40 Years of Brain Infection Caused by Amebas in Recreational Water, United States

[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. Jennifer Cope, a medical epidemiologist at CDC. We'll be discussing trends in recreational water exposure associated with primary amebic meningoencephalitis in the United States.

Welcome, Dr. Cope.

[Jennifer Cope] Thank you for having me.

[Sarah Gregory] So, primary amebic meningoencephalitis, or PAM, is caused by an ameba. What's an ameba? What makes it different from say, a virus or a bacterium?

[Jennifer Cope] So an ameba is a microscopic single-celled organism, and what makes it different from a bacteria is that it's classified as a eukaryote. And this makes it different from bacteria, which are considered prokaryotes, in that eukaryotes are classified that way because they have a nucleus. So that what makes them different from a bacteria.

[Sarah Gregory] So, just give us a little tiny bit of a rundown on a cell. So, what is a nucleus? Where does it fit into a cell that matters?

[Jennifer Cope] So, a nucleus is where the genetic information of a cell is housed. And in this case for *Naegleria fowleri*, which is the ameba, it's the DNA of the cell.

[Sarah Gregory] Okay. So, where is this ameba usually found?

[Jennifer Cope] So, amebas are commonly found in the environment. And this one in particular (*Naegleria fowleri*) likes warm, fresh water, but it can also be found in soil.

[Sarah Gregory] And apparently its existence has been known about since the 1970s. Did it emerge or was it just discovered at that time?

[Jennifer Cope] So, it's likely that it was just discovered, and not that it necessarily emerged right at that time. The first case of primary amebic meningoencephalitis, or PAM, was identified in the 1960s in Australia and it was found to be caused by a new type of ameba that they went on to call *Naegleria fowleri*, and that was after one of the researchers who first described it (Dr. Fowler). And since *Naegleria fowleri* was first identified, actually researchers went back retrospectively then to identify cases of PAM that happened prior to that. So, there was one study in the U.S. out of Virginia where they used pathology records from people who had died previously of maybe unknown causes, and they were actually able to retrospectively identify them as PAM cases. So yeah, we think PAM probably has been around prior to when it was first described, and it was really just our ability to detect it and describe it. And also because it's a rare infection it would have taken a while for it to be detected because of that.

[Sarah Gregory] We've been reading a lot about this ameba in the news over the last two or three years or so. Why are public health officials concerned about it?

[Jennifer Cope] Well, because it's such a highly fatal infection. Most people unfortunately die from this infection. We consider it a high consequence pathogen because of that. And so because of the

implications of getting this infection, that's why it is of concern to public health officials. Because the outcome can be so severe.

[Sarah Gregory] That's terrifying. How common is it?

[Jennifer Cope] Well fortunately, PAM appears to be a rare illness with only a few cases reported each year. So, it's fortunate because most cases do result in death that it is otherwise a rare illness. And there's also likely cases that go unrecognized because it causes meningoencephalitis, which has a lot of different infectious causes as well as noninfectious causes. But even so, even if there are unrecognized PAM cases, we don't think that this is a big number. So overall, this appears to be a rare disease.

[Sarah Gregory] Is it possible to be a little more specific how rare is rare?

[Jennifer Cope] Sure. Oh yeah, of course. So in the United States, we've had...we've been tracking PAM cases since 1962. And we've had anywhere from...we've had years where there's been no cases reported (so zero cases), and the most we've ever had reported in a year is eight cases. So yeah, the range is zero to eight cases, and since 1962 through 2019 (which is our current data), there have been 145 cases reported total in the United States.

[Sarah Gregory] Okay. So it is pretty rare, but tragic for the unfortunate 142 people.

So, encephalitis usually refers to an infection of the brain, as you just said. How does this pathogen even get to the brain in the first place?

[Jennifer Cope] Yeah, so encephalitis (just to elaborate a little bit more on that), that's a general clinical term meaning inflammation of the brain. And the other term to define as well is meningitis, which is referring to inflammation of the spinal cord. So in this infection (primary amebic meningoencephalitis), you have a combination of both of them. And like I said, they can be caused by many types of infections as well as noninfectious causes. So in the case of PAM, it causes both. And the way this happens is when *Naegleria fowleri* is in the water, and if someone gets water that contains this ameba up their nose, that's when the ameba has an opportunity to use…it uses the nerve endings of the olfactory nerve which actually penetrates down through the skull into the top of the nose. And this is the nerve that helps with your sense of smell. And this is what the ameba uses to gain access to the brain.

[Sarah Gregory] There's been some discussion that with COVID, people might be able to get it through their eyes. Could this happen with this ameba?

[Jennifer Cope] So for this specific ameba (*Naegleria fowleri*), it's not known to infect people via the eye. There is another type of ameba that does cause an eye infection, but that's not this one, *Naegleria fowleri*.

[Sarah Gregory] Okay. So that's just an eye infection, not a brain infection.

[Jennifer Cope] Yes, correct.

[Sarah Gregory] Okay. Apparently this ameba can change its shape and appearance in different environments. Why does it do that and how is that possible?

[Jennifer Cope] So, correct, *Naegleria fowleri* does have three different forms that it can take. So, the first is the trophozoite, and this is an active feeding form and it's the form that causes infections as well. Then there is a flagellated form. And this is a very transient form, and it will use this form when food becomes scarce or just the general conditions of the environment are really…are not conducive to

survival. And so it'll form a flagella that allows it to move to a new location. And then the third form is the cyst, and this is the really hardy form that can allow it to really survive harsh conditions.

[Sarah Gregory] So, can you elaborate a little bit on why is this important?

[Jennifer Cope] Sure. I think the one to consider in the importance of it is the cyst form. And I think this is what allows *Naegleria fowleri* to survive harsh conditions like cold temperatures. *Naegleria fowleri* really likes warm water temperatures, and so if the temperatures cool, it will encyst and this might allow it to say, hide out in the sediment of a lake or something, over the winter and it can survive there until the water begins to warm again.

[Sarah Gregory] How is a person diagnosed? I mean, how do clinicians isolate this from other possible causes? I think you mentioned earlier that it's sometimes an issue.

[Jennifer Cope] Yeah, so meningoencephalitis, like I said earlier, is just a general clinical term and it has a lot of different causes, both infectious and noninfectious. And there are causes that are a lot more common than *Naegleria fowleri*. So, it might not be something that a doctor is initially thinking about when they see a patient that they think might have meningitis. One of the clues that they might use is if they might be thinking about it more, say, in the summertime when it is warmer and when we tend to see these cases. And if they ask the patient about possible water exposures (have you been to the lake, have you been swimming lately), that might clue them into the possibility of this infection. And when they're thinking about it then, the way they are going to try to make the diagnosis is, with any type of meningitis you're going to want to get a sample of the patient's cerebrospinal fluid, which is the fluid that surrounds the brain and spinal cord. And this would be something people have heard of, a spinal tap or a lumbar puncture, that's how you get spinal fluid from someone.

And so, in almost all cases of meningitis you're going to get a sample of spinal fluid. And the first way you can try to make the diagnosis of *Naegleria* is actually by observing, looking at the spinal fluid under the microscope. And you can potentially observe the motile trophozoite form of the ameba. So, you can actually see the ameba moving in the spinal fluid. However, this does take some expertise from the person looking at the spinal fluid under the microscope. Or sometimes there might not be enough amebas there for the microbiologist to see. So, really the gold standard now for making the diagnosis is a PCR test, so polymerase chain reaction, which is a test that can detect the DNA of the ameba in the spinal fluid. And that's a test we have here at CDC, and it's in a couple of other places around the country, and the spinal fluid can be sent there to do that testing.

[Sarah Gregory] So if it's diagnosed, it's more just for elimination of other things, right? Because it's fatal. There's no real treatment for it, is that right?

[Jennifer Cope] Well, while it is fatal, in most cases there are a handful of survivors and there are some medications (or some treatment) that can be tried. It's not always successful, but we do think that the earlier the diagnosis is made, there is a better opportunity for survival if treatment is given.

[Sarah Gregory] Your paper is about exposures to waterborne disease during recreational activities. How are these different from other types of exposure pathways? And what are the other ways?

[Jennifer Cope] Yeah so we think this infection is always caused by some sort of water exposure, it's just what type of water we're talking about. And the most common type of water exposure we see is recreational water exposure, meaning exposure in lakes, rivers, streams, basically any water that's not been treated. So this does distinguish it from, say, swimming pool water, which swimming pool water is filtered and disinfected. A well-maintained and disinfected swimming pool should not be a risk factor

for this amebic infection. But yes, untreated recreational water exposure is the most common type of water exposure leading to this infection. And a classic scenario, like something you'll see in a medical school or medical board test question is, say, a child or a teenager who's recently been swimming at the lake or water skiing or wakeboarding and they come in a few days later with headache and fever. And that's a classic scenario for thinking about this amebic infection.

So the other types of water exposures that we've seen more recently are in people who have used tap water for either nasal or sinus rinsing, whether that's for therapeutic or religious reasons. So, a lot of people who suffer from chronic nasal congestion from allergies or other reasons will do nasal or sinus rinsing using like a neti pot or some other sort of device to clean out their sinuses. And then there's also people who do it for religious reasons. They'll do like a cleansing practice that includes nasal rinsing prior to prayer. And we have seen a few cases associated with this use of water, in people who use tap water without doing additional treatment for nasal rinsing. And then one other one that's a little bit different is this ameba actually can survive in hot spring water. And so, we have seen cases associated with people who have used hot springs and gotten water up their nose that way.

[Sarah Gregory] Hot springs, like spa type of hot springs, or…?

[Jennifer Cope] So, usually natural hot springs. So not like a hot tub because again, that would be similar to a swimming pool. Hopefully the hot tub is being well-maintained and disinfected. So yes, I'm referring more to natural hot springs.

[Sarah Gregory] Yes, I guess I'm thinking of some, like people go to what they used to call ‘take the waters’ to natural springs that are hot. Like, I know there's one in Budapest, there's some in Canada, I'm sure there's some all over the world and here in this country. So those could potentially be a risk?

[Jennifer Cope] Yeah. Any hot spring water that’s not having any additional treatment done to it could potentially be a risk, correct.

[Sarah Gregory] Okay. So, I'm a little bit confused about the tap water. Isn't tap water treated?

[Jennifer Cope] Yeah, well tap water is treated, particularly in the United States, our tap water is very safe. However, it is treated to be safe for drinking (so consuming water). But if you're using the tap water in more sensitive areas of the body, say like for nasal or sinus rinsing, or some people use water to rinse their contact lenses which is also not good because then that is going in your eye, those are uses of tap water which actually could cause infection. So, what you're thinking about is more what we thought about back in the day when our water wasn't as safe with fecal contamination, so things that cause more diarrheal illness. But in this case we're talking about organisms like amebas that can still exist even in, and they can still be in, in treated tap water.

[Sarah Gregory] Okay. So back to the nasal rinsing. They sell saline solution, is that safe to use that?

[Jennifer Cope] Yeah, so what we recommend if you are someone who does nasal rinsing using a neti pot or some other or similar type device, and you're going to—this would be for people who might be making their own saline solution, say, with a packet (mixing it) that needs to be mixed with water—we recommend that you...I think the easiest thing to do (a lot of people might find to be the easiest thing to do) would be to buy distilled or sterile water and use that type of water to make your saline solution. The other thing that you can do is you can use tap water that you boil first, and then you let it cool and you can use that water as well. Those are probably the most common ways to make your tap water (or to make nasal rinsing) safer from this perspective.

[Sarah Gregory] Okay, but the manufactured little bottles of saline solution that you just sort of squirt up your nose occasionally, those are safe?

[Jennifer Cope] I believe so. If they're manufactured specifically for that reason, that's probably a product that is sterile. Before you open it, it's going to be a sterile solution.

[Sarah Gregory] What did you do in your study, if a patient didn't know when or where they were exposed or a family member didn't know?

[Jennifer Cope] So, yes, for some cases when we didn't know when they were exposed, we were able to use the date that they became ill or the date that they died to calculate the date that they were likely exposed. Because we do know the average time from when people are exposed to when they become ill is about five days, and then we know the average time from when they become ill to when they die is also about five days. So, we're able to use that data to estimate when they were likely exposed.

For people that say, reported multiple exposures, if all of those exposures were in within a 50-mile radius—for example, say they went swimming at a couple of different lakes but they were all within the same park—we were able to include that exposure location as the center of that 50-mile radius, since the conditions probably didn't differ very much among those different swimming sites. But unfortunately if we didn't have any of that information, we weren't able to include those cases in this particular analysis.

[Sarah Gregory] So your study analyzed 120 PAM cases that occurred from 1978 to 2018. What specifically were you looking for and why did you start at that date?

[Jennifer Cope] So, we had observed anecdotally over the last few decades (mostly actually over the last decade or so) that we were starting to hear about cases happening in states that really had never reported them before. I think the most notable example is the cases that happened in Minnesota. This was really an infection that had historically only been reported from the southern one-third of the United States (or the southern tier, as we call it), which includes all the way in the east over here in Georgia all the way over to say, Arizona and southern California and then all the states in between. That's what we consider the southern tier.

So really states that tend to have warmer weather and hotter summers, that's really where we were seeing these cases (at least historically). But when we started hearing reports coming out of states (say, like Minnesota) that certainly got us a little bit concerned. And what we wanted to do then with this analysis is see if we could show any trends in cases in the United States over the last 40 years, and whether we could find the environmental data about temperatures to help explain those trends. Really what we wanted, we wanted to get the data to support what we were anecdotally seeing. The reason for this time period is even though we've tracked cases going back to 1962, the late 70s was really when we established a laboratory at CDC that was able to better identify and diagnose these infections. So, that's why we started with that time period, because before that it was harder to make the diagnosis.

[Sarah Gregory] What did you find? And did any of your findings surprise you?

[Jennifer Cope] Well, say what we....the two things we focused on in this analysis were where the PAM cases occurred as in what latitude (so, how far north or south), and then we also looked at what the air temperature was around the time that they occurred. And so, in terms of the location, we found that PAM cases appeared to be trending northwards over the time period. Although we did find, we also looked at just the sheer number of cases happening each year, and we found that those did not increase over time. So, the number of cases did not, but the location (as far as how far north they were occurring) did trend north. Five out of the six cases that were reported from the midwest region occurred after

2010—so, really that last decade that we've been looking at. These included two cases in Kansas, two cases in Minnesota, and one case in Indiana. We, as I said before, we really...this has historically been cases seen in the southern U.S., and we didn't see changes in that. We continue to see most of the cases coming from there. But we did see that the range of the cases (meaning how far north they occurred) has increased over time. And overall I'd say, since I...these anecdotal cases being reported from northern states is what spurred this analysis, we weren't necessarily surprised by our findings, but we were really glad to have this more concrete data behind to show these trends.

[Sarah Gregory] Why is it expanding northward?

[Jennifer Cope] So, there's a couple reasons that might be behind what we are seeing. So, I mentioned we also looked at air temperature. So we saw that the temperatures on the days that patients were exposed were higher than the average temperatures over the past 20 years for those locations (so, warming temperatures). This suggests that these rising temperatures could actually...so one thing they might explain is changing how people participate in recreational water activities. So if it was hotter that year that might have driven more people to seek out relief at the nearby lake. And so maybe more people were actually swimming that time. And the other thing is what we, when we talk about this ameba and what it likes, we know it likes warm water. So, increasing temperatures, increasing air temperatures leading to increasing water temperatures might be changing the ecology of this ameba and allowing it to thrive.

[Sarah Gregory] I'm finding it interesting that it has expanded northward, but the number of cases haven't expanded. That seems sort of a dichotomy to me. Do you have any idea why it's not just adding? I mean it seems like it would be, and then subtracting from the south if it's not adding numbers.

[Jennifer Cope] It's hard to explain and I think when you're talking about a rare infection like this where we have so few data points to go on. We might not be...it might take more time to really start to see these trends. So yeah it's hard to say. I mean, I'm glad we're not seeing increasing cases because it is such a scary infection, but yeah for right now we're just seeing changes in the geographic location but not necessarily in the numbers.

[Sarah Gregory] So why don't you give us some highlights of your study?

[Jennifer Cope] Well, I think the main highlights are that this being a ameba that thrives in warm weather it's interesting to see that we are seeing this more northward trend in the location of cases and where they are exposed. It's something we definitely want to keep an eye on and it's a reason why we are going to continue to track this infection, especially in light of the trends we are seeing in the climate in general.

[Sarah Gregory] What were some of the challenges of this study? I mean, you mentioned a couple but what do you perceive as the main challenges of finding what you needed to find?

[Jennifer Cope] Yeah, the main challenge is what I alluded to before. It's the good and bad in this, so I mentioned this is…we only have a few cases reported each year, which I think… fortunately, we don't see a lot of cases because it is such a deadly infection, but it also makes it harder to study. Because we have so few data points to work from. So that's just in any time we're trying to learn more about *Naegleria fowleri* and primary amebic meningoencephalitis, that's what we're always up against, is just the few cases that we have to work with.

A couple other things we discussed before, that some cases we didn't have the full details on the date and location of exposure. So, I think that's something we've been able to improve on a lot of the ones

that we didn't have the full data on were older cases, and so in more recent cases we've been actually able to gather a lot of that data. And then, we did have to rely on secondary data sources from weather stations to gather information on the temperature for the date and location of the exposures, and these aren't the exact location where the exposure occurred. And we also had to use air temperature, which might not be the same (obviously) as the water temperature, although we expect that they are related that when the air is warmer, that leads to warmer water temperatures.

[Sarah Gregory] What future studies or public health actions do you, personally, hope to see?

[Jennifer Cope] So, a couple things I think we'd like to see as it relates to this infection is we'd really like to better understand what makes a body of water a higher risk for someone contracting PAM. We think that there are some certain features because we've had locations that have had more than one case associated with them. Which, when you think about an infection that only has a few cases reported each year, to have them occur in the same place, that tells you something's going on there.

And so we'd really like to maybe identify, say, the specific characteristics of a lake that make it a higher risk for getting this infection. And that would really take going beyond our epidemiology and clinical skillset and getting more into ecology and people who do more study of the environment. But I think ultimately this would help with our prevention messaging. So, instead of just saying be careful about getting water up your nose when you do any sort of recreational water activity in an untreated recreational water (like a lake), we could actually maybe tailor those messages a little bit more to specific types of lakes. So that's a wish on our wish list.

The other thing I'd like to see is currently this infection is only reportable in a handful of states, meaning that it's mandatory that it be reported to state public health authorities. So I'd like to see it reportable in more states. That's not to say that I don't think we hear about all the cases that are identified, but I do think when a disease becomes reportable to public health, it does raise the profile of that and it makes physicians and other healthcare providers more aware of the infection.

[Sarah Gregory] What can people do to protect themselves against getting this ameba?

[Jennifer Cope] So, the main overarching thing to do to protect yourself is just limiting the amount, limiting water going up your nose. And so, there are a couple ways you can do that. I mean, the safest way is just to avoid the activities that will get water up your nose. But we recognize that swimming in lakes, water skiing, doing these types of things are fun, and people want to do these activities. And so, anything you can do to limit the amount of water that might go up your nose while you're participating in those activities. So, whether that’s holding your nose shut, using nose clips, or just keeping your head above the water when you're taking part in these types of activities when you're in warm, untreated freshwater.

Another situation we talked about earlier related to hot springs. If you're someone who's going to be, say, using a hot spring, just keep your head above the water. And I think that's easy enough for, say, adults to do, because I feel like adults are just soaking in the hot spring. But I think paying attention to children in hot springs, because they're probably likely to do more activities that might get water up their nose (just watching kids in those situations). And then just paying attention, consider avoiding water-related activities in warm freshwater during a heatwave when the water temperature is going to be especially high.

And then when we talk about nasal and sinus rinsing, we talked a little bit about how you need to consider the water you're using. So whether that's buying the specific product, as you mentioned, a

prepared nasal saline product or using distilled or sterile water that you buy to prepare your saline solution, or consider boiling your water and letting it cool and then using that water. Those are our main prevention messages.

[Sarah Gregory] Going back earlier, is this ameba settled in the bottom, so stirring up the water in the bottom of the lake, does that have an impact or is it just sort of floating around in the water willy-nilly anyway?

[Jennifer Cope] Yeah, I know that is something people…that is another prevention method that's out there. I don't know that...I think that if you can avoid stirring up the sediment, that's probably a good practice, but I do think that the ameba can also just be in the water column and not necessarily just in the sediment. And so, I wouldn't want to just say that taking that action alone would prevent it. So, it's really going to be focusing on limiting the amount of water going up the nose.

[Sarah Gregory] Right, but additionally, trying not to stir up the sediment at the bottoms probably would be helpful?

[Jennifer Cope] I think it's not going to hurt, for sure.

[Sarah Gregory] Okay. The COVID-19 pandemic, and all the behavior changes that it's caused, has shifted trends in many diseases. Has it affected the incidence of PAM, do you think?

[Jennifer Cope] That's hard to say. And I think, just going back to what we said before with PAM being a rare disease, it's just harder to draw conclusions like that, especially just after based on one year's worth of data. What I can say is we really did see similar numbers last summer (and so the summer of 2020 during the pandemic). And so I don't think we can say...I think this is one instance where we can't necessarily say that there's been major changes due to COVID.

[Sarah Gregory] You're a Commissioned Corps officer at CDC. Tell us about that, what that means, and something about your job and what you like about it and how you became involved with this study.

[Jennifer Cope] Sure, yeah. I am a Commissioned Corps officer in the U.S. Public Health Service, and that means I'm on duty 24/7 to respond to any urgent public health issues. And my specific role is as the CDC's free-living ameba subject matter expert, and that does include *Naegleria fowleri*. And I get involved in...we run a clinical consultation service, actually, where healthcare providers who suspect they have a patient with one of these amebic infections can actually call CDC 24/7 and get a hold of either one of our EIS officers or me to run their case by us and get some advice on how to make the diagnosis and what treatment we recommend.

And so that's a part of my job I really enjoy. I'm an infectious disease physician by training, and so getting to work on these rare infections where if I was an ID doc out in the community just seeing all types of patients, I might never see one of these infections. But being here at CDC and focusing specifically on this, I get to be involved in almost all infections that are identified of this type. And so it's pretty cool. For an ID person like me, it's a really unique position to be in.

[Sarah Gregory] How have things changed for you personally since the beginning of the pandemic? Is what you are doing now different than a year ago? And what are you doing?

[Jennifer Cope] Yeah, I don't think any of us can say that nothing has changed in the last year. I have different coworkers, they're a good deal younger than the ones that I had in the office, working here from home with my family. Looking back on a year ago, I deployed out to the field at the beginning of the COVID response. I was involved in the early work that was going on at the quarantine stations in the

airports to do the screenings in the flights coming from China. And I also had the chance to go to help...I was actually deployed to North Dakota, which is where I did my EIS training at the beginning of my time with CDC, and that was actually the first time I've been out in the field for a deployment since my kids were born. And so while it was hard to leave, it was also rewarding knowing that I was helping in the early days of the pandemic when there was so much that was unknown.

A year into this now, my day job (my work in waterborne) has been very much affected by COVID. We've brought a lot of...my branch also works on topics like handwashing and cleaning and disinfection, which obviously took a lot of attention paid to that, obviously, during COVID. And so a lot of additional work has come into our branch. But that being said, we haven't lost sight of waterborne infections because these things still happen. And I continue to work to track these amebic infections, even in light of all the other things going on with COVID.

[Sarah Gregory] Well thank you for taking the time to talk with me today, Dr. Cope.

[Jennifer Cope] It's been a please, thank you.

[Sarah Gregory] And thanks for joining me out there. You can read the January 2021 article, Geographic Range of Recreational Water-Associated Primary Amebic Meningoencephalitis, United States, online at cdc.gov/eid.

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

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