

From Fictional Pandemics to Potential Reality

The Realities and Myths of 'The Last of Us' Cordyceps Fungus

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Ophiocordyceps unilateralis, also known as the zombie-ant fungus, was discovered over a century and a half ago. It recently garnered heightened attention, largely attributed to its portrayal in the popular TV series *The Last of Us*, adapted from the 2013 video game with the same title. In both forms of media, the narrative unfolds in a world decimated by a pandemic caused by a fungus of the genus *Cordyceps*. Given the real-life existence of this fungus, a question arises: should we be concerned about the possibility of a fungal-pandemic like the one depicted in the show?

O. unilateralis, an insect-pathogenic fungus endemic to tropical forests, exhibits a remarkable life cycle that is tightly linked with its ant-hosts. The infection starts when the fungus spores attach to a traveling ant's exoskeleton, followed by enzymatic penetration and takeover of the host's body. The fungus manipulates the ant's muscles, compelling it to undertake peculiar behaviors. One of these is muscle convulsions, which causes the ant to fall from its tree onto the forest floor. It then compels the ant to climb up a plant stem and use its mandibles to attach itself to the vein; this usually occurs around 26 centimeters above the ground, where fungal growth conditions are ideal. Having secured itself, the ant meets its ultimate fate as the fungus completely takes hold, permanently binding to the plant. The fungus completes its life cycle by generating mycelia and sprouting fruiting bodies out of the ant's head, which eventually rupture and release spores to perpetuate the cycle.

Despite the disparity in infection mechanisms, both real and fictional portrayals in ants and humans converge on a shared outcome – a manipulated host succumbing to its parasitic invader.

In *The Last of Us*, a fictionalized account of a *Cordyceps* outbreak unfolds, deviating from the accurate behavior of *O. unilateralis*. The narrative envisions a scenario wherein rising temperatures cause the fungus to evolve and adapt to prefer the temperature of the human body. The fungus was introduced into the human population through infected crops within the global food chain. Ingestion resulted in an infection within the host, causing them to exhibit aggressive behaviors and display physical deformities. Such deformities involved the fungus expanding over the face, enveloping the eyes, and causing the host to lose vision, with the fungus ultimately gaining control over the entire body. The resulting creature is horrifically mutated and passes the infection on through biting the uninfected. Despite the disparity in infection mechanisms, both real and fictional portrayals in ants and humans

converge on a shared outcome — a manipulated host succumbing to its parasitic invader.

Given the actual existence of the fungus and the rising global temperature, is there cause for concern regarding the mutation causing a fungal pandemic among humans? A grounded scientific assessment offers some reassurance. Firstly, hundreds of *Ophiocordyceps* fungi have evolved to target specific host species. This specificity, developed over millions of years, suggests that a singular environmental change may not trigger cross-species transmission. Secondly, evolutionary constraints limit the extent to which fungi can undergo change. *Ophiocordyceps*, with their specific genetic makeup, may face hurdles in rapidly adapting to infect humans. The likelihood of the fungus causing a pandemic in humans is minimal. However, the discussion raises the broader issue of global warming having profound impacts on organisms surrounding us, potentially leading to issues for human health.

Despite its negative portrayal in the show, the *Cordyceps* fungus appears to not be that harmful in terms of real-life impacts on human health. Ongoing scientific inquiry, particularly in pharmaceutical and medical fields, suggests significant potential for positive applications within drug discovery. However, not all fungi share the same benign or beneficial characteristics.

Beyond *Ophiocordyceps* exists a broad spectrum of fungal species, and some pose a great threat to human health. However, out of the millions of discovered fungi, only a few hundred are harmful to humans. *Candida auris*, a particularly dangerous fungus, has emerged in the past decade. It is known for thriving at a higher temperature than most fungi and is capable of spreading from person to person. The fact that it exhibits multidrug resistance and can rapidly spread in healthcare settings, as emphasized in the CDC's March 2023 warning, highlights its potential as a worldwide threat. The global risk posed by *Candida auris*, especially in the context of bloodstream infections, underscores the significance of focusing our attention on fungal species currently impacting humans instead of those that one day could.

While the fictional narrative of a fungal pandemic might spark fear, it is crucial to differentiate between fiction and reality. *Ophiocordyceps* might have massive prowess against insects; however, it is beneficial rather than harmful to humans. Although fungi are not turning us into disfigured, flesh-hungry creatures anytime soon, they still are capable of serious damage. As we navigate the intricacies of fungal behavior, it becomes evident the focus should not solely rest on *Cordyceps*; rather, attention should be directed towards the existing fungal species already demonstrating the dangers they pose for us. ● ● ●

