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| TPWKY |  | This is Exactly Right. |
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| Erin Allmann Updyke |  | Hey everyone, we just wanted to issue a content warning before this episode. Some parts of this episode, especially our firsthand account, might be difficult to hear. So if you wanna skip that part you can fast forward a few minutes. |
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| Sandra Gompf |  | I'm Sandy Gompf. I'm an infectious disease specialist and faculty with the University of South Florida since 1999. In 2009 our son Philip went boating with his family, his aunt and uncle and cousins, on Lake Arietta in Polk County. It's a freshwater lake, spring-fed and they spent the day swimming and tubing and just really enjoying the day on the water. And about 5 or 6 days after he returned he came over during the evening and said that he had a headache which was kind of unusual for him. So we checked to see if he had a fever, did he have any other symptoms, we thought maybe he was just a bit dehydrated, it's the summer. He seemed like he was okay, he didn't have any neck stiffness, we think about meningitis right away and that wasn't the case so we just let him go to bed. |
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|  |  | By the next morning he was difficult to wake up and I had gone to work early and my husband who's a pediatric hospitalist went in to check on him and his neck was stiff at that time. He had trouble bending his neck forward. And obviously that's a warning sign of meningitis. So he rushed him into the hospital where he works and very quickly had him receive a spinal tap. And shortly after that he was diagnosed with a very severe meningitis, he had a lot of inflammation. And our assumption was that he had a bacterial infection at the time. His spinal fluid was examined for bacteria, they didn't see any, he just had a lot of intense inflammation. The worst inflammation that I have seen. That type of inflammation that's associated with death. The laboratory did look for amoeba, they didn't see any. Within 3 days he began to develop seizures, he was brain dead. So from the time of symptoms it was about 3 days before he was gone. And we had to decide whether to stop life support and donate his organs which we did. |
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|  |  | At the time that was a real shock to us but we're physicians who work in the hospital, we deal with serious infections, serious illnesses and we see this all the time. We didn't expect it to happen to us. Not to our son. And we couldn't do anything for him so it was a very helpless feeling. And we assumed again that it was just bad luck, very back meningitis. And then about 6 weeks later we had requested an autopsy as part of donating his organs and the diagnosis came back with Naegleria fowleri meningitis, amoebic meningitis which is what's commonly known in the media as brain-eating amoeba. And literally that's what it does. |
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|  |  | After this happened it took us a while, took me a while to recover but one of my mentors, our division director of infectious disease at USF at the time, Dr. John Sinnott established a memorial fund, the Philip T. Gompf Memorial Fund for education and possibly research. We thought about what to do with the fund and we figured the most impact that we could make with the fund is to work on prevention and awareness because really even now we have some options for treatment but it takes really early diagnosis, it takes somebody who knows what they're looking for and knows how to treat it and it's really, really intensive and therapy afterwards just for a person to survive. And that's happened in a few cases recently, very fortunately but still the best treatment is prevention. And it's really easy to prevent. |
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|  |  | So that's what we've decided to do with the fund, we decided in 2014 to start a campaign which we call Summer Is Amoeba Season sort of modeling it on flu season. When it's hot and when it's warm and people are swimming in lakes and rivers and ponds and that sort of thing, be aware that there could be a risk of amoebic encephalitis. And we don't wanna scare anybody, I mean this happens rarely however when it does happen it's almost 100% lethal. We say as part of our campaign that it is 99% lethal but 100% preventable. A couple of things that we've done with it is a billboard campaign and then we also have a social media campaign on Facebook and Instagram, we have wristbands and handouts and postcards and informational materials that we give out as well and we mail those materials to people free of charge, anyone who asks. |
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|  |  | Probably one of the most, I hate to say it's wonderful but it's been so positive coming out of two tragedies is that we've partnered with the Jordan Smelski Foundation for Amoeba Awareness. The Smelskis lost their only son from Naegleria fowleri, he was swimming in Costa Rica in a hot spring-fed pool and they have a foundation and we've partnered with them to continue to offer information to the public, to bring together researchers in Naegleria fowleri and parents and the few doctors in the country who are familiar with treating this type of infection. We've helped to develop a best practices treatment regimen using the input from all of these individuals including the CDC. |
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|  |  | We're very proud of our work so far, we know there's a lot more to go, there's so many people that still don't know and so many people that since our children have died that have been impacted themselves and didn't know a thing about it. There's just not enough awareness among even healthcare professionals so we're still plugging away, we're still trying to advocate for awareness and advocated for parents to try to prevent this from happening. Just to say the main tools for prevention are avoiding activities that will force water up the nose during the summer when you're in freshwater or using nose clips and anything that really prevents getting water forced up the nose and avoiding things like using a Neti pot with unboiled water or untreated water. Again just building the awareness, reaching out, monitoring the climate situation and trying to be good advocates for prevention and education has been our goal. |
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| TPWKY |  | (This Podcast Will Kill You intro theme) |
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| Erin Welsh |  | Thank you so much Dr. Gompf for taking the time to chat with us and for being willing to share your story on the podcast, we really appreciate it. |
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| Erin Allmann Updyke |  | Yeah, thank you. |
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| Erin Welsh |  | Hi, I'm Erin Welsh. |
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| Erin Allmann Updyke |  | And I'm Erin Allmann Updyke. |
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| Erin Welsh |  | And this is This Podcast Will Kill You. |
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| Erin Allmann Updyke |  | And today is obviously a doozy of an episode because today we're talking about Naegleria fowleri which is commonly called the brain-eating amoeba. |
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| Erin Welsh |  | Yes. It is I think one of our most requested episodes. |
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| Erin Allmann Updyke |  | Yeah, definitely. We've gotten a lot of requests for this. |
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| Erin Welsh |  | I think it'll be a very interesting and I think enlightening. |
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| Erin Allmann Updyke |  | Yeah, I think so too. I also had heard of it but I think only in a very like sensationalized way I guess. |
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| Erin Welsh |  | I mean, the name. |
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| Erin Allmann Updyke |  | The brain-eating amoeba! |
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| Erin Welsh |  | Right, right. |
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| Erin Allmann Updyke |  | And you know with a name like that I think you would assume it's going to be something horrific but I was not prepared for how terrifying and horrific this disease really is. |
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| Erin Welsh |  | And just like devastating. |
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| Erin Allmann Updyke |  | Yeah. Yeah. |
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| Erin Welsh |  | Yeah, yeah. |
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| Erin Allmann Updyke |  | Yep. |
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| Erin Welsh |  | Well I guess before we dive into the actual part of the episode, should we... |
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| Erin Allmann Updyke |  | Do our important business? |
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| Erin Welsh |  | Yes. I suppose it's quarantini time, huh? |
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| Erin Allmann Updyke |  | I think we might need one to get through this. (laughs) |
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| Erin Welsh |  | Yeah. What are we drinking this week? |
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| Erin Allmann Updyke |  | We're drinking Uncharted Waters. |
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| Erin Welsh |  | Yeah. And it think that the name will make more sense as we go into the episode but basically, spoiler alert, there's still so much we don't know about this amoeba and about how to control it or prevent it or treat it and so we're kinda still dealing with uncharted waters. |
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| Erin Allmann Updyke |  | It's an appropriate name. What's in our drink today, Erin? |
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| Erin Welsh |  | It is mezcal, ginger ale or ginger beer, and pineapple juice, maybe a little squirt of lime juice. It's pretty simple and it's super tasty, so it's how we like 'em. |
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| Erin Allmann Updyke |  | Yeah. We'll post the full recipe for our quarantini as well as our nonalcoholic placeborita on our website thispodcastwillkillyou.com and all of our social media channels. |
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| Erin Welsh |  | And a little bit more business is just that you should go to our website where you can find everything you could ever want to find. We have the sources for all of the episodes that we have ever done, we have all the quarantinis, we have a bookshop.org affiliated account, we have a Goodreads list, we now have a Patreon, we have a place where you can find all the promo codes that we mention, we have transcripts. I mean there probably more. |
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| Erin Allmann Updyke |  | There's a lot. You should check it out. Thispodcastwillkillyou.com. |
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| Erin Welsh |  | Yeah. There you go. All right, should we get started? |
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| Erin Allmann Updyke |  | I think we should. We'll take a quick break and then dive in. |
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| TPWKY |  | (transition theme) |
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| Erin Allmann Updyke |  | So Naegleria fowleri is our pathogen today. Like you said already Erin, this is an amoeba. I actually didn't realize that it had such a kind of interesting life cycle, I just thought it was just an amoeba. |
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| Erin Welsh |  | I mean just saying 'just an amoeba' I'm like I don't know what that is or does really except I just imagine little bloopy edges. |
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| Erin Allmann Updyke |  | That is correct, little bloopy edges. Pseudopods, those are called and that's how they move around. So this is a free-living amoeba, it lives in freshwater sources, warm freshwater although it can exist in colder water, we'll get into it. But it exists pretty much across the globe and I think Erin you're gonna talk even more about where all we find this. And like some other environmental pathogens that we've kind of talked about on this podcast before, it has at least one life stage that's very environmentally tolerant so it can persist even in bad environmental conditions. In this case that stage is a cyst stage and so this is the stage that can persist let's say if a lake freezes over and gets very cold for a period of months, this cyst can persist. |
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| Erin Welsh |  | A little persistent cyst. |
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| Erin Allmann Updyke |  | Yeah, I like that. |
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| Erin Welsh |  | A little overwintering persistent cyst. |
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| Erin Allmann Updyke |  | Exactly. Or if a small body of water dries out and there's not water, the cyst can persist in dust or dirt. And we've seen this before with other, you know like fungus that have spores or bacteria that have spores, etc. So environmental pathogens, not surprising that this guy can withstand harsh conditions. But then there's also another stage of this amoeba that's actually a flagellate stage, it has little flagella, and this is a stage that I didn't know existed of this pathogen but it's also not really that important to the biology in terms of disease so that's all I'm gonna say about it. It's has like an extra fast swimming stage but it just doesn't really do much else. |
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| Erin Welsh |  | I mean it helps it get food from my understanding which is kinda cool. |
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| Erin Allmann Updyke |  | Yes. But it doesn't eat. It just helps it move to a new environment and then it has to go back into the amoeba or trophozoite stage. Anyways. |
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| Erin Welsh |  | It's pretty cool though. |
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| Erin Allmann Updyke |  | It's pretty cool because it also can do that in your body, like it's been found flagellates in our CSF, in our cerebrospinal fluid. |
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| Erin Welsh |  | So it's like moving around, trying to get around to look for food? |
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| Erin Allmann Updyke |  | Presumably, potentially. It's very interesting. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | But in general it's the trophozoite stage or the amoeba, the stage that you think of when you think of the word amoeba. |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | That's the stage that is infective to humans, that's the stage that eats and divides, etc. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | So how does one become infected with Naegleria fowleri? This is an organism that lives in the water and unlike any other organism that we've talked about so far, the route of transmission is specifically getting water up your nose. Not by drinking it, not by being exposed to it on other parts of your body, but specifically getting this amoeba up your nose. It's a very specific and interesting mode of transmission because it's very direct. |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | What happens is this amoeba, once it's in our nose, penetrates the nasal mucosa, so the mucosal lining up in our nose, and then travels through the cribriform plate which is the part of your skull at the very back upper part of your nose inbetween kind of where your eye sockets start in your skull. This is a plate, a little piece of bone that has a bunch of holes in it through which the olfactory nerve, your smell nerve that is responsible for allowing you to smell, travels through those holes in your skull and that's where the nerve fibers come into your nose. So Naegleria fowleri exploits these holes, that's the route of entry that it uses to gain access directly to our brain. So there are a number of other species of Naegleria but they don't do this, they can't infect humans, they haven't been shown to infect humans. There are some that can infect mice but this is very interesting and it is very specific. |
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|  |  | So Naegleria travels along our olfactory nerves, through this cribriform plate directly into our brain. The first place that it invades, unsurprisingly, is the olfactory bulbs which are like that first part of your brain that they're going to access in that region kind of right behind your eyes in the front part of your brain. And then from there, once it's in our brain, it's able to divide, grow, eat, continue to live, and spread throughout the entirety of the brain, literally it travels throughout the whole brain invading potentially any and every part of the brain. |
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| Erin Welsh |  | So what is to stop other pathogens from exploiting those same holes? |
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| Erin Allmann Updyke |  | Right. It's a good question. So we have a lot of barriers, like natural barriers that would normally prevent pathogens from entering. |
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| Erin Welsh |  | Right. Yeah. |
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| Erin Allmann Updyke |  | So your nose is usually full of snot, right, mucus, that's our first line of defense against pathogens that would try and enter through our nose. Turns out that Naegleria fowleri has a number of mucolytics which are certain enzymes that are able to break down that mucus. Then they have to not just invade through that mucus but they actually do have to penetrate through the epithelial cell layers of our nose. |
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| Erin Welsh |  | Okay. So it's a little bit of a brute force entry. |
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| Erin Allmann Updyke |  | Exactly, right. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | It's not just like freeform holes in our skull just absolutely open to the world. |
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| Erin Welsh |  | Right, right. So it would take something that would bust through those cells. |
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| Erin Allmann Updyke |  | Right and do so without causing enough of an immune response that our immune system takes care of it before it actually gains entry into our brain. |
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| Erin Welsh |  | Right but, well that's jumping the gun. |
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| Erin Allmann Updyke |  | Okay. (laughs) |
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| Erin Welsh |  | (laughs) Cause I was gonna say aren't there people who seem to have been exposed but don't...like they have antibodies against it but they've never had PAM or whatever? |
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| Erin Allmann Updyke |  | Right. I read a little bit of that and I also read that there have been very few but a few cases where people have tested, especially children, and found actual amoebas in their nose but with no infection. |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | And so there's a school of thought that is perhaps you need to have quite a high infectious dose and so perhaps that's part of the sort of spectrum of risk is how much amoeba are you exposed to? Then yeah, is there something about the immune response as well that's allowing for only some people to end up becoming infected and others to mount an immune response and not become infected? |
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| Erin Welsh |  | Right. |
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| Erin Allmann Updyke |  | Yeah. These are all still open ended questions, Erin. |
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| Erin Welsh |  | Uncharted waters. |
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| Erin Allmann Updyke |  | Uncharted. So once it does gain entry into our brain and is able to spread throughout our brain it's pretty horrific. It causes something that's called an acute hemorrhagic necrotizing meningoencephalitis, that's the kind of most medical of medical descriptions that you can give it. So what it means essentially is that in environmental water sources where these amoebas are free-living, they're feeding on bacteria and things like that, they're engulfing them with their little pseudopods and that's what they're eating in order to grow and live and continue to divide. |
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|  |  | In our brain they're able to do that by engulfing our cells. They engulf red blood cells, they engulf nerve cells themselves and various other types of cells that they encounter. So they're causing direct damage to the brain tissue which causes hemorrhage and bleeding as well as necrosis which is just a fancy word for tissue death. And this damage, this direct damage caused by proliferating amoeba engulfing our cells unsurprisingly provokes a pretty massive inflammatory response. Our body goes, 'This is not okay.' |
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|  |  | And so you have a lot of fluid and a lot of white blood cells that come into that area to try and help and tamp down this infection. The problem is that in the brain inflammation like that has nowhere to go because our brain is surrounded by our skull which is rigid and immobile and doesn't stretch. So this combination of hemorrhage and severe inflammation causes swelling or cerebral edema and that massive increase in volume of fluid increases the pressure in the brain which can lead to coma and death because that pressure gets too high and it's pushing on the brain. |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | Yeah. It's horrific. So that's kind of the pathophysiology of the disease. If we look at the symptoms of it and what it looks like when someone becomes infected, the disease itself is called primary amoebic meningoencephalitis which listeners of this podcast I think could figure out a lot from that name. It's obviously caused by the amoeba, that's the amoebic part, and meningoencephalitis tells us that we're dealing with inflammation of the lining of the brain and the brain itself. And the reason it's called primary is to distinguish it from other forms of meningitis that can be caused by amoebas but other amoebas like Entamoeba histolytica for example, they invade our brain only after travel through the bloodstream essentially, so they don't go directly to our brain. |
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| Erin Welsh |  | Right. |
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| Erin Allmann Updyke |  | So because of this name we already know a lot of the symptoms because they look a lot like other causes of meningitis or encephalitis that we've actually talked about quite a lot on this show. The difference here is that it's a very, very rapid infection. So usually within anywhere from 1-12 days after infection, average is about 5, the symptoms start with a very, very severe headache and usually one that's unsurprisingly right between the eyes like a frontal headache. |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | With that massive, massive headache you'll have nausea and vomiting and then often a stiff neck which is a very classic meningitis sign because of that inflammation. With this particular form of meningitis you often have loss of sense of smell since your olfactory bulb is very inflamed but all of these other symptoms are kind of so much bigger that you might not even really notice that necessarily. But then often people will have mental status changes, sort of just not feeling right, not thinking right. But very quickly will slip into a coma perhaps having seizures before that. And this disease is almost always fatal. Something like I saw 99% fatal. |
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| Erin Welsh |  | Mm-hmm, 97, 99. |
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| Erin Allmann Updyke |  | Yeah. And usually that happens within 7-10 days after onset of symptoms, often within 5 days. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | So this whole course of disease is happening in less than 2 weeks most of the time. |
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| Erin Welsh |  | Okay so the incubation period is 5 days, you said? |
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| Erin Allmann Updyke |  | Yeah on average. It can be like 1-12 or so but on average it's about 5 and then once onset of symptoms people usually die within 5 days as well. |
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| Erin Welsh |  | And how much variation is there in age groups? Like does the course of infection, is it longer or shorter in certain age groups or...? |
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| Erin Allmann Updyke |  | Good question. I didn't look specifically into that. So in general in the U.S. especially the most commonly infected age group are young teenage boys. That's not the case epidemiologically across the globe in other parts of the world like in the Indian subcontinent it's an older age group but it is still primarily men that are infected. |
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| Erin Welsh |  | Right. |
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| Erin Allmann Updyke |  | But I don't know if there's a difference in incubation period or symptoms between age groups, not that I saw at least in what I read. |
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| Erin Welsh |  | Okay it just is yeah, it's just exposure patterns for that. |
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| Erin Allmann Updyke |  | Yeah, yeah. |
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| Erin Welsh |  | Yeah, okay. |
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| Erin Allmann Updyke |  | But you can imagine that for anyone with such a very rapid acute illness, if somebody is misdiagnosed at first with for example a bacterial meningitis which is much more common or a viral meningitis and started on a treatment for that instead of for primary amoebic meningoencephalitis, then that delay, even a matter of hours, can of course be fatal. But even with prompt identification and treatment it's still a very virulent pathogen. |
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| Erin Welsh |  | What is treatment? |
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| Erin Allmann Updyke |  | Yeah, great question. This is a very rare disease and so there haven't been like large clinical studies and things like that but there is a pretty precise treatment schedule that is recommended based on the few people who have survived with this treatment. So it's a combination of a number of different drugs that are given both IV and intrathecal which means directly into the CSF so usually through a lumbar puncture. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | And it's combination of amphotericin B which we've talked about a number of times on this podcast, it's usually an antifungal. |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | But it basically works by disrupting membranes and so they think that's why it's effective for treatment of this as well as in combination with another antifungal, one of the azole drugs, either fluconazole or ketoconazole, one of those. And then a couple of different antibiotics, rifampin which is often used to treat tuberculosis as well as meningococcal meningitis which is another bacterial form of meningitis. Often also azithromycin which is another antibiotic and then a drug called miltefosine which is an anti-leishmaniasis drug and also a breast cancer treatment, of all things. |
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| Erin Welsh |  | Did we talk about that drug? |
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| Erin Allmann Updyke |  | I don't know. I don't remember. |
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| Erin Welsh |  | Like that name sounds very familiar. |
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| Erin Allmann Updyke |  | Yeah. It sounded familiar when I read it but then I was like I am not good at remembering drug names. Not good for my future career. But yeah so those and then that's not the end of the list, it's a very long list, also steroids dexamethasone to help with the inflammation as well as in some cases people have been treated with something as severe as therapeutic hypothermia where they cool your body down to like 95 Fahrenheit, 35 Celsius or lower to try and help with that swelling in the brain. Or there are other methods to try and reduce that swelling as well but essentially in combination with all of those drugs, keeping track of the pressures in your brain and making sure that your dealing with any increase in pressure. But even despite all of that there have been, from everything that I read, there have been 5 well documented survival cases that we have good records of. I saw one paper that said there's maybe up to 8 but some of those could've maybe not actually been PAM but might have been a different disease. |
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| Erin Welsh |  | Gotcha. So I have a question about testing and how do you test for this? Like obviously you could rule out a bacterial meningitis but how do you test for this PAM, like one that's caused by Naegleria fowleri? |
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| Erin Allmann Updyke |  | Yeah, yeah, that's a great question. So essentially the same way that you would test for any type of meningitis for the most part. So you diagnose it by lumbar puncture which is something that if somebody came in with meningitis symptoms, they're going to get a lumbar puncture. The question is just are you going to analyze it every single possible way including looking for amoebas or do you just analyze it in the ways that you might miss the amoebas if they're not live and swimming around? So there's actually on the website that Dr. Gompf mentioned amoeba-season.com they have a tab for medical professionals and they had a really great algorithm that they recommend for if somebody comes in with acute meningitis. |
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|  |  | And one of the first things is essentially trying to ask someone if there's any history of exposure. So do you have any contact with freshwater sources? Did you go swimming? Did you go rafting? Have you been in a lake, a river, a stream or had contact with well water or groundwater? Have you used a Neti pot? Anything that could potentially put contact between your nose and potentially contaminated water sources. And if someone has that history then you would wanna make sure to do the type of test on that lumbar puncture fluid to check for an amoeba. There are also other tests that you can do, like there are PCR-based tests and things like that but lumbar puncture is kind of the standard. |
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| Erin Welsh |  | So you can see them in the cerebrospinal fluid. |
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| Erin Allmann Updyke |  | Yep, yeah. |
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| Erin Welsh |  | Okay, okay. |
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| Erin Allmann Updyke |  | You can see them swimming around, yeah. So that's the biology of Naegleria fowleri. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | Yeah, horrifying and scary. |
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| Erin Allmann Updyke |  | It is, it is. It is. It's all of those things. |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | So Erin, how did it get here and why are we dealing with something so terrifying? |
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| Erin Welsh |  | I'll try to answer those questions but let's take a quick break first. |
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| TPWKY |  | (transition theme) |
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| Erin Welsh |  | In 1965 a paper was published in the British Medical Journal written by Fowler and Carter, two Australian physicians. And in this paper which is now considered a classic they described 4 case studies of meningitis, all fatal and all originating from a very geographically restricted region, the northern region of the Gulf of St. Vincent in South Australia. 3 of the cases were young children, a boy 9 years old and two girls that were 8. All three were in perfect health before they suddenly started to appear lethargic and then a fever occurred, headaches, sore throat, stuffy nose and for each of them the course of their disease progressed almost the exact same way with a rapid decline almost similar day to day and no response to antibiotics. And the fourth case described in this paper was that of a 28 year old man who's disease progression was a lot longer but also ultimately fatal. The first case that they described which was the 9 year old boy occurred in 1961 but the other three happened in 1965. |
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|  |  | All of these individuals were treated as though they had acute bacterial meningitis and no other causative organism was even suspected despite the fact that none of them responded to any of the antibiotics administered and that cerebrospinal fluid samples didn't result in the culturing of any bacterial pathogens. It wasn't until the doctors performed the autopsies that they began to suspect that what they were seeing were not cases of runaway bacterial meningitis but something else altogether. |
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|  |  | Within some of the brain fluid and meningeal exudate, they caught a glimpse of unusual small amoebae with extremely high abundance in some areas. It wasn't the fact that they were seeing amoebae interesting he fluid that was the unusual part, it was the type of amoebae they were. Amoeba infections had been known to happen like as you mentioned Erin with the obligate parasitic species Entamoeba histolytica as the primary culprit usually and infections with this species did occasionally lead to meningitis as a rare severe complication but like you said, those cases of meningitis usually arose out of this more systemic infection. And also if there was an Entamoeba histolytica infection you would pretty much always find it in the gut at least. |
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| Erin Allmann Updyke |  | Right. Right. |
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| Erin Welsh |  | But there were no amoebae in the gut of these individuals and on top of that the amoebae that the doctors were seeing didn't look at all like Entamoeba histolytica. Maybe it was something new. A few years before Fowler and Carter published this article of their case reports, a couple of researchers had demonstrated that free-living amoebae in the genus Acanthamoeba could be pathogenic, at least when they inserted cultures of the amoeba into the noses of mice which then led to their deaths a few days later. |
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| Erin Allmann Updyke |  | How weird. |
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| Erin Welsh |  | I know, I know. |
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| Erin Allmann Updyke |  | Like why was someone just doing that as an experiment? |
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| Erin Welsh |  | That's a good question, I probably should've read that paper. There are two papers actually. (laughs) But Fowler and Carter were aware of these studies and they cited them in their paper to suggest that the amoebae they were seeing in these four individuals that had died in Australia, they were likely a pathogenic species of this free-living Acanthamoeba. And there was bit of understandable reluctance to suddenly declare that this group of organisms could pose a threat to human health since before these mouse studies, free-living amoebae were not thought to be of any medical interest really. But quote: "Such occasions are not without precedent and we consider that the evidence we have points to some species of Acanthamoeba as the causative agent of acute meningitis in humans." And Fowler and Carter were right except for one thing. The amoebae that had caused the death of those three kids and that one adult were not Acanthamoeba but rather a different species and an entirely separate genus, one that would be given Fowler's name to signify his contribution in bringing this type of meningitis to light. Naegleria fowleri. |
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| Erin Allmann Updyke |  | What about the other guy? |
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| Erin Welsh |  | You know I don't know. I don't know why Carter didn't get any cred. |
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| Erin Allmann Updyke |  | Second author, he didn't get it. |
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| Erin Welsh |  | I know, they were probably co-authors, it's not fair. (laughs) Also if he was second author and there was just two on the paper hen he was senior author so like... |
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| Erin Allmann Updyke |  | It's true. |
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| Erin Welsh |  | I don't know. I don't know. |
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| Erin Allmann Updyke |  | Is the postdoc finally getting credit for something or...? No, I'm just kidding. |
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| Erin Welsh |  | Maybe there's a nonpathogenic Naegleria carteri. |
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| Erin Allmann Updyke |  | Carteri? |
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| Erin Welsh |  | Yeah, carteri. (laughs) So 1965 marked the beginning of people recognizing that Naegleria fowleri could be a cause of meningitis in humans but we know it must have been around before then. And to get a sense of this amoeba's history I need to talk a bit about the global distribution of this species which is in short like global, right? It has been found on every continent except for Antarctica with infections primarily occurring in subtropical or tropical regions or countries. Basically the closer to the equator you get, the more cases of this you're going to see. Although I will say that the distribution is still pretty dang patchy, like very patchy. |
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| Erin Allmann Updyke |  | Very patchy. |
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| Erin Welsh |  | And that completely makes sense, the warm, closer to the equator distribution because the ecology of this amoeba really makes it so that it likes warm things. I'll get into a little bit of that part later. And Erin, you asked when did this get here or how did this get here and I really wish that I could supply some kind of timeline to the emergence of this pathogenic species and then trace when it spread across the globe but I couldn't really find any articles describing that. Maybe that's an oversight on my part, maybe it's just a difficult thing to tease out. Partly because like the number of samples from humans is pretty low. |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | And so it might be difficult to reconstruct this evolutionary history in terms of like a timeline thing. We don't know how fast they evolve, maybe. |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | I don't know. What I did learn though is that Naegleria fowleri is not the same across the globe and that there are different types within the species marked by like a base change here or there, whatever. It's not known whether there's a big amount of variation in the pathogenicity across these different types but by looking at genetic analyses of the different types that are present in different parts of the world, we can get a sense at least as to where this species likely originated. And that looks to be North America where it's thought that Naegleria fowleri evolved from the nonpathogenic free-living amoeba Naegleria lovaniensis. Yeah. And that's based on like so type 1 is present in North America, a bunch more types are present here, and then it's thought to have spread possibly to Europe and then disperse to Asia and then Australia and New Zealand. |
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| Erin Allmann Updyke |  | Interesting. |
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| Erin Welsh |  | Yeah. And that's obviously not a complete story but like I said, we don't have a lot of great data for the different types and prevalences especially because you may have noticed that I left out South America and Africa in that global spread timeline. We just don't have good samples yet or we're still working on getting good samples. |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | Yeah. Although I didn't see any paper that talked about just how long these amoeba have been infecting humans, I would feel pretty comfortable myself guessing that it's been a very long time and that the fact that it was recognized so recently as causing disease is just a product or where we were with medical technology and microbiology knowledge at the time. |
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| Erin Allmann Updyke |  | Yeah, definitely. Definitely. |
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| Erin Welsh |  | And like you said, Erin, the primary sources of exposure are warm pools of freshwater and also like the Neti pot thing. And yes, water warmed by electricity power plants may be a relatively recent thing which is like a place where a lot of people have gotten infected. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | But natural spas and hot springs like geothermally warmed water, those have been around forever as have just like standing pools of warm water. Puddles. |
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| Erin Allmann Updyke |  | Right, puddles, buckets, whatever. |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | And humans have probably always enjoyed a dip in the warmer months to cool down. And so the genus Naegleria had been described all the way bacteria in 1899 but like I said, these were not really thought to be of any medical importance and so they were kind of overlooked as being able to cause any sort of disease. And it was only in the 1940s that bacterial meningitis could even begin to be treated through the use of antibiotics. |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | And even then you weren't guaranteed success. |
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| Erin Allmann Updyke |  | Right. It's like before that of course you're not distinguishing your types of meningitis, of course not. |
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| Erin Welsh |  | Right. Right, exactly. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | And so yeah, you're trying to treat symptoms rather than cause because we had no tools to treat the cause. |
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| Erin Allmann Updyke |  | Exactly. Right. |
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| Erin Welsh |  | And so it's not surprising that these primary amoebic meningoencephalitis cases slipped through the cracks. It's like that saying when you hear hoofbeats you think horses, not zebras. |
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| Erin Allmann Updyke |  | Oh my gosh, Erin, I was going to say that later! |
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| Erin Welsh |  | Really? (laughs) |
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| Erin Allmann Updyke |  | Yes, it's such a common saying! |
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| Erin Welsh |  | Well and I also wrote I guess which animal you think of probably depends on where you live. |
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| Erin Allmann Updyke |  | Yes. |
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| Erin Welsh |  | Like sometimes you may think zebras because whatever. |
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| Erin Allmann Updyke |  | Right. It's a U.S. medicine saying, maybe. |
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| Erin Welsh |  | For sure. (laughs) Anyway so besides me just supposing that it was likely that Naegleria fowleri caused PAM in humans before those first cases were described in 1965. There's also actual evidence. So once Fowler and Carter's paper came out it definitely wasn't ignored or forgotten about, it seemed to spark other people around the world to reexamine past meningitis cases that had maybe seemed a bit unusual or ones where they had seen amoebae floating around in the cerebrospinal fluid but assumed it was Entamoeba histolytica. And that turned up more than a few cases. One of these which is thought to be the earliest example of Naegleria fowleri causing an infection came from an old specimen in a London pathological museum. This specimen which had been set aside for reexamination before being tossed to make room for, quote: "activities more in keeping with a contemporarily scientific approach to medical studies." |
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| Erin Allmann Updyke |  | Ooh, interesting. |
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| Erin Welsh |  | Yeah. (laughs) So they were basically just tossing a bunch of stuff and they were like, 'We should look at these things again.' And one of those things set aside was this preserved brain from 1909. |
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| Erin Allmann Updyke |  | Whoa. |
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| Erin Welsh |  | Yeah. And on this specimen container had the label "cancerous dissemination in the leptomeninges, April 1909, a lad of Essex." But reexamination in the 1960s of this brain showed that it wasn't cancer at all but rather an amoeba that was morphologically identical to Naegleria fowleri and the pathological findings in the brain also mirrored those more recent cases as well. And there were a handful of other suspected or confirmed PAM cases that preceded the 1965 publication by Fowler and Carter, there was like a possible one in Northern Ireland in 1937 and then like immediately in the 1960s there were some, early 1960s in Florida, smattering of cases later on in Texas, Czech Republic, New Zealand, Virginia, and so on. It really became, 'Here it is in Australia' and then people around the world were like, 'Oh, it's also in my backyard. Oh it's here, oh it's there. Everywhere.' |
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| Erin Allmann Updyke |  | Right. As soon as they started looking for it, they found it. |
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| Erin Welsh |  | Exactly. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | Throughout the 1970s, 1980s, 1990s, cases of primary amoebic meningoencephalitis continued to trickle in and one of these cases I learned was cared for by my mom. |
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| Erin Allmann Updyke |  | Nuh uh! |
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| Erin Welsh |  | Yeah. |
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| Erin Allmann Updyke |  | What? |
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| Erin Welsh |  | So I was talking to her the other day about how we were doing this episode and she was like, 'Oh I'll never forget that patient I had.' And I was like, 'Mom, what patient?' And it turns out that she had a patient with primary amoebic meningoencephalitis when she was an ICU nurse, this is sometime during the late 1970s or early 80s. |
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| Erin Allmann Updyke |  | Oh my gosh. |
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| Erin Welsh |  | Yeah. This person had gotten it while swimming in some freshwater near Tampa and unfortunately the kid didn't make it and my mom remembers it as just absolutely devastating. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | She's like, 'I will never forget it. They tried to fly in medication but it didn't get there in time and it was just like horrible.' |
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| Erin Allmann Updyke |  | Oh my god, that's awful. |
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| Erin Welsh |  | Yeah. And that story is like so many others because it doesn't seem as though we've made a whole lot of progress in the treatment arena. But that being said, we have made substantial progress in our understanding of the amoeba itself, Naegleria fowleri. Its biology, its pathophysiology, and its ecology. So this history section isn't super long because this is such a newly recognized pathogen of humans but I do wanna go into one more aspect of this amoeba and that is its ecology and how that plays a role in the number of cases that we see and when we see them. And I know that you're gonna talk about current numbers and a bit more in detail about distribution and so on but one of the questions I wanted to address in this context of ecology is is this an emerging parasite? |
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| Erin Allmann Updyke |  | I read that paper too, Erin. |
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| Erin Welsh |  | I was just gonna say! It's that Maciver et al paper from 2020. There's like such great info in there and there's also a beautiful figure of the worldwide distribution of these cases. |
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| Erin Allmann Updyke |  | Yes. |
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| Erin Welsh |  | I was like ah, perfect. There it is, you can visualize it. But to get at that question of is this an emerging parasite, we need to think no only about whether numbers are increasing but if they are, why they might be increasing. |
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| Erin Allmann Updyke |  | Yes. |
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| Erin Welsh |  | So first of all there doesn't seem to be a sharp increase in the U.S. specifically in terms of cases but it does appear that cases are increasing globally, liker overall around the globe. And it's hard to say whether this increase actually represents more infections or rather just that like growing awareness of this amoeba is driving the increase, especially in areas like Karachi, Pakistan that are increasingly recognized as hotspots. And so maybe that's when you start to shift, you know, when you hear those hoof beats you start to think of zebras and not horses, for example. |
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| Erin Allmann Updyke |  | Right, exactly. It's also too I think, like you mom would probably think of it anytime that she saw a case because she's seen one before. |
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| Erin Welsh |  | Right. |
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| Erin Allmann Updyke |  | So anytime you've seen one before it's gonna be something that comes up earlier to your mind. |
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| Erin Welsh |  | Right, exactly. And so we also know without a doubt that this is a very under-reported disease. |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | For example I saw one number that was for every 3 PAM cases reported in the U.S. there are likely to be another 13 unreported cases. And with this amount of uncertainty surrounding the numbers of cases like are these actual cases vs is this just the tip of the iceberg? It's kind of hard to say what is causing the rise or whether this is on the rise. |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | But that being said, there are a few things that certainly have the potential to increase both prevalence of this amoeba as well as exposure to it. And one of those things is of course climate change. |
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| Erin Allmann Updyke |  | Climate change. |
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| Erin Welsh |  | Climate change. Naegleria fowleri as we've said loves warm water. It's found in freshwater and some brackish water but not saltwater and some researchers believe that part of the reason it thrives in warmer waters is that those temperatures knock out the competition, like other amoebae. Most cases of PAM happen when exposure is most likely, so the summer months when people are more likely to be trying ways to cool down or the water just like happens to be warmer because it's been heated by the sun, etc. And a warming climate means warmer waters. Not only potentially helping Naegleria fowleri to thrive in those places where it's already prevalent but also allowing it to spread polewards. |
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|  |  | This has already been seen with a case in Minnesota, 550 north of a previously reported case. So it's just sort of like isolated out there. And this case there was no outside travel and the person had swum in a lake though in Minnesota that had been uncharacteristically warm that year. And then another case happened in that same lake 2 years later. And then these cases along with another that happened in Northern Pennsylvania have been used as examples of the impacts that climate change is already having on this disease. And it's not just a warming climate that may impact it either. Some areas of the world are predicted to have more drought and although water exposure is the most common way to pick up this amoeba it also appears to be able to breathe in the cyst form of the parasite in dust. |
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| Erin Allmann Updyke |  | I know. I know. I didn't get into that because it's terrifying. |
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| Erin Welsh |  | Yeah. And it's rare. |
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| Erin Allmann Updyke |  | It's very rare. |
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| Erin Welsh |  | Yeah, it's definitely what, less than 10%? |
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| Erin Allmann Updyke |  | Yeah I think I read about 6% or less of cases that we know of don't seem to have any sort of water exposure and so the thought is that it's from dust because the parasite has been found alive and infectious from dust kicked up in the air. |
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| Erin Welsh |  | Right. But I also, not to make this super scary, a lot of the places where it seems to be dust-borne there's really poor monitoring. |
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| Erin Allmann Updyke |  | There's very poor monitoring and those are also the places where people have found the amoeba in people's noses without infection, so it's thought that that is a pretty big route. Well maybe not big but that is an important route of transmission there. |
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| Erin Welsh |  | Yeah, yeah. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | So yeah, so more drought might mean more dust might mean more insisted Naegleria fowleri, more chance for infection. And increasing drought has already led to more people using other ways to store water like rooftop rainwater systems or artesian wells, both of which tend to have higher abundances of this amoeba. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | And roof-harvested rainwater tanks in Australia and South Africa, for instance, Naegleria fowleri is often found in pretty good numbers. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | And there's been a lot of great work looking into how different abiotic factors like temperature, pH, salinity, etc and biotic factors like the presence of predators of Naegleria fowleri and prey abundance, how these things all affect their abundance and life cycle. But it's kind of difficult to put all of these pieces together and I think we're still trying to get a picture of what determines whether or not this amoeba is in this lake vs that lake and at this abundance in this lake. |
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| Erin Allmann Updyke |  | Right. |
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| Erin Welsh |  | Is it seasonal? Is it not? |
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| Erin Allmann Updyke |  | Well and on top of that, how much does abundance in the lake track with infection risk? Cause we still don't know that. How many do you need to be exposed to? What is a safe level vs an unsafe level? We don't know that information. |
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| Erin Welsh |  | Yeah, no, exactly. But I do think that there's one thing that we do know and that is that it doesn't seem as though this amoeba is going anywhere anytime soon. If anything it seems like we can only expect to see more of it. Understanding what drives this patchy distribution of Naegleria fowleri is super important for estimating and predicting risk but also getting that information out there is crucial. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | I feel like increasing monitoring, making that information accessible either on signs or in a public database, like those things seem pretty important in terms of being armed with the knowledge where you can understand risks, I suppose. So to be honest I don't know how much we're doing that here in the U.S. currently. But Erin, maybe you'll tell me what we're doing about this horrible disease in terms of awareness, control, vaccines, all the things. |
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| Erin Allmann Updyke |  | Well I'm not gonna make any guarantees on any of those, Erin, but we'll take a break and then get into some of it. |
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| TPWKY |  | (transition theme) |
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| Erin Allmann Updyke |  | So Naegleria fowleri, primary amoebic meningoencephalitis, it's a very rare disease. But like you said Erin, we absolutely don't have an exact handle on how many cases there are every year because not only are there cases inevitably misdiagnosed, assumed to be bacterial or viral, never confirmed to be caused by Naegleria fowleri. But inevitably as well like you said, in many parts of the world cases are likely never identified because of lack of awareness or because of poor healthcare infrastructure and inability to test for the disease. But with all those caveats in place, let's talk about what these numbers actually are because there's no definitely when we say a rare disease, what does that mean? A review paper, the one that you mentioned Erin that came out in 2020, suggested that there have been a totally of 432 cases reported in the literature. |
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| Erin Welsh |  | Globally. |
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| Erin Allmann Updyke |  | 431 cases from 1965 to now. In the United States annually anywhere from 0 cases to 8 cases are reported, so average is about 3 cases every year in the U.S. But across the globe it's a very uneven distribution and it's also not uncommon for this to be a disease of outbreaks. There have been a number of large outbreaks that have killed anywhere from 16-24 people in one outbreak. |
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| Erin Welsh |  | Mm-hmm, yeah. |
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| Erin Allmann Updyke |  | And over the last decade in Pakistan the number of cases have been increasing dramatically where for example in the United States, from 1968-2019 there were 142 cases reported in the U.S. where in the last decade 146 cases have been reported in Karachi alone. So this distribution of these 431 cases is not equal. The vast majority have been diagnosed in the U.S. and Pakistan and then Australia and a number of other countries. And like you said, Erin, at least one study that has actually tried to estimate what the difference likely is in reported vs true cases estimated that while we see documented reported about 3 cases, that number is likely more like 16 and that was based on epidemiological data as well as diagnostic codes for unspecified or unidentified meningitis. |
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| Erin Welsh |  | Okay. |
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| Erin Allmann Updyke |  | And like you said Erin, this is an environmentally transmitted pathogen that could like continue to increase. Like we don't know how much of this increase is just due to an increase in awareness and reporting which is a good thing vs an increase like a true increase in incidence. But at this point it is still a very rare disease. But I wanna talk about that a little bit because I wanna talk about the fact that sometimes I think when we think about something that's very rare it's easy to kind of brush off. And despite this rarity, this disease has absolutely devastating consequences for individuals and for families when it happens. And the numbers and statistics can only tell us so much about the impact that this disease has. |
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|  |  | And like just sort of stopping to take a minute to recognize that even though you can say there's only been 400 cases documented across the globe in all these years, those numbers might seems so small. But they're not small to the people that they happened to. And so I think that's one of the reasons why we wanted to do this episode is because even though the numbers might be small, that doesn't mean that they don't have a big consequence. |
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| Erin Welsh |  | Mm-hmm, yeah. I mean I think that that goes for a lot of the diseases that we cover. |
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| Erin Allmann Updyke |  | Yes, I agree. |
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| Erin Welsh |  | I think it's also very difficult to capture that in numbers, to capture the impact that these diseases have and will continue to have. |
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| Erin Allmann Updyke |  | Yeah, yeah. So with that being said, kind of looking forward, what's on the horizon? From what I could tell the vast majority of research that's being done is still in pretty early stages. So there's a lot of work kind of in vitro studies in petri dishes as well as in mouse models trying to do things like identifying the underlying mechanisms of virulence and investigating a lot of different potential therapeutics, there's a lot of work on that. There's also a lot of work being done to develop better diagnostic tools and detection tools, not just for the clinical setting but also for environmental detection, like we talked about. And like you said, Erin, there's a lot of work that's being done on kind of the environmental side which I think is really interesting just looking at the basic life history of this amoeba and trying to figure out the more that we know about it, the more that we could potentially use to help treat and prevent this disease. |
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| Erin Welsh |  | Yeah. It's fascinating because like this is a free-living, this isn't an obligate parasite. |
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| Erin Allmann Updyke |  | Right! |
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| Erin Welsh |  | This has a whole other life. |
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| Erin Allmann Updyke |  | A whole other life that has nothing to do with humans, it does not rely on us. I mean it really is incidental in that way, there's no... |
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| Erin Welsh |  | There's no drive for this thing to infect humans. |
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| Erin Allmann Updyke |  | Right and we're not transmitting it on to anyone, you know. |
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| Erin Welsh |  | Right. |
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| Erin Allmann Updyke |  | Yeah. And so I think that a lot of the work too is sort of in focusing on prevention as well. So making sure that especially in areas where the exposure is not necessarily due to recreational water but is due to water that's used for like nasal cleansing or just cleaning in general, making sure that that water is treated adequately in those places and things like that is also a really important part of prevention. |
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| Erin Welsh |  | Yeah, yeah. Gosh. Awareness, awareness, prevention, filtration. |
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| Erin Allmann Updyke |  | Yeah. And speaking of prevention and awareness like Dr. Gompf mentioned in our firsthand account, she has an awesome website, it's amoeba-season.com. There's a lot of great information about Naegleria fowleri, about prevention, and for health professionals there's some really great information there about diagnosis, treatment, all that kind of stuff. So definitely check out that website and thank you again so much to Dr. Gompf for taking the time to chat with us and sharing your story. |
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| Erin Welsh |  | Thank you, thank you so much. We really appreciate it. |
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| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | Well should we do sources? |
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| Erin Allmann Updyke |  | Oh we should, yeah. |
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| Erin Welsh |  | I have a lot of sources. I already shouted out one which was that paper from 2020 titled 'Is Naegleria fowleri an emerging parasite?'. And then there are several papers by De Jonckheere all about Naegleria fowleri, I'm pretty sure he's like the leader in the field because the papers were incredibly thorough and informative and very helpful, especially about the origin and evolution and the different types and so on. And then there were a lot of other helpful papers and I will post them all on the website. |
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| Erin Allmann Updyke |  | I also had a few papers, one that I found very comprehensive was called 'Biology and pathogenesis of Naegleria fowleri' from 2016 and another if you want to read the actual paper where they estimated called 'Estimation of Undiagnosed Naegleria fowleri Primary Amebic Meningoencephalitis, United States'. That's the one where they estimated the difference between reported and actual cases as well as a number of others. We post the sources for this episode and every single one of our episodes on our website thispodcastwillkillyou.com under the EPISODES tab. |
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| Erin Welsh |  | Thank you to Bloodmobile for providing the music for this episode and every single one of our episodes. |
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| Erin Allmann Updyke |  | And thank you to the Exactly Right network of whom we are very proud to be a part. |
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| Erin Welsh |  | And thank you to you, listeners. We know this was a tough episode and thank you for sticking with us. |
|  |  |  |
| Erin Allmann Updyke |  | Yeah. |
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| Erin Welsh |  | Well until next time, wash your hands. |
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| Erin Allmann Updyke |  | You filthy animals! |