

TPWKY

This is Exactly Right.

Erin Allmann Updyke

"Yellow fever had a macabre way of toying with its victim before killing. For three days there was fever and chills followed by a marked improvement. The temperature fell, he could think if it pleased him to fantasize that the worst was passed. Maybe he could tell himself it had been influenza or perhaps a touch of malaria or some unnamed tropical thing of which there were many. But on the fourth day, yellow fever returned with a vengeance. Beads of sweat popped out on the victim's skin as the fever returned and climbed steadily to 103, 104, 105. And then the chills came and the victim's teeth chattered and he begged for covers only to kick them away again when the fever returned. Slowly the patient's skin turned yellow and patches of the inside of his mouth began to ooze blood. Nausea came and passed and returned. There was a pan by the bed to catch the black vomit, a mixture of blood and digestive juices."

"2/3 of the patients eventually recovered and became immune. For those who didn't live the jaundiced skin became yellower and yellower. The end was near when tests detected that protein had begun to leak out of the blood, through the kidney membranes, and into the urine. Shortly after that the kidneys shut down and the flow of urine ceased. When the kidneys died, so did hope. The wracking hiccups began. If the patient was lucky, he went into a coma at about that time. If he was not so fortunate, consciousness faded into delirium and he screamed and cried out in his living nightmare until just before death, which usually occurred between the sixth and the ninth day."

TPWKY

(transition theme)

Erin Welsh

I have chills all over.

Erin Allmann Updyke

Me too. (laughs)

Erin Welsh

Oh my gosh, I hope they're not yellow fever chills.

Erin Allmann Updyke

Oh let's hope not.

Erin Welsh

That's terrifying!

Erin Allmann Updyke

I know, it's really... Ugh, it's horrific.

Erin Welsh

Wow.

Erin Allmann Updyke

Yeah.

Erin Welsh

Well.

Erin Allmann Updyke

Well.

Erin Welsh

If you've just joined us, you know you're listening to This Podcast Will Kill You.

Erin Allmann Updyke

Yes you sure are.

Erin Welsh

(laughs)

Erin Allmann Updyke

Welcome to Episode...

Erin Welsh 10!

Erin Allmann Updyke No!

Erin Welsh I know, we're in the double digits now.

Erin Allmann Updyke Oh that's exciting.

Erin Welsh It really is. Big milestone.

Erin Allmann Updyke (laughs) What a way to start it off.

Erin Welsh (laughs) I'm Erin Welsh.

Erin Allmann Updyke And I'm Erin Allmann Updyke.

Erin Welsh Thanks for joining us.

Erin Allmann Updyke Today we're talking about yellow fever.

Erin Welsh You got it. And what do we have to drink today? What's our quarantini?

Erin Allmann Updyke What are we calling it actually?

Erin Welsh Mello Yello Fever.

Erin Allmann Updyke Mello Yello Fever! (laughs) It's essentially Mello Yello and vodka.

Erin Welsh You know they can't all be winners, guys. (laughs) I mean, we definitely don't think this is delicious but the name was too good to pass up.

Erin Allmann Updyke It was. It just had to be done.

Erin Welsh It really did.

Erin Allmann Updyke Mello Yello Fever.

Erin Welsh (laughs)

Erin Allmann Updyke All right, well that was fun.

Erin Welsh That was fun.

Erin Allmann Updyke That was a quick intro, we just bing-bang-boomed it.

Erin Welsh I know, I think that we're like excited to get to the material.

Erin Allmann Updyke: Yeah I think so too.

Erin Welsh: All right, well let's just get to it. Straight to the biology.

Erin Allmann Updyke: Jump straight into it.

Erin Welsh: Erin, tell me what you got.

Erin Allmann Updyke: Okay.

TPWKY: (transition theme)

Erin Allmann Updyke: So yellow fever is another RNA virus, we've had a few of those.

Erin Welsh: Like what else?

Erin Allmann Updyke: Influenza was an RNA virus.

Erin Welsh: Okay. Cool.

Erin Allmann Updyke: There was another one but I don't remember which one it was. One of our other viruses.

Erin Welsh: At some point the facts begin to blur.

Erin Allmann Updyke: They all mush together.

Erin Welsh: (laughs) Superbug.

Erin Allmann Updyke: Superbug mush. This actually was, you'll probably talk about this so I hope I'm not stepping on toes, but it was the first viral disease that was shown to be transmitted by mosquitoes.

Erin Welsh: I don't really mention that, but hey.

Erin Allmann Updyke: Well then here we go. I think that's really cool, good old Walter Reed.

Erin Welsh: Yeah.

Erin Allmann Updyke: WTG.

Erin Welsh: You'll learn... WTG?

Erin Allmann Updyke: Way to go.

Erin Welsh: Oh. (laughs) You will learn a lot more about Walter Reed and that whole situation.

Erin Allmann Updyke: Oh good. I'm excited about that.

Erin Welsh: Yeah.

Erin Allmann Updyke: So this is a virus that's transmitted by mosquito, I think our third vector-borne disease so far this season.

Erin Welsh: Yeah. Plague, malaria, and yellow fever.

Erin Allmann Updyke: And now this, pretty exciting. So it's transmitted by a squito - a squito - it's transmitted by-

Erin Welsh: A skeeter!

Erin Allmann Updyke: A skeeter. (laughs) That even if you've never heard of anything about mosquitoes, there's a good chance that you've heard of this mosquito because it also transmits dengue, chikungunya, zika virus which is all over the news right now, so this is a pretty gnarly mosquito named *Aedes aegypti*.

Erin Welsh: Aw.

Erin Allmann Updyke: Yeah. So there's also another... So *Aedes aegypti* is called the yellow fever mosquito, so that's the common name for it.

Erin Welsh: Oh I didn't know that.

Erin Allmann Updyke: Yeah. That's the common name. There's another mosquito, *Aedes albopictus* that's also capable and very commonly transmits this disease to humans, that's the tiger mosquito.

Erin Welsh: Okay.

Erin Allmann Updyke: So if you've ever heard of the tiger mosquito or the yellow fever mosquito, that's the mosquitoes we're talking about today. They're black and they have white striped on them, they're actually cute as far as mosquitoes go.

Erin Welsh: What is the geographic distribution of those currently and where do they come from?

Erin Allmann Updyke: So I believe they come from Africa.

Erin Welsh: Both do.

Erin Allmann Updyke: I believe so. I should probably double check that, *Aedes albopictus* might have come from Asia cause it's often called the Asian tiger mosquito. That one might have come from Asia. But at this point they're pretty well distributed throughout the tropics and both of them are increasing in range.

Erin Welsh: Okay.

Erin Allmann Updyke: *Aedes aegypti* and *Aedes albopictus* are both found in the southern United States, in Florida, things like that. And they actually have been expanding, one of our lab mates has been doing research on the expanding distribution of these guys even into Illinois.

Erin Welsh: Yeah, shout out to Allison Parker. Woo woo!

Erin Allmann Updyke

Woo woo! (laughs) Yeah so they're kind of ubiquitous throughout the tropics which is one of the things I'll talk about later that makes yellow fever a scary disease to talk about is that the mosquitoes that transmit this exist in a lot of places, even where this virus doesn't exist currently. So there is a fear that this virus could then spread to places that it isn't currently.

Erin Welsh

Gotcha.

Erin Allmann Updyke

Yeah. So similar to malaria, you get infected when a female mosquito bites you and injects her saliva into your bloodstream and that saliva is full of these little viral particles. And *Aedes aegypti*, part of the reason that they're so gnarly and they transmit so many diseases to humans is that they're really well adapted to human habitats. They're what we call a container-breeding mosquito, so in the quote unquote "wild" they probably lay their eggs into tree holes, ephemeral ponds and things like that but in urban environments they're really well adapted. They can use tires, flowerpots, birdbaths, anything that you have that holds water.

Erin Welsh

Gutters.

Erin Allmann Updyke

Gutters. Shout out to Allison again. (laughs) Yeah so they're the main transmitter of yellow fever in what we call the urban cycle.

Erin Welsh

Mm-hmm.

Erin Allmann Updyke

So there's multiple cycles of yellow fever. The urban cycle is exactly what it sounds like. It's when *Aedes aegypti* transmits yellow fever between humans, so from human to mosquito to human, within an urban environment like say Sao Paulo, Brazil for example.

Erin Welsh

Okay.

Erin Allmann Updyke

Now there's also what they call a sylvatic cycle and sylvatic just means 'wild'. So this is also known as jungle yellow fever which is essentially when you have different species of mosquitoes, actually, a totally different genus in South America and another species of *Aedes* in Africa, when you have virus circulating in monkeys and then you have mosquitoes transmitting this yellow fever virus between monkeys and other nonhuman primates, from monkey to monkey to monkey. And then they eventually might spillover into the human population.

Erin Welsh

Okay. So like a spillover event instead if like in a city, just like an urban human cycle. Gotcha.

Erin Allmann Updyke

Exactly. Right, yeah. So this generally has sort of smaller outbreaks, you can imagine that if a person got infected from a spillover event and went to an urban area that had *Aedes aegypti*, it could result in a larger outbreak.

Erin Welsh

Right.

Erin Allmann Updyke

But yeah so the sort of enzootic cycle, which just means the endemic cycle in animals, is really really important in sustaining this yellow fever virus and it's why the hope of ever sort of eradicating it is basically nonexistent.

Erin Welsh

Really?

Erin Allmann Updyke

Yeah. Because of this enzootic cycle, it's almost impossible to imagine a situation in which we could eradicate yellow fever as a public health problem.

Erin Welsh: Interesting.

Erin Allmann Updyke: Yeah.

Erin Welsh: Also bummer.

Erin Allmann Updyke: Yeah, bummer! (laughs)

Erin Welsh: From that earlier description, yeah. It would be really nice to never-

Erin Allmann Updyke: To never have to get it?

Erin Welsh: -have anyone experience that.

Erin Allmann Updyke: Yeah. There's also a third cycle that they call a savannah cycle or an intermediate cycle which mostly happens in Africa, which is why they call it the savannah cycle. Which essentially is when you have transmission between mosquitoes, nonhuman primates, and humans. And this happens with yet another species of mosquito. So it's basically just that rather than going from monkey to mosquito to monkey to mosquito and occasionally spilling over into human, this is a more integrated cycle that kind of goes from nonhuman primate to mosquito to human to nonhuman primate. So if you imagine situations where you're maybe living in closer proximity to other nonhuman primates, that's when you might see a cycle like this.

Erin Welsh: Okay.

Erin Allmann Updyke: Yeah.

Erin Welsh: Interesting.

Erin Allmann Updyke: Yeah! And also importantly, before I start to talk really about the symptoms of this disease, the virus in this case can be vertically transmitted between mosquitoes. And what that means, this is some deep mosquito biology here-

Erin Welsh: Yeah but it's so important in the transmission.

Erin Allmann Updyke: It's so important, yeah. A vertically transmitted infection means that female mosquitoes transmit the virus to her eggs. So then when those eggs hatch, larval mosquitoes are already infected with the yellow fever virus. And this is really important because that means that when they emerge as adults and are about to take their first blood meal, they can infect that first organism that they bite whereas with malaria and a lot of other mosquito-borne diseases, the mosquito has to get infected by taking a blood meal first.

Erin Welsh: And so what do we call that form of transmission?

Erin Allmann Updyke: That would be just horizontal transmission.

Erin Welsh: Okay.

Erin Allmann Updyke: Yeah. So yeah, so this is super important in terms of viral transmission because you don't have to have that initial blood meal to infect the mosquito, they're potentially infectious right out of the gate, which is really important. You wanna get to some symptoms?

Erin Welsh: That is very scary, actually.

Erin Allmann Updyke: It's really scary, yeah.

Erin Welsh: You have basically this pool of mosquitoes that can always be infected for generations and generations.

Erin Allmann Updyke: They're just emerging infected basically.

Erin Welsh: Yikes.

Erin Allmann Updyke: Yeah.

Erin Welsh: Yeah but I do wanna get to some symptoms.

Erin Allmann Updyke: Let's do it. So yellow fever is one of a number of what we call viral hemorrhagic fevers.

Erin Welsh: Ugh!

Erin Allmann Updyke: Yep, it's as bad as it sounds.

Erin Welsh: What are some of those other ones? Just as a quick...

Erin Allmann Updyke: Dengue can be a hemorrhagic fever. You also have things that are not transmitted by mosquitoes like Marburg or Nipah.

Erin Welsh: Ebola!

Erin Allmann Updyke: (laughs) Next episode! Right? Second to next. Next next. That's not right.

Erin Welsh: Yeah there's no word for that. The day after tomorrow episode. No.

Erin Allmann Updyke: (laughs)

Erin Welsh: The episode after the next.

Erin Allmann Updyke: Yes.

Erin Welsh: The ultimate episode of this season.

Erin Allmann Updyke: (gasps) Oh my god.

Erin Welsh: Yeah.

Erin Allmann Updyke
Wow. So yes, those are some other viral hemorrhagic fevers. So here's how things happen. When a person gets infected by the bite of a mosquito, they generally have about a 3-6 day incubation period. So not symptomatic, the virus is just in your body, starting to replicate. Then for most people symptoms aren't that bad. You get fever, headache, back pain, chills, muscle pain, nausea, vomiting, okay it's pretty bad.

Erin Welsh
That's terrible!

Erin Allmann Updyke
(laughs) So you're generally feeling really crappy. And generally this lasts for about 3-4 days and then you recover. However in about 15% of cases, which is actually kind of a lot-

Erin Welsh
Yeah, absolutely.

Erin Allmann Updyke
They say it's a small number but that's not that small.

Erin Welsh
(laughs) No. A small number would be 0.0001.

Erin Allmann Updyke
(laughs) Yeah. So about 15% of cases enter a second phase. They call it the toxic phase, it's the hemorrhagic phase, it's the gnarly phase.

Erin Welsh
This is the 'you're probably not gonna recover from this' phase?

Erin Allmann Updyke
There's a 20-60% chance or higher that you won't recover.

Erin Welsh
Wow.

Erin Allmann Updyke
That you'll die. By the way that's what I mean by don't recover cause those are you two options here. You end up with a fever that recurs. So you sort of get better from that first round like we heard in the firsthand account. You get better and then all of a sudden your fever spikes again, then you end up with jaundice which is where we get the name yellow fever. Your skin really turns yellow and this is because of how much damage the virus does to your liver. So if your liver stops functioning well then it can't break down and recycle your red blood cells so you end up with bilirubin in your blood which literally turns your skin yellow.

Erin Welsh
Wow.

Erin Allmann Updyke
Yeah. So you can imagine that liver damage, like that's not a good thing.

Erin Welsh
No!

Erin Allmann Updyke
You need your liver.

Erin Welsh
You only get one of those.

Erin Allmann Updyke
You only got the one. Then you can end up with bleeding from your eyes, your mouth, your GI tract which then causes that bloody vomit that we heard about.

Erin Welsh
Oh my god.

Erin Allmann Updyke: Because of how much you're bleeding into your GI tract. So the Spanish name for yellow fever is actually 'vomito negro', which means black vomit. I didn't know that.

Erin Welsh: I didn't either.

Erin Allmann Updyke: It's disgusting.

Erin Welsh: Yeah. Yeah your whole insides are bleeding, right?

Erin Allmann Updyke: Your whole insides are just bleeding, yeah.

Erin Welsh: There was something in the early descriptions of the disease, a doctor is showing an as per usual lack of knowledge about women's health and other things-

Erin Allmann Updyke: Of course.

Erin Welsh: And they said that it causes older women, like post-menopausal women, to spontaneously menstruate.

Erin Allmann Updyke: Oh jesus.

Erin Welsh: When really it was just your uterus is bleeding cause your whole body, everything is bleeding on the inside.

Erin Allmann Updyke: Yeah. Your whole body is just bleeding.

Erin Welsh: So that's another horrifying symptom.

Erin Allmann Updyke: Oh god. That would also be terrifying. Can you imagine? I can't.

Erin Welsh: The whole thing.

Erin Allmann Updyke: Yeah.

Erin Welsh: If you're even not delirious.

Erin Allmann Updyke: Right.

Erin Welsh: Right.

Erin Allmann Updyke: Yeah. Yep. So then we get even worse, you end up with kidney failure which again you really need your kidneys, those are really important.

Erin Welsh: Yeah. Your whole body is shutting down!

Erin Allmann Updyke: Your whole body is shutting down. And that is how you end up with death is just organ failure. Also the hiccups are a really common symptom which I find so interesting.

Erin Welsh: And hiccups are the worst.

Erin Allmann Updyke Oh my gosh. I think they're Brett's number one least favorite thing in the entire world.

Erin Welsh (laughs)

Erin Allmann Updyke Yep. So that is the toxic phase of yellow fever. The fatality rate, again, is 20-50% or higher. So that makes the overall fatality rate somewhere between 3-7.5% of everyone who gets infected with yellow fever.

Erin Welsh And that's based on modern estimates with adequate care for the most part.

Erin Allmann Updyke Yes. For the most part. Yeah. And you die, it's fairly quickly. Most people if they get to this stage of this severe illness, it's within 10-14 days they're dead.

Erin Welsh Wow.

Erin Allmann Updyke And case fatality rates are generally lower in Africa than they are in South America which are the two main areas where yellow fever is currently endemic is Africa and South America. And some of this might have to do with strain differences in the virus itself between Africa and South America but there's also a lot to do with host factors like prior exposure and your individual immune response. And especially the lethality of that hepatic disease seems to be very correlated to the viral load in your blood, so how much virus you actually have in your blood will determine whether or not you die from it once you get to that severe stage. Yeah so the viral load in your blood is a factor of both the initial infection, so how many viral particles that mosquito spit into you, and also your individual immune response, how good your body is at actually squashing that infection.

Erin Welsh That's crazy.

Erin Allmann Updyke Yeah so that's pretty much yellow fever. There's no treatment.

Erin Welsh Besides just like...

Erin Allmann Updyke Supportive therapy. You can try and prevent complete liver failure and kidney failure with supportive therapy and things like that, so hospitalization is important if you have yellow fever to be able to monitor you and things like that. But there isn't any actual antivirals that are good at treating this. There is a vaccine which is great and I'll talk a lot more about it when I talk about what's going on with yellow fever today, cause the vaccine is really important. And if you survive your immune for life.

Erin Welsh Hey, that's great.

Erin Allmann Updyke So that's great. If you survive.

Erin Welsh If you survive.

Erin Allmann Updyke If you survive. (laughs)

Erin Welsh Wow.

Erin Allmann Updyke Yeah. Well I think that's all I have for the biology.

Erin Welsh	Oh is it my turn?
Erin Allmann Updyke	It's your turn!
Erin Welsh	It's my turn!
Erin Allmann Updyke	Teach me everything about the history, I can't wait.
Erin Welsh	I can't wait either.
Erin Allmann Updyke	(transition theme)
Erin Welsh	Opening scene: the camera pans across to post-Civil War Memphis, Tennessee, USA. Late spring 1878. The city is bustling, full of shops, restaurants, frilly dresses. Lively music plays over the scene. Yes the streets may smell like horse poop but this is 1878, what city doesn't? Memphis is the place to be. As heavy clouds gather over our picture of Memphis, you notice the streams and streets are already full to bursting with water. The gentle hum of a mosquito sounds over the picture, soon joined by dozens, hundreds more. Cut to September of the same year. The contrast is shocking, a shot of deserted streets, empty storefronts, houses abandoned seemingly in the middle of a meal. Cannons fire in the distance. As the camera passes over the lonely streets to a graveyard on the edge of town, you are horrified to see bodies stacked, swollen and rotting in the summer heat. So many bodies, so little time. In the next scene you come face to face with the manifestation of this horror, a person thrashing wildly in a bed stained with black vomit while a doctor tries in vain to restrain his patient. You can almost feel the burning heat coming off of the skin of the poor victim and as the camera goes in for a closeup, you get a glimpse of the eyes darting back and forth frantically, their normal white color turned a bright, deadly yellow.
Erin Allmann Updyke	Oh my god. I want that movie.
Erin Welsh	Right? (laughs)
Erin Allmann Updyke	I want to see that movie!
Erin Welsh	Yeah, I really want to too.
Erin Allmann Updyke	Ugh that was amazing! I am there.
Erin Welsh	Here we go. So yeah, that is how I imagined the 1878 yellow fever epidemic in Memphis.
Erin Allmann Updyke	Wow.
Erin Welsh	Which this epidemic would end up being the deadliest yellow fever epidemic in U.S. history.
Erin Allmann Updyke	Wow!
Erin Welsh	Yeah.

Erin Allmann Updyke

I think a lot of people probably don't realize that yellow fever ever existed in the U.S. much less how serious it was.

Erin Welsh

Oh yeah. Well, now you're gonna learn.

Erin Allmann Updyke

Yes!

Erin Welsh

So before the epidemic, Memphis was the second biggest city in the south.

Erin Allmann Updyke

Wow.

Erin Welsh

It was hugely important in trade, commerce, and culture since it was next to the Mississippi River at the southwest corner of the state. However its link to travel and trade came with a serious downside. As we know by now, money and goods aren't the only things exchanged at port cities.

Erin Allmann Updyke

Yep.

Erin Welsh

Pathogens and parasites are just as happy to check out the next stop along the trade route, usually to the detriment of the town or city. Memphis had seen a few yellow fever epidemics in the 1800s but none as devastating as the one in 1878. That year happened to be an El Niño year, which means that the ocean temperatures are warmer than usual which then can really strongly affect global weather patterns.

Erin Allmann Updyke

Yeah.

Erin Welsh

In El Niño years, certain areas get warmer and rainier, some get colder and drier, it just depends on where you are. Memphis in El Niño years gets hit with a ton of rain.

Erin Allmann Updyke

Oof.

Erin Welsh

Do you know who loves rain?

Erin Allmann Updyke

(singing) Mosquitoes!

Erin Welsh

Yep because that means there will be no shortage of breeding spots.

Erin Allmann Updyke

Yeah.

Erin Welsh

When in the summer reports started pouring in of a possible yellow fever epidemic in New Orleans, Memphis remained unconcerned. Quote: "We need not fear in Memphis," one contemporary newspaper said. "We were never in as good a condition from a sanitary point of view."

Erin Allmann Updyke

Famous last words.

Erin Welsh

Right. Well and of course no one yet knew that yellow fever was transmitted by mosquito not bad air.

Erin Allmann Updyke

Oh. They're like, 'Don't worry we cleaned up our air guys, it's gonna be fine. Oh, everyone's dead.'

Erin Welsh

Everyone's, yep. (laughs) Yeah. And so a quarantine was voted against.

Erin Allmann Updyke

Wow.

Erin Welsh

Mm-hmm.

Erin Allmann Updyke

Cool.

Erin Welsh

On public health official who was really in favor of a quarantine resigned cause he was like, 'This is going to be on my conscious forever that you guys are refusing a quarantine.'

Erin Allmann Updyke

WTG, guys.

Erin Welsh

Yeah, no kidding. The first Memphis case was announced in August. Almost immediately a mass exodus out of the city ensued. Anyone who could afford to pick up and go, did.

Erin Allmann Updyke

Wow.

Erin Welsh

And though it probably saved many of the escapees, it was too late for others who died along the way. In the city deaths ramped up to where about 200 people were dying everyday.

Erin Allmann Updyke

Oh my god.

Erin Welsh

Houses containing dead bodies were identified by the overwhelming presence of flies.

Erin Allmann Updyke

Ugh!

Erin Welsh

Some bodies weren't discovered until they were more than, quote: "a lot of bones in a puddle of green water."

Erin Allmann Updyke

(gasps)

Erin Welsh

(laughs) I know.

Erin Allmann Updyke

That's what was left of their bodies.

Erin Welsh

Yes.

Erin Allmann Updyke

Oh my god!

Erin Welsh

Just putrefaction.

Erin Allmann Updyke

Just green water!

Erin Welsh

If you have sensitive ears-

Erin Allmann Updyke: Then why are you listening to this podcast?

Erin Welsh: Right. But here's some pretty horrifying descriptions.

Erin Allmann Updyke: Okay so fast forward like 30 seconds. Go.

Erin Welsh: Children were found sick in the same bed as their deceased parents. And the worst thing that I read is that one mother was found dead beside a starving infant still trying to breastfeed.

Erin Allmann Updyke: Aw.

Erin Welsh: Yeah. It's really sad.

Erin Allmann Updyke: Oh my god.

Erin Welsh: Dead bodies accumulated as willing and able, or even just living, gravediggers dwindled. One mass grave in Memphis still contains the bodies of 1500 yellow fever victims from this epidemic, unidentified.

Erin Allmann Updyke: Oh my god.

Erin Welsh: During the peak of the crisis, the mayor wrote to the U.S. president who was Rutherford Hayes, begging, pleading for assistance. The president's reply?

Erin Allmann Updyke: No thanks.

Erin Welsh: Quote: "I suspect the Memphis sorrow is greatly exaggerated by the panic-stricken people. We do all we can for their relief."

Erin Allmann Updyke: Oh wow.

Erin Welsh: The mayor tried one more time to secure aid before he too became a victim of yellow fever.

Erin Allmann Updyke: Sounds like DJT, bro.

Erin Welsh: (laughs) I was like, I think I wrote on my notes, "parallels to today in Puerto Rico".

Erin Allmann Updyke: (laughs) Yup. Yeah. It's not funny.

Erin Welsh: No it's not funny.

Erin Allmann Updyke: It's terrifying.

Erin Welsh: We're laughing because we're just like in shock at how horrifying.

Erin Allmann Updyke: Oh my god.

Erin Welsh: The virus finally burned itself out by mid-October. By that point it had infected almost every person remaining in the city.

Erin Allmann Updyke That's amazing.

Erin Welsh Let's crunch some numbers.

Erin Allmann Updyke Love numbers crunching!

Erin Welsh Before the epidemic hit, 45,000 people lived in Memphis.

Erin Allmann Updyke That's a good number.

Erin Welsh Yeah.

Erin Allmann Updyke Back then.

Erin Welsh About 19,000 stuck around for the duration of the epidemic.

Erin Allmann Updyke Oh dear.

Erin Welsh 17,000 of those, 17,000 of 19,000 got yellow fever.

Erin Allmann Updyke Oh my god. How many died?

Erin Welsh 5150

Erin Allmann Updyke Wow.

Erin Welsh So almost 1/3 of those remaining.

Erin Allmann Updyke Wow.

Erin Welsh It was this epidemic that prompted the U.S. to form the Yellow Fever Commission.

Erin Allmann Updyke Yeah.

Erin Welsh But before I get to that story, let's start at the very beginning.

Erin Allmann Updyke Yay!

Erin Welsh Okay, our story starts again as it has before in the forests of central and western Africa thousands of years ago. There a virus was circulating, hiding out in the bodies of those horrible creatures known as mosquitoes.

Erin Allmann Updyke They're just trying to get by.

Erin Welsh I don't like mosquitoes.

Erin Allmann Updyke Yeah.

Erin Welsh

(laughs) Until one day it made the jump to primates hanging out in the trees. Once in its new host it caused utter devastation, wiping out huge numbers of its mammal population until it couldn't be sustained. Then it disappeared for a while, the primate population regrew, and the virus was all but forgotten. But it would return and when it did, again the primate population was destroyed and again the virus disappeared and this cycle would continue for thousands of years until one day the virus made its way into a new host, a human host. And what it did in human populations wouldn't be very different from the death and destruction and what it did in nonhuman primate populations. For generations it ran through this epidemic cycle until it in some ways lost its punch. The humans that were continuously exposed to the virus grew an immunity until, in most cases, yellow fever was more of a childhood infection than the horrifying disease that would later be the cause of such fear and panic.

Erin Allmann Updyke

Yeah.

Erin Welsh

How do we know that yellow fever has its origins in Africa? Well first, African primates are pretty much resistant to the virus.

Erin Allmann Updyke

Mm-hmm. Yeah.

Erin Welsh

While New World primates like in the Americas are very susceptible. In addition, Europeans and Native Americans were also super susceptible to the illness, resulting in death rates 5-7 times higher than those in individuals born in Africa, in historical outbreaks.

Erin Allmann Updyke

Yeah.

Erin Welsh

Any guesses as to how it got from Africa to the Americas?

Erin Allmann Updyke

Ooh, ooh, ooh! Let me guess. Slave trade!

Erin Welsh

You got it!

Erin Allmann Updyke

(laughs)

Erin Welsh

Yeah. Or as one of the books I read called it, transoceanic shipping.

Erin Allmann Updyke

Oh my god. Yeah well in, I think it was the WHO website or something, it just said like it made its way to the Americas or something. And I'm like it didn't make its way, okay? Yeah. Slave trade.

Erin Welsh

Both the virus and its mosquito host were brought over during the slave trade. The mosquito would breed in small pockets of water aboard ships and the virus circulated in the blood of the slaves that were brought over.

Erin Allmann Updyke

Right.

Erin Welsh

And the slave trade had really ramped up during the 17th and 18th centuries, and this is a common thread that we've seen and that I've talked about before, so basically European invasion, a lot of Native Americans died which the Europeans viewed as their workforce dying so then they had to go to Africa. And they chose to go to Africa to get slaves. So. But then them going to Africa means that they brought over things like malaria and yellow fever which then killed even more Native Americans, I mean it was just... Yeah. Lots of disease. Okay back to yellow fever. I can't emphasize enough how much this disease gripped susceptible regions with fear and panic. It would be similar to the alarm over Ebola except that yellow fever did actually cause epidemics in the Americas where Ebola hasn't yet.

Erin Allmann Updyke

Right. Thank goodness.

Erin Welsh

Yeah, thank goodness. Before the insane Memphis epidemic, one epidemic in particular stands out in a series of the 18th century epidemics. 1793 was once again an El Niño year and Philadelphia was having a heck of a rainy summer.

Erin Allmann Updyke

(laughs) A heck of a rainy summer there, huh?

Erin Welsh

(laughs) Exactly. And you know what that means?

Erin Allmann Updyke

Mosquitos.

Erin Welsh

Uh huh. At this time the U.S. was in its infancy as a country and Philadelphia was the new nation's temporary capital.

Erin Allmann Updyke

Not anymore.

Erin Welsh

It was also full of people and one of the more popular port cities. Soon after ships containing refugees and slaves from the Caribbean docked in the harbor, reports of yellow fever began appearing. Misguided public health officials decided that it meant that the disease wasn't imported and that the rotting coffee and garbage down by the harbor were to blame.

Erin Allmann Updyke

Oh my god, people.

Erin Welsh

I know right? Miasma strikes again.

Erin Allmann Updyke

Yeah.

Erin Welsh

Soon the numbers of infected were in the thousands and the government effectively shut down. George Washington, John Adams, Thomas Jefferson, Alexander Hamilton, basically all of the Founding Fathers of the U.S. were witness to the fever. And Alexander Hamilton actually came down with it and survived.

Erin Allmann Updyke

Really? A. Ham!

Erin Welsh

I don't know about the Hamilton musical very much, even though it's like the most popular thing in the world right now.

Erin Allmann Updyke

Well it's because we can't afford tickets because we're grad students.

Erin Welsh: No. (laughs) But if any of your listeners are big fans, I really wanna know whether they talk about him getting yellow fever.

Erin Allmann Updyke: Me too, tell us!

Erin Welsh: Let us know please.

Erin Allmann Updyke: I mean we could ask my mom.

Erin Welsh: Yeah you could.

Erin Allmann Updyke: My parents went and saw it cause they're cooler than me.

Erin Welsh: (laughs) So all in all, over 10% of the Philadelphia population of 40,000 died during the epidemic.

Erin Allmann Updyke: Wow. So I have heard that yellow fever specifically was a large part of the reason that the capital ended up moving. Is that the case?

Erin Welsh: So I did a little bit of research into this and I don't know whether that's necessarily the case.

Erin Allmann Updyke: Okay.

Erin Welsh: So Washington D.C. and the White House and that whole area was being built from like 1790-1800.

Erin Allmann Updyke: Okay.

Erin Welsh: And so I think that Philadelphia was chosen to be a temporary capital but I do think it started out as being more or less the U.S. capital. But I don't know if yellow fever was the reason it moved or if it was, you know, building was pushed forward more.

Erin Allmann Updyke: Right. Or something. Maybe a historian could tell us.

Erin Welsh: Yeah. That'd be great.

Erin Allmann Updyke: Yeah.

Erin Welsh: Switching gears a little.

Erin Allmann Updyke: Yeah.

Erin Welsh: Do you know what the Louisiana Purchase is?

Erin Allmann Updyke: Yes I've heard of it!

Erin Welsh: Okay.

Erin Allmann Updyke: That's thrilling.

Erin Welsh (laughs) So basically it's the deal that took place in 1803 where the U.S. bought a ton of land from the French. This land didn't just include Louisiana, now the land from the Louisiana Purchase makes up 15 states. It was a huge change that totally impacted the future of the U.S. and expansion into the west.

Erin Allmann Updyke Oh yeah. Big time.

Erin Welsh Without the Louisiana Purchase the history of the U.S. would be very, very different.

Erin Allmann Updyke Yeah.

Erin Welsh Now did you also know that the reason for its existence can be traced in part to yellow fever?

Erin Allmann Updyke (gasps) Was it because like all the French people were dying of yellow fever and they're like, 'We wanna get the hell out of here'?

Erin Welsh Well not so much.

Erin Allmann Updyke Oh.

Erin Welsh But it's a little bit similar.

Erin Allmann Updyke Okay tell me it. I'm not good at guessing.

Erin Welsh (laughs) So in the years leading up to the 1803 Louisiana Purchase, France controlled a fair bit of land both in what is now the U.S. and in many Caribbean countries. And in 1802, France and the U.S. almost went to war over some trading and taxation crap which is actually interesting but I don't wanna go into cause we have no time.

Erin Allmann Updyke No, no. This is a disease podcast not a tax podcast or whatever.

Erin Welsh Oh god. (laughs) Snooze. War was so close at hand that Thomas Jefferson, who was the U.S. president at the time, sent like 50,000 troops to New Orleans.

Erin Allmann Updyke Wow.

Erin Welsh But they never had to fight. And they didn't have to fight because of yellow fever. Napoleon who was at the time not Emperor Napoleon-

Erin Allmann Updyke Okay.

Erin Welsh -was assembling troops in western Haiti, which was a French colony. Both to quell the recent slave uprisings in Haiti and to prepare to go to war with the U.S. He started with 20,000 troops.

Erin Allmann Updyke Uh oh.

Erin Welsh And when they started to die by the thousands due to yellow fever, he ordered 20,000 more. And he ordered more troops after his replacement troops died.

Erin Allmann Updyke

Oh my god.

Erin Welsh

In total an estimated 3000 troops were left alive at the end of this ordeal with over 50,000 of their comrades killed by the illness.

Erin Allmann Updyke

What? Holy heck!

Erin Welsh

Yeah, it's insane. Obviously this left them powerless and humiliated.

Erin Allmann Updyke

Uh yeah.

Erin Welsh

And the few French that remained left Haiti which became independent. And soon after, Napoleon signed away Louisiana stating that he could in no way afford a campaign against the U.S. All because of yellow fever.

Erin Allmann Updyke

Wow!

Erin Welsh

Isn't that crazy?

Erin Allmann Updyke

Yeah.

Erin Welsh

It's so cool. During the Civil War soldiers died of yellow fever by the thousands, and this is where we see a particularly despicable act of attempted bio warfare. I had to throw this is cause this is just one of my favorite little tidbits of everything I've read.

Erin Allmann Updyke

Tell me, I've never heard about biowarfare with yellow fever.

Erin Welsh

Dr. Luke Pryor Blackburn of my home state Kentucky-

Erin Allmann Updyke

Kentucky!

Erin Welsh

-earned his nickname 'Dr. Black Vomit' after sending soiled clothing of yellow fever victims to northern cities in an attempt to help the South win the war.

Erin Allmann Updyke

Oh my god. That's so misguided.

Erin Welsh

(laughs) Oh wait. He also had plans to burn New York City to the ground and poison the water supply.

Erin Allmann Updyke

(laughs)

Erin Welsh

But he wasn't done there. He tried his hand at assassination by packing up clothing and bedding again from yellow fever wards and shipping them to president Abraham Lincoln. Obviously it didn't do anything! (laughs)

Erin Allmann Updyke

Hey, check out these dirty clothes! They're covered in black vomit. See how that treats yeah.

Erin Welsh

Oh my god. Yeah obviously it didn't do anything.

Erin Allmann Updyke Well but they had had no idea, they didn't know how... I mean it worked so well with smallpox to kill off Native Americans.

Erin Welsh Yeah he's like, 'That's a great idea!'

Erin Allmann Updyke Let's do it again!'

Erin Welsh Well it also didn't do anything to hurt his career.

Erin Allmann Updyke (laughs) Everyone was like, 'You're full of good ideas man, just keep trying. Just keep trying.'

Erin Welsh He later became governor of Kentucky. (laughs) Oh my god. Okay. So now let's pick up where I left off earlier. After what happened in Memphis and in response to the high death toll caused by the virus during the Spanish-American War, the Yellow Fever Commission was formed. Their goal: to try desperately to find out what the cause of yellow fever was and to try and stop it. This four person super team based in Cuba was made up of two army physicians, Walter Reed whose name you've heard, and James Carroll and two civilian physicians, Jesse Lazear and Cuban-born Aristides Agramonte.

Erin Allmann Updyke Jesse? Is that a man or a woman?

Erin Welsh It's a man.

Erin Allmann Updyke Damn.

Erin Welsh I don't think women were allowed to practice medicine at the time.

Erin Allmann Updyke Do anything? Besides bear children.

Erin Welsh Each of these men would come onto the project with their own unique personalities, sometimes clashing, sometimes complementary and their own preconceived notions about yellow fever. Jesse Lazear, who was an easygoing man devoted to his family, had a hunch that it could be the mosquito, a theory originated by a Cuban researcher named Carlos Finlay. As per usual, Finlay's early work supporting this theory was ignored by the research community. But he kept going, thank goodness. And so when Jesse Lazear approached him about it, he was delighted and helped by sharing his data and samples.

Erin Allmann Updyke Aw!

Erin Welsh He was just like, 'Great, yeah! I'm totally down to help and collaborate.' Super cool.

Erin Allmann Updyke Cool! That's awesome.

Erin Welsh All Lazear had to do was design an experiment. This was the late 1800s so he went with human experimentation.

Erin Allmann Updyke That's what you do.

Erin Welsh Naturally, yeah. He fed mosquitoes on a yellow fever patient, collected them, and then had them feed on unexposed people.

Erin Allmann Updyke Oh god.

Erin Welsh Fortunately for them and unfortunately for the commission, no one became infected. Lazear was a touch disheartened by this but kept at it. In order to have a research colony of mosquitoes, you have to keep them fed.

Erin Allmann Updyke Yeah.

Erin Welsh And while today there exist really cool contraptions for mosquito feeding, back in the day you were their meal.

Erin Allmann Updyke A lot of people still do that.

Erin Welsh Yeah it's true.

Erin Allmann Updyke It's like easier and faster and just like, well, here you go. Here's my arm.

Erin Welsh (laughs) Sounds horrible.

Erin Allmann Updyke We don't study mosquitoes. (laughs)

Erin Welsh I don't have to keep my ticks alive, I just kill them.

Erin Allmann Updyke Me neither.

Erin Welsh About 12 days after this first failed experiment, Carroll, who was another member of the commission, stopped by the lab to see how things were going. Lazear asked him, 'Hey, you wouldn't mind offering up your arm. One of these mosquitoes hasn't been fed in a while.'

Erin Allmann Updyke Oh.

Erin Welsh Carroll was like, 'Yeah, sure.' He probably viewed it as low risk. It had been a long time since the mosquito had fed on a yellow fever patient and Carroll didn't believe too strongly in the mosquito-borne idea anyway. Guess what? He became the first experimentally-infected person for the commission.

Erin Allmann Updyke Wow.

Erin Welsh After days of high fevers, delusion, and wracking pain he survived.

Erin Allmann Updyke Wow.

Erin Welsh Yeah. But the infection would impair his health for the rest of his life.

Erin Allmann Updyke Wow.

Erin Welsh Lazear was horrified that he had done this to his friend and collaborator-

Erin Allmann Updyke

But thrilled?

Erin Welsh

But like also, what was he expecting?

Erin Allmann Updyke

Yeah! Was he also like, 'Oh I'm so sorry that you got sick but also yes, I was right.'

Erin Welsh

Yeah I think he was a bit encouraged at this point. And he kept at the experimentation until the U.S. was like, 'Hey man, you've got to stop experimenting on people. We're not doing this anymore.'

Erin Allmann Updyke

(laughs) He was like, 'I told you so guys. I told you so.'

Erin Welsh

He was like, 'God, are you kidding me? Fine. Fine.'

Erin Allmann Updyke

Wink wink, nudge nudge.

Erin Welsh

Yeah. And in his lab notebook where he kept track of every person who had been fed on by an infected mosquito, one final entry noted that quote: "guinea pig number one was fed on." Every other person who he had kept track of in his journal had their name and information.

Erin Allmann Updyke

But then the last person-

Erin Welsh

Guinea pig.

Erin Allmann Updyke

Interesting. But it wasn't an actual guinea pig was it?

Erin Welsh

No.

Erin Allmann Updyke

A human.

Erin Welsh

We don't know who this guinea pig was but many believe it was Lazear himself. It wouldn't be the first time he'd intentionally exposed himself to the virus but it would be the last. After days of battling the infection, he succumbed. He never got a chance to see his wife, son, or newborn daughter again whom he had sent home during a yellow fever outbreak months before.

Erin Allmann Updyke

Aw, that's sad.

Erin Welsh

It's really sad.

Erin Allmann Updyke

What a way to go.

Erin Welsh

I know. And though his death did convince many that mosquitoes were the vessel for the virus, it wasn't airtight science. After all we don't know that he was guinea pig number one for sure.

Erin Allmann Updyke

Right.

Erin Welsh

And no one could say that conclusively because if he had intentionally exposed himself after the U.S. had handed down this order to not do it anymore, his wife and kids would be left with no-

Erin Allmann Updyke: Because he violated orders?

Erin Welsh: Not because he violated orders, because it would have appeared as suicide.

Erin Allmann Updyke: Oh!

Erin Welsh: So the life insurance policy, it would have been nullified.

Erin Allmann Updyke: Oh interesting. Whoa.

Erin Welsh: Yeah.

Erin Allmann Updyke: That's, I guess, why he didn't write his name down. That would be evidence to point o, that it was him.

Erin Welsh: Mm-hmm.

Erin Allmann Updyke: Interesting.

Erin Welsh: Yeah.

Erin Allmann Updyke: What a crazy person though, why would he do that?

Erin Welsh: He felt so close to proving that mosquitoes were the vector for yellow fever.

Erin Allmann Updyke: Wow.

Erin Welsh: He was just too passionate about science.

Erin Allmann Updyke: I guess. Not me.

Erin Welsh: (laughs) So yeah, even though he died after being bitten by, well we assume being bitten by the infected mosquito, it wasn't conclusive and so more experiments would be needed with more human volunteers.

Erin Allmann Updyke: Yeah.

Erin Welsh: Which did actually continue to happen, strangely.

Erin Allmann Updyke: Weird.

Erin Welsh: I will say that in these later experiments, the mortality of those infected was 0 or very close to it. Eventually the mosquito was accepted as the transmitter of yellow fever and this knowledge was used in control strategies like the ones I talked about with malaria and the panama canal and so on.

Erin Allmann Updyke: Yeah. Yeah.

Erin Welsh: Even though there was the knowledge necessary to get rid of the mosquito, the world needed a more permanent solution.

Erin Allmann Updyke: Yeah.

Erin Welsh: The yellow fever vaccine was developed by Max Theiler in the 1930s and was deployed globally in a massive vaccination campaign. Theiler, by the way, would be the only yellow fever Nobel Prize winner. After these vaccination campaigns ended, the disease picked up speed causing more and more infections particularly in African countries during the 50s through the 90s. During the 1960-1962 epidemic in Ethiopia, about 100,000 people were infected and 30,000 died.

Erin Allmann Updyke: Whoa. Wow that's a 30% mortality rate!

Erin Welsh: Yeah and that was in a population of 1 million.

Erin Allmann Updyke: Wow!

Erin Welsh: Mm-hmm. So 10% got infected and of those infected, 30% died.

Erin Allmann Updyke: Oh my gosh.

Erin Welsh: And that's where I hand it off to you.

Erin Allmann Updyke: Oh my goodness.

Erin Welsh: Tell me about yellow fever today.

Erin Allmann Updyke: (laughs) Okay.

TPWKY: (transition theme)

Erin Allmann Updyke: So yellow fever today. It's either considered endemic or important, meaning there's outbreaks and things like that, in 34 countries in Africa and 13 countries in Central and South America.

Erin Welsh: Okay.

Erin Allmann Updyke: Mostly just South America. As far as I can tell in Central America it's just half of Panama, that's it for Central America.

Erin Welsh: Which half of Panama?

Erin Allmann Updyke: The eastern half.

Erin Welsh: The Darién side?

Erin Allmann Updyke: Yeah, exactly. It's really just in the Darién.

Erin Welsh: Okay.

Erin Allmann Updyke In 2017 so far there've been outbreaks or reports of outbreaks in Nigeria, Brazil, French Guiana, and Suriname. And in 2016 there were reports from Angola, the Democratic Republic of Congo. There were actually several cases in China but they were all imported from Angola.

Erin Welsh Oh, okay.

Erin Allmann Updyke Yeah. So case reports really vary wildly from year to year and I think that part of the reason is that surveillance is just really not good for this disease.

Erin Welsh Why do you think that is?

Erin Allmann Updyke I don't know. And I've had a really hard time trying to figure out why it's so difficult to get hard numbers on how many people are getting infected with yellow fever every year. Because it's endemic in a lot of the same places as malaria and WHO is like, 'We have this yellow fever task force, blah blah blah,' where they're putting out, they're trying to get everyone vaccinated. And I would think if you're trying to get everyone vaccinated, you know how many people are getting infected. But the most recent numbers that I found were from 2013 where they were estimating that between 84,000-170,000 people came down with the severe form of yellow fever in Africa alone.

Erin Welsh What? Can you say those numbers again?

Erin Allmann Updyke Yeah. 84,000-170,000.

Erin Welsh Wow! The severe.

Erin Allmann Updyke The severe.

Erin Welsh Like black vomit.

Erin Allmann Updyke Exactly.

Erin Welsh Oh my god.

Erin Allmann Updyke And of those there were between 29,000-60,000 deaths.

Erin Welsh (gasps) That's a really high mortality rate.

Erin Allmann Updyke It's high mortality and it's a lot of people and it's a huge range which means we really don't know.

Erin Welsh Yeah.

Erin Allmann Updyke And its estimated that the actual number of cases are anywhere from 10-250 times higher.

Erin Welsh I'm sorry.

Erin Allmann Updyke Right?

Erin Welsh: 250 times?

Erin Allmann Updyke: 250 times.

Erin Welsh: Okay.

Erin Allmann Updyke: And I think that, my guess is that a large part of this is that we really only hear about the severe cases. And remember that that's usually only about 15% of cases that end up with that severe form because a mild form of this disease, you're either not gonna go to the doctor at all or... Well really you're just probably not gonna go to the doctor at all. So you're never gonna get reported on, essentially.

Erin Welsh: Right.

Erin Allmann Updyke: You're just gonna assume it was influenza or malaria or dengue or whatever. Right?

Erin Welsh: Yeah it's just so interesting to me that this one... I don't know, like why we have such terrible, terrible estimates for it.

Erin Allmann Updyke: Yeah! And I didn't think, I mean I thought that especially because it's vaccine preventable, I would just be able to google, beep-boop-bop, how many people get yellow fever? But no, I can't find that information. If someone knows where to find it that I'm just not finding, please let us know.

Erin Welsh: Right. A better resource, that would be...yeah.

Erin Allmann Updyke: There are not great hard numbers out there. Yeah. But there are definitely outbreaks that happen every year and so there's, you know, information on specific outbreaks. Like there's one going on in Brazil, it mostly seems to be over at this point, it was really from like July to October where there was about 70 cases that they suspected might be yellow fever. Only two of them have so far tested as positive for yellow fever.

Erin Welsh: Interesting.

Erin Allmann Updyke: And so especially in South America a lot of the surveillance is actually done on monkey populations.

Erin Welsh: Mm-hmm.

Erin Allmann Updyke: So they keep track, or they try to keep track of any what they call 'epizootics' or outbreaks in animal populations.

Erin Welsh: Okay.

Erin Allmann Updyke: So for example there's been at least 120 cases this year so far in Brazil that have been confirmed of yellow fever in nonhuman primates.

Erin Welsh: Oh, okay.

Erin Allmann Updyke

So that's when you can end up with then spillover from those nonhuman primate populations into humans.

Erin Welsh

Yeah.

Erin Allmann Updyke

And one thing that's really important to talk about yellow fever today is the information that this *Aedes aegypti* and *Aedes albopictus*, these mosquitoes are everywhere.

Erin Welsh

Right?

Erin Allmann Updyke

I mean basically everywhere. And their ranges are expanding and this is why we've seen outbreaks of things like Zika and chikungunya recently in places that they never existed before is because if you introduce an infected person, a human who's infected with this virus into a new environment, all it takes is one single mosquito to basically start a brand new epidemic. Because remember mosquitoes are transmitting this virus vertically to their offspring. So it really just takes one.

Erin Welsh

Yeah. That's really scary.

Erin Allmann Updyke

It's really scary. So currently yellow fever isn't a problem in Asia. It never has been for some reason, people really aren't quite sure why it hasn't been a bigger problem there because you do have dengue and things like that. So it's kind of a mystery as to why we haven't seen yellow fever outbreaks there the way we've seen them in South America and in Africa.

Erin Welsh

Interesting.

Erin Allmann Updyke

Yeah. You definitely have *Aedes* mosquitoes there. You have dengue infection so you have mosquitoes that are capable of transmitting this virus, so you're kind of already ready to go on that front. So the introduction of an infected person could be really devastating because the population of humans is totally naïve, presumably.

Erin Welsh

Mm-hmm.

Erin Allmann Updyke

And to a certain extent you have seen things like this happen where you have migration of transmission into, for example, Amazonian regions of Peru from more coastal regions and things like that.

Erin Welsh

Okay.

Erin Allmann Updyke

So yeah, on that front it's really scary. The potential for this to become a much more widespread disease definitely exists. So a lot of countries actually require that you show proof of immunization for yellow fever if you show that you've been traveling to any areas that are considered endemic for yellow fever.

Erin Welsh

This is like the yellow card, the transport card?

Erin Allmann Updyke

Exactly, yeah that yellow yellow fever card.

Erin Welsh

Yeah, we've been vaccinated.

Erin Allmann Updyke

Yes. Thank goodness cause I don't wanna get yellow fever.

Erin Welsh: Yeah.

Erin Allmann Updyke: So one of the other big problems besides globalization that's affecting yellow fever distribution is deforestation. So as humans are further encroaching onto forested areas, they're exposing themselves more to the sylvatic cycle of the disease by coming into closer contact with animals and the sylvatic mosquitoes that usually feed on these animals. And this is true in both Africa but also especially in South America where that enzootic cycle is definitely occurring.

Erin Welsh: Okay. Man, stop cutting down trees, people!

Erin Allmann Updyke: Right?

Erin Welsh: Your life depends on it.

Erin Allmann Updyke: Yeah. And the good news is that there is this vaccine. And the vaccine is pretty awesome.

Erin Welsh: Yeah!

Erin Allmann Updyke: It's an attenuated vaccine, so it's a live virus, and there's at least about 10% of children for whom it doesn't seem to work so they need to get boosters, I'm not entirely sure why it is but for some kids it just doesn't quite work that well, it doesn't provide long-lasting immunity. But recent studies have shown that especially for adults, this vaccine provides extremely long-lasting immunity to the point where they're no longer even recommending booster shots for adults.

Erin Welsh: Wow.

Erin Allmann Updyke: Yeah. The immunity is really great from this vaccine.

Erin Welsh: That's awesome.

Erin Allmann Updyke: Yeah. The problem is how to get this vaccine delivered to everyone in endemic areas. So that's a problem for so many things.

Erin Welsh: Yeah but I mean, I guess the thing is like malaria we can definitely see how difficult it is to control and monitor and get the drugs out and there is no malaria vaccine.

Erin Allmann Updyke: Right.

Erin Welsh: But for something like yellow fever when you can vaccinate a population, I guess since you can't eradicate it from the environment there are still going to be susceptible pockets.

Erin Allmann Updyke: Exactly, there's still going to be I think low levels of transmission.

Erin Welsh: Right.

Erin Allmann Updyke: Because of that enzootic cycle.

Erin Welsh: It just seems so high, those numbers seem so high though.

Erin Allmann Updyke: Yeah I mean they are! Because not everyone is vaccinated.

Erin Welsh: Yeah.

Erin Allmann Updyke: There's also issues with your immune status at the time that you get the vaccine is really important. So if you have like a compromised immune system whether from HIV infection or malnutrition which is a problem in a lot of areas where this is endemic, then the evidence is still out on how effective the vaccine actually is.

Erin Welsh: Okay.

Erin Allmann Updyke: But there have been quite a lot of mass vaccination campaigns, especially in Africa. I think WHO estimates that they've vaccinated over 105 million people in the last few years in Africa.

Erin Welsh: Wow.

Erin Allmann Updyke: Which is pretty great.

Erin Welsh: Yeah.

Erin Allmann Updyke: It's also important to note that while very rare, there is the possibility of what's called vaccine-associated viscerotropic - and that's a big word - disease. It basically means that you can get a disease very similar to regular yellow fever from the vaccine.

Erin Welsh: That's not yellow fever?

Erin Allmann Updyke: It is yellow fever but... So the vaccine is derived from a specific strain of yellow fever and has been attenuated to be even less virulent but for some reason in a very small number of cases, like 0.4 per 100,000 people.

Erin Welsh: Oh that's very small.

Erin Allmann Updyke: It's very small. You get this disease that is essentially looks just like normal yellow fever.

Erin Welsh: Okay, bad news.

Erin Allmann Updyke: And it can be really devastating, it has a fatality rate of about 63% so it's really bad.

Erin Welsh: Whoa.

Erin Allmann Updyke: Yeah. But again there was only about 65 cases of that between 2001 and 2011.

Erin Welsh: Oh okay.

Erin Allmann Updyke: So it's pretty low, you know. It exists.

Erin Welsh: Yeah, yeah.

Erin Allmann Updyke

So overall how scared do you need to be? I'd say keep your eye on it because of globalization, global travel, urbanization and deforestation-

Erin Welsh

Climate change.

Erin Allmann Updyke

And also climate change. There's a real possibility that we could see expansion of or changes in the range of yellow fever and it's hard to say for sure that current vaccine stockpiles would be enough to prevent epidemics. Because when an outbreak happens, you need to have vaccination, like bring vaccination around all the people or the whole area where you have an outbreak of at least 80-90% of people, and that's really high coverage that you would need for everyone to be vaccinated in order to prevent spread. But I mean this vaccine does exist and it's really great.

Erin Welsh

Yeah, that's good. There's a vaccine.

Erin Allmann Updyke

There's a vaccine. So if we could just get that vaccine to every person who's living in endemic areas then we really wouldn't have to worry too much about yellow fever.

Erin Welsh

Yeah. And nor would they.

Erin Allmann Updyke

Nor would they, exactly. (laughs) So yeah.

Erin Welsh

So that's yellow fever.

Erin Allmann Updyke

I think that's yellow fever.

Erin Welsh

That was a really interesting one.

Erin Allmann Updyke

It was.

Erin Welsh

Yellow fever is one that kind of just goes under the radar a bit.

Erin Allmann Updyke

Yeah. I think because there is a vaccine for it, people kind of forget about it. Like, 'Oh we don't need to worry about yellow fever, there's a vaccine!'

Erin Welsh

Mm-hmm.

Erin Allmann Updyke

But not everyone has gotten the vaccine.

Erin Welsh

Clearly. Yeah clearly it's still causing a lot of problems.

Erin Allmann Updyke

Right.

Erin Welsh

Well should we cite ourselves?

Erin Allmann Updyke

Let's cite our citation sources.

Erin Welsh (laughs) I've got a few books here. 'The American Plague' by Molly Caldwell Crosby is really great, and this focuses mainly on the Memphis epidemic in 1878 and the formation of the Yellow Fever Commission. Yeah and she just does a really good job telling these stories. It's a historical narrative and so it reads really well, I really enjoyed it.

Erin Allmann Updyke Yeah! That was one of the first disease books I read for fun.

Erin Welsh Me too! Yeah. (laughs) The other one is called 'Viruses, Plagues and History' by Michael BA. Oldstone and it's a really good overview. And I didn't read this this time but as a kid I read a young adult book called 'Fever: 1793' by Laurie Halse Anderson and it's about the 1793 Philadelphia epidemic of yellow fever. I remember loving it as a kid, so I put it on the book list as a 'hey, you guys should read this'.

Erin Allmann Updyke Awesome. You should read this. We forgot to cite also where that firsthand account came from.

Erin Welsh Right, I was thinking about that.

Erin Allmann Updyke I realized, woops. So that came from a book called 'Guinea Pig Doctors: the drama of medical research through self-experimentation' by John Franklin and John Sutherland.

Erin Welsh Cool.

Erin Allmann Updyke Cool. And then I also have to cite a couple of articles that were really interesting to read about the biology especially of yellow fever. One is called 'Yellow Fever' by Monath and Vasconcelos in 2014, and the other called 'Efficacy and duration of immunity after yellow fever vaccination: systematic review on the need for a booster every 10 years' by Gotuzzo et al 2013. And we have a book list that we will be posting, it's on our Facebook page, it's on our website thispodcastwillkillyou.podbean.com, so if you ever want to find these articles and books you can go there and find them there.

Erin Welsh Yeah and we'll also post the books and articles for every episode that we do when the episode comes out. Got a Goodreads list, yeah, there are a lot of different resources but yeah, we want you guys to read cause reading's fun. (laughs)

TPWKY (transition theme)

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

Erin Allmann Updyke Yeah. Thanks for listening everybody.

Erin Welsh Rate, review, and subscribe. Now wash your hands.

Erin Allmann Updyke Filthy animals!