

Role of Oral Rabies Vaccines in Eliminating Death in People from Dog Bites

[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. Ryan Wallace, a veterinary epidemiologist at CDC. We'll be discussing the use of oral rabies vaccination in stray dog populations.

Welcome, Dr. Wallace.

[Ryan Wallace] Hi. Thank you for the opportunity to talk today.

[Sarah Gregory] Ok. To start, what is rabies and what causes it?

[Ryan Wallace] So, rabies is a virus. It's called a zoonotic disease, meaning it's a...it's a virus that can spread between people and animals. Rabies is...is pretty unique in that it's almost universally fatal if you...if you get it and you don't seek the right medical care, and it also causes quite a few deaths globally—59,000 people die from this virus every year.

[Sarah Gregory] How many?

[Ryan Wallace] 59,000.

[Sarah Gregory] Ok, that's...wow. In movies, we often see dogs with rabies foaming at the mouth. Can you tell us more about the symptoms involved with rabies infection?

[Ryan Wallace] Yeah, rabies is a really unique virus that is inoculated usually through a bite into...into the body of any mammal, and it then tries to find a nerve (a peripheral nerve). So you can imagine if you are bit in the hand or in the leg, it's going to be in the tissue, it's going to find a nerve and it gets inside and then it moves really, really slowly towards the brain—again, towards the brain of a person or...or a dog or any other mammal. It moves at about 1 centimeter per day, and eventually when it reaches its end goal (the brain) it can replicate quite rapidly. And that sort of causes all sorts of unusual neurologic disorders that we tend to associate with rabies. So the foaming at the mouth is the virus's attempt to get more virus out so that it can infect the next animal through a...through a bite. It causes some discomfort in the throat, so you don't swallow the saliva and more of it comes out and infects other animals and people. And then it also causes some pretty unique behavioral changes such as the aggression or paralysis.

[Sarah Gregory] Are bites the only way rabies is spread?

[Ryan Wallace] Bites is a primary way that rabies is spread, but there are two general ways in which this virus can get into a person or...or an animal. And so we call those bite and nonbite exposures. Again, almost all rabies transmission, whether it's dog-to-dog or dog-to-human, is going to be through a bite. But we also do know that it is possible for the virus to be spread by a scratch that's contaminated with saliva, mucous membranes, very, very rarely inhalation of concentrated virus (and we've only seen that in a laboratory setting), and then also organ transplantation. So you can imagine this virus is replicating in the nerves and can move throughout most major organs in the body. If you don't know why someone died and transplant those organs into the next individual, you can actually move the virus and transmit the virus that way. All of those nonbite modes of transmission are very rare. There are precautions to prevent

them from happening, but by and large the biggest concern and the biggest public health preventive action are focused on preventing those bites.

[Sarah Gregory] I've actually done a podcast in the past about rabies and organ transplants. And I...and I knew somebody who went to a petting zoo and was told later they had to get rabies shots from petting. I guess they were concerned that the saliva was on one of the animals and it might get in a scratch.

[Ryan Wallace] Yeah, the virus can be...is certainly found in saliva of...of affected animals. And in rare situations, the—it can get into a scratch and find a virus or into a mucous membrane like our eyes or mouth—likely the virus would find...a nerve and get in and then move on towards the brain, which is what we want to try to prevent from happening. While those instances are very rare (these nonbite exposures are...are very rare), it's a 100% fatal disease and so we don't want to take any risk if we know there's a possibility that someone was exposed then any of these bite or nonbite methods.

[Sarah Gregory] Ok. So as you just said if you get rabies, you're going to die from it. So if it's left untreated, that's it—there's...there's no chance you're going to live?

[Ryan Wallace] So there are approximately 15 known survivors of clinical rabies. So that...that is if you....let's take a little step back. Rabies is absolutely preventable through postexposure prophylaxis or vaccination. So we can...that we can prevent this disease two ways in people. One is giving people we think are at higher risk of an exposure something called preexposure vaccination, and it's a series of two to three vaccines (depending on your local recommendations). And...and that's really largely preventive. If you ever get exposed in the future, you need to get a booster. But we...we have very, very few failures of preexposure vaccination.

But we don't do that for the general population. We...for the general population, our preventive measures are based on recognizing that you've had an exposure, seeking healthcare, and then getting postexposure prophylaxis. And again, when that's done in a timely and appropriate manner, failures are incredibly rare. Unfortunately if you don't...if you are exposed and you don't get the appropriate vaccination and you do go on to develop clinical rabies, there's no known effective treatment. Only 15 people globally have ever survived the clinical stage of rabies, and they have...largely all had pretty severe sequelae or pretty severe, long-lasting medical issues from that infection. And you can imagine 15 survivors ever out of 59,000 people that die of it every single year, those are not odds that...that anybody should want to play.

[Sarah Gregory] What's the timeline, say you get and have an exposure to when you start having symptoms?

[Ryan Wallace] The virus moves fairly slow, and so most of our incubation periods are going to be somewhere between 3 weeks and 3 months from exposure until when...when clinical signs will appear, but it's incredibly variable. And there's a lot of biological processes that go into how long it's going to take from...from, again, that exposure to developing clinical signs. So you can imagine if you're bitten on the...on the foot by a rabid dog, that virus has to travel quite a long distance to get to the brain. And you're not going to see clinical signs until the virus is in the brain and replicating quite...quite fast. And in those situations, we've seen reports of several

years before people go on to develop clinical signs. Know that that's very rare, but it does happen. Alternatively if someone is bitten on the head, the virus has a very short path—a very short distance—to get to the brain where it wants to be. And we can see clinical signs develop as early as 14 days if you have a severe bite to the head.

[Sarah Gregory] So 59,000 people die of rabies each year globally, and apparently most of those cases are from domestic dogs. Why is this and why not some other animals, like bats or cats?

[Ryan Wallace] Yeah. This virus is one of the oldest described zoonotic viruses known to man. There...it goes back thousands of years, with reports from...from rabid dogs transmitting, you know, this virus in Mesopotamia. So you could imagine, a virus that's had the opportunity to move in and out of different animal populations for thousands of years...it's had quite a few evolutionary jumps. The biggest one that is the risk to people is when the virus jumped into dogs. That's not necessarily because they transmit the virus any better, but they're...they have a very close association to people. So dogs, they...they sleep in our beds, they're all over our communities, there's just a lot of interaction and opportunities for them to expose people when you're in...in a country that has the virus that spreads through dogs. Whereas animals like bats and (in the United States) racoons, skunks, foxes...we don't interact with those animals quite as much. So even though the virus is found in a lot of other wild mammals, they keep the virus in their population and it's...it's relatively rare that people interact with...with a sick, wild animal and then that virus is transmitted.

[Sarah Gregory] What about cats?

[Ryan Wallace] So, the rabies virus can infect any mammal. You know, there's some stories out there that possums can't get rabies. That's not true, possums can get it. They have some...some biological defenses that make them a little bit less susceptible, but we have rabid possums in the United States almost every year. But there...there are two cycles for this virus. There's the reservoir cycle—the enzootic cycle that's always going on in the background with the...with the key species. So in most of the world, that's dogs. And there's a special version of this virus that is spread from dog to dog to dog—we can differentiate it with lab tests, we can see which type of virus it is. Any mammal can get that version of the virus and die, but it is maintained in the dog population.

[Sarah Gregory] I see, okay. Where is it most common to find dogs with rabies?

[Ryan Wallace] Around 120 countries have the virus that is spread from dog to dog, which we call the canine virus variant. Now the...the level of endemicity (how bad it is) can really vary quite a bit between these countries. Some are...are very close to elimination and doing very...very strong...just running very strong control programs, and others are still at the very beginning stages of elimination. And...and rabid dogs are unfortunately quite common. India has the highest number of human rabies deaths globally, but it's also a very large country and they...they have some pretty strong control programs that are being implemented now. But if we look at a...a rate or, say, risk of rabies in a biting dog, most countries in sub-Saharan Africa are heavily endemic. And then Southeast Asia has a very high rate of rabies as well.

[Sarah Gregory] So how effective are the pre- and post- vaccines? Are they different or they're the same? And do they have the same efficacy?

[Ryan Wallace] Yes, so today—pretty standard across the globe—we use cell-culture vaccines, which are highly, highly efficacious. They work really, really well. There are two different regimens that we...we use with preexposure vaccinations. So, if you're traveling to another country and you're worried you might become exposed, there's a...there's a simplified version of the vaccination series and it's really, really efficacious on its own. But, just to be 100% certain you don't get rabies if you do become exposed in these countries, there is still a booster recommendation. So, just because you're preexposure–vaccinated doesn't mean you don't have to do anything if you are bitten by a dog or a bat. You still have to go seek medical care, wash that wound, and get your booster vaccination. But it's a much more simplified process. Postexposure vaccination can range anywhere from 3 to 5 vaccines depending on the country you're in, and then rabies immune globulin. And that's a process that provides both passive and active immunity, since we know you were exposed and potentially susceptible. When these are given appropriately and per international standards, they're almost 100% effective. Failures by either regimen are incredibly rare.

[Sarah Gregory] Okay. So I think you already said this, there's basically just one type of vaccine in terms of what goes into it for each type? Is that right?

[Ryan Wallace] Yeah. In general, they're referred to as cell culture vaccines and they're really standard all across the world right now. You know, several decades ago, there was something called nerve tissue vaccines and it's probably what a lot of people picture from the movies when...when you get 13 shots in the stomach and it's a really painful process. Those vaccines are not used anymore. WHO has come out and recommended their complete discontinuation across the globe. They had a pretty high rate of adverse events, and the cell culture vaccines are much more effective and much safer. The nerve tissue vaccines are hardly ever used, it would be very uncommon to come across them and if you do, you should really question what you're getting and contact a health official to make sure you're getting high-quality vaccine.

[Sarah Gregory] So, people traveling to high-risk areas, as we said, they can get a preexposure vaccination. And I've gotten vaccines for rabies (at least in the US) every year. Are these two vaccines different?

[Ryan Wallace] The two vaccines are actually quite similar in that they are going to be cell culture (killed) vaccines, but they're formulated and processed a little bit differently. All vaccines need to be not only developed for their target species, but also the studies that go into how effective they are, the dose that's given, the frequency that they're given....they are all based on species-specific studies. And so the vaccine that we use in people, while structurally they're very similar, they are slightly different. They're produced in a different way and they're only studied for efficacy in...in people. So you wouldn't want to get....if you were exposed to a rabid animal, you wouldn't want to go get a dog vaccine. There would be no data to say whether that's going to be effective in a person. Likewise for animals, they shouldn't be getting people...you know, human vaccines.

[Sarah Gregory] People seem to need just this one series of rabies vaccines, plus a booster if you get bitten. But dogs are supposed to get one every year. Why do dogs need to get one every year?

[Ryan Wallace] Yeah, there's a couple of reasons for why that is the state of the world. First, it is based on the studies that are done to obtain licensure. The recommendations for people or animals are going to be based on how the manufacturers have designed their study. And there's a

lot of...a lot of reasons why certain vaccine regimens are studied a certain way and recommended a certain way. But it all comes down to there has to be data for us to make our decisions on frequency, route, dose, all of those things are based on data-derived decisions. The big reason why particularly dogs get the vaccine almost every year (depending on what version you use) is that dogs...we're vaccinating dogs for a different reason than when we vaccinate people. Dogs are a known reservoir species. They can transmit this virus quite effectively. So with vaccinating dogs, they're our frontline defense against people getting...getting this disease. And that security and confidence that we've got that frontline defense vaccinated really requires annual or, in certain situations with...with newer 3-year vaccines (every 3 years vaccination). But it is routine vaccination in our high-risk susceptible species, and that provides a nice buffer to keep people from becoming exposed.

[Sarah Gregory] So your study was about oral vaccines and stray dogs. So, how do you get oral vaccines...well, how do you get vaccines to stray dogs, period?

[Ryan Wallace] It's incredibly challenging. There are two ways we can vaccinate dogs. We have what we call parenteral vaccines—this is the normal needle and syringe. You have to restrain the dog, you know, it goes into the muscle and...and then that dog becomes vaccinated. The other option are oral vaccines, and this is where you can put the...the vaccine in a little bait and then you feed the dog. And when it ingests that bait, it becomes exposed to the vaccine and develops the appropriate immune response. So you can imagine, stray dogs aren't really used to people handling them, they're not used to receiving veterinary care, and you can expend a lot of time chasing these dogs down with nets and catch poles and...and trying...trying to confine them and get that shot in. Or, with the use of oral vaccines, we can just feed them. And you know, obviously one of those requires a lot of effort and would be really expensive with a lot of really well-trained staff, and the other one is quite easy and...and people might even just volunteer to go feed dogs since it's something a lot of us like to do.

[Sarah Gregory] So, tell us a little bit about the oral vaccine itself. What does it look like? You know, how do you get it into the food, I mean?

[Ryan Wallace] They...they have a matrix around them called a bait matrix. And that...that has two functions. The first is it protects the vaccine that's inside, but it also has the flavor that hopefully is going to attract that animal to come and actually want to put this bait...this vaccine in its mouth. Within the bait matrix, there's usually a little full sachet—it can be made of light plastic or some other, you know, food-safe materials—and that holds a liquid vaccine. So the whole process of...of orally vaccinating an animal requires that the animal wants to put this bait in its mouth. So, there has to be a flavor in that bait matrix that they...they want to ingest. They have to chew it, so it punctures the liquid sachet and then that liquid vaccine inside of it has to coat the inside of the mouth. And one of the concerns about using oral vaccines is that all 3 of those steps has to happen to successfully vaccinate the dog.

And so there are a lot more considerations into planning a vaccination campaign that includes oral vaccines and...and the type of vaccine that you are going to use in a certain country. Not all dogs like the same flavors. In Thailand, there was a study that found that they really like the curry-flavored bait matrix, which is kind of hard to find these days. We did one in Haiti, and they very much preferred pig intestines. That's the one they all wanted...all those dogs wanted to eat. Other studies have found that cheese is the preferred...preferred bait...bait flavor, and others have

found fish. So, there...there's this added complexity that you have to sort of tailor the flavor to the local dog population. And it will probably reflect what they are used to eating. With these being stray dogs, probably what they are used to...what their human counterparts in the community leave out for...for food and...and rubbish. And then, the dog has to be able to puncture it. So if you make your bait too thick—that bait matrix is too thick or the bait is just too large in general and they can't put it in their mouth—you're not going to get the vaccine into the oral cavity, and so vaccination will fail as well. So, there are a lot of other considerations. You have to be pretty smart in how you plan and prepare these things. But the alternative of...of chasing dogs down with nets, oral vaccines look quite...quite favorable.

[Sarah Gregory] Yes. So going back to these little sachets, you know, my dogs get (of course) the monthly chewable heartworm, etc. And they hate them. They're supposed to be delicious to dogs. I have to pulverize them and then mix them well with their other food for them to eat them.

So what have you found works best for dogs? Not just the flavor, but in what? So, in...in wet...like canned dog food? Or are you...or are you just trying to get them to eat it on its own? I'm not quite sure what we're saying here.

[Ryan Wallace] Yeah, that's a...it's a really good question and one that the rabies community and vaccine manufacturers are still...still studying. Because...I'll go back to the study we did in...in Haiti back in 2016, we...we used an oral vaccine to try to get a lot of these stray dogs to stop an outbreak that was occurring. And they loved pig intestines. So we could put the sachet (that plastic liquid bait) into the...into a pig intestine and then go out and...and feed all the dogs and they got vaccinated. And it worked quite well. But you can't mass produce, you know, pig intestines. That...that's not something we could...we could make millions of those bait matrixes and...and vaccines and distribute them across the world for everyone to use. So, manufacturers are currently working on trying to identify a universal bait flavor and universal bait matrix. And there are a couple of good prospects. Egg flavor seems to be generally universally liked by dogs. But there are always—and the more we study this...the process of oral vaccination and get out and do field trials—there are always exceptions. And I think that Thailand one is probably the most interesting. I mean, who would have thought that dogs would prefer curry-flavored bait? But that's what they were used to eating from...from people in the community and that's what worked best.

[Sarah Gregory] Yeah, this is...this is really fascinating. Because EID has done articles about orally vaccinating raccoons, and I've actually done a podcast on that. And this being discriminating didn't come up. And you don't really think of stray dogs as being discriminating either. So this is really interesting.

[Ryan Wallace] The spectrum of...of the term 'stray dog' is really wide as well. In Haiti, their stray dogs are loosely owned (largely they are loosely owned). They belong to a community, someone cares for them, but they're really living off of the scraps and garbage left behind. And they would probably eat almost any of the baits that we...we might have tried there. But in other settings, stray dogs are really well-cared for by communities. They're given, you know, food everyday by people in the community. People leave leftover dishes out. They can be really well-fed. We've been in communities in Bangladesh and Vietnam where these dogs are really well-fed and taken care of. You'd never know they're...they're unowned or community-owned dogs. And they can be quite picky.

[Sarah Gregory] Ok. So with these oral rabies vaccines with dogs, is it...are there side effects? Or, I mean I know in people there's been issues with some...some oral vaccines with smallpox and polio mass vaccination programs. There's nothing like that you've seen with these oral ones for these dogs?

[Ryan Wallace] So it's a...there's no blanket universal answer to that. It...oral vaccines, there are a lot of different ways to produce and manufacture oral vaccines. And there's a long history of...of oral vaccine use, not...not just for rabies, but for numerous other diseases like you just mentioned. So if we were, again to go back, you know, 10 or 20 years ago and look at the safety profile of some proposed oral vaccines for...for rabies, some of them actually failed safety reviews. And there were organizations like WHO and OIE (The World Health Organization for animals) that came out against the use of certain oral vaccine products because there were some pretty major concerns about their ability to...to cause adverse events or even revert back to a virulent state. Luckily the process for attenuating and modifying viruses to make an effective oral vaccine these days are much, much better. And so there are several products that are being proposed—and even several that are being used in field trials right now—that have been thoroughly assessed by WHO, OIE, groups like mine at CDC, and largely found to be highly efficacious and incredibly safe. But, the...the best answer to that question is that every...every time you are going to use a live-vectored vaccine, you need to do a thorough safety evaluation of that product and...and ideally, look to your international organizations like WHO and OIE to see if they've reviewed these products and if they have, you know, provided their safety assessments.

[Sarah Gregory] Are oral vaccines expensive? When you have a mass vaccination program, who pays for it? I'm talking about rabies. Are there any US government-funded programs?

[Ryan Wallace] So, yes they are expensive, comparably expensive. And it's a...it's a nuanced question...alright, well, it's a good question, it's a nuanced answer. A lot of different factors go into the cost of vaccinating a dog. And so if we look at the standard shot (the injectable shot that most dogs get these days), the vaccine itself costs less than \$1. You know, \$0.50 or less in...in most settings if you're using high-quality vaccine. But the average cost (full cost) to vaccinate a dog is over \$2. So, the majority of the cost to vaccinate a dog is actually in the logistics. It's in the staff, it's in the cold chain, it's in the consumables. It's not actually the vaccine itself.

Oral vaccines, on the other hand, while they're not widely available yet, they'll probably cost somewhere between \$2 and \$4 just for the vaccine. So quite a bit more expensive than parenteral vaccines. But from what we've seen from...from our field trials and in our experience in the field is that the surrounding cost can go down quite a bit. We can vaccinate more dogs faster with oral vaccines than we can with parenteral vaccines, especially when we are talking about stray dogs. And so, you've got this balance of parenteral vaccines...the vaccine itself is cheaper, but your staff costs are probably going to be higher because it's more effort to go out and vaccinate those dogs. Oral vaccines, the vaccine cost is much higher but staff costs we expect to be quite a bit lower because you can do more dogs in a day.

[Sarah Gregory] Going back to something you said earlier about people just in the community feeding the dogs with these vaccines. So is that part of what's being done? It's not just health...public health workers out there feeding dogs, but is this...are there vaccines given to community members to hand out to these dogs?

[Ryan Wallace] Not yet. And that's not the recommended way to use oral vaccines right now. But we are at the very infancy of...of developing programs that will include oral vaccines as one of the strategies. It's kind of crazy, we've been using oral vaccines to control rabies in wildlife for decades. Hundreds of millions of oral vaccines have been distributed for control of red fox rabies in Europe and raccoon rabies and coyote rabies here in the United States. But we don't have it as a tool (a standard tool) for control of rabies in dogs, which causes 59,000 or more human deaths every year. So, the...the paper that was published in December is really about getting some of....setting some of the facts straight about how these vaccines should be incorporated into standard dog vaccination programs, particularly in canine rabies–endemic countries, and tries to focus some of the attention on where there's...where they will truly benefit an aid of vaccination program.

[Sarah Gregory] So tell us about the Global Strategic Plan for eliminating rabies death in people caused by dogs.

[Ryan Wallace] Yes. So this was an initiative developed back in 2015. There are...our three main international organizations are supporting this initiative—that's WHO (World Health Organization), OIE, and then FAO (the Food and Agricultural Organization of the United Nations). And they are providing an overarching structure and gathering governments and international agency support to try to eliminate dog-mediated human rabies deaths by the year 2030. And...so clearly, vaccinating dogs is going to be a huge component of...of the plan to...to reach this 2030 goal. But also included in that is postexposure prophylaxis and preexposure prophylaxis for people.

[Sarah Gregory] Are you optimistic about this plan actually being achieved by 2030?

[Ryan Wallace] I think any...any program, any large-scale elimination or eradication goal, it has to start somewhere. We can't just say it needs to be eliminated. That could happen, you know, in 50 or 100 years if we don't set a date. So, setting a target puts expectations on endemic countries' governments, it puts expectations on international agencies and...and donor governments that are going to ideally support this goal. It also allows us to start more effectively planning how we would even approach something like global elimination of rabies or elimination of dog-mediated human rabies. We still have, you know, 9 years left to see where we get by 2030. I think this is probably a...a goal that will go on for...for quite a while because countries are at different stages. But I think it was quite...quite bold and ambitious and then really, really good that these international agencies established the goal, set a date, and they are putting down real strategic plans for how we can help other countries address...address this really significant public health issue.

[Sarah Gregory] So what factors need to be considered for creating effective rabies vaccination campaigns?

[Ryan Wallace] The number one consideration really needs to be the type of dog that you have. There are some countries where we can use really easy methods of vaccination. So picture, like brick and mortar veterinary clinics, and people just bring their dogs in and the veterinarian gives them a shot and then they go home in their cars. So there are settings like that, communities and then whole countries where that's totally possible. And you need to know what types of dogs you have. So if you have those types of dogs, we're going to design a very different type of vaccination program than we would if you have a lot of dogs that are...are free-roaming or

unowned or just a population of dogs where people aren't used to providing veterinary care and can't put them on a leash and walk them somewhere. So, under...putting in some effort—doesn't need to be a lot of effort and it doesn't need to delay your implementation—but putting in some effort to understand the type of dogs and the quantity of dogs is going to allow you to...to design a much more effective, a much more efficient vaccination campaign. And then when you run into situations where there's either a country or a community where there are a lot of stray dogs or dogs that aren't easily accessible by a routine vaccinator, these are the situations where oral vaccines are going to become much more important and it's going to be...it's going to make a much more efficient campaign and a much more effective campaign if we have that oral rabies as a...as a tool to get those particular types of dogs.

[Sarah Gregory] I think you already touched on this a little bit, but why did you write this report and what are the most important public health messages in it that you want to get out there?

[Ryan Wallace] This report is really important because it's the first time that our two major international organizations (OIE and WHO) have come together with an aligned statement in support of the effective and safe use of oral rabies vaccines. There have been statements and...and publications and guidance documents developed over the last 30 years that are reflective of the knowledge of rabies vaccines at the time, but have not truly been aligned nor fully supportive of how oral vaccines should be used to control canine rabies. And so, I think it's very exciting that this is the first time where we've really sat down with these partners and global experts in the field, and...and really detailed exactly how these can be used—exactly what the barriers are and how to overcome them—and really put out there that...that we all recognize in the right place, under the right conditions, oral vaccines do have a role in canine rabies elimination. And we need to start stoking the international communities and manufacturers, and the governments of these endemic countries to recognize when the appropriate place is and how they can access them and really push this 2030 goal closer to fruition.

[Sarah Gregory] How can we protect our pets and ourselves?

[Ryan Wallace] So the best way to protect our pets is to keep them up-to-date on their rabies vaccinations. And you know, likewise, the best way to protect us is to keep our pets updated on the rabies vaccinations. They are our frontline defense. Our dogs and our cats and other susceptible species (depending on where your listeners are...are tuning in from), they're the ones that are hot...most likely going to come into contact with a...a rabid animal, you know, be that out in the wild or be that a rabid dog. And you don't want them bringing that virus home to you or your kids. So, keeping them vaccinated is that...that frontline protection.

And then, if you do unfortunately become exposed, postexposure prophylaxis is highly effective. It's a really simple regimen, it's no longer 13 shots in the stomach. It's just...just like getting your flu vaccine (except you need to get a couple extra). But...but it's really simple, quite painless, and extremely effective. And so, making sure that you're aware of what an exposure is, that you seek medical care, and that you get your vaccines when indicated is our second line of defense and very important.

[Sarah Gregory] Okay. So, if a person does get bitten by a stray dog, they need to get vaccinated. But exactly what's the process? I mean, wash their hands immediately, call 911? What exactly should a person do?

[Ryan Wallace] Okay. So if you think you've had a rabies exposure—for this scenario let's say it's a bite from a dog you think has rabies or could have rabies—the first step is to go wash that wound with soap and running water for at least 15 minutes. There's a...there's a really positive effect of washing that virus out if you can do it quickly. And then the next step is getting to some medical care. So you're going to need to go find your doctor or a PEP clinic, and there's going to be not only an evaluation of the wound and maybe some wound care, but also a risk assessment. And that risk assessment is going to look at the...so, they're...they're going to ask you questions about the type of animal that bit you, the...the circumstances of that bite, what were you doing with the animal when it bit you, the vaccination history. They'll probably ask if the animal is available to be quarantined, and that can be done in home or at a special facility, and they'll observe the animal for 10 to 14 days just to make sure it stays healthy. Or if it's a wildlife or suspect rabid animal, they're going to probably try to assess if they can test that animal and get a diagnostic....you know, tell you if it actually did have rabies. And all of those factors are going to go into a decision on whether or not you should get the rabies vaccination series that we've been calling postexposure prophylaxis.

In a heavily endemic country, a lot of these exposures are going to clearly be a risk and you're going to start your vaccination series right away. When you are in a situation where rabies is...is much better controlled, you have a little bit more time to look at the whole situation—maybe wait for a test result for a few days, maybe wait for the outcome of a quarantine if it's a healthy, known dog—and then make your PEP decision based on those outcomes.

[Sarah Gregory] What are the biggest challenges to eliminating rabies in people from dog bites?

[Ryan Wallace] So, that's a...it's a good question. Maybe the....I'll answer it backwards. So, we have the tools to eliminate rabies in dogs—there are numerous countries that have eliminated dog-to-dog transmission of rabies (or the canine rabies virus variant). We have the methods, we have a lot of pilot studies that have shown you can eliminate...eliminate this virus even in low- and middle-income countries. But what we haven't seen, and what I think is probably the biggest barrier is the sustained commitment that's required to truly eliminate a disease. Whether we're talking about elimination in a community or a country or globally, elimination is a big word. It's not something where you do one campaign and...and a virus is magically gone. That's not how this works...and it...it really takes strong commitment, it does take funding, it takes a skilled workforce, and it's something that...that each country that decides to take on this goal...they'll probably be vaccinating dogs for the next five to ten years before it's truly gone. And then even after it's gone, you go to your neighbor and see if your neighbor got rid of it. If your neighbor didn't get rid of it, they might be, you know, unfortunately inadvertently sending rabid dogs back into your country and you're going to need to keep up some level of vaccination.

So, I think the biggest barrier is...is the ability to operate sustainable programs for zoonotic disease in low- and middle-income countries. That's a huge challenge, a huge barrier. Definitely is going to require international assistance. It's going to require governments from countries that have eliminated canine rabies already to...to really step up and help provide support to...to these countries that are heavily affected.

[Sarah Gregory] Are there any actions or further studies that you would like to see at this point?

[Ryan Wallace] The...the big question right now is largely on logistics. How do we scale up very successful pilot programs? What are the technical resources that are needed? The funding that's needed? How do you operationalize an effective campaign in a low- or middle-income country to be something that is scalable? I think that's the big gap right now, and we're looking for strong examples of how that was done. If we go back to oral vaccines specifically, one of the biggest questions right now is, is there a universal bait flavor and how can we mass produce these...these vaccines. We...we can't make a...a curry-flavored vaccine for...for use in Thailand and, you know, pig intestines-flavored bait for...for use in Haiti. The manufacturing for that's probably...the manufacturing that would be required to...to have that type of differentiation just doesn't exist right now. So, identifying a universal flavor and getting it to a stage where we can mass produce...mass manufacture, I think, is a...a big need right now and we know there are some groups that are working on it. And then overcoming the stigma of...of oral vaccines. For decades, there has been major concerns (legitimate concerns) about the safety of these vaccines. How do we get governments and community members and dog owners to understand that new methods of creating these vaccines have made them very safe and very effective? And so we're overcoming...we need to overcome these several decades of...of messaging, because that messaging has changed.

[Sarah Gregory] So do you and your coauthors in this report have any recommendations for implementing oral vaccines for dogs?

[Ryan Wallace] Yeah, we do. We...we provide a summary of...of recommendations that countries should...should...to go through before they try to implement the oral vaccines into their vaccination program. And these are derived from several other pivotal oral rabies vaccine guidance documents produced by WHO and OIE. And so they...I guess I won't list them all for you here. You can go to our article if you want to see, I think, all (I think there might be) 13 steps that countries should take. But in general, you want a surveillance system that can detect exposures (unintended exposures) so if you're going to use a modified live vector vaccine, we need to have infrastructure in place to know if people have made contact with it. And while these vaccines...any vaccine that has been evaluated and found to be very safe, there are still very, very low risks that there could be an adverse event and we want to be able to detect when those exposures occur, and make sure that we can provide appropriate public health reactions. So that, that's a big piece of infrastructure that needs to be in place if you're going to think about using the oral vaccine.

And then, it's the assessment of your dog population. These are not inexpensive vaccines and they're not widely available yet. And so you want to make sure you're using them correctly. So you need to understand your dog population—in which fact...which dogs you are going to target with the oral vaccine, and then are you using the right bait flavor and the right bait construct.

[Sarah Gregory] Dr. Wallace, tell us about your work now and what you enjoy most about it.

[Ryan Wallace] Well, my work for the last 11 months has actually been doing COVID...COVID response. And I think that's what we're seeing across the...across the globe. A lot of people that are traditionally running rabies vaccination programs are now being pulled in to...to help with the pandemic response. It's great that a lot of our colleagues and partners around the world have been able to help out on this and use their experience controlling a similar zoonotic disease and to

help...help with pandemic efforts. But it does...it does raise a major concern about how we're going to sustain the successes that have been made in controlling canine rabies if our workforce is diverted. And if a lot of these programs are (like dog vaccination), are put on hold for a year or two while we're addressing safety concerns and making sure that our teams can go out and do this safely. So, I think there's...the next year or two is going to be very important to ensure that we're maintaining dog vaccination programs. But we need to make sure we're doing it safely and that we're doing it in the context of the priorities of its elements.

[Sarah Gregory] I heard a dog barking earlier. Do...so you obviously have at least a dog. Do you have any other pets? Do you want to tell us about them?

[Ryan Wallace] I have a lot of pets. I have four fish tanks that have a different variety of freshwater fish. I have two Lionhead rabbits that my...my two daughters take care of. And I have two dogs, both rescues. One...one actually looks like a...a Haitian street dog, even though it was found here in DeKalb County, Georgia. But the similarities are quite strange. When I look at pictures of myself in the field vaccinating all these dogs, you would not be able to tell if I was holding my own dog or one of those dogs from Haiti. And then...and then another elderly rescue dog that we picked up from a rescue organization.

[Sarah Gregory] I also have two dogs and two rabbits, that's interesting. But not the four fish tanks.

[Ryan Wallace] If you want one or two I can...I can send them over.

[Sarah Gregory] They wouldn't survive. Thank you for taking the time to talk with me today, Dr. Wallace.

[Ryan Wallace] No problem. Thank you for highlighting this article and the 2030 goal and all of the really good work that our partners around the world are doing. We really appreciate the opportunity to talk.

[Sarah Gregory] And thanks for joining me out there. You can read the December 2020 article, Role of Oral Rabies Vaccines in the Elimination of Dog-Mediated Human Rabies Deaths, online at [cdc.gov/eid](https://www.cdc.gov/eid).

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

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