in patients with impaired immunity suspected of having invasive pulmonary aspergillosis (IPA)?

* In patients with severe immune compromise, such as those with hematologic malignancy or recipients of hematologic stem cell or solid organ transplants, who present with unexplained lung infiltrates suspected of IPA, we recommend the use of serum GM testing. (Strong recommendation, high quality evidence)

* In patients, suspected of having invasive fungal diseases, including those with a negative serum GM, but strong risk factors for IPA, or positive serum GM but confounding factors for false positive GM results (e.g., those patients undergoing chemotherapy or at risk for mucositis where cross-reactive epitopes from other fungi or bacteria can penetrate the intestinal mucosa causing positivity of the test), we recommend BAL testing with GM (Strong recommendation, high quality evidence)

2) Should diagnosis of suspected aspergillus infections in severely immunocompromised patients be based on the application of polymerase chain reaction (PCR)?

* In patients with severe immune compromise, such as those with hematologic malignancy or recipients of hematologic stem cell or solid organ transplants, who are suspected of having IPA, we recommend the use of blood or serum Aspergillus PCR testing. (Strong recommendation, high quality evidence)

* In patients with severe immune compromise, such as those with hematologic malignancy or recipients of hematologic stem cell or solid organ transplants, who are suspected of having IPA, we recommend the inclusion of Aspergillus PCR on BAL testing as part of the evaluation. (Strong recommendation, high quality evidence)

* In patients with severe immune compromise, such as those with hematologic malignancy or recipients of hematologic stem cell or solid organ transplants, who are strongly suspected of having IPA, but in whom PCR testing for Aspergillus is negative, we suggest consideration of biopsy and/or additional testing with or without additional PCR or galactomannan testing. (Conditional recommendation, low quality evidence)

3) In critically ill patients with suspected invasive candidiasis, is the (1-3)-β-D-glucan (BDG) assay alone sufficient for diagnostic decision-making?

* In critically ill patients in whom there is clinical concern for invasive candidiasis, we suggest against reliance solely on results of serum BDG testing alone for diagnostic decision-making. (Conditional recommendation, low quality evidence)

4) Should diagnosis of the common endemic mycoses (i.e., histoplasmosis, blastomycosis, coccidioidomycosis) be based on serology and antigen testing?

* We recommend the use of Histoplasma antigen in urine or serum for rapid diagnosis of suspected disseminated and acute pulmonary histoplasmosis where timely diagnosis and treatment are paramount to outcome. (Strong recommendation, high quality evidence)

* We suggest the use of Histoplasma serologies in immunocompetent patients with suspected pulmonary histoplasmosis. Adding Histoplasma antigen to serological testing might improve the diagnostic yield. (Conditional recommendation, moderate quality evidence)

* In patients with appropriate geographic exposure and illness compatible with infection or pneumonia due to blastomycosis, we suggest using more than one diagnostic test, including direct visualization and culture of sputum BAL or other biopsy material, urine antigen testing, and serum antibody testing. The current evidence cannot support a single best test as being sensitive enough to be ordered in isolation of other testing. The approach should be tailored based on the severity of

illness, the clinical context and availability of tests. (Conditional recommendation, moderate quality evidence)

* In patients with suspected blastomycosis, we suggest that serum antibody testing specifically directed against the anti-BAD-1 antigen for blastomycosis be used along with clinical and epidemiological data to establish the diagnosis. (Conditional recommendation, low quality evidence)

* In patients with suspected blastomycosis, particularly in immunocompromised patients, we suggest that urinary antigen testing for blastomycosis be used along with clinical and epidemiological data to establish the diagnosis. (Conditional recommendation, moderate quality evidence)

* In patients with appropriate geographic exposure and illness compatible with infection or pneumonia due to coccidioidomycosis, we suggest using more than one diagnostic test, including direct visualization and culture of sputum, BAL, or other biopsy material, urine and serum antigen testing, and serology (serum antibody testing). The current evidence cannot support a single best test. The approach should be tailored based on the severity of illness, the clinical context and availability of tests. (Conditional recommendation, moderate quality evidence)

* In patients with suspected coccidioidomycosis, particularly in immunocompromised patients, we suggest performing urinary and serum antigen testing to aid in establishing the diagnosis. (Conditional recommendation, moderate quality evidence)

* In patients with suspected community acquired pneumonia from the endemic area, we suggest initial serological testing with close clinical follow up and serial testing. (Conditional recommendation, moderate

quality evidence)

Due to the increasing incidence of invasive fungal infections, Dr. Limper said that clinicians must be attentive to the serious complications they can cause in immune compromised and critically ill patients. "As always, application of any guideline information must be integrated into the overall clinical context for an individual patient when confirming the diagnosis of invasive fungal infection," he added.

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