

Control Strategies for *Taenia solium* Cysticercosis, Peru

[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. Seth O'Neal, an associate professor of epidemiology at Oregon Health & Science University in Portland, Oregon. We'll be discussing control strategies for *Taenia solium* cysticercosis in people and pigs in Peru.

Welcome, Dr. O'Neal.

[Seth O'Neal] Good morning, Sarah. Thanks for the invitation. It's a pleasure to speak with you.

[Sarah Gregory] Let's talk about pigs first. Why are pigs such an important global food source?

[Seth O'Neal] Yeah, so that's a great question. Sort of on a global scale we've seen an increase with development and increase in the wealth and conditions in lower and middle-income countries, in particular. And that's led to a large increase in demand for high-quality meat protein, like pork, and that's of course led to increased production. That production is happening both on the large scale on the big farms like the ranges that we're accustomed to in North America and Europe, but also on a very small scale where we have these small landowners in rural areas raising just a few pigs for subsistence-level agriculture eventually.

And locally on those small farms, it's not just that pigs are a good source, an important source of pork, it's also that those pigs are an important part of the economy and the cash economy. So pigs are raised there, people buy them as piglets or have their own piglets and essentially they let them roam around and scavenge for food and so it's a very low input source of raising animals. And in six months to 12 months, those pigs are large enough to sell and that's a great source of cash in these cash limited areas. And the pigs themselves are also sort of a piggy bank (a savings bank, if you will) where people will slaughter the pigs and sell them when they need cash, so moments like for school supplies or for dealing with accidents, that kind of thing. So they're both for meat but they're also for a cash economy and savings.

[Sarah Gregory] So you can just take a pig and let it loose and it will find enough to eat that it thrives and grows? That's interesting.

[Seth O'Neal] Yeah. That's how people raise them, yeah. They let them run and scavenge.

[Sarah Gregory] And thievery is not an issue? Are they branded? How do they protect their pigs from your neighbor's pigs running around?

[Seth O'Neal] It's funny, because pigs actually know their homes and will often return to their homes and people will sort of encourage that behavior by, you know, feeding them table scraps and that brings the pigs back to home. Typically at night they come back after roaming and will stay at the home. And they're also herding animals (the pigs are), so they group together, they move together, and they come back.

[Sarah Gregory] Ah. So many cultures and religions don't even allow for eating pigs. Is that historically because pigs have had issues with parasites?

[Seth O'Neal] It's an interesting question to think about. There's parasites like *Trichinella* and *Taenia solium* (which we're going to talk about) which cause severe disease

in humans and are a food safety problem. But whether or not, you know, that's the reason that some cultures and religions have stayed away from them, not really sure but it's potentially related. Yeah.

[Sarah Gregory] Okay. So what is *Taenia solium*?

[Seth O'Neal] So *Taenia solium* is a parasite, and it's in particular what's called a cestode parasite, which is a segmented flatworm. Most people would commonly know this as a pork tapeworm, and it's a parasite that infects both humans and pigs and it...in fact its lifecycle depends on being able to have different life stages of the parasite developing in both humans and pig hosts. And there's really three main life stages for this parasite. There's the adult worm, which is the one that produces eggs and lives in the human intestine, that's what we commonly think of the tapeworm—the two-to-three-meter worm living inside someone's intestine. And then there's the egg stage which are shed by that adult and those are shed in the human feces and contaminate the environment. And then there's what's called the metacestode stage (or the larval stage) of the parasite, and that infects the muscles and other tissues of pigs. And you would see these in pigs as sort of small fluid-filled sacs, maybe a centimeter or less, that have the parasite within them. And the lifecycle depends on all three of those stages occurring.

[Sarah Gregory] Can this parasite be found in domesticated livestock other than pigs?

[Seth O'Neal] There's thousands, actually, of species of tapeworms. *Taenia solium* only infects pigs and humans, and to a lesser extent, dogs where consumption of dogs occurs. But in terms of other livestock, no. There are other tapeworm species that infect cattle—*Taenia saginata* is that one in particular—but that's less of a health concern for humans.

[Sarah Gregory] And why are pigs so prone to having this parasite?

[Seth O'Neal] I don't think it's so much a question of pigs being prone to this parasite, it's more that the parasite itself has developed within this context of this predator-prey relationship between human and pig. And it sort of takes advantage, if you will, evolutionarily of that relationship and also how we raise pigs in close proximity as a food source. So it's—the parasite has specifically developed within that context and so it targets that.

But there are aspects of pig behavior and how we raise pigs that lead to the conditions for pigs to become infected. So the first is that pigs are coprophagic which means they seek out and consume human feces and other feces, and that's to get the minerals (particularly iron) that's in the stool. And they'll actually compete among them and there's sort of a pecking order, apparently, on which pigs are able to access the feces. But in impoverished rural areas that we're talking about—these sort of small landowner scenarios—there's also less resources there for sanitation and so open defecation is common where people are defecating outside. And because people are raising pigs in this sort of scavenging way, those pigs have access to feces, they desire human feces, they consume the feces, and when those feces have tapeworm eggs, that's how they get the parasite infection.

[Sarah Gregory] In your article you mention cysticercosis and taeniasis. What are they and how are they related to *Taenia solium*?

[Seth O'Neal] So those are the conditions—those terms refer to the conditions of being infected. So taeniasis is the condition of having the adult intestinal tapeworm infection, and that's called taeniasis, or the disease would be called taeniasis. And cysticercosis is when you have that metacestode larval stage infection in the tissues, that disease would be called cysticercosis.

[Sarah Gregory] And, okay we get how pigs get it but how is it transmitted to people?

[Seth O’Neal] Yeah. So yeah, I described a bit how pigs get infected—they forage, they consume feces that contains eggs and these eggs come from a human that’s been infected with the adult tapeworm. So those eggs, once they develop into the larval stage in the pigs, when that pig gets slaughtered and the human consumes infected pork (or contaminated pork) that cyst that I described inside the meat—which is likely not visible to the person consuming it—that will hatch inside their intestine. This sort of baby tapeworm, if you will, will emerge and latch on to the intestinal lining and then grow into that adult that then will lay eggs and keep that cycle going. It’s also important to mention though it’s not part of the lifecycle that keeps the parasite transmitting and its life stages going, people can become infected and get cysticercosis (that is the tissue stage) if they ingest eggs accidentally in fecal contamination. So this is a dead end from the, you know, point of view of the parasite because that parasite at the larval stage is not going to be consumed, but from the human standpoint it causes important disease. And that’s really primarily why we were interested in this parasite and preventing the harm it causes because humans can get cysticercosis.

[Sarah Gregory] And clearly people aren’t deliberately eating feces (human feces), so does it...it gets on their hands or something? How does that happen?

[Seth O’Neal] Yeah. These eggs that I described, you know someone who has the tapeworm sheds these eggs in their stool. And the eggs are really sticky, they can stick to hands, they can get in water sources, they can get on food. And so they’d be transmitted sort of as fecal–oral route that other, you know, more familiar diseases like you know, *Shigella* or *Salmonella* might be. Yeah, it’s an accidental ingestion of fecal contamination.

[Sarah Gregory] I see. Do people and pigs get the same symptoms or are there different symptoms once you have this parasite in any form?

[Seth O’Neal] So only humans get taeniasis. The pigs don’t actually get that intestinal stage of the worm. So for taeniasis, this is not really a relevant question. For cysticercosis, it’s hard to say what the pig is experiencing really. But yeah, pigs can have some of the symptoms that we see in humans that are of concern, like seizures, and we can talk about that later.

[Sarah Gregory] Okay. And what are the signs that someone might be infected with these parasites?

[Seth O’Neal] So, again, humans have two forms that they can get. They can get the taeniasis which is the intestinal infection with the adult tapeworm, and people who have that typically have mild symptoms or no symptoms at all. And those mild symptoms might be like transient GI (gastrointestinal) upset. But typically people don’t even know they’re infected. They may pass small segments of the worm. So remember the cestode is a segmented flatworm, and the segments themselves can pass in the stool and are sometimes visible, so if someone sees them they might know. These segments kind of look like, if you had captured dogs before and you see little white segments within their stool, you’d know kind of what it looks like in humans. But because people don’t know they’re infected and because the eggs that they’re shedding are dangerous to humans, taeniasis is a dangerous condition in terms of public health and infecting others. So it’s something that we take very seriously.

The other way that people can become infected is having cysticercosis—so that’s the cyst developing in the body tissues—and that really depends on where those cysts develop. For the

most part, most of the body—if the cyst develops, for example, in the muscle tissues—there may be no symptoms at all and the person may never know they’re...they’ve been infected. But symptoms do and can occur when it happens in the brain, and that’s a condition called neurocysticercosis and that’s the main health concern with this parasite.

[Sarah Gregory] So tell us more about this neurocysticercosis.

[Seth O’Neal] So, again, it’s when the parasite larval stage infects the brain or the spaces around the brain in the central nervous system. And it’s really—we talk about neurocysticercosis as if it’s one thing. But it really presents itself as almost the neurocysticercoses, like many presentations, and that’s because the disease is really dependent and how it manifests is dependent on how many cysts form within the brain, where they are, how big they are, and what sort of their stage of development is. So these cysts kind of grow and develop within the tissues and eventually die, and that can also modify and change how the disease is presenting. So if the parasites were within the brain parenchyma (so this is what we think about as the brain tissue) it’s called parenchymal cysticercosis. And the symptoms there are typically—the main one is seizures. So particularly when this parasite dies and the body recognizes it and causes inflammation as it attacks that infection, seizures can result. And that’s really the main presentation that we think about with neurocysticercosis. But chronic headaches occur, brain inflammation (encephalitis) occurs, cognition issues occur. It can present in many ways.

And then there’s in the form of the neurocysticercosis that occurs when the cysts actually form, not in the brain tissue itself, but in the spaces and the fluid that circulates around the brain and that’s called extraparenchymal cysticercosis. And that actually can present more severely. It can have a condition called increasing intracranial pressure that would occur when those cysts would sort of block that flow of fluid, and that’s an emergency that can cause the brainstem to herniate and potentially leading to death. So those are the two, sort of main presentations of neurocysticercosis, but really it can present in many different ways.

[Sarah Gregory] Is there any treatment for it? Or any form of cysticercosis, for that matter?

[Seth O’Neal] Yeah, there is. We have some treatments; the treatments are imperfect. If you can imagine, I talked about the inflammation occurring and seizures being triggered when the parasite dies in the brain, so treating—if you’re treating and using a drug that might kill that parasite, you can trigger inflammation that can then trigger worsening symptoms in the patient. So decisions to treat need to be taken on an individual basis and again, depending on how many cysts there are, where they are, their life stage, et cetera.

So there’s antiparasitic drugs that will kill the cysts and there’s also drugs like antiepileptic drugs and antiinflammatory drugs that can help reduce the symptoms that are associated with the infection. And then in the case of the extraparenchymal cysts, those are the ones that develop, you know, in the fluid in spaces around the brain tissue. In some instances, sort of specific cases, surgery may be involved and that could be surgery like placing a shunt to reduce some of that pressure that’s forming within the brain cavity. Or in some sort of very specific, not super common instances, surgery could actually take the cyst out.

[Sarah Gregory] What types of tests are used to identify and diagnose this infection?

[Seth O’Neal] So for the neurocysticercosis you really need some form of brain imaging, and the ones that are typically used are either a CT (computed tomography) scan of the head or a magnetic resonance imaging—so the MRI of the brain. And those will help you visual the cyst

but also give information about, again, the number of cysts, how big they are, where they are, and their life stage, which can help you think about treatment indications and how to treat people. So really the neuroimaging is really important for diagnosis. There are some blood tests that can be done, and those can look for things like parasite antigens or antibodies against them, and those have a role in sort of supporting the diagnosis of what you see on imaging. And in some cases they're used to indicate whether someone gets imaging or not.

And then for the other disease, taeniasis in humans (the intestinal tapeworm infection), the typical tests are looking at the stool and using microscopy to look for parasite eggs or segments. And then there's some other tests that are used more often in the research setting that look for, you know, different markers of infection, like antigens or DNA.

[Sarah Gregory] Cysticercosis is considered a neglected tropical disease. What are the other neglected tropical diseases and why is it important to make people aware of them?

[Seth O'Neal] Yeah, that's a really important question. So neglected tropical diseases are really a diverse set of diseases and conditions that cause a large public health burden around the globe, and particularly in areas—low- or middle-income countries—that are still developing. And their impact in terms of the disease and the burden that they cause is larger in many ways than the attention that they get and the resources they get. They tend to not be known about as much, discussed as much, or funded as much and as such they remain largely without intervention. Most of these diseases have some preventable nature to them that could be worked upon, but as the name suggests they're typically neglected. So the World Health Organization has prioritized a diverse group of about 20 different conditions, and these are bacterial infections and parasitic infections and even things like snake bites (venomous snake bites) that would fall into this category.

[Sarah Gregory] Speaking of WHO, apparently they feel that neglected tropical diseases are of enough concern that they have created a roadmap to reach goals. What's in this roadmap?

[Seth O'Neal] Yeah. So the roadmaps have been developed a couple of different times, and they just recently published their newest roadmap which is essentially a set of targets which they hope to reach and hope to promote countries to act upon to reach with respect to these diseases. So the new targets and the new roadmap are for the year 2030. And there are things like reducing by 90% the number of people requiring treatment for neglected tropical disease, having at least 100 countries having eliminated at least one neglected tropical disease, things like that. So there are these large, ambitious targets to hopefully pursue and get governments interested in and addressing.

For *Taenia solium*, it is one of the neglected tropical diseases that's on that list. And the targets for this in particular are related to the number of countries with intensified control programs in place. So essentially, currently there aren't any countries that really have large-scale, established control programs going on specifically for this disease and WHO is interested in promoting this to occur. And so over the next 10 years or so, they want to see countries step up and adopt and adapt and implement some of these control strategies. That's what's in the roadmap.

[Sarah Gregory] What's been done previously to try and control *Taenia solium*? When I was young, people talked about pigs having parasites and that you had to cook pork thoroughly. And then later it seemed people were saying that was no longer true and you didn't have to worry about that. Do pigs not have *Taenia solium* in North America?

[Seth O'Neal] So, yeah. Essentially in North America right now, pigs don't have *Taenia solium* and that relates to the conditions, again, of how transmission occurs. So this parasite thrives in those environments in which pigs have access to and can consume human feces. And with development over time and improving how we raise pigs, and particularly raising pigs in these sort of large, cleaner farms. Well, cleaner maybe is relative in particular to what you're talking about, here I mean not being exposed to tapeworm eggs and feces. So if that condition is changed with development, and this has happened not just here but also in Europe and in places in China, the disease is starting to go away because it doesn't have the conditions to transmit. But still there's many places around the world where those conditions exist.

In terms of other strategies to control apart from development, there are a number of different approaches that could be taken, and these range from education to behavior change, health promotion kind of activities to application of antiparasitic drugs in humans and pigs or vaccines. And there are—these have been primarily applied in the research setting, and that's exactly the kind of work that our study that we'll be talking about was looking at.

[Sarah Gregory] So you carried out your study in Peru. How big a problem is the parasite there?

[Seth O'Neal] It's kind of hard, you know, from this standpoint. Here in North America, we kind of consider it as sort of a strange or unique or not common disease, though we do have people with this infection here. In Peru, it's fairly common. It's common to the point where if you have conversations with people—say, neighbors, taxi drivers, family members—they're likely to know somebody who's had neurocysticercosis and are familiar with the disease in that way. So the more, specifically, as you get into the rural areas where the disease is really transmitting frequently and commonly, there's a couple different ways we've looked at it. We've done some studies in adults in some of these rural areas, small villages, where if you look at CT scans of heads of people, 10%–20% of people will have signs that they've been infected (this is infection of the brain). And that leads again to most of those cases actually don't have symptoms or severe symptoms, but many of them do end up having things like seizures. And in the areas where we do our study, about 45% of people who have epilepsy (that is recurrent seizures), they also have cysts in their brain that appear to be the cause of that epilepsy. So it's a common problem and it causes fairly severe morbidity in humans.

[Sarah Gregory] Is it a bigger problem there than in other places and where is it most endemic?

[Seth O'Neal] So it's pretty much endemic in most places where you find those conditions that we talked about—pigs roaming free and having access to human feces—you tend to find the parasite there. This occurs in many parts of Latin America, Africa, Asia, and particularly in the rural regions of those countries. In sub-Saharan Africa, there are some reports of some very high transmission areas where we see more disease than we do perhaps in Peru and other parts of Latin America.

[Sarah Gregory] You previously did a pilot study in Peru. How did those findings affect how you approached your current study?

[Seth O'Neal] So in addition to that pilot study, really this study that we're going to talk about today, that's really been informed by really three decades of work and research by what's known as the Cysticercosis Working Group in Peru, which is a network of investigators. So there are many people involved in this research, and like most science, we build on each other's results and collaborate to address the problem. And these studies have worked to, you know, understand

the scope of the problem and how transmission occurs and also help come up with some of the potential ways to intervene that we are trying.

I think there's a bunch of different lessons that are pertinent to this study that I would say that we applied in this study. And the first is, you know, while long-term development is certainly the goal—and I'm talking about things like infrastructure improvement and reduction in poverty—that is what we should all be working for and that will help take care of the disease. But in the short-term there's things that we can do while development is underway that can reduce disease and suffering. So that's the first sort of main lesson.

Other things that have informed the study are that we found that there's pockets of transmission—what we call clusters—clusters of transmission that occur within villages. It's not that the disease is happening uniformly, either across villages or within villages or across regions. Human and pig infection cluster together, and that's something that we can potentially take advantage of in our control interventions.

The third thing that I would say is relevant is that pig infection is visible (it can be visible). Most light infections and most infections, in fact, will not be seen—that is if you cut open a pig and it's infected and it has two or three cysts in the whole carcass, you won't see it and it will likely get consumed. But some of the pigs (the heavily infected pigs) are really, really, really apparent. So they slaughter the pig and it is immediately apparent that the meat is full of cysts. We can talk about hundreds and thousands and tens of thousands of cysts. That is something that we can use, that visible indication, and also pig tongue. When the pig is alive, if they're very heavily infected, we can look at the tongue and feel the tongue and see these cysts at times when the pig is still living and that can help us indicate where these clusters of infection are. So that's another point. We use heavily infected pigs as a visible, readily apparent indicator of where clusters of transmission might be, and we take advantage of that.

I think a couple more points that we've learned over the years, one is that, you know, it's a two-host parasite so you can think about putting your resources towards treating humans or treating pigs if we're talking about chemotherapy. And while both strategies could work, there's reasons to target human taeniasis in my mind, and one is that it's prolific. These tapeworms produce tens of thousands of eggs a day over a course of infection that can be years long. So they have the potential to cause a lot of further infection in both humans and pigs, so targeting them makes sense. And also from a practical aspect and practical point of view, in many rural areas where these disease occur, they're sort of far away from government attention and government resources, and veterinary resources are fairly scarce. So having the veterinary infrastructure in place to deal with pigs is not always available. I think those are the main things that we've learned over the years that informed this new study.

[Sarah Gregory] So both ring treatment and mass treatment were used and investigated in your study. What's the difference between the two?

[Seth O'Neal] Yeah, so we did. The study was comparing what we refer to as ring treatment which is a strategy that tries to take advantage of this clustered transmission that I was talking about—the proximity of humans and pork and pig infection—and mass treatment which is what you might think it would be and what it sounds like—this is providing chemotherapy or chemotherapeutic drugs to either all people or all pigs or both regardless of sort of their underlying risk. So mass drug administration or mass treatment would be something like how we

did it in the study, which is going door-to-door on a every six-month basis and providing antiparasitic drugs to people. So everyone gets it or has the opportunity to take it.

Ring treatment is basically a strategy in which we use surveillance, that is we look for these heavily infected pigs that can be either detected upon slaughter because you see the cysts or by examining their tongues while the pigs are alive. And when you find those heavily infected pigs, the ring treatment is just treating people who are nearby, so focusing your treatment resources only on those areas where you see a heavily infected pig. And we used this strategy in which we treated people within...that lived within 100 meters of where that heavily infected pig was found. So the main difference is mass treatment is used to sort of treat everybody uniformly, ring treatment is trying to provide treatment to clusters of infection within community.

[Sarah Gregory] Tell us briefly about your study and how you went about conducting it.

[Seth O'Neal] Yeah. So our study was—the objective of the study was to try to look at these different options and try to see which would be more effective or the effect that they would have. And really the idea was to do this study in a way that would inform future public health interventions. In other words, we would like to see, as WHO would like to see, control strategies adopted. So we conducted a study in which we looked at 23 villages in northern rural Peru, and this is a population of about 10,000 people and about 3,000 sort of backyard raised pigs at any given time. And we divided those villages up into three different groups, and those groups received either mass treatment—so that was where we went to each house every six months and offered antiparasitic drug to treat taeniasis and we did that for two years—or the other villages received (the other groups received) one version or another of ring intervention. So one was ring treatment in which we went through the villages every four months and looked for pigs, that is we caught all the pigs and looked at their tongues. And when we found a heavily infected pig, that is a pig with a cyst on its tongue, we provided the antiparasitic drug to people who lived within 100 meters and we did that every four months for two years.

Ring screening was similar, we had the same kind of surveillance where we went through and looked at tongues every four months. But rather than just providing the drug to people within 100 meters, we collected stool and looked at the stool under a microscope and using another test to look at antigens and only treated those people who we knew to be infected. So that's three different groups. Those are all based on different ways to provide the antiparasitic drug for taeniasis to humans, and we also split those—each of those groups up into two and we added treatment of the pigs with the antiparasitic drug oxfendazole, which treats the cyst. So that was in half, so we had six groups total. And how those pigs were treated in each group depended on, you know, whether they were part of a ring intervention or a mass intervention. So in the mass treatment we just provided the oxfendazole to all pigs, and in the ring strategies we provided the oxfendazole drug only to those pigs living within 100 meters of where that other pig was found.

So that was the general structure (six study groups) and we followed and did this intervention for two years. And then we measured the effect of our study by taking blood samples from the entire pig population and looking at, in particular, the pigs that were born in this study—that was during the time that we were conducting this study—and looking for antibodies. And over time, we were looking for changes in antibodies—how many pigs, what proportion of pigs had antibodies—as an indicator of how our interventions were doing.

[Sarah Gregory] So you looked at pigs (you focused on pigs) in villages and not in slaughterhouses. I guess that's because there aren't actually slaughterhouses in these rural areas? Or is there some other reason?

[Seth O'Neal] Yeah, that's exactly right. In these rural areas, pigs are raised sort of in the backyard and they are often slaughtered in the backyard. There is no formal existing meat inspection. Again, this is a neglected tropical disease. Rural, sort of isolated regions that don't have much attention from government essentially, so no formal meat inspection happens.

[Sarah Gregory] You mentioned in your study you looked at pigs' tongues to see if they were infected. Was there any other way you checked?

[Seth O'Neal] That was the main reason, the main way we checked. We had our teams go through the villages door-to-door, ask for permission, and then literally chase down the pigs which are basically sort of semiferal, if you will, free-roaming pigs. And it's a lot of work to catch them. But when we would catch them, we would temporarily restrain them physically (just hold them), and then we'd open the mouth and feel the tongue and look at the tongue (particularly the underside of it) to see whether or not it had cysts. So that's how the tongue exam works and we actually learned that from the villagers themselves who often use tongue inspection prior to sale as an indicator of whether that carcass (the pig carcass) later will have a lot of cysts or not, and that influences the value of the meat and whether or not it's sold. We also gave the opportunity to villagers sort of to self-report. So instead of us going through and just finding cysts on tongues, we, you know, told villagers that if they slaughtered a pig and found it heavily infected with cysts, they could let us know and we would come verify and then do the ring intervention.

[Sarah Gregory] So when you found infected pigs, you gave them some kind of treatment...all of them? Or were some pigs control groups that you didn't do anything with?

[Seth O'Neal] Essentially when you find an infected pig, it's a food safety hazard, it's a human health hazard, so we're ethically obligated to do something about that. And we essentially offered two things to people: we offered to treat the pig with oxfendazole, which is effective in killing the cysts in pigs, or if people did not want to treat it, we also offered to just purchase the pig and remove it from the community. And so people chose both options for different reasons. But essentially, we didn't leave these pigs in the community to cause further disease.

[Sarah Gregory] I see. So there's an infected pig and they opt for treatment and the pig is treated. Is it actually safe to eat after being treated?

[Seth O'Neal] Yeah, that's a really important question. A lot is known about the drug that's used (oxfendazole) and what's called its withdrawal period. And so the drug itself is cleared from the carcass of the pig and the tissue of the pig about three weeks after it's been treated. And so from that point of view, in terms of drug clearance, yes it's safe. The drug is also very effective in killing cysts in most of the pig—in the pig's muscles and, you know, body tissues. Other than the brain, it's very effective. Some cysts persist in the brain. And so if people decide that they want to treat the pig, we tell them we have to wait three weeks before you would slaughter this pig and eat it and that you also have to be careful not to consume the brain because there might be living cysts in there, you know. The carcass itself—the pig meat, the pork after you treat it—is safe to eat in terms of infection. It may not look the same, and in heavily infected pigs the scars that result from killing all these cysts in the pig, often they get less palatable if you will. And so

heavily infected pigs after they've been treated may not be consumed just for that preference reason.

[Sarah Gregory] What about cooking? Does proper cooking have any impact on this?

[Seth O'Neal] It does. If you were to reach proper temperatures, if you were to cook and have the pork reach 160° uniformly and throughout, that should take care of the cysts and should kill it. You know, that said, it's hard to do. It's hard to tell when pork has uniformly reached that temperature, I think we've all experienced that. It also depends on how people prepare the meat. So if you're, you know, preparing a dish that has sort of large pieces of pork or pork that's near the bone, those places may not reach the same temperature. And so cysts that are still infectious could persist. You know, people in this area in Peru where we work, they eat—the primary way they eat pork is chicharron, which is essentially boiled and deep-fried in chunks. And you would think that that kind of treatment would definitely work, but it seems that transmission still occurs.

[Sarah Gregory] What were your findings about the difference between treating pigs versus humans for this parasite and which is the better approach? I think you mentioned that for logistical reasons, it was better to treat humans (people). Is that right?

[Seth O'Neal] So we chose, in all of our study arms, we chose to treat humans. So it's not that we studied and could tell from our study if it was better to approach in a pig only or human only way. What we did is treated all humans for the reasons I mentioned, both because taeniasis is that direct cause of disease in pigs and humans. It's prolific, and in other words it causes a lot of infection, it has the capability to cause a lot of infection. And then also that practical question of not only that it's hard to have the veterinary resources to treat pigs, but also that the pig population turns over very quickly. And so interventions in the pig population—you're constantly seeing new groups of pigs that would have to be treated, whereas in humans it's relatively stable in comparison. So I can't really say whether there is a...you know, pig only or human only is beneficial because our study didn't really look at that.

[Sarah Gregory] And what about reinfection? So you get this parasite, you get treated for it, the parasite's gone. Then you eat another pig and have the same infection?

[Seth O'Neal] Yeah. Yeah, people definitely do become reinfected, and we see that. There doesn't seem to be an effective immunity for taeniasis in humans. So people do get repeat infections. And often you see those repeat infections, again, in these sort of areas where, you know, sanitation may be less and poverty may be greater and pigs are having more access to feces, and they are being consumed regardless of what they look like even if they are...seem to be infected, they get consumed anyway. So in those scenarios, reinfection is common.

[Sarah Gregory] So possibly repeating ourselves a little bit here, but of all the intervention strategies used, was there one that stood out the most, found to be the most effective?

[Seth O'Neal] There wasn't. And actually this was one of the really important findings of the study. So all three of the studies when you look at antibodies in the pig population in terms of, you know, transmission, they all showed about 65% reduction over two years. And that's regardless of whether, you know, we treated everybody, we treated only people in rings, or we screened people in rings and treated only those who were infected. They all worked. And that's really good news in terms of scaling up and implementing some of these strategies to prevent diseases, public health programs, there's options.

There were some differences between them. And one of the main reasons for a targeted approach (which is these ring approaches) versus a mass approach is to limit the amount of drug that you use. So by only treating people within the rings, you don't have to give as much drug to the population. Again, in the mass intervention, you're giving drug to everybody. And typically in these villages, you might have 2%–3%, so two to three out of every hundred people might have taeniasis at a given time. That's sort of a typical scenario. And if you're treating everybody, you're treating 97 people who aren't currently infected for those two or three who are. With the ring interventions, we were trying to improve that. So although we had the same effect in all three of those main interventions, when we did mass treatment we gave drug to about 90% of the entire population; when we did ring treatment, it was only about 20% of the population; and then when we did ring screening and only treated those people we knew to be affected, we only treated 1% of the population. So a lot less drug was used with the ring approaches, and particularly with screening.

[Sarah Gregory] Okay. So other than having to use more drugs in different approaches, were there any other disadvantages of using one strategy over another?

[Seth O'Neal] Yeah. I think the main differences between these—and try to look at this in context—these are options, essentially, for strategies that might work and they should be perhaps tailored to what the resources are, that are available in those regions. So for ring interventions, probably the main advantage there, as I mentioned, is that you don't use as much drug. There also is some advantage, I believe (though we haven't really measured this) in that when you treat just small groups of people, the message there is that, you know, this group has more risk and people should be taking the drug because of that risk. And it helps to reinforce this idea that hey, we found an infected pig and the cause was a human who has the tapeworm, and so we need to treat the human. It reinforces that lifecycle to villagers who otherwise would not connect these things. So that's one of the advantages there. The disadvantage is that you have to have some sort of surveillance in practice where you either go out and actively find pigs that are heavily infected or some sort of system in place in which people can report those infections to you so that you can actually intervene in those rings and give the drugs or screening as needed.

On the other side, the mass treatment...it's really familiar. It's an approach that's used for many parasitic drugs. It may be, again, less efficient than in other parasitic infections because there are so few people as a proportion that have taeniasis to make this disease endemic. It's only a couple percent of the population, typically. So there may be a lot of waste in that way. And it's not just waste, you're also, you know, potentially—although we use safe drugs—you're potentially exposing these people who may not need the drug to the potential adverse effects from those drugs.

The other thing that's been noted with some of these mass treatment programs is that participant participation can decline over time and that may be related to, again, the sort of perception of risk—if everybody's being treated over and over again, why do I individually have to do it? And for other diseases (so we didn't see this here), there's sort of mixed evidence for other parasitic infections whether mass drug administration is effective in the long term and sustainable. So those are some of the disadvantages of the mass side.

[Sarah Gregory] Was there anything that surprised you?

[Seth O'Neal] So in doing this study, I think the results we expected to see—and a good control effect with all of the approaches that we took—I think what was surprising to me that they were

equivalent in the context or had a similar control effect in the context of using such a different amount of drug between the different ones. I thought the amount of drugs applied was quite a stark difference and still had the same effect. So that was interesting and somewhat surprising.

The other sort of surprising result was that within the ring screening study group—so this is the one where we offered diagnosis and only treated people who were known to be infected—that had the most rapid decline in transmission in all of them. And you would think that by applying less drug (because this applied the least amount) that that wouldn't be the case. But in fact, it had the most rapid decrease. And this may be related to the fact that once we identified someone with a tapeworm infection and treated them, we went back to verify whether they were cured and if they were not, we retreated them. So there may be some treatment effect or ineffect—in other words, the drug not being completely effective—that if you're using a mass approach where you're not diagnosing, you're just applying the drug to people who you think might be infected, they might have persistent infections that could keep transmission going. So those are, I think, maybe the two sort of surprising results that we had.

[Sarah Gregory] Yeah, that is interesting.

Is there a pig vaccine for this? We haven't talked about vaccines, and would a vaccine for a parasite work?

[Seth O'Neal] Yeah. So there is...there has been work done on vaccines and parasites, and a few different ones developed in the research setting and one even now on a limited basis, but it is commercially available called the TSOL18. And that is a really effective vaccine, it blocks transmission to pigs. You vaccinate pigs and essentially they don't get cysticercosis in these environments. It has, you know, from that side it's very effective and it has some great utility. The downside is practical application. So as we talked about before, the pig population turns over rapidly in these areas. So every time you come back to a village, if you come back—we came back every four months—and every time we'd come back, you know, half of the pigs would be new (the pig population would turnover). So if you're vaccinating pigs, you have to be vaccinating pigs all the time. And this vaccine also currently requires two doses. So not only do you have to capture all pigs, you have to vaccinate them twice and the population is turning over really rapidly. That's the main...those are the main downsides for them, and hopefully someday that will be addressed and those will be improved, and it would be something that would be more practical for us to introduce in our strategies.

[Sarah Gregory] What about people? Is there a vaccine for it in people?

[Seth O'Neal] So there's actually no reason to suspect (no main reason to suspect) that that vaccine that's available for pigs now would not also work in humans to prevent people from getting cysticercosis and neurocysticercosis if they were exposed to eggs. The problem is, again, goes back to the theme of neglected tropical disease and developing a vaccine in humans is an inordinately expensive, time-consuming affair. And essentially I think the decisions that are being made, maybe not directly but as a consequence of these being neglected, that the market is not—the demand is not there, basically. The market wouldn't support the development costs and so it hasn't been pursued.

[Sarah Gregory] That's a shame, because that would seem to be the most effective way to deal with all of this, but maybe someday.

In what ways do you hope your findings contribute to public health?

[Seth O’Neal] Yeah. I think this is what motivates me and motivates others to do this work. I mean, we’re motivated by, you know, seeing the consequences of disease in the places that we work and what we really want to see is control interventions in place that would prevent this. This is very much in line with what the World Health Organization is also trying to promote. So my hope is that we can take and build upon these findings showing that there are multiple effective strategies, there are many ways that you can target control interventions, and these are with tools and strategies that are readily available and actually appropriate for these sort of isolated areas. So there’s feasible ways forward and my hope is that these become implemented into public health programs. And that’s a large area of our research currently and ongoing research is working with government sides and trying to understand the best way and best practices to implement these control programs so that they can be effective and sustainable, not just in the research setting but also as ongoing public health programs.

[Sarah Gregory] So on that note, tell us about your job and how you became interested in this particular topic.

[Seth O’Neal] Yeah. So I’m an academic, I’m a physician and an epidemiologist by training. And I work at the Oregon Health Sciences University where I’m on faculty. My work is primarily research related, and that means that I, you know, do the standard stuff for research. I think about study designs and come up with designs and try to get them funded. Again, my focus is on this parasite in particular with an eye towards control and developing ways to control transmission. And again, my motivation from that comes from living in some of these countries and working in some of these countries and seeing the effect. Also seeing some of the effect on people here in the United States during my training, neurocysticercosis does occur in the United States. In fact, it’s one of the more common neglected tropical infections that we see here in the U.S., primarily among migrant populations. And just seeing that how the strength of the impact and how greatly it impacts people and families is what made me interested and knowing that this is entirely preventable.

[Sarah Gregory] How has the COVID-19 pandemic affected your research? I imagine it must be difficult trying to conduct a study in another country with everything that’s going on.

[Seth O’Neal] It has been. The impact has been really hard. It’s drastically affected our ability to do the research that we planned to do. It’s impacted us both in terms of, you know, having to halt activities because of safety issues for participants and staff, not wanting to draw resources away from the hospitals and other public health resources. We work with the public health agencies, so wanting them to remain focused on COVID and not distracted. There’s also been in Peru social unrest as a result—not just Peru, in other places—social unrest as a result, and that’s impacted our ability to do work. And then finally what we’re seeing now further down the line is supply chain issues, getting the drugs that we need to do the work. But all of this leads to uncertainty and a lot of adjustment and a lot of continued adjustment, but I think what helps is just keeping this in context and perspective. I mean, COVID is a global public health emergency and that’s where our attention needs to be. You know, certainly cysticercosis, taeniasis is an important problem but it can take the back seat for now. So, a little bit of perspective and patience I think helps get through that.

[Sarah Gregory] And on that note, thank you so much for taking the time to talk with me today, Dr. O’Neal.

[Seth O’Neal] Sarah, it’s a pleasure to talk to you and I’m happy to do it.

[Sarah Gregory] And thanks for joining me out there. You can read the September 2021 article, Geographically Targeted Interventions versus Mass Drug Administration to Control *Taenia solium* Cysticercosis, Peru, online at [cdc.gov/eid](https://www.cdc.gov/eid).

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

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