The Last of Us: Why making fungal vaccines is so challenging

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Fungus Infected Frog. Credit: Wikipedia Commons

Warning: this article may contain spoilers.

HBO's hit TV adaptation of the popular video game "The Last of Us" has just aired its season one finale.

While there are some aspects of the series' premise that are far from realistic (such as the possibility of a fungal pandemic), other elements are more grounded in reality.

Take the fact that even 20 years after the outbreak of the apocalyptic fungal pandemic there was no cure or vaccine to protect against the deadly cordyceps fungus. This isn't all that unrealistic, considering in reality there are currently no vaccines available which can protect against fungal infections.

This is largely due to the number of difficulties developing fungal vaccines presents.

First, the people most likely to get sick from fungal infections would not be able to receive a vaccine.

The most effective type of vaccine is usually a "live vaccine." Essentially, this gives people a safe form of the pathogen which is unable cause a proper infection. This in turn trains the immune system to fight the disease, preparing it for attack by the real, dangerous bug.

But people with weak immune systems (due to cancer, certain types of drugs or viral infections, for example) can't receive these types of vaccines, because even a safe form of the bug might harm them. Yet most of the people who get sick from fungal infections have weak immune systems. This means that even if a live fungal vaccine was created, the people that would most benefit from one would be unable to get it.

While there are other types of vaccines—such as the sub-unit vaccine, which uses an even smaller part of a virus or bacteria to train the immune system—these tend to be even less effective, although often safer for people with weak immune systems.

Another problem with developing fungal vaccines is that many fungi are shape-shifters.

Fungal infections typically start after inhaling spores. Our immune systems are good at killing spores and preventing them from causing disease. But an infection happens if the immune system fails to do that. Once inside the body, the fungus then shape-shifts into a new cell type that the immune system may not have seen before.

The purpose of a vaccine is to train the immune system to see and fight a pathogen in order to prevent infection. But since fungal cells change shape, this makes developing a fungal vaccine very complex since we can't predict how the cell may shape-shift once inside the body.

Antifungal treatments

Another approach to stopping fungal infections is medicines that can fight them off.

One approach is by making drugs that kill fungi or stop them from growing (antifungals). Unfortunately, like vaccines, developing new antifungals is very difficult.

This is because fungal cells are similar to our own in many ways. As such, finding targets for a drug that won't be toxic to our own bodies is tricky. Not to mention there's the growing problem of antifungal resistance, where fungi can no longer be destroyed by the drugs designed to kill them. This would explain why in the last two decades, there have been no new types of antifungal drugs developed, either to treat an infection or prevent them for happening in the first place.

Immune-boosting drugs have also been used to help treat fungal infections in some cases. This approach relies on researchers learning

how a healthy person's immune systems fights an infection, and then using this information to repair a patient's weakened immune system to help protect them against infection. This type of approach has given early successful results for some types of fungal infections in humans, and may be able to work alongside antifungal drugs to improve how we treat these infections.

Cordyceps vaccine

In "The Last of Us" TV show, they would almost certainly have come upon many of these difficulties—which may explain why they'd been unable to develop a cordyceps vaccine. A major hurdle that would need to be overcome is getting to know the cordyceps fungi causing the zombie-like infection.

As with all vaccines, it's essential to understand the bug and figure out what mechanisms it uses to avoid being destroyed. This is needed to decide which vaccine strategy has the best chance of working.

But growing real cordyceps in a laboratory is difficult and time-consuming. This is true for many fungal species, since it's hard to replicate natural growth conditions in a lab. This slows our progress in understanding these microbes and how we can use their natural defenses to prevent them from causing infections.

Having access to a patient who is immune (such as Ellie) may give some clues about how to develop other types of treatments. Antibodies (protective proteins produced by the immune system) can be helpful for treating infections and may be injected into patients as a treatment. Patients who are immune can also help us learn which antibodies are effective and which protect against infection. Luckily for us, antibodies can be drawn from the blood or tissue of living patients.

While things may not be looking very hopeful in the fictional world of "The Last of Us," things are looking a little more hopeful in reality. A number of fungal vaccines that have made it into clinical trials have shown promising results in humans—including a vaccine which protects against yeast infections. This is an important step in preventing further harm from fungal infections, which currently cause hundreds of thousands of deaths every year alongside billions of infections.

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