

# 'The last of us': How likely is a fungal apocalypse?

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HBO's hit series "The Last of Us" envisions a world decimated by a

fungal apocalypse.

A real-life insect [fungus](#) called Cordyceps makes the leap into humans, turning those stricken into violent zombie-like creatures that spread it to others through bites. Society collapses in a matter of days after the fungus emerges.

But viewers can relax: There's very little real risk that Cordyceps itself could actually evolve to present the sort of risk to humanity displayed in the show, [fungal infection](#) experts say.

However, the show does accurately portray a number of factors—climate change, [drug resistance](#), few reliable antifungal agents—that are increasing the health risks that various fungi and mold pose to humans, the experts add.

"I tell people sometimes these are the most clinically important infections that you've never heard of, because of the staggering numbers of people that they actually affect," said [Karen Norris](#), chair of immunology and translational biomedical research at the University of Georgia's College of Veterinary Medicine.

Fungal infections are responsible for more than 75,000 hospitalizations and nearly 9 million trips to the doctor every year in the United States, according to the U.S. Centers for Disease Control and Prevention.

But newer data suggest that the threat of fungal [infection](#) is even more pronounced, and growing.

More than 666,000 [fungal infections](#) were diagnosed in about 35.5 million U.S. hospitalization cases documented in 2018, according to a Norris-led study published last year in the journal [Open Forum Infectious Diseases](#).

A diagnosis of fungal infection "doubles their hospitalization costs, their hospitalization stay, and it doubles the risk of death compared to individuals with the same sort of comorbid situations without a fungal infection," Norris said. "So these are really, really serious infections."

Reports like those have led the United Nations Environmental Program to issue a new report earlier this month, "Bracing for Superbugs," that cite climate change and antimicrobial resistance as two of the [greatest threats](#) to human health.

## A fungal nightmare

The real-world Cordyceps fungus is blood-chilling—for [carpenter ants](#).

Ophiocordyceps unilateralis spores slip inside an ant's body on the jungle floor and begin to replicate, eventually making their way to the brain.

The fungus hijacks the ant's brain, slowly taking over its behavior. The fungus forces the mesmerized ant to leave its hive and find humid terrain that promotes its growth.

At the end, the fungus compels the ant to lock its jaws into the underside of a leaf, where it remains while being eaten alive from the inside. The fungus eventually erupts from the head of the dead ant and bursts, spraying a cloud of spores intended to infect more ants.

It's a horrifying fate to contemplate, but one not likely to occur in humans, said [Dr. Scott Roberts](#), associate medical director for infection prevention at Yale New Haven Hospital.

"It seems to really infect a very specific niche in nature, which is this certain species of ant," Roberts said, noting that the fungus does not appear capable of infecting even other [insect species](#).

"For this specific Cordyceps to make the leap from this ant species to humans is really impractical, unless it went through a significant amount of evolution in a short period of time," Roberts added.

Fungus and mold species also don't tend to spread the way viruses or bacteria do, with one infected person passing the bug on to others, Roberts continued.

"By nature, fungus and molds really do not spread person to person, with few exceptions," Roberts said. "The vast majority are in the environment. We inhale them every time we walk outside—certainly in a forest, where there's just tons of fungus and mold in the air. And really in only rare instances, mostly with patients with profoundly decreased immune systems, can they cause problems."

## **Climate change favors fungi**

The Cordyceps pandemic in "The Last of Us" occurs when climate change prompts the fungus to evolve around humankind's best defense against fungal infections—body temperature.

That part of the show is accurate, experts say.

Rising temperatures associated with climate change appear to be eroding humankind's evolutionary advantage against some types of fungal infections.

"A very prominent mycologist who I follow academically, [Dr. Arturo Casadevall](#), said that he hypothesizes that the reason we're 98.6 is because that's really the threshold at which a lot of fungal species cannot grow," Roberts said.

Norris points to an emerging fungus of concern called Coccidioides,

which causes a lung infection called Valley fever. The fungus thrives in hot, dry soil.

"It's mainly present in the southwest U.S., and for different reasons—climate change and extended development in areas where people hadn't lived before—that organism has spread up to California and extensive regions in the West," Norris said.

Valley fever most often is not a serious infection, Norris added.

On the other hand, *Candida auris* is a very serious fungal threat that also appears to have been spurred on by climate change, Roberts said.

A type of yeast found in soil, *Candida auris* "was not previously a human pathogen, so it has adapted to the higher body temperature and now is a very serious concern," Norris said.

*Candida auris* can cause a life-threatening blood infection if it infects a hospitalized person already weakened by other health problems.

"This is a fungal species that nobody knew about before 2009, and all of a sudden it was detected independently on four continents at the same time, suggesting that [climate change](#) led to the rise in this new organism that evolved to adapt to higher temperatures," Roberts explained.

*Candida auris* also spreads more easily than other fungal threats, prompting the CDC to list the fungus as a potential infection threat among people in health care settings.

"It sticks to the environment really easily, and studies have shown it can spread patient to patient," Roberts said. "*Candida auris* can really stick to surfaces and spread through reusable medical devices, for instance."

## Few medicines

The rise of *Candida auris* reflects another fear experts regularly express, in that it doesn't respond well to antifungal medicines.

"One of the reasons that make it a very serious threat is that many of the clinical isolates that have been observed are resistant to one or more of the antifungal drugs. That's a problem," Norris said of *Candida auris*.

There aren't a lot of antifungal medicines available at all, compared to the array of antibiotics and antivirals available for people with bacterial or viral infections, Norris and Roberts said. If resistance grows in fungi, people with severe infections will be left with few options.

"It has been an area that has been underfunded and understudied for a long time. There's a core group of people that have been toiling in the vineyard for a long time on these, but it has not been an area that has been supported for the kind of research that is necessary," Norris said.

Doctors also lack good tools for diagnosing a fungal infection and differentiating it from a bacterial or viral infection.

"An individual that's in the hospital or even in the ICU for other conditions, there's a little bit of a delay. We don't have the best diagnostics still for fungal infections, compared to bacterial infections or viral infections," Norris said.

That delay can cost patients their lives.

"Sometimes just a couple of days of delay in diagnosis of a fungal infection is critical," Norris continued. "These can be very rapidly progressing infections. Once they get a hold, it is difficult to treat them. And the treatment that is the standard of care, antifungal drugs, there's a



limited number of those."

Severe fungal infections occur most often in people with compromised immune systems, such as cancer patients or people with an autoimmune disorder, Norris found in a 2021 study published in the journal [\*Clinical Infectious Diseases\*](#).

But even folks with common inflammatory conditions like diabetes, lung disease, rheumatoid arthritis or Crohn's disease are more vulnerable to an opportunistic fungus, Norris found.

"Then there are individuals who have other infections, for instance, influenza," Norris said. "Some individuals are more susceptible to getting an infection with an invasive fungal agent on top of their influenza.

"And then, of course, COVID. We saw a very high uptick in patients with serious COVID in the hospital, in the ICU, who then also acquired a fungal infection. And that accounted for a significant amount of the mortality in the ICU during the height of COVID," she continued.

## **Fungi to watch out for**

Norris' 2022 study found that three fungi accounted for more than three-quarters of fungal infections diagnosed in hospitals:

- Candida, and in particular *Candida auris*
- *Aspergillus fumigatus*, a common mold that infects the lungs and sinuses
- *Pneumocystis*, which causes pneumonia.

Norris and her team are working on a vaccine that could protect against all three of these fungal threats.

"Individuals that would be highly susceptible to all of these infections are susceptible to all of them," Norris said. "The thing that makes this potentially a game changer is that the vaccine induces an immune response that is effective against at least three pathogens, and we are testing it against others."

The fungus vaccine is now in animal trials. If the research team finds funding, Norris says they could start and finish human trials for the vaccine within the next five years.

Other researchers are working on a vaccine for Valley fever, Norris added.

But while fungi are a rising health threat that need to be taken seriously, both Norris and Roberts emphasize these pathogens are very unlikely to cause a "Last of Us" scenario—or even the next pandemic.

"The way that fungal and mold species spread so slowly, I really don't have a major concern for any sort of pandemic threat from a fungus or a mold," Roberts said. "Were I watching the show, I would have no concerns that this is a realistic portrayal of what's going to happen with the next fungal species. But I'm very grateful for the show because it's raising awareness."

**More information:** The World Health Organization has more about [health-threatening fungi](#), while the U.S. Centers for Disease Control and Prevention has more on [fungal diseases in the United States](#).

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