Tackling Human Fungal Infections

FUNGI INFECT BILLIONS OF PEOPLE EVERY YEAR, YET THEIR CONTRIBUTION TO THE GLOBAL BURDEN of disease is largely unrecognized. Most are “relatively” minor infections, but millions contract diseases that kill at least as many people as tuberculosis or malaria. Although true mortality rates are unknown because of a lack of good epidemiological data, the incidence of invasive fungal infections is rising as a result of modern medical interventions and immunosuppressive diseases, such as AIDS. Despite the high mortality rates of invasive fungal infections, they remain understudied and underdiagnosed as compared with other infectious diseases. What can be done to remedy this unfortunate situation?

Most important is to raise the general awareness of the problem. Over 600 different fungi have been reported to infect humans, ranging from common to fatal infections, including those of the mucosa, skin, hair, and nails, and other ailments including allergies. Even influential international organizations, such as the World Health Organization and the Bill & Melinda Gates Foundation, appear not to fully appreciate the burden imposed by infection with fungi.

Three issues require immediate attention. Robust, rapid, simple, and cheap diagnostics are needed to allow quicker implementation of antifungal therapeutics. Most diagnostics still suffer from long assay times and poor specificity and/or sensitivity. These problems, combined with subtle clinical presentations, often result in missed or delayed diagnosis and compromise clinical care. Appropriate diagnostics would immediately affect mortality and reduce morbidity.

Safer and more effective antifungal drugs are also needed. Although several classes of antifungal drugs are clinically available, they have had only modest success in reducing the high mortality rates of invasive mycoses such as candidiasis and cryptococcosis. Although this is due in large part to delays in disease diagnosis and fungal identification, antifungal drugs also suffer from restrictions in route of administration, toxicity, a narrow spectrum of activity, detrimental drug interactions, the development of drug resistance, and bioavailability in target tissues. These factors, and the high cost of many antifungal therapies, exacerbate the problem in resource-limited settings, where mortality rates are consequently much higher. Although combinations of existing drugs may yet prove to be more efficacious, new and cheaper drugs are needed that are rapidly fungicidal and overcome the various deficiencies listed above. Only a few drugs are currently in preclinical development, and it will be years before any of them reach the clinic (if they do). We also need a better understanding of who is at risk of infection, to facilitate targeted preventative measures.

Finally, fungal vaccines must be developed for clinical use. There are currently no approved human vaccines for any fungal pathogen, despite the advances in our understanding of antifungal immunity. Although effective in animal models, few vaccines have reached clinical trials, which is due in part to a lack of commercial interest. In addition to preventing invasive infections, an effective vaccine could also benefit those with fungal-related allergies and mucocutaneous infections, such as vulvovaginal candidiasis.

Accurate data on fungal disease burdens and their economic impact are needed to raise scientific interest and increase global investments. The major U.S. and UK funding agencies currently invest only about 2% of their infectious disease budgets in fungal research. More private funding can be generated through partnerships with academia and public health institutions. The population at risk for life-threatening fungal infections is growing worldwide, and tackling the challenges of these pathogens should become a much higher priority.*

– Gordon D. Brown, David W. Denning, Stuart M. Levitz

10.1126/science.1222236

*Neil Gow, Mihai Netea, and Theodore White contributed equally to this editorial.
Tackling Human Fungal Infections
Gordon D. Brown, David W. Denning and Stuart M. Levitz

Science 336 (6082), 647.
DOI: 10.1126/science.1222236