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American Thoracic Society Issues Guidelines on Treating Pulmonary Fungal Infections

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January 12, 2011 — The American Thoracic Society (ATS) has issued updated clinical guidelines on treating pulmonary fungal infections, according to a statement published in the January 1, 2011, issue of the American Journal of Respiratory and Critical Care Medicine. The new recommendations, which replace 1988 ATS guidelines and target pulmonary and critical care practitioners and trainees, describe new medications and treatment approaches to pulmonary fungal infections, as well as provide an overview of emerging fungi.

Increase, Severity in Fungal Infections

"The incidence, diagnosis, and clinical severity of pulmonary fungal infections have dramatically increased in recent years in response to a number of factors," said lead author Andrew Limper, MD, professor and chair of Pulmonary Medicine at Mayo Clinic and chair of the ATS Fungal Infections Working Group, in a news release. "In addition to growing numbers of immune-compromised patients with HIV and other diseases, the number of patients receiving drugs to suppress the immune system following organ transplant or as the result of autoimmune inflammatory conditions has also increased."

The development of newer diagnostic methods and techniques has significantly facilitated a definitive diagnosis of pulmonary fungal infections. These new approaches include antigen detection, polymerase chain reaction, serologies, computed tomography and positron emission tomography scanning, bronchoscopy, mediastinoscopy, and video-assisted thorascopic biopsy.

"At the same time, the introduction of new medications has significantly broadened the options that are available to the physicians who treat these patients," Dr. Limper said. "In view of all of these developments, the ATS convened a working group of experts in fungal infections to develop an expert yet concise guide to currently available therapeutic options for the treatment of the myriad fungal infections that are of particular relevance to pulmonary and critical care practice."

During the past several years, the ATS Fungal Working Group met on multiple occasions at ATS meetings, reviewed journal articles and previously published guidelines, and performed a comprehensive search of online databases to gather all relevant diagnostic and treatment data. The resulting recommendations are a complete revision and expansion of the 1988 ATS fungal treatment guidelines.

"The treatment of fungal infections has undergone tremendous change since the earlier ATS treatment guidelines were published in 1988," Dr. Limper said. "These new guidelines offer physicians a source of updated treatment recommendations backed by relevant clinical data, including the use of novel drugs and the treatment of emerging fungi."

New Arsenal of Drugs

Amphotericin B, flucytosine, and a few clinically available azole agents (eg, itraconazole and fluconazole) were the mainstay of traditional antifungal therapy. Now, however, the pharmacotherapeutic arsenal includes potent new triazoles (ketoconazole, itraconazole, fluconazole, voriconazole, and posaconazole), polyenes, and newer antifungal drugs including the echinocandins (caspofungin, micafungin, and anidulafungin), which act by inhibiting the formation of the cell walls of fungi. Newer representatives of the polyene class include amphotericin B deoxycholate; lipid-associated liposomal amphotericin B, which is less toxic to the kidneys; and amphotericin B lipid complex.

"The expanded availability of agents offer[s] clinicians a broader range of treatment options, which is especially critical in treating some of the more recalcitrant infections," Dr. Limper said. "This statement offers recommended guidelines for the optimal use of these new and promising drugs."

The statement highlights 3 main areas of treatment recommendations: the endemic mycoses (eg, histoplasmosis, sporotrichosis, blastomycosis, and coccidioidomycosis); fungal infections with increased prevalence in immunocompromised and critically ill patients (eg, cryptococcosis, aspergillosis, candidiasis, and Pneumocystis pneumonia); and rare and emerging fungal infections.

Endemic Mycoses

Mild to moderate histoplasmosis, sporotrichosis, and blastomycosis can be treated with itraconazole. However, antifungal agents are not needed for most immunocompetent patients with primary pulmonary coccidioidomycosis and no risk factors for dissemination, although triazoles are recommended for all patients with disseminated infection. Severe histoplasmosis, sporotrichosis, and blastomycosis should be treated initially with amphotericin B, followed, if needed, by systemic glucocorticosteroids for histoplasmosis or blastomycosis or itraconazole for sporotrichosis.

Immunocompetent patients with pulmonary cryptococcosis should receive fluconazole, whereas those with disseminated or central nervous system disease should receive amphotericin B plus flucytosine, followed by azole drugs. Depending on the severity of aspergillosis, treatment options may include prednisone, intravenous voriconazole, liposomal amphotericin B, or itraconazole.

Central venous catheters should be removed, and ophthalmology examination should be performed in patients with candidiasis. Indicated antifungal drugs may include fluconazole, amphotericin B, echinocandin, voriconazole, or combined fluconazole and amphotericin B.

"We also cover infections with Candida and Aspergillus species, which are increasingly common in the environment of the intensive care unit," Dr. Limper said. "The specific recommendations are concisely organized and should be readily applicable to practice."

Fungal Infections in Immunocompromised Patients

Immunosuppressed patients and those with HIV infection should receive prophylaxis for Pneumocystis pneumonia. Oral trimethoprim and sulfamethoxazole, oral primaquine plus clindamycin, or oral atovaquone are recommended for mild to moderate Pneumocystis pneumonia, whereas immunocompromised patients with moderate to severe pneumonia should be treated with trimethoprim and sulfamethoxazole, and possibly prednisone.

Emerging, Rare Fungal Infections

For treatment of emerging or rare fungal infections, such as the zygomycoses, hyalohyphomycoses, phaeohyphomycoses, and Trichosporon-related infections, the statement recommends reducing use of immunosuppressive agents, treating with immunostimulant drugs, and controlling underlying conditions. Necrotic tissues, cysts, or abscesses should be debulked or debrided; and specific antifungal agents can be administered locally, systemically, or for wound irrigation.

For zygomycosis, recommended treatment is amphotericin B; for fusariosis, lipid-associated amphotericin B, voriconazole, or posaconazole; for scedosporiosis, voriconazole; and for phaeohyphomycoses, itraconazole, voriconazole, or posaconazole. For trichosporonosis and Paecilomyces infections, extended-spectrum triazoles may possibly be effective.

The ATS Fungal Working Group is considering developing a future statement detailing only diagnosis of fungal infections using newer techniques such as serologies, antigen testing, nucleic acid amplification methodologies, and immune-detection strategies.

Some of the statement authors have disclosed various financial relationships with AlphaMed Pharmaceuticals, Pfizer, Ortho-McNeil, MiraBella Technologies, AstraZeneca, GlaxoSmithKline, Bayer, Novartis, Aradigm, Astellas, Enzon, Merck, and/or Schering-Plough.

Am J Respir Crit Care Med. 2011;183:96-128. Abstract

Clinical Context

Pulmonary fungal infections have recently increased in incidence and severity. The diagnosis has increased because of advances in diagnostic methods. The mainstay of treatment was previously amphotericin B, flucytosine, and azole drugs. However, current treatment options include azoles agents with extended antifungal activity; lipid forms of amphotericin B; and a new antifungal class, the echinocandins.

The ATS working group reviewed primarily English-language articles and guidelines to develop this statement that addresses the treatment of fungal infections in adult pulmonary and critical care patients, with attention to the endemic mycoses, fungal infections in immune-compromised and critically ill patients, and rare and emerging fungal infections.