Rise in antifungal resistance may portend global health crisis

Infectious Diseases in Children, November 2016

“[The antimicrobial] cycle just sets us up to continuing to breed all the types of resistance, including fungal infections,” she said. “I think we could decrease our antibiotic use, that would be one thing; secondly, antifungals have always been more difficult for us to use unlike antibiotics, since in bacteria we have really defined breaking points of what is susceptible, what is not, and the turnaround time on that information is very quick in labs, which is not the case with most fungi.”

A change in armaments

Aside from difficulty differentiating and treating infections from Candida and other drug-resistant fungal organisms promptly, treatment of invasive fungal infections is especially costly. Candida is the most common perpetrator in health care-associated bloodstream infections in the U.S., and according to a study by Juliette Morgan, MD, and colleagues, candidemia represents an estimated additional cost of $6,000 to $29,000 with 3 to 13 days added to length of hospital stay.

Antifungals that are presently used, including amphotericin B, caspofungin and voriconazole, are sufficient to eliminate some strains of Candida but not others, and combination therapy is generally advised against for multidrug-resistant Candida.

“Antifungal drugs are often used blindly to protect patients at risk for candidemia and elusive mold infections, further contributing to: high costs; newly recognized toxicities, such as skin cancer and; of course, antifungal resistance.” Farmakiotis said. “There is an urgent need and promising ongoing research to develop reliable diagnostic methods to diagnose fungal infections early, such as blood and even breath tests. New modalities are expected to help diagnose invasive fungal infections accurately and in a timely manner or rule them out with near certainty, thus limiting the inappropriate use of antifungals.”

In a recent study published in Nature Medicine, Jian Zhang, MD, associate professor of microbial infection and immunity at The Ohio State University, and colleagues demonstrated that inactivating the CBLB gene in mice produced an increased pro-inflammatory response from the immune system to C. albicans, and protected mice from disseminated candidiasis.
“It is very clear that through this process, we can boost our immune response against fungal pathogens and reduce the invasive fungal infection,” Zhang told *Infectious Diseases in Children*. However, there is still an additional need for newly developed antifungal therapies, he added.

Identifying a pathogen quickly, followed by immediately isolating the pathogen and preventing spread of the infection, is critical to containing a multidrug resistant fungus and possibly developing new antifungals, according to Del Poeta.

“I think that during the next 5 years we will see a dramatic increase of new antifungal agents compared to what we have right now – and the fungal community is very united in this,” he told *Infectious Diseases in Children*. “The FDA have granted Fast Track, Qualified Infectious Disease Product and orphan drug designations for many antifungals, in comparison to other antibiotics, suggesting that the government recognizes the dire need for new drugs to combat invasive fungal infections.”

**Peter G. Pappas, MD, FACP**, William E. Dismukes professor of medicine in the division of infectious disease at University of Alabama at Birmingham, claims that the prevalence of invasive fungal diseases is just not as alarming as bacterial infections, and that is the main obstacle in developing new antifungals: simply not enough is known about them.

“It takes something drastic like *C. auris* to get you to start doing the right things sometimes,” Pappas said in an interview. “The truth is that we are dealing with several multidrug resistant fungi, both yeasts and molds, that really require our attention and we need to respond in a similar way, especially as it relates to unnecessary use of antifungal agents.”

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