

Erin Allmann Updyke

"The laboratory assistant Marga K. had worked since March 1967 in the Marburg Serum factory. Her job was to fetch newly removed kidneys from the postmortem room to clean them and to prepare them for further processing. The prescription was that she had to wear gloves and mouth cover in order to avoid the contamination of the cultures. Occasionally she helped with the fixation of the killed animals on the examination table. On August 18, 1967, malaise and myalgia took place. On the following day she developed fever up to 39 Celsius. On August 20th, the third day, for the first time vomiting occurred. One day later burning and reddening of the conjunctiva. The temperature now rose to 40 Celsius.

On the fifth day, she was admitted to our infectious ward. At this time there appeared in the face, on the trunk, and on the proximal parts of the extremities a macular-papular rash, a red enanthema of the soft palate that reached to the hard palate. There were enlarged lymph nodes at the neck, along the sternocleidomastoid, and in the axillaries. On the sixth day, the conjunctivitis decreased, the vomiting went on, and a watery not mucous or bloody diarrhea occurred which made an intravenous substitution of fluid and electrolytes necessary. On the eighth day, a diffuse cutaneous erythema developed over the whole body, the diarrhea went on, the vomiting stopped. On the ninth day the state of health improved significantly, the diarrhea decreased. In the 27th day the skin began to peel off, especially in the face, the palms, and the lower extremities. On the 36th day after the beginning of the illness, the patient left the hospital. She did not show any more clinical signs but the reconvalescence was delayed and she continued feeling weak for several weeks."

TPWKY

(This Podcast Will Kill You intro theme)

Erin Welsh

Ooh.

Erin Allmann Updyke

That does not sound good.

Erin Welsh

No, that's a long course.

Erin Allmann Updyke

But she did survive.

Erin Welsh

She did survive.

Erin Allmann Updyke

Yeah.

Erin Welsh

Yes. So that was a case history of Marburg virus disease in a chapter titled 'Clinical Syndrome' by G. A. Martini in a book called 'Marburg Virus Disease' published in 1971. So it was like the first and still in many ways is like the definitive textbook of that outbreak in 1967 that we'll talk about.

Erin Allmann Updyke

Yeah. Wow.

Erin Welsh

Yeah. Hi, I'm Erin Welsh.

Erin Allmann Updyke

And I'm Erin Allman Updyke.

Erin Welsh

And this is This Podcast Will Kill You.

Erin Allmann Updyke

Today, if you haven't clued in, we're talking about Marburg.

Erin Welsh: We are. Yeah. There are a lot of reasons to cover this disease. Most pressing is that it's been in the news lately.

Erin Allmann Updyke: Yeah, there is an ongoing outbreak as of the day of recording, which is April 4, 2023. The outbreak remains ongoing so we'll get there eventually.

Erin Welsh: We will, we will. Yeah. Yeah. But first-

Erin Allmann Updyke: It's quarantini time!

Erin Welsh: It is. What are we drinking this week?

Erin Allmann Updyke: We're drinking, in honor of Ebola, Still Spilling Over.

Erin Welsh: Yep. If you are a long time loyal listener-

Erin Allmann Updyke: Very long time.

Erin Welsh: Or you're just someone who happened to listen to our Ebola episode that came out over five years ago, five years ago in 2018.

Erin Allmann Updyke: 5 and half.

Erin Welsh: 5 and a half. Yeah. You may remember that in our Ebola episode, we titled our drink Spillover because of the fact that like many other viruses and other pathogens, Ebolavirus spills over into humans. And guess what? So does Marburg virus. So we're still spilling over here. And also they're closely related which like maybe that's jumping the gun but...

Erin Allmann Updyke: Yeah.

Erin Welsh: In any case-

Erin Allmann Updyke: What's in Still Spilling Over, Erin?

Erin Welsh: In Still Spilling Over it's kind of like a variation of the original Spillover. And so it contains Mezcal and maple syrup and sparkling lemonade. And I don't know, like a slice of an orange or a lime. I don't know. But the point is you fill it to the very top so that it almost spills over.

Erin Allmann Updyke: All the way.

Erin Welsh: But you don't want it to spill over because it's not great when that happens.

Erin Allmann Updyke: I like it.

Erin Welsh: Yeah.

Erin Allmann Updyke: We'll post the full recipe for that quarantini as well as our nonalcoholic placeborita on our website thispodcastwillkillyou.com and all of our social media channels.

Erin Welsh	We certainly will. Okay, podcast business. We've got website.
Erin Allmann Updyke	Check it out.
Erin Welsh	Check it out. It's got lots of good stuff, transcripts, links to many things. It's a good resource. And in other podcast news, we will be back to our regularly scheduled programming next week. So we will be releasing one of our special episodes, our Book Club episodes, the following week there will be a normal regular season episode and we'll do a little bit of that until we wrap up our bonus episode series. But from this point on, we are back to at least one new regular season episode every other week. I think that about does it for business.
Erin Allmann Updyke	I think so too. Shall we get into the biology of Marburg virus?
Erin Welsh	Let's do that please, right after this short break.
TPWKY	(transition theme)
Erin Allmann Updyke	So as you alluded to Erin, for long time listeners of this show, the episode today on Marburg virus may sound hauntingly familiar in a lot of ways and that's because this particular virus, Marburg virus, is very closely related to Ebolavirus which we covered in our very first season. Ebolavirus is a pathogen whose name still makes people usually unnecessarily absolutely lose it with terror. And Marburg virus is a very close relative. So it's probably unsurprising that a lot of what I'm going to talk about seems very similar. Let's get into it. Marburg virus, it's an RNA virus in the family Filoviridae which includes essentially just Ebolavirus and Marburg virus in terms of human viruses. I did learn there's a newly discovered filovirus called Lloviu virus, it's in the genus Cuevavirus.
Erin Welsh	Yeah.
Erin Allmann Updyke	It was discovered in 2011 in Spain in bats. That's all I know about it. So moving on. Literally just didn't know about it until today.
Erin Welsh	Okay.
Erin Allmann Updyke	So Marburg looks under the microscope a lot like Ebolavirus, it's kind of that filamentous curvy long shape. And while Ebolavirus has several different species, Marburg virus is literally just one species of virus, it's Marburg Marburgvirus. It does have several different lineages and there are two classifications of virus, Ravn virus and Marburg virus. Virus phylogeny is very confusing but in short, they're both the same species of virus, they both cause disease in humans, and from now on will just be called Marburg.
Erin Welsh	Sounds good.

Erin Allmann Updyke

So this is a virus that thankfully, as you will see as I continue through the description of its symptoms, has caused relatively limited scale disease in humans and very limited scale outbreaks for the most part. It is not something that has to this point very commonly caused disease. Primarily disease in humans is happening, like we mentioned in the intro, from spillover events from zoonotic reservoirs, a lot of times bats and in some cases nonhuman primates, though it seems that this has really only happened in laboratory settings and not in kind of non laboratory settings. But it can and does also spread person to person. And transmission tends to be like with Ebolavirus via direct contact with bodily fluids. That means blood, saliva, sweat, stool, urine, literally any and all bodily fluids as far as we have studied. The incubation period, the time between when someone is exposed and starts to show signs of disease, can really range between 2-21 days.

Erin Welsh

It's such a huge range. It's so interesting.

Erin Allmann Updyke

I know. And I think, I mean there's a lot that goes into that like what's the infectious dose? But also how much data do we have on this?

Erin Welsh

Right. Not much.

Erin Allmann Updyke

Not much. On average it seems to be like 5-10 days for the most part.

Erin Welsh

And when is someone first contagious?

Erin Allmann Updyke

Great question. First contagious potentially as soon as symptoms start, but like Ebola, the most contagious towards the end of convalescence as this virus builds up in those bodily fluids.

Erin Welsh

Okay.

Erin Allmann Updyke

And in some cases potentially contagious for quite some time because like with Ebolavirus, we have found this in bodily fluids even after somebody recovers from a Marburg virus infection.

Erin Welsh

Right. Which is like part of the question around ecological sources of infection.

Erin Allmann Updyke

Exactly.

Erin Welsh

Yeah.

Erin Allmann Updyke

Right.

Erin Welsh

It's difficult.

Erin Allmann Updyke

Yeah. I couldn't get a sense of what the R-0 is, the reproductive value of Marburg, largely most likely because there have been relatively few outbreaks and with two exceptions, all of these outbreaks have been very small in size, which is a good thing. And I'll mention more about this but the World Health Organization has like a powerpoint that they developed recently on ring vaccination strategies. And in that the World Health Organization at least estimates an attack rate of 1%-2%. So that means that in say close contacts, 1%-2% of close contacts of an infected person, in their models at least, are susceptible to infection or are likely to get infected.

Erin Welsh

That's lower than I thought. That's interesting.

Erin Allmann Updyke

Yeah, yeah. Which is a good thing.

Erin Welsh

That's great. Yeah.

Erin Allmann Updyke

But again, very limited data on that. So grains of salt a-plenty. In terms of reservoir hosts, bats are thought to be the primary reservoir host of Marburg virus as with Ebolavirus, specifically the common Egyptian fruit bat, *Rousettus aegyptiacus*, I think seems to be a really big contender at least from the data that we have so far though it has been detected in other bat species as well and can infect nonhuman primates and possibly others that we just don't know about. So let's get in to the symptoms, shall we? The symptoms have been broken down into three major phases of disease. An initial phase sometimes called a generalized phase, an early organ phase, and then either a late organ phase, which is not good, or a convalescent phase, which is better but as we heard in the first hand account can be very prolonged.

Erin Welsh

Yeah, okay.

Erin Allmann Updyke

So this initial phase tends to start with a fever. Often a pretty high fever, 39-40 Celsius, so that's like 102-104 Fahrenheit.

Erin Welsh

Oh dang, that's high.

Erin Allmann Updyke

It's pretty high. Often a severe headache, chills, muscle aches, malaise, and sometimes kind of a prostration, like not really being able to move beyond just laying down because of all of these body aches and kind of general symptoms. Most of the time, like 50%-75% of the time, this then is followed within the next couple of days by pretty significant gastrointestinal symptoms. So lack of appetite or anorexia, abdominal pain, nausea, vomiting, diarrhea, the whole shebang of GI symptoms. This then often progresses to sores in the mouth and sores probably in the throat because a lot of pain with swallowing and some difficulty swallowing. And all of that is happening over the course of 4-5 days, so days 0-5.

Erin Welsh

That is a rough 4-5 days.

Erin Allmann Updyke

It is. And people are clearly very, very sick at this point. But all of those symptoms are also pretty nonspecific.

Erin Welsh

Yeah.

Erin Allmann Updyke

It's called generalized because it's really just affecting your kind of whole entire body. After this phase, usually after about day 5 or so, there might be a rash and this rash is called maculopapular. We've talked about this type of rash a lot of times. It isn't very specific. But in the case of Marburg, it tends to happen on the back, the trunk, and the neck and kind of relatively limited to those areas at least at first. And maculopapular means it's little spots with maybe little raised bumps in the middle. And this type of rash might be the first thing that makes it seem less like a malaria or an influenza and more like a Filovirus infection, an Ebola or a Marburg.

Erin Welsh

Okay.

Erin Allmann Updyke

These symptoms then continue to progress to things that are resulting more directly in organ damage. And this is when we enter the early organ phase. You're likely still experiencing all those other symptoms that I already mentioned but now new symptoms are starting to arise, like neurologic symptoms, encephalitis, confusion, behavior changes. You might also start to see signs of vascular permeability, so that means leaky blood vessels. So depending on where blood vessels are leaking, that might look like difficulty breathing if your lungs are starting to get fluid in them. It might be generalized edema or swelling if it's kind of just underneath the skin in your arms or your legs. And then it may and often does progress to some kind of clear evidence of hemorrhage. Marburg virus is a viral hemorrhagic fever.

So this evidence of hemorrhage bleeding could be petechiae which are little pinpoint purplish spots that you see underneath the skin. Or it might be mucosal bleeding, like bleeding from the nose or the gums. It might be bleeding into the eyes, so conjunctival injection. Or bloody diarrhea, bloody vomiting, or even just easy and large bruises that appear with seemingly very little pressure. So all of this is going on from about day 5 until about day 13. And it's not just these signs that are easily visible. What's happening inside of the body is also this direct damage to the organs. So in terms of what we see on laboratory values, we see evidence of kidney damage, we see evidence of liver damage, pancreas damage, even discrepancies in blood counts like increases or decreases in white blood cells and platelets, etc.

At this point people either succumb to this overwhelming infection, their organs cease to function, they develop even worse neurologic symptoms, and eventually progress to severe shock, multiorgan failure, and death. And this tends to happen between days 8-16 after the onset of symptoms, so kind of towards the end of that early organ phase. And death most often is coming directly from shock and from organ failure, from all of this leakage from the blood vessels and just your organs not being able to keep up. And again, that usually happens by about day 16. If people don't die, then this is the time period in which they start to show signs of remission and then have a pretty prolonged course of convalescence as they slowly recover. This can happen over weeks to months.

Erin Welsh

What is the virus doing?

Erin Allmann Updyke

Yeah. Replicating and replicating and replicating.

Erin Welsh

In what cells?

Erin Allmann Updyke

Yeah. So how can this virus make us so sick? So the answer, I mean as always is we don't fully understand, blah, blah, blah, we know that. But we do know that the way that this virus makes us so sick is at least in part due to its tropism, the cells that it's infecting. So we are being exposed, this virus is getting into our tissues and our bloodstream, either through our mucous membrane or from breaks in our skin, right, from direct contact with infected bodily fluids into our mucus membranes or breaks in our skin. From there, this virus tends to infect cells first like our macrophages, our dendritic cells and other of our white blood cells.

But then they have a tendency to infect our endothelial cells. These are the cells that line our blood vessels, right, in all of our various organs, which means not only can this virus spread anywhere cell to cell as they replicate, but they also can then as they break out of these cells to go on and infect other cells cause that leakiness of the blood vessels, right. Because they're directly damaging especially the basement membranes, the bottom part of these endothelial cells that line all of our blood vessels. It's not only our endothelial cells. Marburg virus can also infect our liver cells themselves, so they can cause direct damage to our hepatocytes, our liver cells. And they infect a lot of other lymphatic tissues besides just our macrophages and other white blood cells. So in doing that, they're causing damage to our spleen, our lymph nodes, and that's just making it even harder for our body to fight off this virus.

Erin Welsh

Jeez. Okay.

Erin Allmann Updyke

But in addition to the direct damage to our cells and our endothelial cells, Marburg virus, much like its cousin Ebola, interacts very heavily with our innate immune system. So it causes an additional and kind of spiraling inflammation in ways that we, say it with me, don't fully understand.

Erin Welsh

Don't fully understand.

Erin Allmann Updyke

But we know that they're really important in the overall development of that severe organ dysfunction and shock and death, right. It's the damage to the tissues themselves caused directly by the virus and it's the way that this virus upregulates our own immune system to then cause this spiraling inflammation.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah.

Erin Welsh

This is interesting.

Erin Allmann Updyke

Yeah.

Erin Welsh

And in nonhuman primates does the course of disease look fairly similar?

Erin Allmann Updyke

As far as I understand, yes.

Erin Welsh

Okay.

Erin Allmann Updyke

Pretty similar. Nonhuman primates are definitely the kind of model species because of that, because it infects nonhuman primates and causes very similar disease. It's been difficult to find good animal models for Marburg virus and Ebolavirus in other animals other than nonhuman primates, which are really difficult to work with in the lab for a lot of reasons.

Erin Welsh

So if you are fortunate and you enter the convalescent stage, do you have lifetime immunity?

Erin Allmann Updyke

Great question.

Erin Welsh

Or at least any immunity.

Erin Allmann Updyke

That's a really good question. I didn't read that specifically but I know there's pretty good immunity that comes from Ebolavirus and there's a lot of work being done on vaccines. So I suspect that you develop pretty robust immunity if you do survive a Marburg virus infection.

Erin Welsh

Okay.

Erin Allmann Updyke

But I don't know kind of the longevity, how forever it is kind of a thing.

Erin Welsh: And do we know anything about like again, in the people who recover from Marburg virus disease, are there long term effects? Or is it just like again we're dealing with such few numbers that it's...

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah. Okay.

Erin Allmann Updyke: That's what it is. We're dealing with such few numbers that we don't have data on it.

Erin Welsh: Okay.

Erin Allmann Updyke: Probably, I wouldn't be surprised but we don't have the data to say it.

Erin Welsh: So can we talk a little bit more about the hemorrhage part of this?

Erin Allmann Updyke: Yeah.

Erin Welsh: So not everyone who is infected with Marburg virus develops hemorrhaging and that hemorrhaging can look very different.

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah. Can you say more about that?

Erin Allmann Updyke: I think that the word hemorrhage in this context is very different than in the context that a lot of people are maybe more used to hearing the word hemorrhage. So in the case of things that are sometimes called viral hemorrhagic fevers, probably more accurately not called viral hemorrhagic fevers, but viruses like Marburg which can cause disruptions in our coagulation cascade, they can cause disruptions in the way that we're able to clot our blood and therefore put us at risk, higher risk for bleeding, especially from our mucosal surfaces, which are already more prone to bleeding than just like your skin for example. In the case of Marburg virus, this could look like a lot of different things like I mentioned. It could be bleeding from the nose, it could be bleeding in the eyes, it could be bleeding in the GI tract which would come out in a lot of ways.

But in all of these cases, it's not as if someone had like a massive wound and is bleeding out or hemorrhaging from a very large wound. It's more slow bleeding and just not being able to stop and clot that bleeding that we tend to see with this type of viral infection. And it's not specific to Marburg by any means. And you're right, not every person who has Marburg virus is going to necessarily have either the same types of disruptions and the same types of bleeding or any signs of bleeding necessarily.

Erin Welsh: Okay, yeah.

Erin Allmann Updyke: Yeah. It's just based on the damage to that coagulation cascade. See our hemophilia episode.

Erin Welsh: We refer back to that a lot.

Erin Allmann Updyke: It's a really good ep and the coagulation cascade is kind of important.

Erin Welsh	It's pretty crucial, pretty crucial.
Erin Allmann Updyke	But kind of along those lines, I think the thing that's interesting about Marburg virus is that when this virus first emerged, and Erin I can't wait for you to walk us through that story, and for quite some time after it was thought to be not as deadly, not as virulent, not as scary as its cousin Ebolavirus. Because Ebolavirus has a case fatality rate as high as 90% which is terrifying. But as outbreaks of Marburg virus have continued and have grown in size, what we have seen is that in fact the case fatality rate of Marburg is as high as Ebola, 80%-90% if you average across all of these outbreaks. So I think that that's very interesting and I think that it kind of just shows that even though this is a virus that thankfully hasn't caused thousands of human cases, it is still something to be very wary of in kind of the broad sense of how we think about zoonotic viruses and spillover events.
Erin Welsh	Yeah. It indicates a lot. And the case fatality rate indicates a lot beyond just the characteristics of the virus.
Erin Allmann Updyke	100%.
Erin Welsh	And you mentioned how it was thought that Marburg had a lower case fatality rate than Ebola initially and then that later was sort of like yeah, maybe not. But part of the reason for that, and I'll get into this more, is that when Marburg first emerged it was in Germany.
Erin Allmann Updyke	Right.
Erin Welsh	And the case fatality rate was like 21% or something relatively low compared to later numbers. And a big part of that reason is probably treatment, which I know there's no Marburg-specific treatment really but what does supportive care look like that's driving these differences?
Erin Allmann Updyke	Yeah, exactly. Exactly. That supportive care is supportive care. We talked a lot about it in our sepsis episode because this progression to shock and organ failure is really very similar to what we talked about in our sepsis episode. And it involves access to hospital level care, it involves aggressive fluid resuscitation, it involves being able to identify which organs are being affected the most and how to support those particular organs, whether that means maybe dialysis or maybe just fluids or maybe less fluids. So it's a lot of different things but it really is access to high level ICU level of care, especially as it progresses to these late stages of organ damage. So yeah, that's going to look very different in different parts of the world whether or not people have access to that kind of care.
Erin Welsh	Yeah, I feel like that's a piece that often gets left out.
Erin Allmann Updyke	It always gets left out, especially of the discussion around case fatality rate.
Erin Welsh	Yeah.
Erin Allmann Updyke	But in any case, that is the biology of Marburg.
Erin Welsh	Okay. I mean it's still scary.
Erin Allmann Updyke	Oh yeah. It really is. I mean it's amazing how much havoc a virus can wreak.
Erin Welsh	Yeah.

Erin Allmann Updyke

Really I think that that's what it comes down to. It's just it's incredible how this virus can just absolutely wreck a body.

Erin Welsh

Yeah.

Erin Allmann Updyke

So Erin, tell me how did we get here? Tell me about these first outbreaks and what we know about this virus and how it started infecting us. What did we do to deserve it? Just kidding.

Erin Welsh

Yeah, I'll do my best right after this break.

TPWKY

(transition theme)

Erin Welsh

So we've already talked about how we covered Marburg the teeniest tiny bit in our Ebola episode from all the way back in February 2018. And if you are a TPWKY listener with like just the world's best memory, then you may remember exactly what I talked about. I did not. So I went back to our transcripts to see like okay, what did I say? What do I need to recover stuff? And no, basically all I talked about was that when Ebolavirus was first observed in 1976, people initially thought that it could be Marburg virus which had shown up nine years before in 1967 when workers at a lab in Germany came down with this hemorrhagic fever. That's about it. That's like all I really talked about. And we even joked about how like oh, now we don't have to do an episode on Marburg virus.

Erin Allmann Updyke

We were so naive.

Erin Welsh

Right? Right. Because that is far from the full story of Marburg virus and even if there weren't currently an ongoing outbreak, this is still a really important virus to cover. And I think that remains true despite the fact that Marburg has kind of been I think overshadowed by Ebola in recent decades.

Erin Allmann Updyke

Totally, totally, totally.

Erin Welsh

Yeah. Okay, so we're recording this on April 4, 2023. As we speak, like we've mentioned, there's an ongoing outbreak of Marburg virus in Equatorial Guinea as well as Tanzania. That's the first ever cases observed there. And this is of course part of our reason for choosing to cover this topic to give a little context to what's happening today or at least close to today because this will be coming out quite some time in the future. And we'll go into these current outbreaks in the current event section in a bit. But along with providing this additional context and answering where this thing came from and how did we get here and all those questions you asked, I also wanted to talk a bit about Marburg virus in history.

As in what impact did this virus' emergence have on public health or epidemiology or disease ecology? Because it really did mark a sort of turning point in the history of infectious disease. The story of Marburg virus hits on some themes that at this point in the podcast and at this point during COVID, we are all probably very familiar with. One in particular being the spillover of a zoonotic pathogen from wildlife to humans. Even before COVID brought this concept to a much wider audience, things like SARS-CoV-1, Hendra virus, Nipah virus, which we still need to cover both of those.

Erin Allmann Updyke

I know.

Erin Welsh

I can't believe we haven't covered it.

Erin Allmann Updyke

Listen, there's a lot of ground.

Erin Welsh

There's a lot of things out there, yep. Sin Nombre virus, West Nile virus, and others had shown that as humans, as our domestic animals, and as wildlife interact with each other more and more, as habitat is destroyed, as the climate changes, pathogens will be unavoidably exchanged. As global travel continues to become more widespread, those pathogens will more easily cause outbreaks that turn into epidemics that turn into pandemics, rapidly spreading to all corners of the world too fast for containment.

Erin Allmann Updyke

Too fast, too furious.

Erin Welsh

Too fast, too furious! But we know this, right. We've lived this. Scientists have warned about this, possibility doesn't seem like quite strong enough of a word here, this inevitability.

Erin Allmann Updyke

Reality?

Erin Welsh

This reality for a long time, long before COVID, so long that it seems like ingrained knowledge, like we've always been waiting for the next pathogen, probably a virus to spillover. But it hasn't always been that way.

Erin Allmann Updyke

Ooh, okay.

Erin Welsh

Of course the circumstances for pathogen spillover have always existed, that's how we got so many of our old friends. But the number of emerging infectious diseases has risen over time, even controlling for reporting bias. And the majority of these emerging pathogens have their origins in wildlife. It's taken us some time to notice this pattern. As the mid 20th century approached, things were looking pretty good in the war against infectious disease. We had antibiotics, we had pesticides that had drastically reduced rates of arthropod-borne disease, we had vaccines for many diseases that had been the biggest killers historically, including most recently polio during that time.

And it seemed like only a matter of time before we got a handle on the rest. But this starry eyed optimism would be short lived. First with the rise of antibiotic resistance chipping away at our confidence to handle bacterial infections and then the emergence of extremely deadly never before seen viruses that seemed to serve as this reminder that humans hadn't quite conquered the natural world. The first of these viruses to make an appearance was Machupo virus in Bolivia in 1962 which causes Bolivian hemorrhagic fever and which we will cover someday. And the second was the topic of today's episode, Marburg virus.

Erin Allmann Updyke

Wow. Second. Okay.

Erin Welsh

Yeah. Like I mentioned first described in 1967, after 31 laboratory workers in Marburg and Frankfurt, Germany and Belgrade, Yugoslavia, now Serbia, became extremely ill after handling African green monkeys, with seven people ultimately dying. Both of these viruses, Machupo and Marburg, they sort of marked the beginning of a new chapter in the history of infectious disease. One that we could reasonably call spillover, thanks David Quammen, and one that we're still deep in today. Although I feel like we may be shifting to like even more like spillover 2, more intense spillover than ever before. Still spilling over.

Erin Allmann Updyke

Still spilling over. I mean yeah.

Erin Welsh: And the emergence of these two viruses kind of served as a wake up call that we actually weren't close to shutting the door on infectious disease, that our increasing contact with wildlife and the ease of global travel had potentially deadly consequences. Let's get into what those consequences looked like in late summer and fall of 1967.

Erin Allmann Updyke: Okay.

Erin Welsh: In August 1967, Marburg, Germany was not the place to be.

Erin Allmann Updyke: Oh dear.

Erin Welsh: Even before the outbreak of a deadly virus.

Erin Allmann Updyke: Oh gosh.

Erin Welsh: The heat wave had driven anyone who could get out of town up to the mountains or over to the sea while anyone left behind had to suffer through the unrelenting heat day after day. And a handful of those unfortunate enough to not have a means of escape out of Marburg were about to get a whole lot more unlucky.

Erin Allmann Updyke: Oh dear.

Erin Welsh: Because within a few weeks, about 20 people living in or near Marburg began to get sick.

Erin Allmann Updyke: Uh oh.

Erin Welsh: Fever, malaise, headache, vomiting, rash, conjunctivitis. Their doctors chalked it up to summer diarrhea or dysentery and the patients were instructed to take lots of fluids and relax and recover at home. But that wasn't working, they weren't getting better, they were getting worse. And about five days after symptoms first showed up, most of them had checked into the hospital of the University of Marburg where they were promptly put into an isolation ward for infectious disease.

Erin Allmann Updyke: Wow. Just imagine working at that hospital at that time.

Erin Welsh: Yeah. I mean people still weren't wearing gloves until like later to handle specimens and stuff.

Erin Allmann Updyke: Oh wow.

Erin Welsh: Yeah. Because it was like this is probably a disease that we know about.

Erin Allmann Updyke: Yeah. But also you wear gloves with those.

Erin Welsh: Yeah. Well maybe not-

Erin Allmann Updyke: Maybe not in 1967.

Erin Welsh

Yeah. Yeah. But this was looking less and less like a GI infection, less familiar overall, and much more terrifying as word spread that an additional four people with similar symptoms were being treated in Frankfurt. Doctors at the hospital in Marburg ran test after test, first looking for the usual suspects like salmonella, Shigella, rickettsias, chlamydia, yellow fever, Leptospira, and others. And then when each of those tests came back negative, they enlisted the help of a dozen labs around the world to test for the unusual suspects, things like arboviruses or other pathogens that were known to cause hemorrhagic fever. And it was looking more and more like it was going to be a rare zoonotic pathogen at the root of all of this, especially since interviews with patients had revealed the one thing they all had in common. They all worked in a lab either directly with African green monkeys, their organs, or cell cultures derived from these monkeys' organs, namely kidneys.

Erin Allmann Updyke

Wow. Okay.

Erin Welsh

Why were they working with monkey kidneys in the first place? The polio vaccine.

Erin Allmann Updyke

Oh. I was going to say I feel like I should know this because I feel like we've talked a lot about the African green monkey kidney cells.

Erin Welsh

Yeah. I should have done a search through our transcripts to see where else I've talked about African green monkeys or you have.

Erin Allmann Updyke

Yeah.

Erin Welsh

Yeah, they've come up quite a bit.

Erin Allmann Updyke

Yeah.

Erin Welsh

Probably in our polio episode to be honest. But yeah, so if you remember in that polio episode that we also released forever ago at this point it feels, like Sabin's polio vaccine used a live attenuated strain of polio and this polio vaccine strain had to be propagated in monkey kidney cells. But why African green monkeys? Well in the first half of the 20th century, researchers had primarily used rhesus macaques in biomedical research. But it turned out that they couldn't be used for vaccine production because these monkeys are natural hosts of herpes B virus, whereas the African green monkeys were thought to not carry any viruses or other pathogens whatsoever that could be infectious to humans.

Erin Allmann Updyke

I mean the hubris.

Erin Welsh

I know. It still happens. Yeah. But that thought changed once this outbreak happened. And we can look back now and think okay, 31 total cases, that's not that many, that's just a few dozen.

Erin Allmann Updyke

I mean...

Erin Welsh

It is a lot but like-

Erin Allmann Updyke

It sounds really scary.

Erin Welsh

It is. I mean absolutely. But like in the scheme of things, it's like okay, 31 and it was done within a few months. That's done, right.

Erin Allmann Updyke

And they all worked at this place. I feel like that's the thing that makes it the least... Like okay, at least we have a source.

Erin Welsh

They all initially worked at this lab or at a different lab.

Erin Allmann Updyke

Uh oh.

Erin Welsh

But then it started to spread to other people.

Erin Allmann Updyke

Oh dear.

Erin Welsh

Okay. So that's when things were getting really scary, right?

Erin Allmann Updyke

Yeah.

Erin Welsh

31 and that seems like okay, they were able to contain it, they were able to isolate it. But when cases were still happening and when those cases were not just in Marburg, in Germany, but also in Frankfurt, and then when they were also in Belgrade in then Yugoslavia and now Serbia, also in a vaccine facility that also handled African green monkeys. And then things started to get scarier when it was not just people who had direct contact with those monkeys or monkey organs or cells, but also healthcare workers and then a family member or two.

Erin Allmann Updyke

Here we go.

Erin Welsh

They started to kind of like whoa, whoa, whoa, what is the actual limit of what this outbreak is going to be? And in the 1960s, tens of thousands of African green monkeys were exported each year from Ethiopia, Sudan, Eritrea, and Uganda which is where the monkeys linked to the 1967 outbreak were ultimately traced. I couldn't find an exact number but it seems that at least several hundred monkeys were shipped from Entebbe, Uganda to Germany via London. Normally they would have been sent straight to Germany but the direct flight was disrupted due to the Six-Day War. And this detail would become relevant when researchers were trying to track down where exactly the virus came from. Because in London, they were against regulations, kept in a room with other animals from other places. And like one of the animals got sick later for instance. And then in the final transport to Germany, two of the monkeys escaped and then were later captured.

Erin Allmann Updyke

Oh no.

Erin Welsh

But just like did it have to be these monkeys? You know what I mean? Like are you kidding me? Yeah, yeah. But all this confusion and this contact with the other animals kind of obscured where this virus originated.

Erin Allmann Updyke

Right.

Erin Welsh

Did the monkeys have it when they were captured in Uganda or did they get it from another animal that they were temporarily housed with?

Erin Allmann Updyke

Right, right, right.

Erin Welsh

It also of course lead to fears that if it did come from the monkeys, it would have spread to the other animals, which was a legitimate fear.

Erin Allmann Updyke

Yeah.

Erin Welsh

Because when the monkeys arrived in Belgrade for quarantine, those three shipments of 100 monkeys each, 21% of one shipment, 32% of another, and 46% of another died during quarantine.

Erin Allmann Updyke

Oh my goodness.

Erin Welsh

Yeah. And because of the super high mortality rate, a vet at this facility was assigned to do necropsies, that vet ended up getting infected with Marburg virus. And about 10 days later, his wife who was taking care of him developed symptoms.

Erin Allmann Updyke

Oh dear.

Erin Welsh

They both survived fortunately. And later on it would be revealed that there had been a major outbreak of a deadly disease in the monkeys in the places that they were usually caught before being shipped to Germany.

Erin Allmann Updyke

Oh gosh.

Erin Welsh

But at the time of this 1967 outbreak, no one could say for sure that the virus was from Africa. It was only later, about 8 years later, when a 20 year old man from Australia who was traveling in South Africa was diagnosed with Marburg virus disease and later his companion and a nurse caring for them also got sick. But that suggested pretty strongly that he had picked it up in his travels, likely in a cave where he slept near bats. Yeah. But I'll get to these later cases of Marburg virus in a second but I want to head back to 1967 for now. So by mid September, 7 of the 31 infected individuals had died of their infections. So a 23% case fatality rate. But the disease did not seem to be spreading, which was a huge relief as you can imagine. And less than three months after the first cases, the responsible virus had been isolated, characterized, identified, and named.

Erin Allmann Updyke

Wow.

Erin Welsh

Marburg, of course, after where the cases occurred. Most of the cases, I should say. The last case of Marburg virus in 1967 developed in November, the spouse of someone who had recovered from the infection a couple of months prior, thought to be sexually transmitted in that case. Yeah. But yeah, I feel like all of that was over a fairly short course of time, right?

Erin Allmann Updyke

Right.

Erin Welsh

Just over the period of a few months. But the impact of this outbreak would last a lot longer and spread much wider than the virus itself did. Because first this outbreak showed that these monkeys, these African green monkeys were not as safe to work with as had been previously thought. For instance before this outbreak, lab employees would handle the brains of these without any PPE.

Erin Allmann Updyke

Oh my god.

Erin Welsh

PPE was limited at best, like it didn't protect against aerosols for instance. And even initially, like I mentioned, the samples taken from infected people were handled without any extra precautions by hospital staff.

Erin Allmann Updyke

Aye aye aye.

Erin Welsh

Obviously all of that changed because of Marburg.

Erin Allmann Updyke

Right.

Erin Welsh

Secondly, the remaining monkeys that had been imported in the same batches as the infected ones were culled, future imports were super restricted, and tons of monkey kidney cells had to be thrown away along with the polio vaccine produced from them, all of which led to a pretty big shortage in polio vaccine in Germany, which then led to an increase in cases of polio.

Erin Allmann Updyke

Wow.

Erin Welsh

It's amazing like these cascading effects.

Erin Allmann Updyke

Yeah, seriously.

Erin Welsh

Yeah. But fortunately, having the virus identified and described meant that existing batches of vaccines could be tested and future monkeys or kidney cells from those monkeys could be checked for presence of the virus. Sidenote, some vaccine manufacturers switched to using crab-eating macaques from Southeast Asia for vaccine production because they were thought to not carry any potentially harmful pathogens or at least that was the belief until 1989 when Reston virus and Ebolavirus was discovered in macaques in a research facility in Reston, Virginia, near Washington DC.

Erin Allmann Updyke

I just, I mean, we learn but we don't learn but we learn but we don't.

Erin Welsh

It's like a little bit of absence of evidence is not evidence of absence. And also like we know this. And it's like well we screened for everything that we know.

Erin Allmann Updyke

Yep.

Erin Welsh

That's how we find something we don't know. Yeah. I mean fortunately Reston virus, like this is a huge dodge, right? It's not pathogenic to humans.

Erin Allmann Updyke

Right.

Erin Welsh

Or at least doesn't appear to be at this point in-

Erin Allmann Updyke

Time.

Erin Welsh

2023. Okay but I wanted to just throw that in there because I thought that was a come on, do we need to keep learning this? Yes.

Erin Allmann Updyke

Yes, we do.

Erin Welsh

Yeah. All right. But okay, back to Marburg. After the 1967 outbreak, Marburg virus was not detected again until those three cases that I mentioned in 1975. The next year, 1976, was when the first recognized outbreak of Ebola occurred which was initially thought like I said to be Marburg virus. And since then, Marburg has mostly been overshadowed by Ebolavirus, partially because by the mid 90s, Ebolavirus had caused sizable outbreaks involving hundreds of people with a super high case fatality rate, like you mentioned, on the order of 65%-80%-90%.

Erin Allmann Updyke

Right.

Erin Welsh

Whereas Marburg virus had really only caused one or two cases at a time outside of the 1967 outbreak, I counted like eight cases total between 1968 and 1997 or something.

Erin Allmann Updyke

Yeah.

Erin Welsh

And a couple of those eight cases were lab accidents from like a needle stick. But things would change in 1998 because that year an outbreak of Marburg virus began in Durba, a gold mining village with an estimated population of 25,000 in North Eastern Democratic Republic of the Congo. From October 1998 to September 2000, a total of 154 cases were detected or suspected and 128 people died.

Erin Allmann Updyke

Wow.

Erin Welsh

That's a case fatality rate of 83%. Yeah. Very high.

Erin Allmann Updyke

Yep. And very different again than-

Erin Welsh

Very different.

Erin Allmann Updyke

Most of the cases that we had seen prior.

Erin Welsh

Yes. Yeah. This seemed unusual at the time. We now know that it is not unusual. Because in October 2004 there was another big outbreak but this time it was in northern Angola in West Africa where the virus had not been detected before because all earlier outbreaks had origins in East Africa. So that alone was sort of like whoa, what's happening here? Why is this going on? And the size of this outbreak in Angola and the case fatality rate was also unprecedented. A total of 252 cases and 227 deaths. It was 90%.

Erin Allmann Updyke

Yeah.

Erin Welsh

Yeah. One of the things that I found really interesting about these two outbreaks is comparing the viral genetics between these outbreaks because researchers observed two pretty different patterns. So in the DRC outbreak, they found at least nine genetically distinct viral lineages during the outbreak.

Erin Allmann Updyke

Wow.

Erin Welsh

So that suggests multiple introductions from a natural reservoir.

Erin Allmann Updyke

Ooh.

Erin Welsh Suspected to be those Egyptian fruit bats that you mentioned. So that's like multiple spillover events.

Erin Allmann Updyke Right. A bunch of different people were exposed to a bunch of different bats in that outbreak.

Erin Welsh Yep. Whereas in the Angola outbreak, researchers found what looked like a single introduction of Marburg virus.

Erin Allmann Updyke That is so important and interesting, Erin.

Erin Welsh Yes. Right? Okay. Because the other thing that this outbreak did was challenge not only like oh, it is geographically restricted to this area, but also there was... I mean it was hard to say because there were so few cases still and case histories were really difficult to get and like all of that, but there was sort of this prevailing idea that secondary infections, so if somebody picked up the virus from an infected person rather than from a natural reservoir, that it was going to be less deadly.

Erin Allmann Updyke Right, less virulent. Yeah.

Erin Welsh Yeah. And that obviously was not the case in Angola.

Erin Allmann Updyke Well I think it also just can show the scale or the potential scale of person to person transmission to begin with.

Erin Welsh Yeah.

Erin Allmann Updyke Because previously we hadn't seen any outbreaks on that scale. And so knowing that it could have been potentially from a single introduction means that all of the other cases are from person to person transmission.

Erin Welsh Yes. Yeah. And it gets even more kind of interesting because so we've talked a lot about RNA viruses on the podcast before as being highly mutagenic. They mutate frequently, they mutate a lot. I don't know, and I probably should have looked up the mutation rate of Marburg compared to something like influenza or SARS-CoV-2 or something. But in some of the genetic analyses from this Angola outbreak, they found that the virus didn't really seem to change very much even after going through like 2-3 human to human transmissions. Where you would normally expect at least some changes to occur, the genomes were identical.

Erin Allmann Updyke Fascinating.

Erin Welsh Yeah. So I think that suggests that the mutation rate in general for Marburg virus is pretty low.

Erin Allmann Updyke Right.

Erin Welsh But why that is is a fascinating question.

Erin Allmann Updyke Yeah.

Erin Welsh I don't know what causes mutation rates to be different.

Erin Allmann Updyke

I don't know the answer but I now want to know.

Erin Welsh

I do too. So since the first outbreak in 1967 and excluding the current outbreak that I'm sure you'll talk more about, Erin-

Erin Allmann Updyke

Oh yes.

Erin Welsh

There have been approximately 474 cases of Marburg virus. But that's probably an underestimate.

Erin Allmann Updyke

Certainly.

Erin Welsh

Yeah. Number one, there have probably been, like very, very, probably, additional cases that were contacts of confirmed cases that never developed disease or were never tested in the first place. And second, because Marburg virus has probably been around for quite some time, causing infections before we knew what to look for. For instance, before the outbreak in Durba in DRC, there had been cases of something called hemorrhagic syndrome of Durba associated with living near the mine. And one person who had survived this disease was later found to carry antibodies against Marburg virus.

Erin Allmann Updyke

Ooh.

Erin Welsh

Research into the evolutionary origins of Marburg virus and other Filoviruses tells a similar story, although definitely not a consistent one by any means.

Erin Allmann Updyke

I'm not surprised about that.

Erin Welsh

Some papers put the origin of Filoviruses at 10,000 years or so ago or at least several thousand.

Erin Allmann Updyke

Okay.

Erin Welsh

While others say that it's more like millions of years since Filovirus-like elements have been found incorporated into mammalian genomes, which is pretty intriguing. And if that is the case, then it's possible that Filoviruses have played a pretty big role in mammal evolution overall. Marburg viruses as a group probably emerged much more recently as long as 700 years ago or maybe in the mid 19th century.

Erin Allmann Updyke

What?

Erin Welsh

I know. There's ranges with estimates. I feel like this may seem like a small detail, like why do we care precisely when or where this thing emerged? But it's important because it helps us predict and contain future outbreaks, it helps us understand how this virus might change during an outbreak, how those changes could be related to the severity of disease that a specific variant causes, and for developing an effective vaccine. And all this is important because one thing is certain, the outbreak that we're seeing now is not going to be the last time that this virus makes headlines. And before I hand it over to you to talk about what's happening today, Erin, I want to take a quick moment to talk about those headlines. Both Marburg virus and especially Ebolavirus have fascinated people, terrified people, and intrigued people since their discovery. They've been the subject of awful fiction such as 'The Virus' by Stanley Johnson, aka Boris Johnson's dad.

Erin Allmann Updyke

Really?

Erin Welsh

Yeah.

Erin Allmann Updyke

Okay.

Erin Welsh

I know, I could not believe it. I'm like is Wikipedia fooling me here? What's happening? Not to mention the movie Outbreak which is terrible but also kind of great in some ways. And also egregiously exaggerated nonfiction books like 'The Hot Zone' by Richard Preston. And don't get me wrong, 'The Hot Zone' is definitely one of the books that got me interested in the history of infectious disease, but it is borderline fiction. I grabbed it off my shelf for researching this episode because I was like okay, I know that there's a part in here about Marburg virus. Where did he get his sources? Are these going to be good places where I can learn about like the sequence of events and stuff?

Erin Allmann Updyke

Yeah.

Erin Welsh

There are no sources listed anywhere.

Erin Allmann Updyke

Love that.

Erin Welsh

None. There's a list of main characters and a glossary at the back. But giving benefit of the doubt, at least in my copy, there's not a single source which was very jarring. And 'The Hot Zone' did get people interested in epidemiology and so on and that's great but I feel like we really should aim higher when it comes to transparency in science communication and reporting. Anyway, Marburg and Ebolaviruses are scary. We've talked about case fatality rates as high as 90% but a frustrating amount of news reports play on that fear, stoking it, describing grizzly symptoms and chaotic hospital scenes, suggesting that the virus appeared out of nowhere, encouraging you to imagine what if it happened here? These news articles rarely talk about why that case fatality rate might be so high, especially considering, like we talked about, that first outbreak in Germany didn't come close to that.

They rarely mention that perhaps things like inadequate healthcare infrastructure, inadequate pathogen testing, inadequate isolation facilities, inadequate access to PPE, and other sociopolitical factors that could play a role in driving that number far higher than it should be. They rarely mention that we know quite a bit actually about the ecological circumstances leading to spillover events, meaning that these viruses don't just come out of thin air, these outbreaks don't just happen in a vacuum. They sometimes mention that we do have vaccines in the works but they may not mention that we are likely equipped already scientifically to bring those vaccines from the lab to the real world but we lack the funds. Because these are rare diseases that happen quote unquote "over there".

Erin Allmann Updyke

Over there. But you should be terrified if they come quote "over here".

Erin Welsh

Right.

Erin Allmann Updyke

That's I think the part that is just on top of everything so frustrating.

Erin Welsh

Yeah. Yep. And the other thing is that part of the reason why these vaccines haven't been completed, I mean and a lot of it is logistical difficulties considering that there have been few cases of Marburg and some difficulty in testing and all of that. But there's no profit in making these vaccines, that's a huge part of it. And that may be so but is that a reason to not make a life saving vaccine? Or at the very least to build up healthcare infrastructure overall? In the regions where Marburg and Ebola cause outbreaks, these Filoviruses are a rare occurrence compared to many other diseases, infectious and non, but they are also indicators of ecosystem degradation and possible climate change, these factors that promote pathogen spillover and they're indicators of how well a region is equipped to deal with a disease outbreak. So I guess my point in all of this is that the sensationalist portrayal of Marburg and Ebolaviruses in much of popular media does a disservice by withholding information or misrepresenting what we do and what we do not know at this point. So speaking of which Erin, what's happening with Marburg virus today?

Erin Allmann Updyke

Oh I'd love to tell you right after a short break.

TPWKY

(transition theme)

Erin Allmann Updyke

So the outbreak that you mentioned Erin, that happened in Angola in 2004-2005 still remains the largest outbreak that we have seen thankfully. And for a long time after that, like you mentioned, it was really just sporadic individual cases or very small single or double digit outbreaks that happened since then. However in the last couple of years, there have been outbreaks year after year. In 2021 there was an outbreak in Guinea from August to September with only one individual but that was the first time that a case was reported in the country of Guinea. And then in July 2022, two cases were reported in Ghana for the first time, both of which were fatal. And then two more cases were identified, so a total of four cases and three deaths overall. And again, these are two outbreaks in two countries where Marburg had never been reported before.

And then that brings us to 2023. Again, we're recording this April 4th and at this time we are looking at two different and thus far much larger outbreaks than we have seen in recent years. One of them is happening in Equatorial Guinea, again the first time that cases were reported in this country. And as of March 22nd of this year, that outbreak is up to nine laboratory confirmed cases and an additional 20 probable cases with seven deaths reported among those that are confirmed Marburg and all of the probable cases have died. So that's 27 people who have died so far. And a second outbreak identified in March in Tanzania, which if you haven't looked at a map of the continent of Africa recently is nowhere near Equatorial Guinea. These are completely disparate outbreaks that are happening to happen at the same time. In Tanzania it's a total of eight confirmed cases and five deaths so far. And the first outbreak reported in Tanzania.

Both of these outbreaks are considered still ongoing because the incubation period is long enough that the World Health Organization doesn't consider an outbreak over until at least 42 days after the last reported case just to like really try and make sure that we're catching every possible case in an outbreak. So these are still ongoing. So by the time you're listening to this episode, dear listeners, there may have been a number of more cases or maybe the numbers will have stayed the same if we're lucky. But obviously, one of the biggest natural questions is like why does it seem like these are increasing in number again? Like is this an increase in number? There's two different outbreaks that's going on?

Erin Welsh

Right.

Erin Allmann Updyke

I mean the outbreak in 2004 was certainly the largest, we're nowhere near that scale yet thankfully. But these are two significantly larger outbreaks than we have seen in quite some time. And because this is happening currently as we speak, we do have to rely on information kind of directly from the World Health Organization as well as journalism articles that are written because we don't have a lot of peer reviewed science thus far from this particular outbreak or these particular outbreaks. But one article that I read from the New York Times that interviewed a number of people mentioned that since COVID, over the last couple of years, a lot of countries have beefed up their capacity for things like PCR testing. So it could be in part that 2021, 2022, now 2023 where we're picking up Marburg, not just more cases but also in more countries than we've ever seen it before, it could be that it's because we're able to actually do the testing. Right?

Erin Welsh

Yeah, that's interesting.

Erin Allmann Updyke

Yeah. So it could very well be that this virus has been circulating far more widely than we realized and we're just now picking up on it for kind of the first time.

Erin Welsh

Yeah.

Erin Allmann Updyke

And that might be part of it, I think only time will tell. One thing that I do think is interesting kind of that might support that idea is that I read a paper from 2015 which is really prior to any outbreaks being reported in the most western parts of Africa, aside from Angola, that had modeled the potential niche for Marburg virus based on all the prior outbreaks that had happened before 2015. And this paper indicated a much broader potential range of risk for Marburg than the places and the countries where outbreaks had up to that point been previously reported. I'll definitely put a link to that paper on our website because the maps are really interesting and they now very nicely overlay with places that in the last few years we have started to see Marburg in fact appear.

Erin Welsh

Yeah.

Erin Allmann Updyke

So that may be part of it is that we finally are beefing up the capacity to be able to pick up on these viruses that previously were just going undetected, just generic people are dying from some kind of viral hemorrhagic fever or some kind of unknown undetected virus. Right?

Erin Welsh

Right, right.

Erin Allmann Updyke

But of course, as you mentioned Erin and as we always get to on This Podcast Will Kill You, certainly things like climate change, land use change, urbanization, encroachment on natural habitats, and this overall increase in wildlife-human interactions, all of these things are going to increase the possibility and probability of spillover events happening. And Marburg is still predominantly a disease of spillover events. So that piece of the puzzle really can't be ignored. And because of that I think that in terms of where do we go from here? What is the future research as it comes to Marburg? I think that some of the biggest areas are really in better understanding the biology and ecology of this virus, right? We need a lot more knowledge on the natural reservoirs, a lot more details on why are we seeing these increases in case numbers? Is it really true increases? Is it better detection? Is it a combination of all of these things? There is a lot I think to be done on the general ecology of this virus.

But there's also a lot of work to be done and that is being done on both vaccines and therapeutics for Marburg. As of right now, neither vaccines nor any specific therapeutic treatments exist. There are a number of candidate vaccines, at least one of which has made it as far as phase 1 clinical trials and has been shown to be safe in humans and a number of others that have had pretty thorough animal testing that have been shown to be very effective in nonhuman primates and are ready for human trials but haven't been able to undergo them yet. So the World Health Organization very recently, like March 2023, put out this very interesting guideline that anyone can access, it's just a PDF of a powerpoint, on what their kind of plan of action is to try and actually do these clinical trials during outbreaks.

Erin Welsh

Yeah.

Erin Allmann Updyke

And this is in an effort to both increase the capacity to do this kind of research because like you mentioned Erin, with a disease that's as sporadic as Marburg, it's really difficult to do clinical trials the way that we typically do them, this is a very rare disease which is a good thing. And the better our public health response is in identifying and isolating cases, the less chance we have for this type of clinical trial, right?

Erin Welsh

Yeah.

Erin Allmann Updyke

Which is a good thing for people.

Erin Welsh

Right, right.

Erin Allmann Updyke

But it still does limit in terms of the data that we're able to gather on these various vaccine candidates. So at this point, we have relied heavily on these animal studies but these guidelines are for things like ring vaccination campaigns during outbreaks. So this would be vaccine trials that involve people who are at very high risk, people who are either already exposed potentially or at very high risk of being exposed, like healthcare workers or family members of people who are identified as infected, etc.

Erin Welsh

Right.

Erin Allmann Updyke

So that's kind of where we stand. Most of the vaccine candidates thus far are viral vector vaccines. So very similar to the AstraZeneca COVID vaccine, people may remember. So they use adenovirus vectors or some other virus vectors. And then in terms of therapeutics, there is research being done on using things like monoclonal antibodies. The word remdesivir might ring some bells for some people because that was used for COVID, originally developed for Ebola, didn't work great for Ebola, has been shown to be effective in nonhuman primates for Marburg. No idea if it works in humans but there's at least potential. But like you mentioned Erin, a lot of the limitation comes not only in the fact that this is a rare disease but also in the fact that especially between outbreaks, the funding kind of just disappears.

Erin Welsh

Right. Yeah.

Erin Allmann Updyke

And it's very difficult to do vaccine research without funding.

Erin Welsh

Yep. It's kind of like investing in healthcare and public health infrastructure is a good idea. But let's just throw money at the problem when we see the problem.

Erin Allmann Updyke

You might come to the conclusion that investing in this technology would serve us well. I don't know, maybe you'd come to that conclusion.

Erin Welsh: One good reason.

Erin Allmann Updyke: But that is Marburg.

Erin Welsh: Sources?

Erin Allmann Updyke: Sources.

Erin Welsh: I have several, I have a bunch. I'm going to shout out two in particular. One that was helpful with the evolution was by Emanuel et al from 2018, I think it was a book chapter called 'Filoviruses: Ecology, Molecular Biology, and Evolution'. And then there was a great paper by Brauburger et al from 2012 titled '45 Years of Marburg virus research'.

Erin Allmann Updyke: I love that paper.

Erin Welsh: It's great. It's very thorough.

Erin Allmann Updyke: That was actually my number one paper, I relied very heavily on that same paper as well as a paper from 2022 that was called 'The Pathogenicity and virulence of Marburg virus'. I had a few other papers with a lot more kind of nitty gritty detail and then I will link to the World Health Organization disease outbreak news kind of generic website because this is where when you're listening to this several months from today, you'll be able to get the most up to date information on what's going on with Marburg and also any other infectious disease that are having outbreaks around the world. And we'll post the sources for this episode and all of our episodes on our website thispodcastwillkillyou.com.

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

Erin Allmann Updyke: Thank you to Lianna Squillace for our amazing audio production and editing.

Erin Welsh: Thank you to Exactly Right.

Erin Allmann Updyke: And thank you to you, listeners, for listening.

Erin Welsh: Yeah. We hope that you learned something.

Erin Allmann Updyke: Yeah. I feel like this was a real kind of throwback episode, like very OG TPWKY. So hopefully it was fun for everyone.

Erin Welsh: For sure, yeah.

Erin Allmann Updyke: Yeah.

Erin Welsh: And a special thank you to our wonderful, generous, amazing patrons. We appreciate you and your support so, so much.

Erin Allmann Updyke: So much.

Erin Welsh: All right. Well until next time, wash your hands.

Erin Allmann Updyke

You filthy animals.