COVID-19 has now been found in 29 kinds of animals, which has scientists concerned

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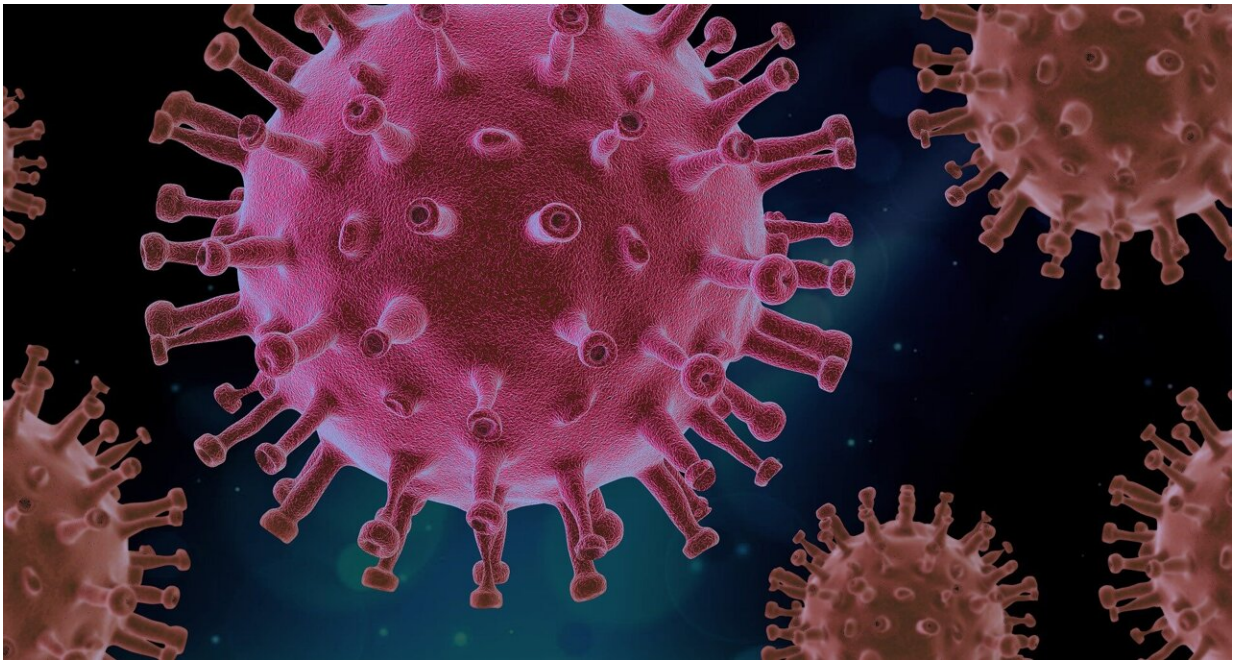

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The 11-year-old cat had been vomiting and lethargic for several days, and showed little interest in food.

When the pet was examined at the University of Pennsylvania's Ryan Veterinary Hospital in September, her owner mentioned a possible clue to the symptoms: Someone in the household had COVID-19.

The animal's nasal swab turned up negative. A fecal sample, on the other hand, told the tale. The shorthair feline was infected with the Delta variant.

Scientists have now found the coronavirus in 29 kinds of animals, a list that has been steadily growing almost since the start of the pandemic and includes cats, dogs, ferrets, hamsters, tigers, mice, otters, and hippos. In most cases, the animals have not been shown to transmit the virus back to humans.

But in at least two cases, it looks as if they can. Minks have spread the virus to people, and in a new Canadian study, scientists identified one person who tested positive after unspecified "close contact" with infected white-tailed deer.

The good news is that with all known variants that have circulated in humans, the vaccines remain very good at preventing severe disease. The concern is that as the virus continues to circulate in other animals, it could accumulate mutations that render the vaccines less effective. Increased surveillance is key.

We spoke to three scientists about what the latest animal findings mean: Eman Anis, assistant professor of microbiology at Penn's School of Veterinary Medicine; Suresh V. Kuchipudi, a professor of veterinary and biomedical sciences at Pennsylvania State University; and Frederic Bushman, professor of microbiology at Penn's Perelman School of Medicine.

Q. How do they find COVID in animals?

A. In the case of deer, scientists typically test animals that have been hunted or killed in car accidents.

With domestic and zoo animals, testing can be done much as it is in people. A sample taken with a nasal swab can be tested just like a human swab—using the laboratory method called polymerase chain reaction (PCR).

The exact procedure might vary from animal to animal. When vets tested a tiger at the Bronx Zoo in April 2020, for example, they wisely sedated her in advance.

For now, the American Veterinary Medical Association recommends against routine testing of pets, as they do not often get sick with COVID, and they are not thought to play a big role in spreading the disease to humans. But testing may be warranted if the animal shows symptoms consistent with COVID, or has come in close contact with an infected human, the association says.

Both things were true for the cat at Penn. In a case study, vets wrote that the animal's symptoms might be partly explained by another condition, a gastrointestinal disorder called chronic enteropathy. But the cat's owners had kept that condition under control by managing her diet. The cat began vomiting only after the household member came down with COVID, suggesting the virus was indeed to blame.

Once the cat tested positive, her sample was sent to Bushman's lab, which used a sequencer to read the entire genome of the virus. It was clearly the Delta variant and was a close match to versions of Delta also found circulating in people in the Philadelphia area.

Q. Why worry about COVID in animals?

A. Every time a virus makes copies of itself inside a new host, it makes a few random "spelling" mistakes in its genetic code—mutations. Most mutations either have no impact on the fitness of the virus, or they may

cause it to become less viable.

But every so often, a set of mutations will improve the microbe's ability to spread to other cells, and ultimately its ability to infect other hosts.

With the right combination of attributes, a virus can even jump from one host species to another. That's how the COVID pandemic got started in late 2019, with horseshoe bats—though a debate is ongoing as to whether bats spread the virus to humans in a live-animal market, through a laboratory accident, or some other means.

Public health agencies have done a fairly good job of tracking viral mutations in infected people, sounding the alarm when a set of worrisome mutations warrants the label "variant of concern." But there is far less surveillance of the virus in animal populations, especially in the wild, said Anis, the microbiologist at Penn's vet school.

"It could be evolving in hosts we are not aware of," she said.

In the infected deer in the new Canadian study, the coronavirus had evolved dozens of mutations not found in other strains, leading scientists to proclaim it as "highly divergent." Translation: on the family tree of the virus, this lineage was off on its own branch—suggesting it had been circulating in deer and racking up new mutations for a while, unbeknownst to science.

This lineage does not appear to be different enough that it would evade protection from the vaccines. That's because the vaccines teach the human immune system to recognize the "spike" protein on the exterior of each virus, whereas many of the mutations in this deer version occurred elsewhere in the virus.

Still, we need to keep an eye on it, said Penn State's Kuchipudi, who was

not involved in the Canadian study but has done his own studies in deer. As the virus continues to circulate in deer, more mutations will arise, and we need to be ready in case.

"There is no need to panic," he said, "but this is not something we can ignore."

Q. How many more tricks does this virus have in store?

A. Early in the pandemic, scientists determined that the coronavirus spike was a very close fit with "receptors" found on cells in human airways, almost like a match between a key and a lock. That's what made it so adept at penetrating cells.

That finding was essential in developing the vaccines. They teach the immune system to make antibodies that bind to the spike, interfering with its ability to get inside a cell.

But the threat of any particular virus is about much more than penetrating cells, said Bushman, the Penn microbiologist. Other segments of the genetic code are involved in making copies of the virus inside the host cells, exiting the cell, and traveling from host to host, among other steps in its virulent journey.

Along came Delta, followed by omicron, both of which had acquired new mutations that made them more transmissible. The vaccines still offered good protection against severe disease from both strains, yet they managed to cause plenty of havoc.

One theory is that omicron developed in an immunocompromised person, evolving more mutations as the person was unable to fully clear

it. Another theory is that the strain evolved somewhere in the developing world, where there is less surveillance, or that it evolved in a wild animal, such as a mouse.

Q. Are more worrisome combinations in store?

A. "It's hard to predict what evolution's going to come up with," Bushman said. "The virus will probably change different ways in different animals. Some of them probably won't infect humans as well. But the fear is that maybe some new one will come along that does infect humans well."

The only answer, he said, is to keep looking.