

## WHO publish fungal priority pathogens list

On October 25 2022, WHO published for the first time a list of 19 fungal priority pathogens. The focus was on fungi that cause invasive disease and threaten public health. Each pathogen has been classified as critical, high, or medium priority using a criteria that takes into account incidence, mortality, drug-resistance, and treatment options. The stated aim of the list is: “to focus and drive further research and policy interventions to strengthen the global response to fungal infections and antifungal resistance”. It is an urgent task. A reasonable estimate as to the population affected by long-term disease caused by fungal infections would number in the hundreds of millions, with at least 1.6 million deaths every year.

Yet, less than 1.5% of all research spending on infectious diseases is directed at fungal pathogens. As a result, only four classes of antifungals are used in clinical practice and there are few new drugs in the pipeline. In many countries, the recommended treatments for *Cryptococcus neoformans* and *Candida auris* are unavailable. Both pathogens have been classed as critical priorities. WHO stresses the importance of developing novel antifungals, but there are similar challenges to those associated with antibiotics. Pharmaceutical companies are put off by the return on investment offered by antifungals, especially given the lengthy development process and the scientific obstacles around identifying new targets.

David Denning, professor of infectious diseases at the University of Manchester (Manchester, UK) and a member of the WHO Advisory Group on the fungal priority pathogens list, pointed out that over the past 3 years a lot of patients infected with SARS-CoV-2 have died from fungal infections. “Fungal pathogens typically attack individuals who are already

vulnerable—patients with severe influenza, for example, or people who are immunocompromised”, explained Denning. Infection with HIV heightens the risk of infection with several opportunistic fungal pathogens. Every year, there are an estimated 220 000 new cases of cryptococcal meningitis and 181 000 deaths, mostly among people living with HIV.

Patients who contract or are suspected of contracting eumycetoma, the fungal form of mycetoma, face the prospect of at least 12 months’ treatment with an expensive broad-spectrum antifungal that has a modest efficacy of approximately 30%. Patients often have no option but to have the affected limbs amputated. It was not until 2017 that the first randomised controlled trial of eumycetoma drugs started (this trial is currently ongoing). The causative agents for the disease have been categorised by WHO as high priority.

“Mycetoma affects some of the poorest people in the world; to see it listed as a priority by WHO is really encouraging”, commented Borna Nyaoke, Senior Clinical Project Manager for Mycetoma at the Drugs for Neglected Diseases Initiative (Nairobi, Kenya). Eumycetoma is mostly found in sub-Saharan Africa, with Sudan accounting for a high number of cases. In low-income settings, the lack of access to diagnostics (ie, trained microscopists, culture techniques, or PCR methods) and the unavailability of a point-of-care test means that fungal infections are frequently missed; it is uncommon for there to be microbiological confirmation of the pathogen responsible for a fungal infection. Prescribing patients broad-spectrum antifungals, in the absence of a confirmed diagnosis, can accelerate the development of drug resistance.

“Laboratories, especially in sub-Saharan Africa, do not have the capacity to properly diagnose fungal infections”,

Nyaoke told *The Lancet Microbe*. “For a disease like eumycetoma, where diagnosis is a drawn-out and expensive process, there is the strong potential for misdiagnosis, misuse of antimicrobials, and resistance”.

The majority of African nations are not capable of diagnosing invasive aspergillosis and *Aspergillus fumigatus* has been classified as critical priority by WHO. Rates of azole-resistant *A fumigatus* vary widely, but are thought to have reached 80–90% in southeast Asia. The spraying of crops with azole fungicides is a huge driver; 90% of plant diseases are fungal. “The only oral medications for any kind of aspergillosis are the azoles. If we lose them, we are in trouble”, said Denning. Multidrug-resistant *C auris* is now endemic to the USA and the Indian subcontinent. Once it becomes established in a health-care facility, it is almost impossible to eliminate.

Surveillance data on the distribution of fungal pathogens and patterns of resistance are woefully inadequate; the exact burden of disease is unknown for every one of the 19 priority pathogens. Only a handful of countries around the world maintain national surveillance programmes on fungal pathogens, and fewer than 20 nations have reference laboratories that specialise in diagnosing fungal infections. Nyaoke believes that the priority pathogen list will throw a spotlight on some of the gaps in global prevention and control efforts. “Donors and policymakers pay attention to what WHO does”, she explained, “I am hoping that we will now see more advocacy and public awareness campaigns related to fungal infections, and more funding released for research and development”.

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