The fungal zombies in HBO's 'The Last of Us' are based on real, horrifying biology

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The Last of Us. Credit: HBO Max

In the premiere of HBO's big budget video game adaption "The Last of Us," a scientist on a 1960s Dick Cavett-like talk show raises the idea that a fungal, not viral, infection will spell the end of humanity. On the

surface, it's laughable, and the idea is met with bemused laughter by the host and audience.

But as the scientist explains his theory, the energy in the room slowly shifts from amusement to horror. All it would take is for one gene in a fungus to mutate and suddenly it "could become capable of burrowing into our brains taking control not of millions but billions of us," he says. "Billions of puppets with poisoned minds, permanently fixed on one unifying goal: to spread the infection to every last human alive by any means necessary."

The scientist goes on to say there are no treatments or cures for this kind of infection. There's only one possible conclusion: "We lose."

In the world of "The Last of Us," those words are prophetic. In 2003, a fungal infection ravages the world, turning humans into ravenous, mind-controlled zombies. HBO's latest hit, and the game that it's based on, might sound like pure science fiction, but it's actually based on real, horrifying science.

The developer behind "The Last of Us," Naughty Dog, took inspiration for its fungal zombies from the cordyceps fungus. A kind of parasitic fungus that infects insects and, in some cases, plants, it's nature's zombifying agents.

The spores dispersed by the cordyceps sit in the soil and attach to the bodies of insects. Over the course of 24 to 48 hours, the parasite grows into the body of the insect, before spreading throughout the body over the course of a few weeks.

"It already starts changing the neurobiology of the host so that it basically makes it a zombie organism, meaning this parasite takes over, producing some kind of neurotoxins or neuromodulators that change the

behavior of the host," says Rebeca Rosengaus, associate professor of marine and environmental sciences at Northeastern.

The parasite surrounds the muscles of an insect, affecting its motor neurons and turning the host into a marionette. David Hughes, an entomologist who consulted on "The Last of Us" game, says there are clear similarities between the fictional infected and how the parasite operates in the ants he studied.

At first, infected humans in "The Last of Us" don't immediately display signs of infection. However, that quickly changes. They start twitching and become hyperaggressive and overly energetic. Survivors in "The Last of Us" call those infected in this stage "runners."

This behavior is somewhat based in reality, Hughes says. The cordyceps parasite releases a chemical compound that causes insects to twitch and convulse.

"They do not enter the brain, but what they do is push chemicals into the brain across the blood-brain barrier so that they can control the brain at a distance," Hughes says.

Ants infected with the cordyceps parasite also start becoming more antisocial, a notable shift in highly social ant societies, and wander off from the rest of the colony. Similarly, the show's infected humans lose all ability to speak and, instead, scream and shriek in rage and pain.

But the parasite isn't just forcing the host to wander mindlessly. There's intent and purpose behind where infected ants—and their fictional counterparts—roam.

Ants are very adept at detecting infected members of their colony through changing chemicals and scents. If an ant is sick, it is killed and

its body is deposited outside the colony. In order to circumvent that, the parasite needs to make its host die outside the colony if it has any hope of infecting more hosts.

This manifests in a behavior called summiting. The infected host will climb to a certain height before lodging its mandibles in a branch, stem or leaf. Up until this point, the host was still alive but totally unable to control its movement. However, at this point, the fungus starts eating the host alive from the inside before sprouting a long tendril-like stalk with a "fruiting body" that disperses spores. From on high, the spores catch on the wind and can infect an even larger area.

"The ants are forced every day to go out looking for food, so as they go out, they walk underneath a sniper's alley of their dead siblings, which are hanging underneath the underside of the leaf, producing spores," Hughes says. "You can imagine a dome of death which is surrounding the colony that the ants have to pass through every day, and this is why the fungus is winning."

Although the 2013 video game featured spores as a method of infection, HBO's adaptation of the "The Last of Us" has done away with them, marking the biggest departure from its scientific inspiration.

As for whether we'll ever have to face a fungal zombie outbreak, Hughes says there's no reason to worry. The motor systems of ants and humans are different enough that the cordyceps can't make the leap into humans—but that doesn't mean fungi can't affect our behavior or even infect our bodies.

LSD is, of course, derived from hallucinogenic fungi. But other kinds of fungi can have a much more dangerous effect. The coccidioides fungus causes a condition called Valley Fever when inhaled and has been found, notably, in California prisons.

In 2022, the World Health Organization released its first list of health-threatening fungi, which included 19 fungi that "represent the greatest threat to public health." According to the report, fungal infections kill about 1.6 million people per year and present a particular danger for severely ill patients who are already immunocompromised. The frequency and geographic range of fungal diseases are also on the rise, due to global warming and an increase in international travel and trade.

"Emerging from the shadows of the bacterial antimicrobial resistance pandemic, fungal infections are growing, and are ever more resistant to treatments, becoming a public health concern worldwide," says Dr. Hanan Balkhy, WHO's assistant director of antimicrobial resistance

While fungal infections are becoming more common, the idea of a fungal apocalypse is still the stuff of science fiction, Hughes and Rosengaus agree. However, Rosengaus says fungal parasites can still provide a new lens through which to look at more common viral infections like the flu or even COVID-19. There's a reason we sneeze and cough while we have the flu.

"The word that we call 'symptoms,' yes, they're symptoms of the disease, but the question I think is interesting to ask is, are these symptoms really the reflection of the [virus] manipulating our physiology, our behavior, in order to be more helpful in transmitting the disease?" Rosengaus says. "It's astonishing the kind of evolutionary back and forth that these parasites have been able to manage in order to manipulate the behavior of the host."

Provided by Northeastern University

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