

Erin Welsh	Hello listeners. Before we get to the episode, we want to take a moment to address the June 24, 2022 Supreme Court decision to overturn Roe vs Wade.
Erin Allmann Updyke	This decision stripped away the right to have a safe and legal abortion. Everyone should have the freedom to decide what's best for themselves and their families including when it comes to ending a pregnancy.
Erin Welsh	This decision has dire consequences for individual health and safety and could have harsh repercussions for other landmark decisions. Abortion is health care and restricting access to comprehensive reproductive care including abortion threatens the health and independence of all Americans.
Erin Allmann Updyke	You can learn more by visiting choice.crd.co . That's choice.crd.co .
Erin Welsh	And if you're able to support others, please consider donating to abortion funds.
Erin Allmann Updyke	We encourage you to speak up, take care, and spread the word.
Erin Welsh	Hey everyone, just a content warning here. The firsthand account does describe the death of an infant and so if you would like to fast forward past that part we recommend jumping ahead about two minutes.
Erin Allmann Updyke	"The patient was a nine month old boy who became ill with fever on August 22, 1970 and two days later developed a rash. He was admitted to Basankusu Hospital on September 1st. On examination it was recorded that the lesions were hemorrhagic, although they showed a centrifugal distribution typical of smallpox. Crusts were collected for laboratory examination. The rash lasted about two weeks. During the scabbing stage the patient developed otitis and mastoiditis as well as enlarged painful cervical nodes which were subsequently incised and drained. The patient recovered and was about to be discharged but on October 23rd he developed measles and died 6 days later. The child had never been vaccinated."
TPWKY	(This Podcast Will Kill You intro theme)
Erin Allmann Updyke	That's a tough one.
Erin Welsh	That's horrible.
Erin Allmann Updyke	Yeah.
Erin Welsh	So that is a case description of the first known human case of monkeypox and it is from a paper by Ladnyj et al from 1972 titled 'A human infection caused by monkeypox virus in Basankusu Territory, Democratic Republic of the Congo.'
Erin Allmann Updyke	Oof, yeah.
Erin Welsh	Yep. Hi, I'm Erin Welsh.
Erin Allmann Updyke	And I'm Erin Allmann Updyke.
Erin Welsh	And this is This Podcast Will Kill You.

Erin Allmann Updyke And today we're covering monkeypox.

Erin Welsh Long awaited, much requested.

Erin Allmann Updyke Long awaited.

Erin Welsh Here it is. Yeah.

Erin Allmann Updyke Yeah. Monkeypox has obviously been making a lot of headlines lately so a lot of you have asked for us to do this episode. We're very excited to dig in and deliver this episode to you because this is a very interesting virus and it's spreading in a way that we have really never seen before which is fascinating and also potentially kind of terrifying.

Erin Welsh Absolutely kind of terrifying.

Erin Allmann Updyke Yeah.

Erin Welsh And we know that during the last and ongoing pandemic, COVID, many of you came to really appreciate our Anatomy of a Pandemic miniseries for updates and information about what was going on and how the science was constantly changing. So that's kind of what we wanted to do here.

Erin Allmann Updyke But not a miniseries specifically.

Erin Welsh Hopefully not, hopefully not.

Erin Allmann Updyke Hopefully not. But we did want to give you background on what we knew about this virus going into the current outbreak and where things stand with monkeypox today as far as we know.

Erin Welsh Yeah. And of course the fact that this is an ongoing outbreak makes it trickier to pack in all of the super up to date info in a more deep dive research podcast like ours. And we learned that difficulty with this episode all too well because we actually initially recorded this episode in early June, June 9th to be precise.

Erin Allmann Updyke Yup.

Erin Welsh But then in the week and a half that it took to edit and put it all together, so, so much changed and we didn't want to put that out and leave you with more questions than answers.

Erin Allmann Updyke Yeah. So we decided to give ourselves a little bit of time to get caught back up with monkeypox and then record the current event section as close to the release date as possible so that we're giving you the most up to date information that we can.

Erin Welsh But since this is a virus that we've known about for quite some time, much of the biology and history section hasn't changed from that first recording and those parts of the episode come directly from that first recording on June 9th while this intro that you're listening to right now-

Erin Allmann Updyke Right now.

Erin Welsh And the current events section is from July 6, 2022.

Erin Allmann Updyke

What can we tell you? Erin's editing is just magic. I'm sure you'll never know.

Erin Welsh

You probably will. But ultimately the purpose of this episode is to give you a solid background on monkeypox, how we have known this virus to act in the past, the history of its identification, and what past outbreaks can tell us about this current one. And finally we'll bring you up to speed on how things have progressed with this current outbreak in 2022.

Erin Allmann Updyke

And speaking of this current outbreak, one more thing that we wanted to bring up before we get started on this episode and that is the naming of this virus. So as this outbreak and the number of headlines about it has grown over the past many weeks, this increased attention has generated a lot of discussion over the potentially problematic naming of this virus and its two clades. For one thing, as we'll talk a lot, about monkeypox is a misnomer and it's also against World Health Organization guidelines to name diseases after animals or people or jobs or food or places because it can lead to discrimination and stigma.

Erin Welsh

Which brings us to the second prong of the bad naming of monkeypox. As we'll get into again later, this virus can be classified into two clades or strains or subtypes of the virus which are currently called and have historically been called the West African clade and the Central African or Congo Basin clade which is where they were first identified. And of course if you've listened to this podcast before, you'll know that naming a disease or virus or clade of virus after a place is also not a good practice. It can lead to discrimination and stigma.

Erin Allmann Updyke

And today a lot of the discussion that's ongoing about the naming of monkeypox and its clades is not just like hey, this isn't good names, but it's also like hey, let's actually fix this and come up with some new names. So it's very likely that within the next weeks or months, I don't know, monkeypox and its clades will have completely different names than what we are using today. But that hasn't happened yet and so to avoid confusion in this episode we'll be using the names that the virus and the disease have historically gone by which is monkeypox and the historic clade names. All right.

Erin Welsh

Yeah.

Erin Allmann Updyke

With all that behind us, I do believe it's quarantini time.

Erin Welsh

It's quarantini time. What are we drinking this week?

Erin Allmann Updyke

We're drinking More Pox on the Rocks.

Erin Welsh

So all the way back in 2017.

Erin Allmann Updyke

2017!

Erin Welsh

Unbelievable. Episode 3 was on smallpox and it was our very third quarantini.

Erin Allmann Updyke

Our very third?

Erin Welsh

And we called it Smallpox on the Rocks. And you know what we just figured we'll stick with that.

Erin Allmann Updyke

It's a classic.

Erin Welsh: And we're calling this More Pox on the Rocks even though we have done other pox viruses.

Erin Allmann Updyke: Yeah but not like a pox named pox virus.

Erin Welsh: That's true, that's true.

Erin Allmann Updyke: Yeah. I also have to say that the smallpox episode was one of my favorites of all time and I still to this day think that Smallpox on the Rocks is one of our best quarantini names. So I love that we get to just sort of bring it back to life here.

Erin Welsh: More Pox on the Rocks.

Erin Allmann Updyke: Yeah.

Erin Welsh: And basically More Pox on the Rocks is take your favorite liquor of choice or liquor substitute of choice, there's a lot of non alcoholic spirits which is super cool, pour it over some rocks, maybe add a little bit of citrus or a couple dashes of your favorite bitters. And it's really up to you what you want to make it.

Erin Allmann Updyke: Yeah. Clink it. Clink it in your glass.

Erin Welsh: And we will post the full recipe for More Pox on the Rocks, the most complicated recipes, as well as the non alcoholic placeborita on our website thispodcastwillkillyou.com as well as on all of our social media channels.

Erin Allmann Updyke: On our website thispodcastwillkillyou.com you can find everything that you'd hope to find on a podcast website. You can find merch, you can find our Patreon, you can find our Goodreads list, you can find a link to our music from Bloodmobile and all of the sources from all of our episodes, you can find transcripts. There is just so much there.

Erin Welsh: There's no end to what you can find. Okay so with this long intro out of the way, I feel like there's no possible way that there's more business to cover. So let's get started.

Erin Allmann Updyke: Let's take a quick break and then get into the biology of this virus.

TPWKY: (transition theme)

Erin Allmann Updyke: Monkeypox and smallpox and cowpox and many other animal-named pox viruses are as we learned in our smallpox episode in fact pox viruses.

Erin Welsh: Stands to reason.

Erin Allmann Updyke: Right. Well they aren't all though. They belong to a family of viruses called the pox viridae specifically in the Orthopoxvirus genus. So Orthopoxviruses and all pox viruses in general are pretty large viruses. They're generally shaped like bricks or big chunky oval shapes, they have an envelope that surrounds them, and they have this very large linear double stranded DNA genome. And we on this podcast have covered the most famous pox virus, smallpox.

Erin Welsh: We have.

Erin Allmann Updyke

Way long time ago now. That virus is known as variola virus. And thanks to vaccination campaigns as well as the fact that that was a human-specific pox virus, smallpox was eradicated in... Was it 1980 that it was declared eradicated?

Erin Welsh

Yep.

Erin Allmann Updyke

Yeah. And then you may also remember we covered another pox virus, myxoma virus although that is in a different genus, the Leporipoxvirus genus.

Erin Welsh

I got a kick out of something about myxoma virus.

Erin Allmann Updyke

Tell me.

Erin Welsh

So I kept stumbling across these papers on monkeypox where the name Frank Fenner was either an author or mentioned in a reference to another paper. I was like that name sounds so familiar and he was one of the big researchers who studied myxoma virus and wrote the book, the textbook that I read for that episode. And so I just got a really fun kick out of that.

Erin Allmann Updyke

I love that, when episodes intertwine.

Erin Welsh

Yeah, exactly.

Erin Allmann Updyke

Excellent. So the majority of pox viruses, especially today I'm really just focusing on this Orthopoxvirus genus since we're talking about monkeypox, these are not human-specific viruses. So like I mentioned some of them at the top, there's smallpox, camelpox, cowpox, the vaccinia virus which is what was used to make the smallpox vaccine which includes various strains like buffalopox and rabbitpox, and then the one we're going to focus on today that is the subject of all the media fervor currently, monkeypox. But all of these various animal-based names are slight misnomers because they might lead you to believe that they only infect that particular animal.

Erin Welsh

Or that they come from that particular animal.

Erin Allmann Updyke

Exactly. But that's not the case. But in the case of monkeypox the name is a real misnomer because while it was first identified from monkeys, evidence suggests that it's rodents and not monkeys that are the primary natural reservoir for this particular virus. And just like many of the other orthopoxviruses, monkeypox can have a relatively broad host range. And what these broad host ranges mean is that sometimes these various viruses can spill over from their animal hosts into us humans. And that is what listeners of this podcast will be very familiar with is often called a zoonotic pathogen. These are transmitted from animals to humans via spillover events. And anyone who listened to our smallpox episode 100 million years ago remembers that this is a thing because of cowpox. Cowpox is what helped serve as one of the first examples of a type of vaccination that... Was it Edward Jenner, Erin?

Erin Welsh

Uh huh.

Erin Allmann Updyke

I feel so proud that I remembered that. Inoculated people with cowpox to protect them against smallpox. And this example illustrates a couple of really key characteristics that I wanted to highlight upfront about orthopoxviruses because they'll be important throughout this episode. And that is A) that these pox viruses can infect a wide range of potential hosts depending on the virus and that infection with one pox virus often confers at least some degree of cross protection against other virus species.

Erin Welsh

Crucial, crucial information.

Erin Allmann Updyke

Very, very crucial. And so when it comes to monkeypox, let's focus on that for now, this is not a completely new virus. We've known since 1970 that it has the potential to both be a zoonotic illness as well as occasionally cause small outbreaks that do include person to person transmission. But today what's happening currently in 2022 is by far the most person to person transmission that we've seen. And we'll get into that later on but I just kind of wanted to set the stage that we've known about monkeypox and its ability to infect humans for quite some time. And in the past, prior to the 1980s, because a lot of the human population was vaccinated against smallpox, humans possessed some degree of protection against monkeypox. And today that's really for the most part no longer the case because the vast majority of people are not being vaccinated against smallpox anymore since it's been eradicated. But let's get into monkeypox, shall we?

Erin Welsh

Yeah.

Erin Allmann Updyke

So the disease that monkeypox causes is actually similar in a lot of ways to smallpox although it is substantially less virulent. So historically the way that we've understood the transmission of monkeypox is actually very similar to the transmission of smallpox and that is by close contact with either the rash itself which we'll talk about in a minute, or by respiratory droplets that are full of virus, and potentially by very short range aerosols because this is a virus that can persist in the environment for a little bit longer than other viruses. And I meant to try and find an exact number for you Erin because I thought you might ask, I don't have a number.

Erin Welsh

Okay.

Erin Allmann Updyke

But it's more environmentally stable for example than a coronavirus.

Erin Welsh

Interesting.

Erin Allmann Updyke

And like smallpox, monkeypox also has a potentially rather long incubation period.

Erin Welsh

Yeah.

Erin Allmann Updyke

It's usually in the range of 10-14 days but it can be as short as a week, it could be even longer than a couple of weeks. And in general as far as we understand, people don't become infectious until the development of the rash.

Erin Welsh

Oh okay.

Erin Allmann Updyke

Yeah. So let's talk about what the symptoms look like, shall we? Most people who get infected with monkeypox will start off feeling cruddy. They'll get fever, they'll have malaise, they'll start to feel very sick for at least one or two days before the development of this rash. Also very commonly people might also notice swelling in the lymph nodes, maybe the lymph nodes under your chin, maybe behind your ears, maybe in your groin, maybe in your armpits. This lymphadenopathy as it's called could be anywhere. And then after one or two days of this generalized feeling really sick is when the rash itself typically begins. And the rash of monkeypox looks a lot like the rash of smallpox and it follows a very classic series. It begins as these small, 2-5 mm flat to maybe mildly raised little bumps, they're called macules and papules. That's the beginning.

Erin Welsh

Okay.

Erin Allmann Updyke

And it tends to start in what's called a centrifugal, and I'm sorry, I feel like I'm pronouncing that word wrong, rash. Anyways this means that the rash tends to start on the extremities, especially the head and then the arms and the legs and then it spreads inwards. This is the same way that smallpox tends to start. It's more concentrated on the head, the extremities and then it spreads to the rest of the body inwards. And that's in contrast to what are sometimes called centripetal rashes which start primarily on the trunk and then spread outwards. A great example of this is something like chickenpox.

Erin Welsh

That's so interesting.

Erin Allmann Updyke

There's a lot of different ways that rashes spread. You might remember when we talked about measles and rubella, they start on the head and then spread downward.

Erin Welsh

Yeah.

Erin Allmann Updyke

That's called cephalocaudal spread. Roseola is another virus that tends to start on the neck and trunk and then spread up to the face and out to the extremities but not in exactly the same way as something like chickenpox would. There's a lot, it's interesting.

Erin Welsh

Is it just different tissue tropisms or what?

Erin Allmann Updyke

That's a great question. I don't actually know.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah. Yeah, I don't know. It's a really good question. That would be a fun whole episode, rash distribution.

Erin Welsh

Oh rashes. I would love that.

Erin Allmann Updyke

That would be fun actually. So it spreads in that way. But then this rash does progress through very similar phases as the smallpox rash. So they start out as those flat or slightly raised maculopapules then they become even more raised and fill with fluid, these are known as vesicles. Then these vesicles will start to form into these pus-filled taut pustules and then these pustules will crust over and then eventually slough off and often leave a scar behind. So this process from papule to vesicle to pustule to scab, this is a long process just like with smallpox, it generally takes between 14-21 days, so 2-3 weeks. And what's interesting is that unlike something like chickenpox, what tends to happen is that all of this rash progresses through those phases at the same time. So all of your rash is papules and then they all around the same time transform to vesicles to pustules, etc. Whereas with chickenpox and other herpesviruses you often see vesicles in different stages of healing. So you'll have some that are crusting, some that are vesicles, etc. Classically.

Erin Welsh

Yeah. I'm really trying to resist just saying like why? How?

Erin Allmann Updyke

Why? Why?

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah, it's really good questions. I don't know, Erin. It's really interesting especially when it comes to the details of the virology of this virus and the pathophysiology. I'll just warn you we don't know much. We really don't.

Erin Welsh

Right.

Erin Allmann Updyke

Yeah. But in contrast to smallpox, this is where we get to the good parts about monkeypox, we don't tend to see a lot of the more severe forms, especially if you remember listening through our smallpox episode and I read over it to remind myself how horrific smallpox is.

Erin Welsh

Oh yeah.

Erin Allmann Updyke

The most severe form, the hemorrhagic form that we describe in that episode doesn't tend to happen, that hasn't really been seen to happen with monkeypox which is very good. But that being said case fatality rates have been shown in some cases to still be relatively high. There are as it turns out and I know you'll talk a little more about Erin, two different clades of this virus and one of them seems to be more virulent where the case fatality rate is estimated on average to be about 10%. Which is actually really high.

Erin Welsh

In unvaccinated individuals.

Erin Allmann Updyke

Exactly, in unvaccinated individuals. And then in the other clade the fatality rate is usually estimated at about 3.5% which again is still really high but is much, much less than smallpox.

Erin Welsh

Right, yeah. I was surprised at how high the case fatality rates were.

Erin Allmann Updyke

Me too.

Erin Welsh

I had no idea.

Erin Allmann Updyke

I did not realize that either. I thought that it was much lower. And it's interesting because it really does vary depending on what outbreak you're looking at and it probably really varies how much data was collected in all of these different cases. So we'll see when we get to what's happening today.

Erin Welsh

Yeah. I think there there are other factors too like the number of confirmed cases vs suspected.

Erin Allmann Updyke

Exactly.

Erin Welsh

And then the other thing too I think is access to healthcare because a lot of the deaths that seem to happen seem to be from secondary causes.

Erin Allmann Updyke

Right. Even in our firsthand account, right.

Erin Welsh

Yeah.

Erin Allmann Updyke

This poor nine month old survived infection with monkeypox but then was left unfortunately susceptible to another infection. So yeah, especially with the way that these pustules can break open, you are very susceptible to overlying bacterial infection of this rash.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah. So that tends to be the symptoms of monkeypox. Most people do recover with relatively little long term effects except for scarring which given how prevalent this rash can be on the face can be pretty significant but generally don't tend to see a lot of long term other problems that arise from monkeypox when people survive.

Erin Welsh

Okay.

Erin Allmann Updyke

And like I said when it comes to the pathophysiology, I don't have a ton of detail to give you Erin. I was trying to look into a lot of specifics and try and compare and contrast this pox virus to smallpox but I guess in our early seasons I didn't talk about pathophysiology a lot because I didn't even mention it in the smallpox episode. But this virus, when we get infected through direct contact with the virus that is contained in these pustules right, I think that's important for everyone to know. And these pustules can be present in our mouth, they can be present in the genitals, they can be present on mucous membranes but also throughout our skin. And this virus, once it then gets into a new host body seem to have a pretty wide tissue tropism. So they replicate in our skin cells but they also replicate in our lymphatics which is why you see that lymphadenopathy.

And then they've also been shown to replicate in a lot of the cells that usually helps clear out bacteria and viruses like our macrophages. And another interesting thing is that the more severe clade of these viruses seem to replicate in an even wider variety of tissues including the genitourinary tract, the respiratory tract, and even the GI tract. And so while we don't fully understand and there's probably underlying genetic basis to the difference in virulence between these two clades and we don't really know the details, it's quite possible based on what we know about the difference in potential tissues that they infect that that's part of that virulence, right. If you have a virus that's infecting basically wider variety of your tissues, you're more likely to get sick, you're more likely to get more severely sick, and then that's leading to a higher case fatality rate.

Erin Welsh

That makes sense.

Erin Allmann Updyke

Yeah.

Erin Welsh

And so in terms of, I just can't resist, monkeypox vs smallpox.

Erin Allmann Updyke

Yeah.

Erin Welsh

Does smallpox also have pretty wide tissue tropism?

Erin Allmann Updyke

Yeah, I believe it's very similar. One thing that I think is very interesting that's quite different between monkeypox and smallpox is this lymphadenopathy, these swollen lymph nodes happen in over 95%-98% of cases of monkeypox and they don't happen at all with smallpox. But it's not because smallpox isn't able to replicate in these tissues, some people think it's actually because we're mounting a better immune response to the monkeypox than we did to smallpox.

Erin Welsh

Right, smallpox is just evading our immune system a little better.

Erin Allmann Updyke

Exactly.

Erin Welsh: Okay.

Erin Allmann Updyke: Yeah, yeah. That's also something that differentiates this disease from varicella, chickenpox. Historically, and when I say historically I don't mean like Erin's history section-

Erin Welsh: Not Egyptian papyri from 1200 BCE?

Erin Allmann Updyke: No, no. I just mean like in past outbreaks, varicella is often cited as the other disease that's most difficult to distinguish from monkeypox. But there are a few pretty solid distinguishers. One is that initial fever which is pretty rare with chickenpox, when it is present it's usually doesn't last as long and it's not as severe of a fever, like most people don't get as sick from chickenpox as they get from monkeypox.

Erin Welsh: Okay.

Erin Allmann Updyke: And then I already talked a little bit about the differences in the progression of that rash where they might progress in different stages with varicella and all the stages progress at the same time with monkeypox. But with varicella, with chickenpox it also progresses much more rapidly, right. Chickenpox is a much shorter duration in general. And then there's that lymphadenopathy, those swollen lymph nodes that are really common in monkeypox and really uncommon in chickenpox.

Erin Welsh: It's so interesting.

Erin Allmann Updyke: Yeah. Chickenpox, not a pox virus.

Erin Welsh: Right.

Erin Allmann Updyke: Yeah. See our chickenpox episode.

Erin Welsh: What type of virus is it, Erin?

Erin Allmann Updyke: It's a herpesvirus, Erin. But yeah, so it does definitely complicate the picture though because they can look very similar in some cases especially if you have never seen a monkeypox case and you don't know what you're looking for.

Erin Welsh: Yeah.

Erin Allmann Updyke: Erin, that's the biology.

Erin Welsh: Wow okay.

Erin Allmann Updyke: Was that enough? Did you want more?

Erin Welsh: I guess my biggest questions really have to do with what's going on today.

Erin Allmann Updyke: Yeah.

Erin Welsh: And so maybe we'll address some of those when we get to the current events section.

Erin Allmann Updyke

We will. So everything that I just described is classic monkeypox.

Erin Welsh

Okay.

Erin Allmann Updyke

This is monkeypox as we have understood it until today. What we'll talk about and what we're seeing today is in fact quite different than monkeypox that we've seen in the past. So we'll get to that. But first Erin, can you tell me where the heck this came from and how we got to where we're going to get to today?

Erin Welsh

I'm so glad you asked. Yeah, I will get to that right after this break.

TPWKY

(transition theme)

Erin Welsh

So again I just want to preface the history of monkeypox by mentioning that when talking about the history of this disease a big part of that story has to do with the different clades of this virus and how they have occurred in different epidemics over the past decades. And even though these names are likely to be changed in the future and for good reason, naming diseases after places can lead to other ring in stigma like we've already mentioned, they haven't been changed yet. And so I'll be using the names that they have been called historically which is the West African and Central African or Congo Basin clade or subtypes. All right. The history of monkeypox.

Erin Allmann Updyke

Yeah.

Erin Welsh

Erin, you are definitely not alone in wondering where did this virus come from and how did we get to where we are today?

Erin Allmann Updyke

Yeah.

Erin Welsh

It seems likely that a good chunk of the world is very curious about the same thing and I'll include myself in that. And in reading for this episode I found out that whereas the biology or maybe more specifically the clinical manifestations of monkeypox and smallpox may be similar in a lot of ways, their histories and importantly ecologies are incredibly different.

Erin Allmann Updyke

Yeah.

Erin Welsh

And again I'll point you towards our smallpox episode to get more detailed info about the history of this devastating disease. But for the purposes of this monkeypox episode, I think it'll be enough for me to say that smallpox ranks up there as one of the deadliest diseases of humans of all time, both in terms of the case fatality rate as well as the sheer number of people it has killed.

Erin Allmann Updyke

Yeah.

Erin Welsh

In the 20th century alone, smallpox is estimated to have killed between 300 million to 500 million people.

Erin Allmann Updyke

In the 20th century alone? And it was eradicated in 1980.

Erin Welsh

Yeah and declining in many places of starting long before then.

Erin Allmann Updyke

Wow.

Erin Welsh

Yeah. Smallpox has helped to topple civilizations, change the outcome of wars, and it has shaped humanity in really innumerable ways, both trivial or seemingly trivial and monumental, like from makeup trends to the development of vaccines, giving vaccines their name. A small part of me wishes that we hadn't covered smallpox yet because I feel like I did not give it the detailed deep dive that it deserved although I can't bring myself to re-listen. But also the other part of me is relieved that we have that massive disease already under our belts.

Erin Allmann Updyke

Yeah.

Erin Welsh

In any case smallpox was one of the most notorious and impactful diseases ever to have infected humanity and emphasis on 'was' because like we talked about it's also one of the most incredible success stories in public health. Smallpox is one of two diseases to have ever been eradicated, though fingers crossed we'll be adding at least one more to that list soon, dracunculiasis maybe. And it remains as of June 2022 the only disease of humans to have been eradicated.

Erin Allmann Updyke

Yeah.

Erin Welsh

Check out our rinderpest episode to learn more about the other disease that has been completely wiped off this planet. Throughout the 1960s and 1970s, public health agencies around the world participated in a tremendous coordinated campaign to determine where smallpox still lurked and to stop the chain of transmission through vaccination. And as we've talked about, their massive efforts paid off. In 1980 the world was declared free of smallpox and vaccination against this virus slowed and ceased. But out of the ashes of smallpox emerged another pox virus, the same one that's been making headlines lately. Of course I'm talking about monkeypox.

Erin Allmann Updyke

Monkeypox.

Erin Welsh

How did people first recognize this virus? Where had it been hiding? How long ago did it evolve? And why was it showing up just as smallpox was disappearing?

Erin Allmann Updyke

Yeah, Erin.

Erin Welsh

Yeah. So these are the questions that I'm hoping to get answered for you in this history section starting with evolutionary history. Although the monkeypox virus was first identified in only 1958, it's been around for much longer than that. Researchers put the origin of this virus at around 2500 years ago, give or take a few hundred years, with the West African clade, that's the less virulent clade showing up only 600 years ago, at least according to one estimate. So yes, it's been around longer than 1958 but it's not a terribly, terribly old virus.

Erin Allmann Updyke

Yeah.

Erin Welsh

And neither is the smallpox virus really which estimates put as a little older, maybe like 3400 years ago or so which is actually more recent than what I said in our smallpox episode which I just said very generically around 10,000 years ago when humans first domesticated animals and began settling in larger groups. And definitely smallpox needed that sort of crowd setting in order to spread but in any case, here's the correction five years later. Initially before these more precise evolution date estimates, researchers suspected that the monkeypox virus could be the ancestor of the smallpox virus since they cause similar disease and the monkeypox virus has a wider host range. The smallpox virus has a smaller genome and just infects humans and so some researchers thought that maybe it had lost some of those genes that had allowed it to infect more species to trade off infectivity for humans. But it turns out that monkeypox is neither the ancestor nor a descendant of the smallpox virus. It likely evolved from the cowpox virus.

Erin Allmann Updyke

Okay.

Erin Welsh

And it was a relief to learn that because not personally speaking but I think scientifically speaking-

Erin Allmann Updyke

And personally maybe.

Erin Welsh

Yeah. Because one of the key characteristics of smallpox that made eradication possible was the lack of a wildlife reservoir. And if smallpox had evolved from monkeypox once then scientists felt like it might be possible for it to happen again, to become once again specifically adapted to humans and transmission from human to human.

Erin Allmann Updyke

Right. Like smallpox 2.0.

Erin Welsh

Exactly. But thankfully that isn't the case. Of course it could become more adapted to humans given the opportunity but at least it hasn't happened before, so maybe the road map isn't as clear.

Erin Allmann Updyke

Okay.

Erin Welsh

Anyway so if monkeypox has been around for thousands of years, why did it take so long for us to notice it?

Erin Allmann Updyke

I have a guess.

Erin Welsh

What is your guess?

Erin Allmann Updyke

Because smallpox existed.

Erin Welsh

That's exactly what I have. Smallpox stole the show.

Erin Allmann Updyke

Yeah.

Erin Welsh

Smallpox was Marcia and monkeypox was Jan.

Erin Allmann Updyke

Poor Jan.

Erin Welsh

By the mid 20th century we had gotten a lot better at being able to actually visualize and isolate and culture viruses which had been tricky before due to their tiny size. And so scientists by then knew what a smallpox virus looked like, as you said a big brick-shaped virus. They had also found other pox viruses as well, some very host-specific like myxoma virus and others that had these wide host ranges. And like you said Erin, the naming trend for many of these pox viruses was to name it after the animal you first isolated it from.

Erin Allmann Updyke

Yeah.

Erin Welsh

Assuming that that species was the reservoir or the natural host.

Erin Allmann Updyke

Right.

Erin Welsh

And I put in some fun ones here and I realized as I was reading for the episode today that I saw in the transcript from smallpox, because I couldn't listen to it, that you have done the same thing.

Erin Allmann Updyke

I know, yeah.

Erin Welsh

We have just a little bit of overlap which is fun. Cowpox, camelpox, mule deerpox, salmon pox, Nile crocodilepox, and so on. Those are just a few of them that I grabbed.

Erin Allmann Updyke

Oh that's funny Erin because in the last one I definitely said dolphinpox and you asked me if there was fish pox and I was like I don't know it just seems like there should be fish pox. And then you said salmon pox. I love it.

Erin Welsh

Salmon pox, yeah. And so this naming convention was how monkeypox got its name. In 1958 a few crab-eating macaques at a polio vaccine research institute started getting sick. About two months after their arrival from Singapore some of these monkeys started showing signs of a pox-like illness. Fever, pustules, swollen lymph nodes. Only about 20% of the monkeys showed any signs of illness although the virus was found in the kidneys of some asymptomatic monkeys, suggesting the potential for a latent infection.

Erin Allmann Updyke

Okay.

Erin Welsh

The outbreak ended pretty soon after it began but not four months later another newly arrived batch of monkeys also from Singapore, held in a completely different room, also came down with this pox-like virus. This time about 30% showed signs of infection. The researchers published their observations and suggested that this pox-like disease could be caused by a previously unrecognized pox virus. Maybe perhaps we should call it monkeypox virus.

Erin Allmann Updyke

Maybe we should.

Erin Welsh

Maybe. This first recorded outbreak of monkeypox at an animal facility was quickly followed by more. The next year monkeys of several different species came down with the infection at a research institute in Philadelphia and then a couple of years after that monkeypox popped up in the primate colony of the Walter Reed Army Institute of Research in Washington, DC. Interestingly this outbreak hinted at what would later be seen in human infections of monkeypox. Several monkeys got sick from the disease but the ones that died had been previously irradiated for some research project, suggesting that this virus posed a greater risk for immunosuppressed hosts. The pattern of monkeypox breaking out in places where animals were held in crowded conditions continued as you might expect with cases popping up in more animal research facilities as well as the zoological garden in Rotterdam, Netherlands in 1964 which was the first time that monkeypox failed to live up to its name exclusively, I guess you could put it. Okay, essentially during this zoo outbreak - I tried to be clever, it didn't work. Not only did a bunch of primate species become infected, orangutans, gorillas, squirrel monkeys, macaques, gibbons, marmosets-

Erin Allmann Updyke

Wow.

Erin Welsh

But so did other non primate species such as giant anteaters.

Erin Allmann Updyke

Oh no.

Erin Welsh

And those anteaters were apparently the source of the outbreak, igniting the outbreak.

Erin Allmann Updyke

Really?

Erin Welsh

Yeah. Even though they're definitely not thought to play a role in the natural history of this virus in the wild. The mortality rate from this outbreak was much higher than had been previously seen. 11 of the 23 affected animals died.

Erin Allmann Updyke

Whoa.

Erin Welsh

Including 6 of 9 orangutans.

Erin Allmann Updyke

Oh god.

Erin Welsh

I know. But more than just showing that this virus could be very deadly and had a wider host range than previously thought, what this zoo outbreak demonstrated was that crowding, multi species mixing, and stress provided the perfect conditions for the transmission of this and likely other viruses. We just keep learning this lesson. Throughout these early outbreaks the warning bells for potential spillover into humans were also sounding, given that monkeypox virus was clearly showing it could infect a number of different species. But so far it was just sort of a faint ringing of bells since none of the animal handlers or research technicians at any of these outbreak sites had gotten sick with the virus. Early papers describing these outbreaks noted that perhaps monkeypox was simply not infectious to humans but they did also point out that all of the people who had come into contact with infected animals had been vaccinated against smallpox.

Erin Allmann Updyke

Aha!

Erin Welsh

Yep. In these papers they acknowledged that it was possible that monkeypox could potentially infect an unvaccinated person but that remained hypothetical until 1970. For the first six or seven years of the 1960s, the smallpox eradication campaign wasn't doing too hot. Funding was limited, projects were understaffed, and smallpox cases didn't seem to be dropping. But by the end of the decade things had really turned around as funding started to flow, agencies began working together, and people got a better sense of the scope of the problem. The smallpox eradication campaign wasn't just about vaccinating every last person, it was identifying where the virus was still circulating so that you could concentrate your efforts in those regions, in those communities. And so a big part of smallpox eradication involved surveys to see where smallpox was or wasn't.

If someone walked into a clinic with a rash or lesions all over their body and a fever that would send up an alert for a smallpox crew to come out, see if it was smallpox, and if it was conduct contact tracing and vaccinate those who were unvaccinated, essentially stop the chain of transmission. And that practice worked really well. Smallpox rates had plummeted by 1970 when one of these alerts of a possible case came in from the Waka Bokaka region of Basankusu territory in the DRC. The last significant outbreak of smallpox in this region had happened in 1968, so two years prior, and since then maybe a few suspected cases but nothing for sure. When public health officials arrived to check out this alert, they found two suspected cases of smallpox. One ended up being chickenpox but the other, the nine month old boy that you heard about in our firsthand account, looked very much like he had smallpox. And as was protocol, his doctor took specimens to verify that it was indeed variola virus. Except it wasn't.

It was monkeypox virus which until this point had not been seen in humans. Initially the reaction to the news of a human monkeypox case seemed almost mixed or uncertain. Was this something to be concerned about or was it just a fluke? Did we only catch it because we're actively looking for smallpox and this happens to look like smallpox? That may be true but it definitely wasn't a fluke because throughout the rest of the 1970s human monkeypox cases popped up sporadically and over a wide geographic range in the DRC, Liberia, Nigeria, Ivory Coast, Sierra Leone.

And although the total case count was low at around the 30s-40s between 1970-1979, it was enough for researchers to draw some patterns. One of these patterns was that human to human transmission seemed very low. Most of the people infected had direct contact with an animal source. Another was that it seemed to predominantly affect children, those young enough to have not gotten the smallpox vaccine. And the third was that there seemed to be a substantial difference in disease severity between the West Africa cases and the Central Africa cases, with infected individuals in Central Africa experiencing much worse illness and a higher risk of death like you discussed Erin, between 1%-5% for the West Africa clade compared to around 10% of the Central Africa clade.

Erin Allmann Updyke

Yeah.

Erin Welsh

But perhaps the most alarming pattern that researchers were observing was the fact that cases seemed to be on the rise.

Erin Allmann Updyke

Yeah.

Erin Welsh

In 1980 smallpox was declared eradicated which meant almost no one was getting vaccinated any longer, although surveillance still continued in many places for a few years, rooting out those suspected smallpox cases that often ended up being chickenpox or more and more likely monkeypox. Like you talked about Erin, the smallpox vaccine provides cross protection against other orthopoxviruses including monkeypox. And with the smallpox vaccination campaign coming to an end that meant a greater and greater proportion of the population was susceptible to monkeypox. And the increase in cases over the '80s and into the '90s and the changing epidemiology of these outbreaks challenged the assumptions previously made about this virus, like human to human transmission being uncommon or that young children were most susceptible or that monkeys were the natural reservoirs for this virus.

From 1980-1986 surveillance identified 338 probable and confirmed cases of monkeypox in the DRC alone which was the country with by far the largest number of cases. The case fatality rate of unvaccinated individuals was around 9.8%, the average patient age was getting older and older, and human to human transmission was much likelier with during the 1980s 28% of cases likely haven't gotten it from an infected individual, another human. Actually observing human to human transmission was alarming but researchers crunched the numbers and came to the conclusion that a monkeypox outbreak could not be sustained without repeated introductions from a primary animal source. I think the lesson here might be just be careful with these assumptions and rules. Because after a few quiet years in the late 1980s and early 1990s, monkeypox made an appearance in 1996-1997 in the DRC when it led to about 88 confirmed cases. In this outbreak 70% of infected individuals reported coming into contact with another human case, while only 27% had known contact with an animal. So that changed very quickly.

Erin Allmann Updyke

Right.

Erin Welsh

And very disturbingly. And the infection chains were getting longer too. It wasn't just you got infected from an animal and you gave it to one other person in your household and it stops with them. Now it seemed more possible for them to pass it on and pass it on and so on down the line. And a big reason for this change was of course vaccination status. In 1980 about 80% of the global population was vaccinated against smallpox.

Erin Allmann Updyke

Wow Erin.

Erin Welsh

I know.

Erin Allmann Updyke

Do we have numbers like that for any other vaccine currently?

Erin Welsh

It's a good question. I'm sure you could compile them.

Erin Allmann Updyke

Yeah.

Erin Welsh

But ready to grab numbers?

Erin Allmann Updyke

That's impressive.

Erin Welsh

Yeah. Well that number has dropped and dropped.

Erin Allmann Updyke

Well logically so.

Erin Welsh

Logically so. And today less than 30% of the global population is vaccinated against smallpox.

Erin Allmann Updyke Does that mean including the people who were vaccinated 40 years ago and who knows if they even have any immunity?

Erin Welsh Right.

Erin Allmann Updyke Yeah, okay.

Erin Welsh Yeah. I guess I should say has been vaccinated.

Erin Allmann Updyke Yeah.

Erin Welsh And we stopped vaccinating for good reason, smallpox was no longer around.

Erin Allmann Updyke Yeah, right.

Erin Welsh And when the threat of a disease is less than potential side effects from a vaccine, the risk calculation changes.

Erin Allmann Updyke Yeah. And the original smallpox vaccine had a lot of potential side effects.

Erin Welsh It did, it did. After this outbreak in the DRC in 1996-1997, sporadic cases of monkeypox continued to pop up in West and Central Africa. But the next big cluster happened in a very unexpected place.

Erin Allmann Updyke I love it.

Erin Welsh I could not believe my eyes when I was reading this. On May 24th, 2003, a three year old girl from Wisconsin was hospitalized with an unexplained fever and rash. Can you think of anything else that was going on in 2003 in the public health sphere?

Erin Allmann Updyke I sure can, Erin. How about SARS-CoV-1?

Erin Welsh SARS-CoV-1. The timing, I could not believe it.

Erin Allmann Updyke I know. Erin listen.

Erin Welsh I know. So yeah, people were understandably a bit freaked out by this unexplained febrile illness. I think we can all relate to that. But her symptoms didn't really fit with SARS. Talking with her mom called up a few more likely suspects because it turns out that the girl and her family had recently attended a swap meet for exotic animals and they came home with a prairie dog that they had purchased.

Erin Allmann Updyke I can't. Okay, I'll let you finish.

Erin Welsh Yeah. This prairie dog was intended to be a pet. And some days later the prairie dog, doing what wild animals do, bit the girl. And later that day the animal started showing signs of illness, discharge from the eyes, enlarged lymph nodes, and skin lesions. A few days later the prairie dog died.

Erin Allmann Updyke Oh gosh.

Erin Welsh: Yeah, I can't imagine how terrifying.

Erin Allmann Updyke: Yeah.

Erin Welsh: And a few days after that the girl was admitted to the hospital. So diseases from prairie dogs, you're probably thinking plague and tularemia.

Erin Allmann Updyke: Yeah.

Erin Welsh: And that's certainly what the doctors thought. But the bacterial cultures came up negative. The girl recovered and the doctors were left with no clear answers until the girl's mother became ill also. This gave them an opportunity for more testing which revealed - tada! - monkeypox virus.

Erin Allmann Updyke: Monkeypox.

Erin Welsh: I know. What? How? How? At this point the virus had only been detected in West and Central Africa and no human cases had occurred outside of those regions, outside of some travel cases. So naturally public health officials began investigating this swap meet, right.

Erin Allmann Updyke: Yeah.

Erin Welsh: Let's find the other prairie dogs this prairie dog was hanging out with. And they turned up a surprising number of cases of monkeypox linked to the swap meet.

Erin Allmann Updyke: Wow.

Erin Welsh: By the end of July, so the first case was May 24th, 47 confirmed or suspected cases of monkeypox had been detected in Wisconsin, Illinois, and Indiana.

Erin Allmann Updyke: Wow. Midwest.

Erin Welsh: The Midwest.

Erin Allmann Updyke: Showing strong.

Erin Welsh: Turns out that an exotic animal distributor in Illinois had gotten a shipment of animals from Ghana via Texas. This shipment consisted of about 800 small mammals.

Erin Allmann Updyke: Oh my.

Erin Welsh: Including species known to be associated with monkeypox, such as rope squirrels and tree squirrels.

Erin Allmann Updyke: Oh dear.

Erin Welsh: Public health officials tested these animals and found that sure enough several of them were infected with monkeypox including some Gambian rats that had been sent to Illinois where they were kept in close proximity to the prairie dogs that were sold to people. And there you go.

Erin Allmann Updyke

And there you go. Monkeypox.

Erin Welsh

Monkeypox. Interestingly as of 2021 no human cases of monkeypox have been reported from Ghana. But it's probably circulating there among wild animals, at least as far as I could find.

Erin Allmann Updyke

I knew that, I have that on my list as well as Ghana but there it has only been identified in animals.

Erin Welsh

Yeah.

Erin Allmann Updyke

Interesting.

Erin Welsh

Yeah. But this outbreak in the Midwest US clearly showed how easy it was for monkeypox to spill over into humans and it led to a ban by the CDC on the importation of any African rodents live or dead into the US.

Erin Allmann Updyke

Wow.

Erin Welsh

Another alarming lesson from this outbreak was how many species the monkeypox virus can infect.

Erin Allmann Updyke

Yeah.

Erin Welsh

Like prairie dogs which likely hadn't ever been exposed to it before.

Erin Allmann Updyke

Yeah and clearly got very sick from it and died.

Erin Welsh

Very sick. I mean can you imagine if the virus had gotten out into a wild population of prairie dogs?

Erin Allmann Updyke

I know.

Erin Welsh

It could have just run rampant and exposed a lot of other animals and it just could go on and on and on. And this I want to say is absolutely still a risk today with widespread travel and transport of not just animals creating opportunities for spillover into humans but also spillback from humans into wild animals.

Erin Allmann Updyke

Yeah.

Erin Welsh

Just important to keep in mind.

Erin Allmann Updyke

Yep.

Erin Welsh

Into the 2000s and 2010s, monkeypox cases continued to climb and the average age of those infected climbed with it. The median age in the 1970s of a person who was infected was four years old, in the 2010s it was 21. Human to human transmission became more common probably for the same reason that the average age was increasing, a decline in smallpox vaccination. And alongside an increased incidence in areas where monkeypox is naturally circulating there have also been higher rates of travel or imported cases where people travel from an endemic country to a non endemic one and bring back monkeypox with them. Although most of the cases of monkeypox have historically taken place in the Democratic Republic of Congo and are from the Central African clade, the West African clade is not far behind with a large outbreak in Nigeria in 2017-2018. This outbreak consisted of 122 confirmed or probable cases and a case fatality rate of 6%.

Erin Allmann Updyke

Wow. That's quite high.

Erin Welsh

It's quite high. So it seems high based on what we know about the West African clade but it turns out that several of the people who died were immunocompromised and others had developed sepsis from secondary bacterial infections and I think another was an infant. And so I think this really highlights how crucial again, how crucial access to healthcare is. Because if you compare this to the outbreak in the Midwest, no one died.

Erin Allmann Updyke

No one died. Yep.

Erin Welsh

And also about this outbreak in Nigeria, the last reported case of monkeypox before this happened 39 years before.

Erin Allmann Updyke

Wow.

Erin Welsh

So yeah.

Erin Allmann Updyke

Interesting.

Erin Welsh

I also want to point out that the case numbers I've mentioned with these previous outbreaks may still seem like low numbers right, 122 cases, 88 cases, 47 cases. But those are just the confirmed numbers generally speaking. Suspected can be much, much higher. Since the few dozens of cases reported in the 1970s, rates of monkeypox have shot up at least tenfold but likely much higher. In the 2000s there were over 10,000 suspected cases of the Central African clade and that nearly doubled the following decade to nearly 19,000.

Erin Allmann Updyke

Wow.

Erin Welsh

In 2020 there were an estimated 6257 in the DRC alone.

Erin Allmann Updyke

Wow! That's way more than I expected, Erin.

Erin Welsh

Me too. And I get your frustration often with these in the current events sections where you're like, 'I don't know the numbers, the numbers aren't good.'

Erin Allmann Updyke

Yeah.

Erin Welsh

And there is a lot of discrepancy between confirmed and suspected.

Erin Allmann Updyke

Yeah.

Erin Welsh

And so I think it's difficult to get a handle on how many of those suspected, how many of those 19,000 were likely to actually be monkeypox.

Erin Allmann Updyke

Right, monkeypox.

Erin Welsh

Compared to chickenpox or something.

Erin Allmann Updyke

I know. It's a huge, huge discrepancy.

Erin Welsh

It is. But what we do know for sure, even if we don't have the best handle on numbers, we do know that cases are going up. This is not just an artifact of reporting or better surveillance, this is a real and concerning increase.

Erin Allmann Updyke

Yes.

Erin Welsh

And part of what makes it so concerning is how much we still don't know about this virus. I mean don't get me wrong, we know a lot, people have studied this virus for years, we have a vaccine specific to monkeypox, we're well ahead of the game compared to how we were with SARS-CoV-2 and COVID at the start of the pandemic.

Erin Allmann Updyke

Yeah.

Erin Welsh

But there are still huge gaps in our knowledge. For instance the reservoir species.

Erin Allmann Updyke

Right.

Erin Welsh

It's been found in some wild animals such as a Thomas's rope squirrel, a tree squirrel, the Gambian pouched rat, a sooty mangabey. But we still don't know for sure the primary source of many of these outbreaks or even if there is just one reservoir species compared to several, whether the West African clade has a different ecology or reservoir species compared to the Central African one, etc. The ecology in general of this virus is not well understood which makes it difficult to predict when and where outbreaks might occur, what time of year, what region, and so on. People have done some really cool ecological niche modeling trying to look for patterns in where past cases have occurred to see if we can get a framework for where future ones might happen but we still have a long way to go, the knowledge gaps are just almost too great. And crucially we need to consider this disease from a one health perspective.

Erin Allmann Updyke

Yeah, we do.

Erin Welsh

We'll never get sick of saying that.

Erin Allmann Updyke

Nope.

Erin Welsh

Researchers have pointed to four primary reasons for monkeypox reemergence and outbreaks, several of which are very much one health aligned. Number one, increased contact between humans and wildlife due to habitat encroachment from urbanization and hunting. Number two, wildlife trade especially of rodents. Number three, ecological and climate shifts bringing animals and humans closer together. And number four, increased proportion of population that is not vaccinated against smallpox.

Erin Allmann Updyke

Yeah.

Erin Welsh

I would also like to add a fifth reason and that is increased global travel.

Erin Allmann Updyke

Yeah.

Erin Welsh

So I'm really curious Erin to hear you bring us up to speed on this ongoing monkeypox epidemic and maybe a question that I feel like we haven't asked in a long time, how scared we need to be.

Erin Allmann Updyke

Yeah, we haven't asked that in a very long time. Let's take a quick break and I'll see if we can, I don't know, come to an answer.

TPWKY

(transition theme)

Erin Allmann Updyke

So just as a reminder, all of that you heard, the history and the biology section were recorded on June 9, 2022. Today we are recording on July 6, 2022. So that is how up to date our data is. Let's get into it, shall we? Prior to this current outbreak that's ongoing, monkeypox was considered endemic in a number of countries across Central and West Africa. In these countries the World Health Organization collects data from an integrated disease surveillance and response system, that's what it's called, which is still in place and was in place prior to this current outbreak. And I want to kind of emphasize here that in these endemic areas every year there are both confirmed and even greater numbers of suspected cases of monkeypox and very often there are deaths that occur every year. So I kind of want to just say that upfront because although this current outbreak that's making headlines is important and it is worthy of these headlines, monkeypox was also important even before this outbreak and we shouldn't only care about diseases when they infect people in Europe or in the US. I think it's very easy to ignore infectious as well as chronic diseases that seem to only affect people living far away or in rural areas or impoverished areas, etc.

Erin Welsh

Yeah, absolutely.

Erin Allmann Updyke

Yeah. So that's up top. But this outbreak is still very significant, So let's get into the details of it. I believe that I mentioned this earlier in this episode But I'll reiterate that any single case of monkeypox that was detected outside of previously considered endemic countries is considered an outbreak. All it takes is one case. And the vast majority of cases that we have seen prior to this, like you discussed in the history section Erin, have been either small geographically or very small numerically, associated with travel or something like that. And today very new things are happening. So this outbreak that is going on between May and so far July of 2022 ongoing was first reported to the World Health Organization on May 13th when two confirmed and one probable case were reported all from a single household in the UK. And then two days later on May 15th, four more confirmed cases were all reported. All these all of a sudden. And these cases through all of the investigation that people could do seemed to have been acquired in the UK and were not related to any travel, especially any travel to endemic areas or any other travel-associated cases.

Erin Welsh

So no one knows the ultimate origins necessarily of monkeypox but those were just the first reported cases, not necessarily the first cases cases.

Erin Allmann Updyke

Exactly. So as we see these numbers pile up, it turns out that there were likely many other cases that people became symptomatic with much earlier than May 13th. But this was just the first that were reported to the World Health Organization.

Erin Welsh: Gotcha.

Erin Allmann Updyke: Yeah. Now since May, since that time these case reports have been piling up.

Erin Welsh: Yeah.

Erin Allmann Updyke: By May 21st it was 92 confirmed cases. By May 26th, 257. By June 8th before our last recording, over 1000 confirmed cases in 29 countries. And now at the time of this rerecording, July 6th, over 6000 cases have been confirmed in 58 countries.

Erin Welsh: And just to clarify, those countries are countries where monkeypox has not been known to happen previously?

Erin Allmann Updyke: Well here is where things get a little bit confusing.

Erin Welsh: Okay.

Erin Allmann Updyke: And the importance of surveillance and good data to begin with is really exemplified. So between January and June of 2022, in the World Health Organization African Region where this is an endemic disease there have been several thousand, over 1500 suspected cases but just over 70 confirmed cases. And so now as of July the World Health Organization is not reporting those separately, they're counting everything in this year as all part of this outbreak, if that makes sense.

Erin Welsh: I see, okay.

Erin Allmann Updyke: So that number, 6000, includes in both endemic and non endemic countries and the majority of these cases in this current outbreak, about 80% have been reported in the World Health Organization European Region.

Erin Welsh: Gotcha.

Erin Allmann Updyke: Yeah. It's also important to note that in this outbreak there has only been one death reported which happened in Nigeria. However there had been over 60 deaths that were suspected to be due to monkeypox but were not confirmed. Those happened in endemic regions before May of this year.

Erin Welsh: Okay.

Erin Allmann Updyke: And so it seems like both for streamlining of data reasons but also to reduce this stigmatization and idea that there is separate things going on in endemic countries and non endemic countries right now, the World Health Organization's reporting only confirmed cases at this point and deaths only due to confirmed cases and everything is part of this outbreak, if that makes sense, once it's a confirmed case.

Erin Welsh: Yeah.

Erin Allmann Updyke

And so obviously this outbreak with these numbers and in the number of countries that we are seeing is drastically different from any monkeypox outbreak that we have seen before and it's in a number of different ways. So what I want to do is kind of go over some of the ways besides just the numbers and the geographic spread in which this outbreak is different and see if I can answer some of the questions as to why.

Erin Welsh

Yeah.

Erin Allmann Updyke

I'll do my best. So first, in this particular outbreak the disease seems to be presenting in some cases with a rather different clinical presentation than that classic presentation that I described in the biology section. So some people seem to not be reporting quite as much of the constitutional symptoms. Those are things like fevers, malaise, overall feeling really sick. Some people don't have those at all. And people seem to have lesions in some cases at least in different stages of development at the same time.

Erin Welsh

Which is very interesting.

Erin Allmann Updyke

So fascinating to me. And that's like we talked about something that's more typical of a varicella, chickenpox, but very much not typical of what we've seen with monkeypox or other pox viruses in the past. Another thing that's different is a lot of people are being identified through sexual health or primary healthcare clinics presenting with lesions primarily in the genitals and perianal region. They are classic monkeypox-looking lesions but starting on the genitals rather than the head or mouth like we've seen in the past. And in some cases they aren't always spreading to the entire body.

Erin Welsh

I think these differences are really interesting because what I'm very curious about is whether these represent new characteristics of a new manifestation of this disease or just things that we previously haven't captured in past outbreaks because surveillance maybe was not that high and it was sort of like unless you had a clear case of monkeypox then, yeah.

Erin Allmann Updyke

Yeah, that is the exact question that everyone is trying to answer. We don't have a full handle on it but I'll get into a little bit more detail that helps us get there.

Erin Welsh

I have a quick question though before we do that. So we have a vaccine for monkeypox.

Erin Allmann Updyke

You're just jumping ahead on all my things.

Erin Welsh

I know, I know, I know. But this is about sort of outbreak control. So when somebody is diagnosed with monkeypox, what happens to them in terms of the treatment that they get, the care that they get? And then public health-wise, what happens to their contacts?

Erin Allmann Updyke

Yeah, excellent question. So first, if somebody presents to their clinic with things that look like monkeypox, especially now that everyone is aware that this is the thing that's happening, ideally samples from these lesions are going to be taken and they're going to be tested to see if it is truly monkeypox. If it is, there is treatment that's available. There is an antiviral that was very recently approved for treatment of smallpox as well as monkeypox. So especially if someone is very, very sick, then hopefully they would have access to that kind of antivirals. I truly don't know what the status of antiviral access is across the world and I suspect it's relatively limited since it's a pretty new antiviral and historically this disease has not been so prevalent. But they do exist. Then isolation is going to be really important.

So a person should avoid close contact with other people, especially contact with the lesions themselves. And then is when comes the real like what we call boots on the ground epidemiology where epidemiologists will come in and say okay, let's go over everywhere that you've been, everywhere that you've traveled in the preceding 2-3 weeks most likely since this is a relatively long incubation period virus. Everyone that you've been in contact with, everyone that you've maybe lived with or shared a bed with or just been in very close contact with. And then those people will be contacted to see if they've developed any symptoms and also just to be made aware that A) if they have symptoms they should isolate and B) they should be on the lookout for symptoms. The last piece of that puzzle is that people who were very, very likely to have been exposed, it is also possible to do what's called post exposure prophylaxis with a vaccine. So we have two different vaccines that are available. And you can do vaccination, I've seen different reports but up to a number of days after exposure and potentially drastically reduce the risk that you would go on to get infected.

Erin Welsh

Okay, cool. Thank you. Yes, I know it was jumping ahead but I just wanted to have in my head step one, step two, step three, what does this look like.

Erin Allmann Updyke

That's okay. Yeah. Like what actually happens?

Erin Welsh

Yeah.

Erin Allmann Updyke

That was a good question. Where were we?

Erin Welsh

We were in talking about symptoms.

Erin Allmann Updyke

Yeah, that's right. So yeah, those are all the symptoms that are a little different. Some symptoms like the lymphadenopathy seem pretty consistent and plenty of people are still presenting with relatively classic-looking monkeypox, so that's important to point out. In very good news reporting the overall fatality rate has been exceedingly low compared to what we've seen in a lot of other cases and outbreaks. So far only one confirmed death from monkeypox.

Erin Welsh

And is that likely due to just access to healthcare?

Erin Allmann Updyke

Well that probably plays a big role but all of the samples that we have been able to identify so far come from that West African, we know that's not a good name, but the West African strain which is much less virulent and this one in particular seems to be even less so. When it has caused outbreaks in the past, it's actually had a mortality rate of less than 1%.

Erin Welsh

Okay.

Erin Allmann Updyke

So this strain in particular seems to have a much lower mortality rate, much less virulent. So that's very good news.

Erin Welsh

Gotcha. Yeah.

Erin Allmann Updyke

So I think a lot of people probably have the question and you kind of asked it a little bit Erin already and that is why is this spreading so rapidly? How can this outbreak be so much bigger than any that we've seen before?

Erin Welsh

Yeah.

Erin Allmann Updyke

And there's kind of a lot of different possibilities. So is it because like I described the symptoms seem to be a lot more mild? So are people spreading it more easily because they just don't realize that they're infected? Maybe. We don't really know because like you said we don't maybe have the best data to begin with to know how much was this virus potentially circulating undetected across the globe potentially.

Erin Welsh

Right.

Erin Allmann Updyke

Another possibility is is this particular virus different than other strains? Is this particular strain more infectious or more easily transmitted especially from person to person?

Erin Welsh

Is it?

Erin Allmann Updyke

Maybe, maybe. We don't really know. We do have some pretty limited data just about what we know about how different this particular strain is from a very closely related one that had caused a few cases in 2018-2019 that were mostly travel-associated. So this particular virus is closely related to that one which caused a number of cases but it has at least 50 new mutations that have not been seen before or were not present in that 2018-2019 cases.

Erin Welsh

Okay, questions here.

Erin Allmann Updyke

Okay.

Erin Welsh

Number one. Sorry, I know you were intaking a breath to continue on.

Erin Allmann Updyke

I was.

Erin Welsh

But I can't stop myself from interrupting.

Erin Allmann Updyke

I love it.

Erin Welsh

Okay. This is a DNA virus.

Erin Allmann Updyke

That's my next sentence, Erin.

Erin Welsh

Perfect. So A) that's a high mutation rate for a DNA virus, right?

Erin Allmann Updyke

It sure is, Erin. It's about way higher, I think we would have estimated so this is like 50 mutations in about 3-4 years. We would expect probably like 1-2 or so a year.

Erin Welsh

Okay. B) or 2), I don't know what I started with, so we have available data to kind of look at that same trend with other monkeypox strains in the past?

Erin Allmann Updyke

Fascinating question, Erin. As far as I can tell I don't think so.

Erin Welsh

Okay. Or at least we haven't done the genomic analysis.

Erin Allmann Updyke

Right, not yet. Not yet. But there's a lot of thought just based on I think not only perhaps the mutations that we're finding but also just comparing the mutations in this virus to the way that other viruses mutate, especially zoonotic viruses. Remember that this has primarily been an animal to human spillover type virus. So there is thought that perhaps this is the result of microevolution. So small changes to be better adapted to evade our human immune response, essentially getting more specific to infecting humans.

Erin Welsh

Okay. So these are not necessarily just random mutations, these are actually functional potentially.

Erin Allmann Updyke

Potentially, yeah. Potentially yes, that's kind of the thought. Because that would help explain why now, right. If this virus picked up these mutations that made it really easy to be transmitted, then it makes sense. It's going to transmit a lot more efficiently.

Erin Welsh

I mean it makes sense but that doesn't make it any less scary.

Erin Allmann Updyke

No, it makes it a lot more scary. But on the flip side it does again seem to be a very, very low mortality rate compared to most other strains that we've seen.

Erin Welsh

Plus we have treatment and vaccines.

Erin Allmann Updyke

Plus we have treatment and vaccines. The other thing that is different about this outbreak that's very important for us to talk about for a lot of reasons is that especially very early in this outbreak in May and June when cases were rolling in, these cases were primarily being reported in men who have sex with men, that's the public health terminology. And when we are in an outbreak situation, a new disease, what have you, it is really, really important to get information as accurate as we have it out and available to the public as quickly as we can so that public health agencies are aware, so that clinicians and health systems can be aware and be on the lookout, so that if more active surveillance needs to be enacted, it can be. And so when there are epidemiological characteristics that link cases together such as in these early reports of quote "in individuals who self identify as men who have sex with men", this is important information because it can help us inform both groups or individuals who are at risk as well as the public health infrastructure at large how to react and how to reduce overall risk, right.

That's imperative information. The problem is especially because of our society's obsession with othering and ostracizing people in general as well as the historic and continued marginalization of gay men, bisexual men, transgender and genderqueer individuals, many of whom are going to fall into this category of men who have sex with men, because of this particular dynamic at play, it's very easy to make it seem as though this is an other problem which can lead to a lot of stigmatization. And not only is that problematic but it also makes it really easy to miss a lot of potential transmission.

Erin Welsh

Right.

Erin Allmann Updyke

And the World Health Organization agrees that that is very likely what has been happening. Based on the rapidity with which we have seen case numbers rise and how long the incubation period is for this disease, this is something that's been circulating for some time but is now being diagnosed.

Erin Welsh

I feel like you use epidemiological characteristics of a disease, patterns of an infectious disease, to prevent it from spreading further and to control. But it seems like what can often happen and what does happen is instead of using those to tell you okay, who might most be at risk? How can we best use this information to control? Instead it's like putting blinders on and being like we only are going to look for it in these individuals.

Erin Allmann Updyke

Right. Or we're going to say well I'm definitely not at risk because that's not me, I don't fit into that bucket.

Erin Welsh

Yeah.

Erin Allmann Updyke

Right. And it's just not good.

Erin Welsh

Yeah.

Erin Allmann Updyke

So yes, in this particular outbreak people who identify as men who have sex with men were possibly some of the first to be exposed or at least the first ones to pay attention and notice a rash and go and get it checked out. And that is still important information for us to have. And what's interesting is that the question that has been raised a lot because of this particular route of transmission is the question of is monkeypox an STI? Is this a sexually transmitted disease now? And the answer is essentially no, not really because as far as we know this is still a disease that is transmitted the way that monkeypox has always been transmitted and that is by close contact. Sexual contact is one type of close contact but any sharing of things like clothes or bedding, any touching of skin lesions, and potentially respiratory droplets or very close range aerosols, given that this virus can be in the saliva or lesions could go undetected in the mouth really is what it comes down to, the same way that they can be undetected on the genitals.

Erin Welsh

Right.

Erin Allmann Updyke

So there's a lot of questions of is this a sexually transmitted disease? And in some ways it's an interesting and important question. Is this virus particularly being housed in say cervical secretions or in semen or something like that? But what it boils down to is that we know that it's the viral particles in these lesions that are on your skin that are infectious.

Erin Welsh

Yeah.

Erin Allmann Updyke

And because sexually transmitted infections are often very highly stigmatized I think it's pretty important to push back against that in this case, especially early on when we really don't know the full extent of this epidemic, pandemic, what have you.

Erin Welsh

Yeah.

Erin Allmann Updyke

Yeah, Erin. That's what's going on as far as we know. We already talked about everything that we're doing to kind of prevent it and help prevent the spread, a lot of that is making the public aware. And so hopefully we're helping with that at least a little.

Erin Welsh

I have one last question for you.

Erin Allmann Updyke

Give it to me, Erin.

Erin Welsh

How scared do we need to be?

Erin Allmann Updyke
Yeah. We haven't asked that question in so long. I would say this is something that the public health powers that be are taking very seriously and are working really, really hard to interrupt this chain of transmission. But overall for most of the 8 billion people in this world this is still something that at this point is pretty low risk overall. It is transmitted in a much more limited manner than something like SARS-CoV-2 for example. It's also generally a self limited disease in terms of severity, we have not seen mortality like we saw and are still seeing with COVID for example. But it is also spreading a lot more rapidly and one of the things that I think about is if it makes its way into wild or domestic animal populations it could definitely establish and become an endemic disease worldwide. Same thing if this virus has really become very well adapted to humans and is now just being very easily transmitted person to person. So it is a big deal for those reasons.

Erin Welsh
It seems like there is cause for concern and there's cause for hope.

Erin Allmann Updyke
Yeah.

Erin Welsh
And I guess the future will tell us how we should have been feeling in retrospect at this moment.

Erin Allmann Updyke
Yeah. I think maybe. I think that people are really paying a lot of attention and so for me that gives me a lot of hope.

Erin Welsh
Yeah.

Erin Allmann Updyke
Yeah.

Erin Welsh
Well maybe we'll be back with a miniseries.

Erin Allmann Updyke
I hope not.

Erin Welsh
I hope not too. I really hope not.

Erin Allmann Updyke
Actually TWiV, This Week in Virology, has been doing a lot of updates. So if people are interested especially in really deep dives on the virology of this, they've got the deets, it's another podcast, check it out.

Erin Welsh
For sure, good rec.

Erin Allmann Updyke
Well then.

Erin Welsh
Well then.

Erin Allmann Updyke
Sources, speaking of?

Erin Welsh
Sources. I have several, a bunch but I'm just going to shout out two. One on monkeypox virus evolution by Babkin et al from 2022 called 'An update of orthopoxvirus molecular evolution'. And then there was a great paper from 2022 in PLOS Neglected Tropical Diseases called 'The changing epidemiology of human monkeypox - A potential threat? A systematic review'.

Erin Allmann Updyke
Can confirm that's a great paper.

Erin Welsh

It's a great paper.

Erin Allmann Updyke

I also had quite a number of papers. One that I liked for the clinical aspect, there was a few but one in particular was just called 'Human monkeypox' and it was in Clinical Infectious Diseases from 2014. There is a very interesting paper with more detail about the specific strain that is causing this outbreak, it's a pre-print from Nature Medicine 2022, obviously I will link to that as well as the World Health Organization page where they are posting all of their disease outbreak news updates. But you can also follow them on Twitter for very rapid fire updates on the state of monkeypox today.

Erin Welsh

Thank you to Bloodmobile for providing the music for this episode and all of our episodes.

Erin Allmann Updyke

Thank you to Exactly Right network.

Erin Welsh

And thank you to you listeners. We hope that you found this episode helpful.

Erin Allmann Updyke

I hope so.

Erin Welsh

And informative.

Erin Allmann Updyke

Yeah. And a special shout out to our patrons. Thank you so much for your support, we can't express how much it means to us.

Erin Welsh

Truly, truly, truly. Okay well until next time, wash your hands.

Erin Allmann Updyke

You filthy animals.