

Animals as Carriers For Alpha- and Betacoronaviruses

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Ria Ghai, an associate service fellow at CDC. We'll be discussing how animals can serve as hosts for emerging coronaviruses.

Welcome, Dr. Ghai.

[Ria Ghai] Hi Sarah.

[Sarah Gregory] Coronaviruses have been around for a long time now. When were they first discovered?

[Ria Ghai] So, coronaviruses that affect animals like livestock, pets, and laboratory animals were actually first discovered in the 1930s. But at that time, what the actual virus was wasn't known. And it wasn't until the 1960s that the first human coronaviruses were discovered. So, they're called HCoV-229E and OC43. These are two coronaviruses that many people might not know are actually still circulating today and cause the common cold in people.

[Sarah Gregory] In this study, you focused primarily on alpha- and betacoronaviruses. Tell us what they are.

[Ria Ghai] So, alpha- and betacoronaviruses are two types of coronaviruses, and they're both species within the coronavirus family that are...have some members that can infect people. So all emerging coronaviruses in people, like SARS and MERS, and now of course SARS-CoV-2 which causes COVID-19, they're all betacoronaviruses. And so what we did for our study was we chose to focus specifically on just those two species (alpha- and betacoronaviruses), because we knew that they each had some members that were able to infect people.

[Sarah Gregory] So how many types of coronaviruses are there actually out there?

[Ria Ghai] It's a great question, and we don't know for sure. Many coronaviruses circulate in wildlife, which is why they might have remained undiscovered. So, we know of one study that estimated that there actually could be thousands of coronaviruses just in bats alone. However, there's only seven known coronaviruses that have ever circulated in people. So, there's four that cause the common cold (I spoke just briefly about two of those a second ago) and there's also three others which we call high-consequence coronaviruses: that's SARS, which only circulated from 2002 to 2004; MERS, which still causes disease in the Arabian peninsula; and now of course SARS-CoV-2.

[Sarah Gregory] Okay. So only those can spread to humans.

[Ria Ghai] Yup, only those ones are known so far.

[Sarah Gregory] And are they all spread in the same way?

[Ria Ghai] So, they can spread through different routes. Like SARS-CoV-2, many are primarily spread through respiratory droplets. Others, however, can also be spread through contaminated objects, or fecal-to-oral transmission is also seen in some coronaviruses.

[Sarah Gregory] Okay. So you mentioned this already, so let's talk a little bit more about this. So alphacoronaviruses and betacoronaviruses can jump from animals to humans?

[Ria Ghai] Yeah, not all of them though. So in fact, only a few have (just the seven that we talked about earlier). And all seven of those coronaviruses were associated with an animal at some point in their evolutionary history, and then they made the jump to people. And then once they were in people, they adapted to human-to-human spread. But most alpha- and betacoronaviruses have not made that jump into people.

[Sarah Gregory] And how does that happen all of a sudden like that? Like COVID-19?

[Ria Ghai] Yeah. So, we know that some viruses (like SARS-CoV-2) are already naturally circulating in animals, and most will probably never spread to people. And there is actually one study that came out back in 2020, which suggested that the parent virus of SARS-CoV-2 (so the progenitor that essentially gave rise) may have actually been circulating in animals for decades before SARS-CoV-2 eventually made that jump into people. So, a virus making that jump to a new species, whether it be people or a new host altogether, is kind of like a game of dominoes. So, there's many pieces that kind of need to be perfectly aligned for everything to fall, and really that's what we suspect happened with SARS-CoV-2. So, there must have been an animal that was actively infected with SARS-CoV-2, and then that animal had close contact with a person. And then that contact must have been close enough, for example, blood or saliva exposure led to a person becoming infected with the virus. And perhaps at first, the virus wasn't perfectly adapted for transmission within people, but it was well enough adapted to survive and replicate in that first person. And then that person would have spread the virus to others. So, hopefully what this shows is that it's a pretty unlikely series of events that are required to occur for an initial spillover, but SARS-CoV-2 and many other viruses have shown us that viruses can and do spillover under that set of kind of optimal conditions.

[Sarah Gregory] That's just kind of amazing to me that all those things can align so perfectly.

[Ria Ghai] Exactly.

[Sarah Gregory] And create such a horrific outcome. Okay, so SARS-CoV-2 is the coronavirus that has caused the current COVID-19 pandemic. So tell us how SARS-CoV-2 is different than other alpha- or betacoronaviruses.

[Ria Ghai] Yeah. So let me compare it to the other two high-consequence coronaviruses that we've been talking about—so, the original SARS-CoV from 2002 to 2004, and then MERS-CoV (which we mentioned) emerged in 2012 but still circulates in the Arabian Peninsula. So, all three of those coronaviruses are biologically pretty similar – they're all betacoronaviruses, they all spread primarily through respiratory droplets, and they're all believed to come from horseshoe bats. The proportion of people who die from COVID-19, interestingly, is actually slightly lower than the proportion of people that have died from SARS, and it's actually much lower than the people who die from MERS infection. So really, while SARS-CoV-2 is biologically quite similar to these other coronaviruses that we've seen, SARS-CoV-2 really stands alone in the breadth of its spread around the globe. So, COVID-19 has been able to gain this tremendous foothold in the human population that is really quite unlike SARS or MERS.

[Sarah Gregory] Partly because it's just not killing off its host, right?

[Ria Ghai] Yeah, that could absolutely be part of it.

[Sarah Gregory] There's a lot of speculation out there. Do we know where this virus originated?

[Ria Ghai] Not precisely. So, we know that all of those first known cases were identified in Wuhan, China. But we don't know if that first person, or patient zero if you will, was in the city of Wuhan or perhaps somewhere else. But we do believe that Wuhan was the epicenter of that initial outbreak.

[Sarah Gregory] Do we know specifically what type of animal caused COVID-19 in humans yet? You mentioned bats earlier.

[Ria Ghai] Yeah. So we do know that COVID-19, like some of those other coronaviruses, likely had a reservoir host of bats from the genus *Rhinolophus*, which are the horseshoe bats. And so we believe those are the likely origin of the virus. However, we don't yet know if the virus passed directly from those bats to people. Or, the alternative is something like what happened with SARS, where there was an intermediate host—so, a different animal that become infected from bats and then passed that on to people. Bamboo rats, pangolins, and raccoon dogs, and actually many other animals have been speculated and considered as potential intermediate hosts for SARS-CoV-2, but there is not enough evidence yet to know for sure if any of those species were truly an intermediate host. So, additional One Health research is really needed to understand the role of intermediate hosts and those original reservoir hosts in the source of this pandemic.

[Sarah Gregory] I know you sort of talked about the chain of how this all worked out, but can you give us a more detailed (maybe a little bit more technical) account of what caused it to spread to people?

[Ria Ghai] Sure, absolutely. So, any virus needs a couple different things to be able to spread. So, first it needs an exposure between a host (and that can be a person or an animal) that is infected and shedding the virus, as well as a susceptible host that it's jumping into. Second, it needs to be able to enter and replicate in host cells. And finally, it needs to make its new host shed the virus so that it can be passed on to another host. So in the case of SARS-CoV-2, we can assume that an exposure occurred between an infected animal and a person. And one of the interesting aspects of SARS-CoV-2 is that it has a protein that binds quite well to mammalian epithelial cell receptors. It uses a specific receptor called angiotensin-converting enzyme 2, and this surface receptor allowed the virus to bind to human cells and enter—so, kind of like a lock and a key. And we think that this is definitely one of the dominoes that needed to be perfectly aligned that we talked about earlier. And finally, the virus was able to take over, essentially, human cell replication machinery to produce more copies of itself and spread to new people.

[Sarah Gregory] So we mentioned bats before, and I know from other podcasts I've done on bats and diseases, they're like the perfect vector. They have the ability to carry all kinds of diseases and not get sick themselves, but then spread them super easily. And they might be thought to be one of the main vectors for coronaviruses (I think you mentioned that earlier). Why is this? Do we have anything specific we know about bats and coronaviruses?

[Ria Ghai] Yeah, it's a great question. So, I think more generally bats are actually the reservoirs of many viral diseases, and we believe this to be the case for at least two different reasons. So first, they are incredibly diverse. Actually, one of the most diverse mammalian orders, second

only to rodents in the number of bat species that there are on earth. So we know that in general, host diversity (so, the number of species there are) tracks pathogen diversity (so, the number of pathogens there are). So, species that have many.... or, sorry, taxa that have many species generally mean that there's more options for pathogens—so, things like coronaviruses—to proliferate. And then, as you mentioned a little bit, bats can do some really interesting things, like suppress the consequences of viral infection through immune regulation, which is an adaptation believed to have occurred because of their ability to fly. And so what this means is that we have animals that may carry many viruses but show absolutely no clinical signs. And then on top of that, they're roosting in sometimes extremely large groups in caves, and that provides a great breeding ground for virus transmission. And then on top of that, they also cover really large distances through flight, which is quite unique for most mammals, and that might also allow them to acquire new viruses. So, all of that put together means that bats can actually be really exceptional reservoirs for many viral diseases. But it might also leave you wondering if bats are really a problem that needs to be dealt with, and I'd just like to preface by saying that bats are also tremendously important parts of the ecosystem as predators and prey and pollinators of countless plants. So, the real problem isn't bats necessarily, it's how people interact with the natural environment in which bats live, and how things like changes in land use have driven bats into closer proximity to us.

[Sarah Gregory] So, coronaviruses can be found in livestock apparently, which is frightening considering that so many people across the country rely on them for food and close contact because of that. Can any of these viruses be passed onto humans from livestock?

[Ria Ghai] The good news is that none of the coronaviruses that we're aware of in livestock are able to be spread to people.

[Sarah Gregory] So, okay, but are camels considered a livestock? I know that you can get MERS from camels. How does that.... or are they not really considered a livestock?

[Ria Ghai] Yeah, so that's a great question. So, some coronaviruses are kind of endemic in livestock, and livestock are their main host. And so for most of those, those coronaviruses that they harbor cannot be passed to people, which is good news. But in the case of MERS, it's maybe the one exception to that. And MERS, the primary host is believed to be camels and camels can cause the infection to spread into people.

[Sarah Gregory] And I know this is something people have been very concerned about with all kinds of diseases, and that's the eating of livestock and getting infected. So, can people get sick from eating livestock infected with a coronavirus?

[Ria Ghai] Yeah, there's still a lot that we're learning about coronaviruses and how they're transmitting, but it's certainly not the primary way that people are becoming infected. And eating livestock that is prepared hygienically and cooked to their recommended internal temperatures shouldn't be a risk.

[Sarah Gregory] Okay. So, we've got bats with coronavirus in them. How do livestock get sick from coronaviruses in the first place? And are they endemic in all livestock, or are the viruses spread from other animals or people or some other chain?

[Ria Ghai] Yes, so it's most similar to how people get coronaviruses. So, the reservoir hosts for most livestock coronaviruses are rodents or bats. So, in most cases, the coronavirus started in a

reservoir host (like the rodents or bats), and then it jumped into livestock and did well enough in livestock that it stuck around and adapted to survive while it spread there.

[Sarah Gregory] But how did it jump to the livestock? Like, get bitten by a rodent? Or how did that happen?

[Ria Ghai] Yeah, we don't know in a lot of cases how that jump might have happened. It could have been rodents in the area that had died and maybe infected the environment. It could have been feces left behind by the rodents or bats. We're not quite sure how those initial spillovers happen for many of these coronaviruses.

[Sarah Gregory] Has SARS-CoV-2 been found in any livestock?

[Ria Ghai] Yeah, so there's been studies in livestock species, like cattle, pigs, poultry, that have been intentionally infected with SARS-CoV-2 under laboratory conditions. And we found that poultry were not susceptible, and cattle and pigs were very weakly susceptible to infection. So that's good news, since livestock are an important part of our food supply. And to date, no traditional livestock species, like cattle, pigs, goats, sheep, or chickens, have been infected by SARS-CoV-2 in any sort of natural setting. So the only farmed animal that has been naturally infected with SARS-CoV-2 are minks.

[Sarah Gregory] Okay, so let's talk about this mink thing. In Europe, several million minks suspected with SARS-CoV-2 were culled. How did the virus get into the mink farm then, do you think?

[Ria Ghai] Yeah, in the majority of outbreaks in Europe, as well as the affected mink farms here in the U.S., minks were first infected by a person, oftentimes a farmworker with COVID-19. And from there, the virus was able to spread among the mink. And in some farms, it was actually also documented to spread from mink to other animals on the farm, like dogs and cats roaming around.

[Sarah Gregory] Do we know why minks are so susceptible?

[Ria Ghai] We don't know entirely. We believe that it might be that they have not only that ACE2 receptor that I talked about earlier, but also that receptor is present in the right areas of their respiratory and gastrointestinal tract. But I think there's still a lot more to be learned about why some species, like mink and ferrets, are so susceptible.

[Sarah Gregory] Are there ways to stop the spread of coronavirus from animals to people?

[Ria Ghai] Yeah, we know that about 3 in every 4 emerging diseases in people are zoonotic, and that means that they're shared between animals and people. And most of these zoonotic diseases originate from wildlife. So, if we want to slow or stop the spread of any new disease, we need to revisit and improve the way that we're interacting with our natural world. So, we know that certain human behaviors like expanding into new geographic areas and encroachment on wildlife habitats, as well as things like climate change, land use change (like deforestation), and then consumption of wildlife has created opportunities for both domestic animals and wildlife to essentially come into closer proximity to people. And that can increase the likelihood of zoonotic disease spillover.

[Sarah Gregory] One Health comes up a lot in my podcasts, I think you mentioned it earlier as we were talking. And you mention One Health quite a bit in your article. Tell us about One Health, and why it's increasingly important? It must relate to what you just said a minute ago.

[Ria Ghai] Sure, yeah. In short, One Health is the idea that the health of people is really closely related and connected to the health of animals and our shared environment. So the concept of One Health is definitely not new, but it has become more important in recent years. And I think that's because of many factors that have changed interactions between people, animals, plants, and our environment, like we just kind of talked about that. And a One Health approach to public health, it essentially brings together experts in human, animal, and environmental health, and other areas as well, to address shared health threats. So, I kind of think of One Health as this bridge that's needed to combat zoonotic diseases like COVID-19, because diseases like COVID-19 aren't respecting species or geographic boundaries. So, I believe One Health is the way forward to combat any health threat that is more than just affecting humans or animals. So, if you want something, an approach that essentially bridges the gap between human, animal, and environment, One Health can give that approach to that interface.

[Sarah Gregory] Why did you do this study and how were you involved?

[Ria Ghai] Yes, so shortly after CDC first activated the Emergency Operations Center in January 2020 for COVID, there was a One Health team that was stood up very early in the response. And so, I was part of that team, and our job was essentially to determine if SARS-CoV-2 could potentially spread between people and animals. And in order to determine that, we started collecting all of the information we could find on other coronaviruses and the closest relatives to SARS-CoV-2, thinking that that could provide us some insight into the biology and epidemiology of this new virus. So, this study was essentially born out of that effort, and of course it expanded to become a little bit more comprehensive as we realized that we could turn this into a manuscript. And as lead author, I designed and wrote a lot of the manuscript, but I'm really, really lucky to be part of a truly exceptional and collaborative team. So when this all happened, we all hit the ground running with research for this manuscript.

[Sarah Gregory] Tell us about the main points of your study now, just a little brief rundown.

[Ria Ghai] Sure. Yeah, I think we've covered a lot of them already. But in short, our manuscript is divided into three sections, and those outline the emerging or reemerging coronaviruses in wildlife, in livestock, and in companion animals. However, my favorite part of the manuscript is actually Tables 2 and 3. I've been using them essentially as quick reference guides for a wealth of information on the hosts and clinical presentation of numerous emerging and reemerging coronaviruses, including SARS-CoV-2, as well as all of the hosts that are known to have been discovered.

[Sarah Gregory] Tables 2 and 3.

[Ria Ghai] Mm-hmm.

[Sarah Gregory] Is that what you said?

[Ria Ghai] Yes.

[Sarah Gregory] Okay, so if readers want to....listeners want to read the article, be sure to look for Tables 2 and 3. In your article, you mention that companion animals might also act as “spillover hosts” for human coronaviruses. Tell us about that.

[Ria Ghai] Yeah, so SARS-CoV-2 is actually a great example of that, and specifically for companion animals, they have essentially been spillover hosts for human COVID-19. So, a lot of people might not realize that one of the most commonly infected animal groups during this pandemic has been companion animals (so, dogs and cats). And people’s pets are really most often being infected by owners with COVID-19. And recently, we’ve even started seeing cases of SARS-CoV-2 variants in pets, such as B.1.1.7, which was first detected in the UK. And this is because pets are becoming sick with whatever their owners are infected with. So to me, this really suggests that there is a need to pay more attention to pets, both in terms of public awareness and investment in research and science to be able to understand the role that companion animals might play for this as well as other zoonotic diseases.

[Sarah Gregory] Yes, I don't think people are aware at all about the interaction between COVID-19 and pets, kind of only heard about a couple dogs or one dog and one cat or something. So, that's very upsetting. Do dogs and cats present the same symptoms as humans?

[Ria Ghai] Yes, so just like people, slightly more than half of infected pets don't show any signs of illness at all. But for those that do, the clinical signs are pretty broad in dogs and cats. So those include respiratory signs like coughing, sneezing, runny eyes or nose, and shortness of breath or difficulty breathing. So, that's a little bit similar to people. And they also show some gastrointestinal signs like vomiting and diarrhea, as well as nonspecific signs like they become lethargic and can sometimes also develop a fever.

[Sarah Gregory] Is the fatality rate about the same as with humans/people?

[Ria Ghai] We don't have a great sense of that yet. So in most pets, COVID-19 or SARS-CoV-2 infection is typically pretty mild and resolves on its own. But we have found in some rare circumstances that the animals with the virus have died or have been euthanized. And we actually just recently released a preprint that's undergoing peer review now, and that paper documents the first 10 companion animals in the U.S. to have died or been euthanized while also positive for SARS-CoV-2. And in that manuscript, we show that eight of those 10 companion animals had SARS-CoV-2, but it was kind of incidental to their death and likely didn't contribute to the reason for their death. But in one dog, there was pathological evidence that COVID-19 may have contributed, and in one cat we believe COVID-19 was the primary reason for the animal's death. Unfortunately, as with people, there's not treatment for COVID-19 in animals. So, just really supportive care. And the majority of pets with SARS-CoV-2 do fully recover.

[Sarah Gregory] Is there a test for it? Is it the same test that humans take?

[Ria Ghai] We don't recommend routine testing for SARS-CoV-2 in animals unless the animal has been recently exposed to the virus and is showing clinical signs. But usually what we're recommending is if your pet has a health concern to call your pet's veterinarian, let them know your pet has been around someone with COVID-19, and they'll be able to take it from there.

[Sarah Gregory] Can my dog get it from my cat? I mean, is it spread from animals to animals?

[Ria Ghai] Yes, so we're still learning a lot about the transmission between animals. So, we definitely know that people with COVID-19 seem to be able to transmit the infection to their pets. But we're still learning a lot in households if one pet can transmit it to another.

[Sarah Gregory] Alright. Just basic hygiene here, what precautions should people that are sick with COVID-19 be taking around their pets?

[Ria Ghai] We generally recommend that people who are sick with COVID-19 avoid contact with their pets and other animals, just like you would with other people. So where possible, it's best to let someone else in the household who is not currently sick care for the pet. And if that's not an option, we recommend wearing a mask while you're interacting with your pet, and hopefully as usual, washing your hands before and after feeding and interacting with your pet.

[Sarah Gregory] What do you think are the most important takeaways from your study?

[Ria Ghai] I think that it's that people, animals, and our environment are really all connected, and because of that, pathogens are often connected as well. So our study really does try and lay bare that most emerging and reemerging alpha- and betacoronaviruses have long evolutionary histories, and they're tied to multiple animal hosts. So, this really does make a One Health approach critical if we're to apply the lessons from this pandemic to whatever pathogen is coming next.

[Sarah Gregory] Do you see your study guiding future One Health initiatives in any particular way?

[Ria Ghai] I think it kind of sets some of the background for future One Health works by being able to provide some of that literature review and synthesis of what's known currently. So when there is something new that pops up, investigators can hopefully hit the ground running a little quicker.

[Sarah Gregory] So you obviously have been incredibly busy with COVID-19 pandemic. You talked a little bit about how you've been involved. Do you want to tell us a little bit more about that and what you do at CDC generally?

[Ria Ghai] Sure. So, pretty much from January 2020 onward, I have been part of the One Health group at CDC that has been tasked with understanding the zoonotic nature of SARS-CoV-2. So, as you can probably guess, our team primarily works to investigate, track, and analyze situations where SARS-CoV-2 isn't just spread between people, but is spread between people and animals. And I've been particularly involved in establishing animal surveillance for SARS-CoV-2 and I have also assisted with many animal investigations that have occurred, especially those that have centered around exotic species that we know can also be infected, like big cats in zoos and sanctuaries as well as, of course, the companion animals that we've talked about.

[Sarah Gregory] Personally now, what have you found useful to help keep you grounded during these very unprecedented times? And do you have any pets?

[Ria Ghai] Yeah, I do. So I'm a little biased, but I have a pet cat and a dog, and they are the absolute cutest and they're also best friends, which a lot of my friends get a kick out of seeing. So, they're always kind of snuggling and playing together. And I think something that has helped keep me grounded is just watching their daily antics as I've been on my Zoom calls, and that has definitely I think given me (as well as probably my team) some good laughs. And then also,

probably to my husband's dismay, I own several hundred plants and those have also helped me keep and grow (pun intended) a hobby that I can kind of sustain through lockdown that doesn't involve, you know, going out and getting into too many things outside of the house.

[Sarah Gregory] So those are indoor plants?

[Ria Ghai] Yeah.

[Sarah Gregory] Oh, goodness. Nice! You must have good light.

[Ria Ghai] Yeah, I do. My house has really good windows.

[Sarah Gregory] Well thank you for taking the time out of your busy life to talk with me today, Dr. Ghai.

[Ria Ghai] Thank you so much, it's been a pleasure to talk with you, and I really appreciate the opportunity to come on today.

[Sarah Gregory] And thanks for joining me out there. You can read the April 2021 article, Animal Reservoirs and Hosts for Emerging Alphacoronaviruses and Betacoronaviruses, online at [cdc.gov/eid](https://www.cdc.gov/eid).

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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