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From *Candida Auris* to The Last of Us *Cordyceps*: Addressing Fungal Infections before it's too late

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Introduction

In 2009, *Candida auris*, a novel yeast species, was first described after its isolation from the ear canal of a patient in Japan (named from the Latin: *auris* means ear). It has been isolated in all continents, except in Antarctica, and it is an emerging pathogen considered an urgent global health threat, with high transmissibility and mortality rates in healthcare settings [1,2]. The widespread and prolonged use of antifungal agents has given rise to multidrug resistance that limits the therapeutic available options. Some superficial fungal infections can be treated or prevented with topical or systemic treatments, however, although high cure rates can be achieved, systemic fungal infections are associated with high mortality [3,4].

In the videogame and post-apocalyptic drama television series launched in 2023, a real-life fungus called *Cordyceps* turns humans into violent zombie creatures that spread it to others through bites. The Last of Us came as a reminder that many fungi can cause life-threatening invasive fungal infections [5].

Resistance of *Candida Auris*

Candida auris is considered a multi-drug resistant (MDR) species, as it has shown innate resilience to fluconazole and emerging resistance to other antifungal drugs, such as 5-flucytosine, amphotericin B and echinocandins, making it comparable to a "superbug". Among the reasons for public health concern is C. *auris's* ability to spread both from person to person and through surfaces. Unlike other Candida species, C. *auris* is also resilient to hygiene and infection control methods, making it easily able to cause deadly nosocomial outbreaks [4,6].

The surfacing of drug-resistant microbes (superbugs) is a well-known problem generally related to the misuse of antibiotics in combating bacteria, usually due to a lack of awareness about the dangers caused by these pathogens. Consequently, the neglect of the adaptability of bacteria has increased antibiotic resilience and created untreatable infections. On this matter, while there has been an emergence in worry about MDR bacteria, mycotic infections continue to be overlooked and, therefore, the limited forms of treatment for such diseases are worrying in the context of emerging superbugs like C. *auris*. The videogame and TV show The Last of us have helped to bring awareness to this issue through the depiction of a fictitious human-infecting strain of *Ophiocordyceps unilateralis*, which causes an unstoppable pandemic that collapses societies worldwide. The fiction succeeds in displaying a major concern toward the lack of effective prophylactic measures, such as antifungal vaccines, and shows how drugs are ineffective toward the depicted strain [7].

Recent developments in antifungal therapy have focused on re-formulating existing antifungal agents, however, death rates from systemic fungal infections are unacceptably high, and new medicines are needed [4]. Although, in real life, the portrayed fungus doesn't infect humans, the possibility of new harmful mutations cannot be ignored. The number and heterogeneity of patients at risk for invasive fungal infections have increased, the selection of therapeutic strategies is complex, and the classes of available antimycotics are well overdue. In this way, the emergence of resistant pathogens highlights the need for the development of antimycotics [8].

Currently, *Candida auris* is the first and only fungal pathogen considered an urgent health threat [7]. To ensure it will be also the last, it is necessary to conduct more research on mycotic infection treatments and prophylactic measures before more species of fungi become MDR.

Conclusion

Antifungal resistance is a growing global public health concern, thus, it is urgent to coordinate pharmacological interventions, monitor patients, and choose the appropriate antifungal to achieve the best outcomes and minimize the resistance.

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