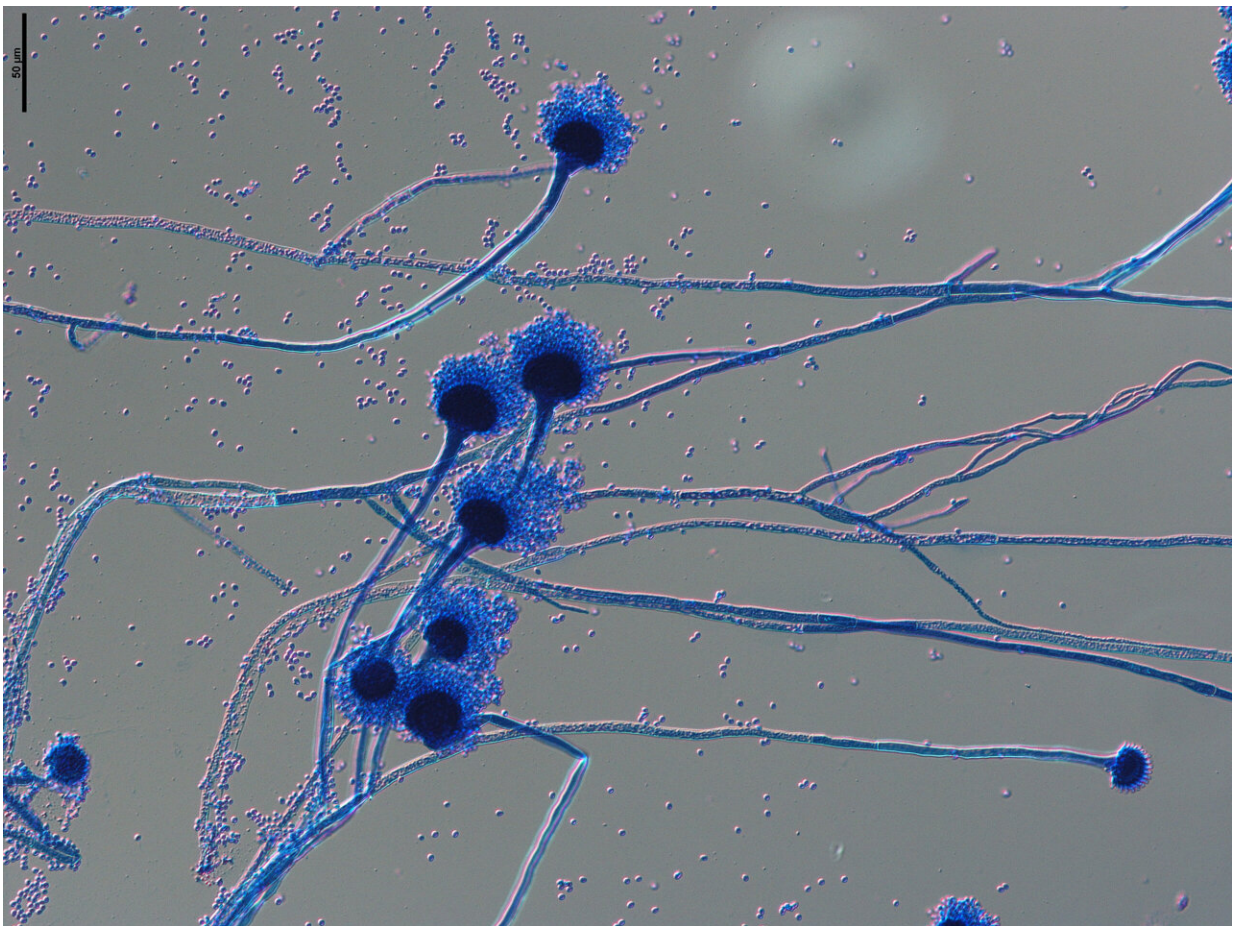


'Too little money is invested in research on life-threatening fungal infections,' says researcher

February 21 2023, by Ronja Münch



Aspergillus fumigatus is a fungus that is common in the environment. In immunocompromised people, it can cause an invasive fungal infection that is difficult to treat. Credit: Grit Walther/Leibniz-HKI

The WHO has published a list of the most important fungal pathogens for the first time at the end of 2022, thus highlighting the high importance of research on the topic of fungal infections. Leibniz-HKI director Axel Brakhage explains his assessment of the WHO list and classifies its importance for the institute.

Mr. Brakhage, what was your reaction to the publication of the WHO's 'Fungal Priority Pathogens' list? Was it overdue?

It was long overdue. And the list confirms that we have taken the right course at our institute. We started to develop our institute into a center for research on these important pathogens and the human immune response to them in 2006. The list emphasizes the importance of the topic, which has not really been recognized by various groups so far, including clinicians.

The topic was acknowledged recently in a commentary in *Nature Reviews Microbiology*: Every year, more than 300 million people are affected by severe fungal infections and more than 1.5 million die from these diseases. The actual number is probably higher. But because [health systems](#), [policy makers](#) and funders underestimate the problem, and because diagnostic capabilities are limited, it is impossible to accurately estimate the global burden of fungal infections.

Do you agree with the WHO classification and what does it mean for the work at the Leibniz-HKI?

The ranking is based on various criteria. Epidemiology plays a role, but also how serious the diseases are. Personally, I think the classification is very good because it integrates many factors. And we at the institute work on three out of the four of the fungi designated as particularly

critical: *Aspergillus fumigatus*, *Candida albicans* and *Candida auris*. These organisms are focal points of our work.

This list provides us with renewed motivation to transfer basic research into new diagnostic procedures and into the development of therapeutic possibilities. Due to the increased attention, we also expect to receive more submissions of sample material. The institute hosts the National Reference Center for Invasive Fungal Infections, which is tasked with diagnosing unusual or complex fungal infections that appear in clinics throughout Germany and, above all, being able to make the right therapy suggestions.

Why are fungal infections so dangerous?

Various factors play a role. On the one hand, they often occur in patients who have a weakened immune system, who are therefore particularly susceptible—for example, cancer patients. Secondly, many infections remain undetected, and this often leads to the death of the patients.

This situation is aggravated by the fact that we basically only have three classes of antifungal agents that can be used against fungal infections: The antibiotic amphotericin B, which, however, has considerable side effects; echinocandins, a class of substances that act against the cell wall; and azole derivatives that inhibit the biosynthesis of fungal membranes.

All of these factors combined, unfortunately, mean that fungal infections cause death in patients much more frequently than bacterial infections. In some groups of patients, severe fungal infections cause a lethality of between 30 and 90 percent.

Why is it that viral and bacterial infections, as well as antibiotic resistance, are now big topics in the media,

while fungal infections have so far received little attention from the general public?

I think that of course it has to do with the fact that we need to inform the public more. That is not to say that [antibiotic resistance](#) is not really a very big problem. However, these resistances now also apply to fungal infections. And that is fatal because, unlike bacteria, we have much fewer possibilities to switch to alternative drugs. We are already seeing multi-resistant fungi, such as *Candida auris*. The WHO report has made it clear that this is not only a national problem, but a major problem worldwide.

For example, there have recently been large outbreaks of mostly fatal mucormycosis in India. This is usually a rare disease, I estimate we normally have about 10,000 patients in the world per year. In India, several thousand suddenly became infected as a result of COVID19. Besides the COVID19 disease, this was probably also due to untreated diabetes in many patients. Increased sugar levels make people more susceptible to fungal infections.

In addition to those already mentioned, which fungi play a special role for research at the Leibniz-HKI?

We also research fungi that are classified as High Priority Pathogens by the WHO. These include fungi that cause mucormycosis—for example the genera *Mucor* and *Lichtheimia*—or *Fusarium*.

The latter infect plants, but can also cause infections in humans. But of course, there are not only pathogenic fungi, those are probably only 150 species at most. According to analyses, there are up to 5 million fungi in total, and those are highly interesting organisms. We are also working on them to discover new active substances—for example antibiotics, but

also substances that act against fungi, so-called antimycotics.

Can you name a few milestones of research at the Institute?

The groups at the Institute have done a lot of work to identify new virulence determinants—that is, to clarify the question of why precisely these few fungi are pathogenic and how they can outsmart the immune system. We have discovered interesting molecules: for example, a certain melanin on the surface of *Aspergillus fumigatus*, which only occurs in very few fungi and which helps the fungus to hide from the immune system.

And we have discovered a new peptide toxin, Candidalysin, the first toxin ever in a eukaryotic microorganism. It helps *Candida albicans* to become pathogenic. We have also researched how the human immune system fights fungi. We have discovered, for example, that small extracellular vesicles produced by immune cells are able to kill [fungi](#). These are also promising gateways to develop new therapies.

Where does research into fungal infections in Jena stand in a global comparison?

We have had the opportunity here in Jena since the 2000s to establish a center for the study of fungal pathogens. And of course, we cooperate with the other centers around the world, but there are not very many of them. I would rank the Leibniz-HKI among the largest in the world.

In summary, what do we need to be better equipped against fungal infections?

What we need, based on the very good analysis of the WHO, is much greater financial support, also from the public sector. Too little money is invested in research on life-threatening fungal infections, much less than in viral or bacterial infections. I hope that this WHO report will also make it clear to decision-makers that we need to substantially expand research and development in order to solve this urgent problem. We need much more training in the natural sciences as well as among clinicians.

We need more researchers dedicated to this very complex issue. They need to develop much better and faster diagnostics, that is crucial. Every hour counts. And we need better therapeutic options.

More information: List of pathogens:
www.who.int/publications/i/item/9789240060241

Matthew C. Fisher et al, The WHO fungal priority pathogens list as a game-changer, *Nature Reviews Microbiology* (2023). [DOI: 10.1038/s41579-023-00861-x](https://doi.org/10.1038/s41579-023-00861-x)

Provided by Leibniz Institute for Natural Product Research and Infection Biology - Hans Knoell Institute -

Citation: 'Too little money is invested in research on life-threatening fungal infections,' says researcher (2023, February 21) retrieved 2 May 2024 from <https://medicalxpress.com/news/2023-02-money-invested-life-threatening-fungal-infections.html>

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