TPWKY	This is Exactly Right.
	(Skype calling sound)
Erin Welsh	Hello?
Ummat Somjee	Hey!
Erin Allmann Updyke	Yay! (laughs)
Erin Welsh	How's it going?
Ummat Somjee	It's going well. I just made it back home and I frantically prepared a gin and tonic, a gin and tonic with a lemon slice.
Erin Welsh	We'll accept it.
Erin Allmann Updyke	(laughs)
Ummat Somjee	(laughs) Okay.
Erin Welsh	So for this episode we decided to sit down with our good friend Umat to ask him about his personal experiences with malaria.
Ummat Somjee	I'm Ummat Somjee, I grew up in Nairobi, Kenya. Right now I'm a graduate student at the University of Florida Gainesville and I met Erin and Erin in Gamboa, Panama while we were doing fieldwork at this tropical research station. I remember I had just come from a camping trip in western Kenya and I had been back in Nairobi where I lived and my parents lived for about two weeks. One day I was just feeling really lethargic and tired and I had this lower back pain, that was really memorable, this pain in my lower back. And I went to bed and in the morning I was confused, I had a fever, I was really sick, my body hurt a lot. So I remember just having like really weird, wacky dreams you know and having these high fevers.
	And so my parents took me to the doctor's and I got blood tests. Living in the tropics, there's a lot of different things that you could get. Of course they did the malaria test and they didn't find malaria. But I had these very cyclical fevers, I would get really, really cold and suddenly I'd be really, really hot again. And I remember when I had the fever, when I was feeling really cold, I would be shivering so much that my muscles would contract so much that they'd be hurting. And I went for another blood test cause my mom was suspicious that this actually might be malaria. And still there was no positive malaria diagnosis.
	But then my mom took me to the hospital at 2am and I didn't know what was happening, I didn't know why we were going to the hospital in the middle of the night. And I got a blood test done that time and they diagnosed me with malaria. And I didn't learn until later that it's really common for malaria not to be in your peripheral bloodstream until the middle of the night. So yeah, that was kind of an interesting experience. I feel like malaria was such a big part of life growing up in Kenya. I feel like it was the disease that whenever somebody had a fever or any sort of sickness, you'd always wonder like, is it malaria? Cause it could be, you know. It's really common there. So when you're really young you learn about the Anopheles mosquito. So I remember like in primary school growing up, we learned about Anopheles and what it looked like when it was resting, it has this very unique posture when it's resting and you can recognize it immediately and it's something that everybody learns in school from a really young age.

	When I was really young, you know how as a stereotype every young kid hates to have the chore of doing their beds? Just like any kids I hated doing my bed but there was something else I had to do, I had to fold up and roll up my mosquito net every day and every night I had to unroll it and tuck it around my bed so I could go to sleep for the night. And you know I hated doing it, it's a chore and it's this extra thing you have to do and I would do it badly sometimes. I remember lots of times my parents waking me up and I had gone to sleep a rebellious teenager not putting my mosquito net on. (laughs) I was the worst, yeah. And you know, I'd be like, 'Okay fine! I'll do it!'
Erin Allmann Updyke	That is the most beautiful introduction we could've ever asked for for this episode. (laughs)
Ummat Somjee	(laughs)
Erin Welsh	Yeah. Absolutely.
Erin Allmann Updyke	It was like textbook perfection. (laughs)
Ummat Somjee	Oh really? Okay.
Erin Welsh	So thank you for going through that experience! (laughs)
Erin Allmann Updyke	Yeah. (laughs)
Erin Welsh	So that was incredible.
Erin Allmann Updyke	Amazing.
Erin Welsh	Thank you so much Ummat for sharing your story about malaria and wow...
TPWKY	(This Podcast Will Kill You intro theme)
Erin Allmann Updyke	Hi and welcome to Episode 8. Holy crap.
Erin Welsh	Holy crap.
Erin Allmann Updyke	Of This Podcast Will Kill You.
Erin Welsh	I'm Erin Welsh.
Erin Allmann Updyke	And I'm Erin Allmann Updyke.
Erin Welsh	Thanks for joining us.
Erin Allmann Updyke	We're very excited.
Erin Welsh	This week we're talking about malaria.
Erin Allmann Updyke	Yeah.

Erin Welsh	Which is a big one but we're gonna have a good time today.
Erin Allmann Updyke	Totally. It's gonna be really fun, I'm thrilled about it.
Erin Welsh	Malaria is fascinating.
Erin Allmann Updyke	It's a really... It's actually one of the first diseases that made me want to study disease, so I'm really excited.
Erin Welsh	Oh I didn't know.
Erin Allmann Updyke	Yeah, malaria and schistosomiasis.
Erin Welsh	Oh!
Erin Allmann Updyke	They're like really close to my heart. (laughs)
Erin Welsh	That's so cool.
Erin Allmann Updyke	Yeah.
Erin Welsh	All right.
Erin Allmann Updyke	I'm excited about it.
Erin Welsh	Learned something new about you.
Erin Allmann Updyke	Right? But before we jump in, we have a correction to make.
Erin Welsh	Yes, we do.
Erin Allmann Updyke	We always say if we get something wrong, please let us know. And this is proof that we're not lying. All of this is outside of our area of expertise.
Erin Welsh	We expect to get things wrong.
Erin Allmann Updyke	So in the very first episode, eight whole weeks ago at this point-
Erin Welsh	Whoa!
Erin Allmann Updyke	I know, right? We talked about influenza and I mistakenly said that influenza was a retrovirus. That is incorrect. Thank you, Dustin, for letting us know that.
Erin Welsh	Yeah, thank you.
Erin Allmann Updyke	But anyways, that's our correction. Influenza is an RNA virus but it is not a retrovirus. So if you have a correction for us, you can go ahead and send that to thispodcastwillkillyou@gmail.com or you can message us on any of our social media profiles as well.

Erin Welsh	Yeah.
Erin Allmann Updyke	That is all.
Erin Welsh	All right. That means that we're on to quarantinis.
Erin Allmann Updyke	Ooh!
Erin Welsh	What are we drinking this week?
Erin Allmann Updyke	This week is the Fever Reliever. (laughs)
Erin Welsh	Wonderful. And what is in the Fever Reliever?
Erin Allmann Updyke	Well since we're talking about malaria today, we're drinking basically a gin and tonic.
Erin Welsh	Okay.
Erin Allmann Updyke	And when I say 'basically' I mean it's a gin and tonic, people.
Erin Welsh	With a lime.
Erin Allmann Updyke	Yes.
Erin Welsh	All right. And we're gonna get into why that has anything to with malaria later on in the episode. So stay tuned.
Erin Allmann Updyke	Yes. Make sure your tonic water has quinine in it.
Erin Welsh	Yeah. It won't be any sort of effective dose, but...
Erin Allmann Updyke	No, no. No. Just enough to be delicious. (British accent) Cheers.
Erin Welsh	(British accent) Cheers, cheers.
Erin Allmann Updyke	(British accent) Cheers, cheers. Yes, with a British accent for many reasons. Cheers. Delicious.
Erin Welsh	Gin and tonics, when I was living in Panama, they were my drink.
Erin Allmann Updyke	Too bad that you weren't living in an area of Panama where malaria was a real risk factor.
Erin Welsh	I don't think that's too bad.
Erin Allmann Updyke	Self-medicating. (laughs)
Erin Welsh	(laughs) I'm pretty okay with that fact.

Erin Allmann Updyke	You're happy about it? All right.
Erin Welsh	Cool.
TPWKY	(transition theme)
Erin Welsh	So now that we've got our quarantinis underway, we're going to delve right into the biology. Erin, tell me about malaria.
Erin Allmann Updyke	I will try my best. (laughs) Malaria is a big one and one of the things that makes malaria so interesting is the fact that it has a really complex life cycle, which means it's gonna be complex to talk about today.
Erin Welsh	But we're gonna simplify it as much as possible.
Erin Allmann Updyke	Yes. So malaria is caused by a parasite. This is the first disease that we're talking about on the show that's caused by a parasite.
Erin Welsh	Can you explain to me the difference between a parasite and a pathogen?
Erin Allmann Updyke	Yes. So we usually use the word pathogen to refer to viral and bacterial diseases.
Erin Welsh	Okay.
Erin Allmann Updyke	A parasite is usually referred to only for what are called protozoans or like parasitic worms and things.
Erin Welsh	Okay. And protozoans are not bacteria.
Erin Allmann Updyke	Right. So protozoa, it's not a great term but it essentially means it's still a single-celled organism but it's much larger than a bacteria or a virus and it's more closely related to plants and animals than it is to bacteria.
Erin Welsh	So a little more complex.
Erin Allmann Updyke	Exactly, yeah. So malaria is a protozoa.
Erin Welsh	All right.
Erin Allmann Updyke	There are several different species of parasite that cause malaria. The one that causes the worst disease in humans and is the most widespread is called Plasmodium falciparum. This is the species that's the most common throughout most of Africa and it replicates really quickly so it causes a very severe form of disease. The other species are Plasmodium vivax, which is the most common species in Asia and it along with another species called Plasmodium ovale have these dormant stages that kind of hang out in your liver for a long period of time where they're not really causing any active infection, not really causing any real symptoms but they can just hang out there and then re-emerge later in your life, like months or years later.

Erin Welsh	Which is important also in the distribution for the mosquito and the seasonality of this because something like falciparum has to occur where the species occurs year round, the mosquito species occurs year round.
Erin Allmann Updyke	Right, yeah.
Erin Welsh	Whereas something like vivax can exist in a place that has more seasonality to it in terms of cold and warm.
Erin Allmann Updyke	Yeah. Definitely. And then finally there's Plasmodium malariae which is found pretty much worldwide and causes the most chronic infection if untreated. I should also note that there are other species of malaria that infect other mammals as well as birds. Avian malaria is actually really important and is a major cause of decline of native bird populations in Hawaii and other places but unfortunately we don't have the time to talk about those today. Maybe we could have a future episode on avian malaria?
Erin Welsh	Yeah, yeah.
Erin Allmann Updyke	Anyways, let's talk about the life cycle, shall we? (laughs)
Erin Welsh	Let's do it.
Erin Allmann Updyke	So malaria infection starts when an infected female mosquito, put my entomologist hat on here, because it's only female mosquitoes that bite you and suck your blood, male mosquitoes just drink nectar, they're just little beep bops.
Erin Welsh	Okay.
Erin Allmann Updyke	So an infected female mosquito takes a blood meal, meaning sticks her snout into you and sucks your blood, and as she does this the parasites which are in her salivary glands are injected into your bloodstream. These parasites which look kind of like little spores, they're just little balls at this point, once in your blood will infect your red blood cells or in some cases they'll travel through your bloodstream to your liver and infect your liver cells directly. Then once inside of your cells, the parasites begin to replicate. They replicate and replicate and eventually explode out of your blood cells and they'll fly freely through your bloodstream again.
Erin Welsh	Uh oh.
Erin Allmann Updyke	And this is what's actually causing the symptoms that we see in malaria, is when these thousands of millions of parasites explode open your red blood cells and then travel through your blood to find new cells to infect. So now these parasites are free-floating in your bloodstream and they can be picked up by another mosquito as it feeds on you. Then within the mosquito, the parasites have to travel through the mosquito's gut, survive through the stomach, replicate, reproduce, then they have to exit the gut which isn't easy to do because they're basically punching through the gut wall of this mosquito, then they have to travel to the salivary glands where they can then get ready to start the cycle all over again.
Erin Welsh	All this tells me is that I'm amazed that this is a real thing. Like it's so cool the way it's so complex how long it took for this to evolve.
Erin Allmann Updyke	Right.

Erin Welsh	Such a complex life cycle. It's very cool.
Erin Allmann Updyke	This is what I love about vector-borne diseases is how much more complex this becomes because you have this entire other organism and there is a part of this life cycle of this parasite that takes place only in the mosquito is dependent on that mosquito.
Erin Welsh	All players have to be there.
Erin Allmann Updyke	Exactly.
Erin Welsh	Cool.
Erin Allmann Updyke	Yeah. So transmission of malaria isn't direct person to person, it happens just from the bite of this infected mosquito. Specifically it's an Anopheles mosquito. There are several hundred species but only about 30 or 40 that are important in terms of human malaria transmission. And there's some evidence that once a mosquito is infected with malaria, like once these parasites are in the salivary glands and ready to infect a human, mosquitoes are more attracted to hosts, more persistent in their attempts to feed, and they feed on more hosts per feeding attempt. Which is crazy cause it's basically the malaria parasite going, 'Hey I'm Here! I'm ready to go! Better take a meal. Better take a meal. Better take a meal.'
Erin Welsh	That's super cool. It's host manipulation by a parasite.
Erin Allmann Updyke	Yeah! It's crazy.
Erin Welsh	That's one of my favorite themes, I guess, or like favorite things. Yeah like the zombie fungus, maybe we'll do an episode on cordyceps.
Erin Allmann Updyke	Definitely.
Erin Welsh	Cool.
Erin Allmann Updyke	No question, we have to.
Erin Welsh	Okay, sorry to interrupt.
Erin Allmann Updyke	No, you're fine. One thing I think that's really interesting about this, and I'll talk more about it later on, is just that in terms of thinking about prevention of malaria. On the one hand it makes it a lot harder to deal with prevention when you have an entire other species that you're trying to deal with, but it also means that there's a lot of stages of the malaria parasite that you could potentially target that are outside of the human, which I think is really interesting. So I'll talk more about that when we talk about the status of malaria in the world today.
	What else about malaria? So the incubation period, which again is the time from when you're infected to when you show symptoms, in this case from when you're bit by a mosquito until you have your first round of symptoms is between 7 and 30 days. And this large range depends on the species of parasite that you're infected with.
Erin Welsh	Okay.

Erin Allmann Updyke	So Plasmodium falciparum, the one that's sort of the worst, has the shortest incubation period while Plasmodium malariae has the longest.
Erin Welsh	That would make sense because you said falciparum replicates so quickly.
Erin Allmann Updyke	Exactly. So in some cases, because you can have this really long incubation period, diagnosis and treatment can be somewhat harder. Especially for example if you're traveling or you become infected while your traveling and you come back to a country where maybe malaria isn't very common, it can be really difficult to diagnose because it might be several weeks or months until you actually have any symptoms.
Erin Welsh	That makes sense.
Erin Allmann Updyke	Yeah.
Erin Welsh	So malaria's inside you, you've been bitten by a mosquito that has injected a bunch of parasites. What's my body gonna do?
Erin Allmann Updyke	Well first there's something that's called classic malaria which has a cold stage with shivering, feeling very cold' a hot stage where you have fever, headache, vomiting, young children can have seizures; and then a sweating stage where you just sweat a lot. But I don't know why they call it classic malaria because apparently this is a very rare presentation, like it doesn't usually happen this way.
Erin Welsh	Really?
Erin Allmann Updyke	Yeah, I don't know if maybe people have written about malaria in this way a lot and that's why it's called classic, but realistically what happens is all at once you have fever, chills, sweats, headaches, nausea, vomiting, body aches. You feel like absolute sh-
Erin Welsh	Human garbage?
Erin Allmann Updyke	Human garbage. And this happens in cycles. A classic attack lasts for between 6-10 hours and happens every 2-3 days depending on the parasite species. So Plasmodium falciparum replicates every two days, as does vivax and ovale, whereas malariae replicates every 3 days. So that means that in your cells, they're basically taking two days to have a full cycle of replication and then they're bursting out of your cells.
Erin Welsh	Okay.
Erin Allmann Updyke	And so that is how you end up with these fever and headaches is all of these parasites all at once are bursting out of your cells and into your bloodstream.
Erin Welsh	So each time you have this intense spike in all these symptoms it's in response to the parasite reproducing.
Erin Allmann Updyke	Exactly. And that is also when you're going to be most infective for mosquitoes because that's when these stages that are infective to the mosquito are free-floating in your bloodstream as well.
Erin Welsh	Okay that makes sense.

Erin Allmann Updyke	Yeah. So that's most of what you need to know, I think, about malaria biology. One thing that makes it difficult to control also is that diagnosis is really difficult. So typically it's done by microscopy, so you need a person who's very highly trained to actually take a smear of your blood on a microscope slide and look through it. And it's effective but you have to have people that are very well-trained, and even very well-trained people, because you have these cycles if you just take blood at the wrong time you might not see them or you might see things that look like malaria but aren't actually malaria. So basically microscopy is imperfect. There are other molecular methods that you can use for detection of malaria but they're also not perfect and in many cases they're expensive and sometimes cost prohibitive. But yeah, I think that's it for malaria biology.
Erin Welsh	Okay. So do you wanna hear about the history of malaria?
Erin Allmann Updyke	Oh I'm really excited about it.
TPWKY	(transition theme)
Erin Welsh	It spans eons.
Erin Allmann Updyke	Eons?
Erin Welsh	Oh, millions and millions of years.
Erin Allmann Updyke	What!? That's gotta be... That's the first time we've talked about millions of years on this show.
Erin Welsh	It probably is. Malaria's history is, yeah, it's enormous. And we're gonna get through it all.
Erin Allmann Updyke	Yes! In the next 10 minutes. Go! (laughs)
Erin Welsh	Uh oh. Well first, we're gonna go back to the dinosaurs and malaria's evolutionary origins. Then I'm gonna talk about malaria before treatments were discovered, then Panama Canal time.
Erin Allmann Updyke	Yes!
Erin Welsh	Just a little bit. And the failed eradication campaigns of the 20th century.
Erin Allmann Updyke	I'm thrilled.
Erin Welsh	Let's do this.
Erin Allmann Updyke	Give it to me.
Erin Welsh	Malaria is an ancient, ancient disease. Definitely prehistoric. Some researchers think that the parasite evolved from a free-living plant species.
Erin Allmann Updyke	A plant species?
Erin Welsh	Yeah, like algae or something.

Erin Allmann Updyke	What?
Erin Welsh	Yeah. So it has a bunch of genetic fragments that are similar to those used to make chlorophyll.
Erin Allmann Updyke	What?
Erin Welsh	Yeah.
Erin Allmann Updyke	That's so cool, I never knew that.
Erin Welsh	It's very strange.
Erin Allmann Updyke	I just assumed that everything is like an animal, cause I'm... Oh, what does Matt call it? I have plant blindness. Yeah, I do.
Erin Welsh	Yeah, you do. I think we both do.
Erin Allmann Updyke	Yeah definitely.
Erin Welsh	A lot of disease ecologists have plant blindness.
Erin Allmann Updyke	Definitely.
Erin Welsh	Okay, anyway. So in prehistoric times, I'm talking like time of the dinosaurs prehistoric, the ancestor of malaria made the jump from plant species to parasite. Scientists have found the DNA of a malaria species in a biting midge, which is an insect, preserved in amber from 100 million years ago.
Erin Allmann Updyke	(gasps) Stop it.
Erin Welsh	Yeah!
Erin Allmann Updyke	That's thrilling.
Erin Welsh	(laughs) Like Jurassic Park style.
Erin Allmann Updyke	No that's really Jurassic Park. Oh that's so cool!
Erin Welsh	Oh yeah. So long, long, long before malaria became a parasite of humans, it was probably a parasite of dinosaurs.
Erin Allmann Updyke	Oh my god.
Erin Welsh	Which makes sense considering that there are malaria parasites in so many different groups of animals today, including birds and reptiles. Okay but we know that modern malaria is transmitted by mosquitoes, not biting midges, so when did that happen? Probably around 30 million years ago. Eventually it became a parasite of humans maybe 8 million years ago.
Erin Allmann Updyke	Wow.

Erin Welsh	Or ancestors of humans.
Erin Allmann Updyke	Right.
Erin Welsh	Maybe 15,000 years ago? I mean, there's a lot of debate.
Erin Allmann Updyke	Everyone's like, 'Maybe then. Well, maybe in the year that I study.'
Erin Welsh	Plus or minus 8 million years.
Erin Allmann Updyke	(laughs)
Erin Welsh	In any case, once it was in humans it never really left. Ever since malaria emerged as a human parasite it has infected and killed billions. That's with a B.
Erin Allmann Updyke	That's will a B?
Erin Welsh	Of people throughout history.
Erin Allmann Updyke	Oh man.
Erin Welsh	And it doesn't really have the same like wham, epidemic storyline that some of these other diseases we've talked about have.
Erin Allmann Updyke	Dinosaurs are a pretty big wham though.
Erin Welsh	Oh yeah, absolutely. But like in terms of a pandemic or an epidemic.
Erin Allmann Updyke	Right.
Erin Welsh	But the numbers are still absolutely staggering both in ancient and modern times. Are you ready for the body count?
Erin Allmann Updyke	(laughs)
Erin Welsh	Malaria probably killed half, 50%, of all of the humans who have ever lived.
Erin Allmann Updyke	What?
Erin Welsh	About 108 billion people have existed at some point or another throughout history. That means that malaria has probably killed about 54 billion of them.
Erin Allmann Updyke	What on earth does that even...
Erin Welsh	You can't even?
Erin Allmann Updyke	How? I literally can't even. (laughs)

Erin Welsh	(laughs) If you didn't know we were millennials before, you do now.
Erin Allmann Updyke	You know now. But also-
Erin Welsh	That's number seemed really outrageous.
Erin Allmann Updyke	Also, it's just too... Ugh.
Erin Welsh	It's too much, you can't wrap your brain around it, all those things. Yeah. But I was like, alright, that seems... Hold on, let's take a step back.
Erin Allmann Updyke	There's gotta be someone exaggerating?
Erin Welsh	I saw that and I was like I really wanna put that in the podcast, and then I was like I don't know, that seems a little bit bogus. I looked into it and it may be on the upper end of things but it seems certainly possible.
Erin Allmann Updyke	It's within the confidence interval.
Erin Welsh	Yeah. Well I don't know if you can make a confidence interval with this type of back of the cuff calculation. But it is possible.
Erin Allmann Updyke	Wow.
Erin Welsh	It's insane.
Erin Allmann Updyke	That is really a cool statistic. Now that's the kind of thing you wanna whip out at a party.
Erin Welsh	Yes. Statistics.
Erin Allmann Updyke	Like hi, nice to meet you. Did you know...
Erin Welsh	(laughs) Only whip out statistics.
Erin Allmann Updyke	(laughs) This is why I have so many friends.
Erin Welsh	(laughs) Okay so I don't really have an estimate for when malaria first popped up in humans. The reality is that malaria has been with us throughout our evolutionary history and actually plays a pretty big role in it. As we all know, the cradle of human evolution is in Africa so it's also likely that that is also where malaria evolved. As you mentioned-
Erin Allmann Updyke	I did.
Erin Welsh	Malaria is caused by several different species of organisms. I'm gonna focus on just two of them because they probably made the biggest impact on human history.
Erin Allmann Updyke	Cool.

Erin Welsh	All right. So we've got Plasmodium vivax and Plasmodium falciparum, which I'm just gonna call vivax and falciparum from here on.
Erin Allmann Updyke	That's good.
Erin Welsh	Vivax is the less severe and more ancient one, falciparum is more deadly and more recent.
Erin Allmann Updyke	Interesting. I didn't know that falciparum was more recent.
Erin Welsh	Mm-hmm. Vivax probably showed up in hunter-gatherer groups many thousands of years ago and caused sporadic but deadly outbreaks. And we know this because of something called the Duffy antigen which prevents vivax from entering the blood, like the red blood cell.
Erin Allmann Updyke	What?
Erin Welsh	So if you are a person with the Duffy blood type then you are protected from vivax malaria.
Erin Allmann Updyke	That is really cool.
Erin Welsh	And because vivax was probably so severe in those early years and this mutation was so beneficial, the Duffy antigen spread like wildfire throughout much of Africa. And by around 5000 years ago, nearly every person born on the African continent had the Duffy blood type.
Erin Allmann Updyke	And so is that why you basically don't see vivax in Africa?
Erin Welsh	Exactly.
Erin Allmann Updyke	That is so awesome!
Erin Welsh	Yeah.
Erin Allmann Updyke	Cool!
Erin Welsh	And today the proportion of black individuals from Africa with this blood type is between 90-100%.
Erin Allmann Updyke	Wow, so it's persisted.
Erin Welsh	Oh, absolutely.
Erin Allmann Updyke	Man, that is very advantageous.
Erin Welsh	And despite the Duffy mutation, Africa would not remain malaria-free for long. Another malaria parasite was about to take vivax's place. Enter falciparum.
Erin Allmann Updyke	Ooh.

Erin Welsh	Falciparum probably made its appearance when people began to farm in or near rainforests in central Africa. So there a new malaria parasite emerged, taking advantage of settled groups so more stable where it could actually persist in a community whereas vivax was able to survive prior to large settled groups because of the dormancy.
Erin Allmann Updyke	Ah, that makes sense.
Erin Welsh	Super cool. Yeah and then there was also a more efficient mosquito for falciparum disease transmission. Falciparum, when it first popped up, would have been really devastating. So devastating in fact that when yet another mutation, this one protecting against falciparum malaria, appeared it rapidly spread through the African continent. This one you may have heard of: sickle cell. I'm not gonna delve too deeply into the biology or the genetics of this one but basically people with one copy of the sickle cell allele have blood cells - actually people with one or two copies of the sickle cell allele - have blood cells that have a shape that prevents the falciparum parasite from entering them.
Erin Allmann Updyke	They're sickle-shaped.
Erin Welsh	Yes.
Erin Allmann Updyke	Yeah.
Erin Welsh	There are other mutations with a pretty high prevalence that are linked to malaria such as G6PD deficiency, thalassemia, and about 1 in 14 people on earth has one of these mutations.
Erin Allmann Updyke	Wow.
Erin Welsh	Yeah. Anyway with these two very protective mutations, malaria should have been history. Right?
Erin Allmann Updyke	Right?
Erin Welsh	Yeah not so much.
Erin Allmann Updyke	It's too sneaky.
Erin Welsh	By the time that pretty much everyone in Africa was protected against vivax malaria, it had escaped to Europe and Asia. And falciparum would continue and continues to wreak havoc on the African continent. Malaria doesn't leave any traces on skeletons but we can track its history through human genetics, like I just talked about, through examining mummies, and through ancient writings.
Erin Allmann Updyke	What can we see in mummies?
Erin Welsh	I was just going to say. (laughs) This is so cool. Malaria antigens were found in 5000 year old Egyptian and Nubian mummies.
Erin Allmann Updyke	No dang way.
Erin Welsh	Tested their tissues.

Erin Allmann Updyke	God, mummies!
Erin Welsh	Science.
Erin Allmann Updyke	Science.
Erin Welsh	And there are mentions of a cyclic fever, probably malaria, in ancient Chinese, Greek, Roman, Sumerian writings.
Erin Allmann Updyke	Wow.
Erin Welsh	In Rome, vivax probably contributed to the fall of the Roman Empire, yada yada yada, like every stinking week I say something about the fall of the Roman Empire.
Erin Allmann Updyke	(laughs) Yeah it's not This Podcast Will Kill You if we don't mention Ancient Rome.
Erin Welsh	Ebola might be another story. But that's okay.
Erin Allmann Updyke	Ooh, maybe. I'll find a way.
Erin Welsh	(laughs) Yeah, but I gotta tell you, I'm not gonna talk about the Roman Empire. But I do wanna tell you about some of these Roman cures for malaria because what were they thinking. All right. So you're a citizen of Ancient Rome.
Erin Allmann Updyke	I have my toga on and someone is holding grapes that I'm eating.
Erin Welsh	Exactly. Oh my gosh, so perfect.
Erin Allmann Updyke	I'm there.
Erin Welsh	I'm your doctor, you probably shouldn't trust me.
Erin Allmann Updyke	I don't.
Erin Welsh	You have no choice.
Erin Allmann Updyke	I do!
Erin Welsh	(laughs) Oh wow, you have recurrent fever and chills? Well that sounds like malaria. I could prescribe you some honeysuckle dissolved in wine.
Erin Allmann Updyke	Ooh it sounds delicious.
Erin Welsh	Right? It sounds pretty nice. Or I could instruct you to consume the liver of a 7-year-old mouse.
Erin Allmann Updyke	(laughs) How are you even gonna find a 7-year-old mouse for god sake?
Erin Welsh	I assume it's killed and then preserved for seven years?

Erin Allmann Updyke	Ugh, that's even worse than just a really old, creaky mouse running around.
Erin Welsh	(laughs) Well I could also tell you about my famous meal combo of bed bugs, eggs, and wine.
Erin Allmann Updyke	Okay, what?
Erin Welsh	Not bedbug eggs, but bed bugs, eggs, and wine.
Erin Allmann Updyke	Like a chicken egg?
Erin Welsh	Yeah.
Erin Allmann Updyke	Why?
Erin Welsh	I don't have those answers.
Erin Allmann Updyke	How do you prepare the eggs?
Erin Welsh	Again, I assume over easy.
Erin Allmann Updyke	(laughs) Oh my god, this sounds... I wanna leave Rome.
Erin Welsh	(laughs) Well whichever one of those you choose-
Erin Allmann Updyke	Honeysuckle, duh.
Erin Welsh	Sorry but I'm gonna prescribe you whatever I think is best. And I'm also going to prescribe you a piece of papyrus that you're gonna wear around your neck with the powerful word 'abracadabra' on it.
Erin Allmann Updyke	Not the-
Erin Welsh	Yes. No, abracadabra. That is where 'abracadabra' comes from.
Erin Allmann Updyke	Stop it right now.
Erin Welsh	Malaria. It was to prevent malaria in Ancient Romans.
Erin Allmann Updyke	Stop it right now!
Erin Welsh	It took everything I had to hold this factoid from you. (laughs) Cause I wanted maximum impact.
Erin Allmann Updyke	Abracadabra means 'go away malaria'?
Erin Welsh	Mm-hmm.
Erin Allmann Updyke	Oh my god.

Erin Welsh	Well I don't know if it necessarily means...
Erin Allmann Updyke	We're gonna say it means...
Erin Welsh	I looked up the etymology and it seems like nonsense, but...
Erin Allmann Updyke	Go away malaria.
Erin Welsh	Yeah.
Erin Allmann Updyke	Oh my god. That is the best news I've ever heard.
Erin Welsh	Yep. Okay so we got abracadabra, we got some mouse livers, we got some bedbugs, we're done with Ancient Rome. There's nothing more I can say on that.
Erin Allmann Updyke	I need to leave this place.
Erin Welsh	I'm gonna talk a little bit about more modern Rome, I guess. Like not modern day but it's important because Rome in like the 1500s, I think, I probably where malaria actually got its name.
Erin Allmann Updyke	Oh.
Erin Welsh	So malaria: 'mal' meaning mad and 'aria' meaning air. Bad air.
Erin Allmann Updyke	Yeah. Bad air.
Erin Welsh	So remember the theory of miasmatism?
Erin Allmann Updyke	I do.
Erin Welsh	The idea that disease is caused by foul-smelling air and certain weather patterns?
Erin Allmann Updyke	Yeah.
Erin Welsh	That is what was at play here when malaria was coined.
Erin Allmann Updyke	Right, it's just the bad air that you're breathing in.
Erin Welsh	Right. People noticed that it occurred more frequently in the summer and in low-lying marshy areas which also happen to be when and where mosquitoes are most abundant.
Erin Allmann Updyke	Great mosquito habitat, those marshes.
Erin Welsh	Yeah. But the route of transmission wouldn't be figured out for a while.
Erin Allmann Updyke	Yeah.
Erin Welsh	And we'll get there. But first let's head to the New World.

Erin Allmann Updyke	Let's go on the boat.
Erin Welsh	Before Columbus and the European invasion of North and South America, the western hemisphere was free of malaria.
Erin Allmann Updyke	What?
Erin Welsh	Mm-hmm.
Erin Allmann Updyke	I don't think I even knew that, that's embarrassing.
Erin Welsh	(laughs) That's why you're here. That's why I'm here, too. Yeah so both vivax and falciparum were brought over by Europeans, particularly during the slave trade. In fact some historians suggest that the slave trade was so massive because two things: one, widespread colonization of Africa by Europeans hadn't been successful because falciparum, the more deadly malaria, would kill so many of the European invaders while Africans had been exposed to the disease as kids and were more protected. So there was more emphasis of invasion and colonization of North and South America instead where all of the indigenous people were killed by the invading diseases as well.
Erin Allmann Updyke	Right like smallpox and then malaria. You know I guess I actually did know that about the slave trade and malaria, so I'm not that stupid.
Erin Welsh	(laughs) Okay but there's a second reason why the slave trade may have been so massive because of malaria.
Erin Allmann Updyke	Why?
Erin Welsh	So as we've heard in other episodes, Europeans brought with them a bunch of diseases that wiped out up to 90% of the Native American population in the first few decades of colonization.
Erin Allmann Updyke	See Episode 3.
Erin Welsh	Mm-hmm. Which the Europeans saw as wiping out their potential workforce/slaves.
Erin Allmann Updyke	Wow.
Erin Welsh	So they turned to Africa and ramped up the slave trade to compensate.
Erin Allmann Updyke	Cool.
Erin Welsh	Mm-hmm. Although malaria was new to the western hemisphere, there was a secret there hidden in the forests and hills of the Andes: the cinchona tree. The bark of this tree contains a chemical called quinine which when ingested reduces the symptoms of malaria and basically cures you. The Quechua people of Peru, Bolivia, Venezuela, and Ecuador have been using bark from the cinchona tree for ages prior to the European invasion. But when malaria started popping up they saw that it was also an effective treatment for that illness. Some Jesuits from Spain noticed this Quechuan practice of treating malaria with this bark and co-opted it, bringing the powdered bark back to Spain, announcing it as a miracle cure - which it really was - and calling it Jesuit's Bark, claiming that they had discovered it and its practice.

Erin Allmann Updyke	Pretty typical.
Erin Welsh	Uh huh. It's like come on guys, really? Europe was still very much malarious - I think that's a word - at this time, which is like the mid 1600s. And when the news spread about this miraculous fever tree, the race was on to find these trees, get their bark, and most importantly control their production.
Erin Allmann Updyke	Yeah.
Erin Welsh	There were many missions, failed and successful, to harvest saplings, collect seeds, and bring them back to Europe to be planted. It became a huge commercial venture with a lot of political turmoil. The cinchona tree was almost harvested to extinction.
Erin Allmann Updyke	Wow.
Erin Welsh	Mm-hmm. Exporting these trees out of Peru and selling the seeds was quickly outlawed but that didn't stop it from happening. And the Dutch maintained some pretty huge cinchona plantations in Indonesia while the British had some in India.
Erin Allmann Updyke	Wow.
Erin Welsh	Of course only wealthy people could afford to purchase the treatment which kind of set the precedent for malaria being a disease of poverty.
Erin Allmann Updyke	Yeah.
Erin Welsh	The other thing that cinchona bark did was to enable the colonization of parts of the world that had previously resisted because of the amount of malaria there. Now Europeans could travel to and invade these places, such as India, such as parts of Africa, as long as they took with them a suitcase full of cinchona bark.
Erin Allmann Updyke	Wow.
Erin Welsh	I mean, so I'm kind of speculating over here but I don't think it's necessarily a coincidence that the whole manifest destiny, British imperialism movement really hit its stride soon after access to a malaria treatment was possible and fairly easy.
Erin Allmann Updyke	Oh definitely not.
Erin Welsh	I mean British officers in India invented tonic water as a malaria preventative because quinine on its own was too bitter. So those of you who are drinking along with us or have ever had tonic water, you have ingested quinine. Erin is guzzling the rest of her... (laughs)
Erin Allmann Updyke	(slurping sounds)
Erin Welsh	You heard it, that was the last sip.
Erin Allmann Updyke	Holding my glass waiting for the moment in which I could.

Erin Welsh	(laughs) So quinine is really bitter-tasting, apparently it has some really nasty side effects, and so in order to take it and not vomit immediately afterwards-
Erin Allmann Updyke	You gotta mix it with gin. (laughs)
Erin Welsh	Gin, sugar, tonic water contains a lot of sugar.
Erin Allmann Updyke	Yeah.
Erin Welsh	Yeah. So it's in all tonic water. Even though by the late 1600s there was an available treatment for malaria, people didn't discover the cause or transmission route of malaria until the late 1800s. In 1880 a French surgeon named... I don't know how to say his name.
Erin Allmann Updyke	You want me to do it?
Erin Welsh	Okay, I'm gonna give you, I'm gonna prompt you. Alphonse.
Erin Allmann Updyke	(French accent) Alphonse.
Erin Welsh	Laveran.
Erin Allmann Updyke	(French accent) Laveran.
Erin Welsh	Thank you, that's beautiful.
Erin Allmann Updyke	De rien.
Erin Welsh	(laughs) What?
Erin Allmann Updyke	That means you're welcome. (laughs)
Erin Welsh	Clearly I know zero French. Okay so this guy Laveran-
Erin Allmann Updyke	(French accent) Laveran.
Erin Welsh	-glanced into a microscope at a smear of blood from a malaria patient and saw something wriggling in the blood cells.
Erin Allmann Updyke	Ugh!
Erin Welsh	He knew that this was not a bacterium, it was something new. Something he had never seen before.
Erin Allmann Updyke	Yeah. Wriggling!
Erin Welsh	Uh uh. And he figured that it was the causative agent of malaria and he presented his findings.
Erin Allmann Updyke	Cool!

Erin Welsh	Yeah. Which were met with scorn by the leading bacteriologists of the day-
Erin Allmann Updyke	Typical.
Erin Welsh	-who had already decided that malaria was caused by an airborne bacterium, thus supporting the whole miasmatism theory.
Erin Allmann Updyke	(laughs) Oh, I just love it.
Erin Welsh	(laughs) They completely shut him down. But-
Erin Allmann Updyke	(French accent) Laveran.
Erin Welsh	-didn't back down. Instead he doubled down, also claiming that malaria was transmitted by mosquitoes even if he didn't have any evidence to back that up.
Erin Allmann Updyke	He just was like, 'I've decided.'
Erin Welsh	Yeah so the role of the mosquito in filariasis had recently been discovered and so he was like just jumping on that train.
Erin Allmann Updyke	Oh. Well I mean, that makes sense.
Erin Welsh	Oh yeah he clearly had a good instinct.
Erin Allmann Updyke	A wriggling thing and you're like, 'That doesn't look so different from what causes this, it's gotta be a mosquito.'
Erin Welsh	Yeah.
Erin Allmann Updyke	Seems like a smart guy to me.
Erin Welsh	I think he eventually did get the Nobel Prize.
Erin Allmann Updyke	Cool.
Erin Welsh	But all of his findings at the time more or less fell on deaf ears. Eventually he would be proven right about both but that would take a couple of decades.
Erin Allmann Updyke	Wow.
Erin Welsh	In the meantime, the French had decided to build a canal through the little landmass connecting North and South America. You know, Panama.
Erin Allmann Updyke	Aw, such nostalgia.
Erin Welsh	We both did our fieldwork in Panama.
Erin Allmann Updyke	Yes.

Erin Welsh	The entirety. We spent months.
Erin Allmann Updyke	Many months, especially in your case.
Erin Welsh	Yeah I spent years. Literally years.
Erin Allmann Updyke	(laughs) Literally.
Erin Welsh	Panama had been the bane of Europe's existence for a while since it inconveniently blocked easy transport form the Atlantic to the Pacific oceans.
Erin Allmann Updyke	How rude of it.
Erin Welsh	I cannot believe it. At its narrowest, Panama is about 50 miles or 80 kilometers across, actually a little bit less than that.
Erin Allmann Updyke	So small.
Erin Welsh	It's very small. And the Spanish had previously built a trail, actually the Spanish had their slaves build a trail known as the Camino de Cruces to link these two oceans. But the forests were full of malaria and yellow fever and in the rainy season huge parts of this trail would be washed away. And I should know because I used to walk along what remains of this trail every week during my fieldwork.
Erin Allmann Updyke	Yeah, didn't you find a lot of really cool old bottles and junk on that trail?
Erin Welsh	Yeah.
Erin Allmann Updyke	So cool.
Erin Welsh	It was my favorite thing in the world. Anyways, fresh off the success of the Suez Canal, the French engineer Ferdinand de Lesseps was hired to cut into Panama. Construction began but progress wasn't really made. Workers were dying by the thousands from malaria and yellow fever. In eight years over 22,000 workers died in the construction.
Erin Allmann Updyke	Wow. Eight years.
Erin Welsh	Eight years, 22,000 lives lost.
Erin Allmann Updyke	That's half the students at this university.
Erin Welsh	It was a complete disaster.
Erin Allmann Updyke	That is awful.
Erin Welsh	Yeah. So the French, after this they were like, 'Okay this isn't working.' So the whole project was abandoned for a number of years.
Erin Allmann Updyke	Oh my god.

Erin Welsh	A few years after the canal was canceled, a couple of researchers finally showed conclusively that malaria was transmitted through the bite of a mosquito. And this finding though would come too late for the thousands of workers who died during the first canal efforts. But not for the second, successful attempt to build the canal. When the U.S. took over canal construction, they hired a guy named William Crawford Gorgas to act as medical specialist.
Erin Allmann Updyke	Gorgas!
Erin Welsh	Gorgas. One of the first things that he did was to start a full on war against the mosquito. He put in screens, drained swamps, oiled puddles, and fumigated buildings in the area known as the canal zone. As a result malaria was more or less driven from that part of Panama but not outside it. Only in those areas that he targeted, which of course were the areas where the Americans were living.
Erin Allmann Updyke	Just a bunch of white people.
Erin Welsh	Mm-hmm. And also since living quarters were segregated by race, only the buildings for white people received screens or were treated with pesticides.
Erin Allmann Updyke	Oh my god.
Erin Welsh	Yep. It was really typical and crappy of them. Horrible of them. Anyway. But it was enough to get the canal built. It's funny because Gorgas is hailed by so many as the man who conquered the mosquito but he was very specific. The only reason that it persisted, that malaria control persisted in the canal zone is because Americans stayed in that canal zone until like the 1970s.
Erin Allmann Updyke	Right. So they kept up with that type of control.
Erin Welsh	Exactly.
Erin Allmann Updyke	Right.
Erin Welsh	Once it became widely known that the mosquito was responsible for malaria, many countries took the same approach as Gorgas. Control the mosquito and you control malaria. This is when we see DDT and other pesticides make a big appearance.
Erin Allmann Updyke	DDT.
Erin Welsh	Spraying campaigns were going so well in the first half of the 20th century that people started to talk about eradication.
Erin Allmann Updyke	Yeah.
Erin Welsh	Let us spray-
Erin Allmann Updyke	Let us spray.
Erin Welsh	-was their motto. (laughs)

Erin Allmann Updyke	And let us spray.
Erin Welsh	Let us spray. I love that. Malaria was completely eliminated from areas that had been so badly afflicted before until a new case popped up here and there, which was confusing since there shouldn't be any mosquitoes left.
Erin Allmann Updyke	Yeah.
Erin Welsh	That's right, pesticide-resistant mosquitoes.
Erin Allmann Updyke	Oh man.
Erin Welsh	Bad news. Bad, bad, bad news. Malaria-infected mosquitoes quickly reestablished themselves and caused disease which was so much worse because people didn't have the past exposure to gain a bit of immunity to protect themselves.
Erin Allmann Updyke	Yeah.
Erin Welsh	The death tolls were super high and the spraying campaigns stopped both because of the evolution of resistance but also because of the devastating effects of these pesticides on wildlife.
Erin Allmann Updyke	DDT is...
Erin Welsh	That's with the Rachel Carson Silent Spring.
Erin Allmann Updyke	Right, it's really gnarly.
Erin Welsh	Okay. Public health professionals were like, "well I guess we'll have to try another approach'. This time they targeted the parasite rather than the mosquito with drugs. Again, huge numbers of people were mobilized to administer newly-developed powerful drugs to treat and prevent malaria. Again, it worked. But again, only for a while before the first drug-resistant cases popped up. Efforts were soon abandoned and by the 1970s and 80s a lot of the funding for malaria had dried up. There was a huge upsurge in cases around this time but no real focused efforts to relieve the malaria burden in those areas most impacted. Because a lot of the early 20th century campaigns focused on wealthier countries, so the southern U.S. I mean, malaria was endemic in a lot of the United States, the southeast United States.
Erin Allmann Updyke	Right.
Erin Welsh	It went up the east coast, it was in Europe... So once those areas which were first targeted for eradication, once those were cleared, it was kinda like, 'Well, I mean, you know...'
Erin Allmann Updyke	The white people are safe so, hey, we've done our job.
Erin Welsh	Mm-hmm.
Erin Allmann Updyke	Yeah.

Erin Welsh	My story kind of ends around then with the sad facts that the incidence of malaria really increased following this decline in funding and sort of the shut down of all of these spraying and drug campaigns. So tell me whatchu got for today.
Erin Allmann Updyke	Yeah, that's where I should step in then. (laughs)
Erin Welsh	Got it.
TPWKY	(transition theme)
Erin Allmann Updyke	So first of all, as of 2016 nearly half of the world's population lives at risk of malaria.
Erin Welsh	Half.
Erin Allmann Updyke	Half. So that's like 3.5 billion people or so? Putting that on the table right away, it's literally over 3 billion people live in areas that have malaria transmission in 91 different countries.
Erin Welsh	Wow.
Erin Allmann Updyke	That's a lot of countries.
Erin Welsh	That's a lot of people at risk for malaria, a lot of people probably getting malaria.
Erin Allmann Updyke	Right. And the money that you're talking about that dried up back in the 60s, 70s, 80s didn't really start flowing back towards malaria research and prevention until 2000.
Erin Welsh	Whoa!
Erin Allmann Updyke	Yeah, I know. I thought that had to be wrong. But the other thing that's really important to keep in mind when we're talking about malaria is that when you look up these numbers of cases and numbers of deaths, they're basically guesses. They're educated guesses, they're guesses that are based on some surveillance and a lot of statistical and mathematical modeling but they're still just guesses. And depending on who you talk to or whose paper you read, they're either really great guesses or they're maybe not that great of guesses. And this is especially important because the guesswork in this case extends not just to guessing how many cases and deaths there are but how effective the interventions have been in reducing those cases and deaths.
Erin Welsh	It would have to be like a massive reduction to detect any sort of...
Erin Allmann Updyke	Kind of, yeah. And just to really understand like how big of an impact is this intervention having vs. that intervention.
Erin Welsh	Right so any sort of evaluation is really difficult.
Erin Allmann Updyke	It's really difficult, yeah. So in 2006 WHO estimated that there were 216 million cases of malaria worldwide and 455,000 deaths.
Erin Welsh	(gasps)

Erin Allmann Updyke	That was last year. Let me just say that again.
Erin Welsh	Yeah I need to repeat that. It bears repeating.
Erin Allmann Updyke	Last year there were 216 million cases of malaria and 445,000 deaths estimated. 285,000 of those deaths, this is larger than the population of the town I grew up in, were children under the age of five.
Erin Welsh	For a disease that has a cure and prevention by preventative drugs.
Erin Allmann Updyke	Mm-hmm. Yeah.
Erin Welsh	That is horrifying.
Erin Allmann Updyke	Yeah. Almost 90% of these cases and 91% of the deaths happen in Africa. So one study that I read... And so this is where we'll start to talk about the interventions and the fact that believe it or not these numbers are better than they were.
Erin Welsh	Wow. That's really hard to believe.
Erin Allmann Updyke	I know. So this one paper that I read estimated that in 2000 in Africa alone there were 321 million cases of Plasmodium falciparum.
Erin Welsh	The bad one.
Erin Allmann Updyke	The bad one. And by 2015 that number had dropped to 187 million, so that's a 40% reduction and it took 15 years for that 40% decline.
Erin Welsh	And since this is so much guesswork, I mean, do we think that that's a real decline?
Erin Allmann Updyke	Do you wanna know what caused it? Well, it seems like it's a real decline. So this study specifically could detect that about 68% of this reduction could likely be explained by the use of insecticide-treated nets. So bed nets treated with long-acting insecticide, long-lasting insecticide, are one of the main intervention methods that people us to control malaria, to prevent malaria. They're quite effective, they're cheap to make but they haven't always been available cheaply to people.
Erin Welsh	Right, I saw somewhere that it said $5 a bed net in an area where the average daily income was less than $1.
Erin Allmann Updyke	Yeah, it wasn't until very recently in the 2000s that the WHO made it one of their main goals to get these insecticide-treated nets to every household especially in Africa. And so I think, I don't know I hope that that number on $5 per net came from prior to that time.
Erin Welsh	Yes, it did.
Erin Allmann Updyke	The other things that are commonly used to control malaria, besides bed nets, is something called indoor residual spraying which essentially means instead of the massive DDT campaigns of the past where we just sprayed DDT throughout the whole air and all over everything, this is just spraying the inside walls of your house because what mosquitoes do - this is fun.

Erin Welsh	(laughs) She's very excited.
Erin Allmann Updyke	Yeah. After a mosquito takes a blood meal it's all fat and full of blood and it's like, 'Oh, I'm tired'.
Erin Welsh	It's hard for it to fly.
Erin Allmann Updyke	Oh it's a lady, so she goes, 'I'm sleepy'. That's so ridiculous. Anyways. So she flies off and she takes a rest and she usually lands on a wall to take that rest, a vertical surface.
Erin Welsh	Oh!
Erin Allmann Updyke	Yeah.
Erin Welsh	Sorry, I jumped the gun. I think I know where you're going with this.
Erin Allmann Updyke	Yeah so-
Erin Welsh	Treat the walls, kill the mosquito.
Erin Allmann Updyke	Treat the walls, kill the mosquitoes. So there are several problems with this. One is that you kind of have to spray at least 80% of the houses for this to be effective, which is a hell of a lot of work.
Erin Welsh	Yeah that's gonna be really hard.
Erin Allmann Updyke	Right? The second is it only lasts for about 3-6 months so you have to do this every 3-6 months.
Erin Welsh	Oof.
Erin Allmann Updyke	And lastly, do you wanna take a guess?
Erin Welsh	Resistance?
Erin Allmann Updyke	Resistance.
Erin Welsh	Uh oh.
Erin Allmann Updyke	Yeah. So insecticide resistance is already happening, it's been happening, right. In many parts of Africa and in many parts of the rest of the world where malaria is still endemic, you have resistance to all four classes of insecticide that are used.
Erin Welsh	Uh oh.
Erin Allmann Updyke	Yeah.
Erin Welsh	I mean that doesn't really quite cover it. (laughs)

Erin Allmann Updyke	There's like four different main entire classes of insecticide that act in totally different ways on totally different systems and some species of mosquito have shown resistance to all four of those classes. We don't have a lot of options left. Because of this, physiological resistance, potential behavioral resistance, indoor residual spraying, while it can be effective, might not be that effective.
	The other scary thing that you talked about already is this drug resistance because the other main way of malaria control is combination therapy. At least two different types of drug. The problem is that this parasite is already resistant to the main drug that's used and in a lot of countries, in a lot of places, it's developing resistance to some of the secondary drugs that are used as well. Yeah so that's pretty scary. Another thing, I don't know, is climate change.
Erin Welsh	Oh! Yeah. This is my sweet spot.
Erin Allmann Updyke	It is, it's like your favorite thing.
Erin Welsh	Yeah, well. (laughs)
Erin Allmann Updyke	I mean to talk about intellectually.
Erin Welsh	Well...
Erin Allmann Updyke	No? (laughs)
Erin Welsh	I would say that that's more in my wheelhouse in terms of my dissertation.
Erin Allmann Updyke	Definitely. There's a lot of conflicting opinions out there on what the effects of climate change are going to be on vector-borne diseases.
Erin Welsh	Yes.
Erin Allmann Updyke	And at this point what we know for sure is that things are likely going to change.
Erin Welsh	That seems very reasonable.
Erin Allmann Updyke	(laughs) We don't necessarily know the exact direction of these changes, we don't necessarily know if things are gonna get better in some areas and worse in other areas or if they're just gonna get worse or better overall but what seems pretty clear is that-
Erin Welsh	In talking about infectious diseases or vector-borne diseases.
Erin Allmann Updyke	Right, in talking specifically about vector-borne diseases that is.
Erin Welsh	Right, it's gonna be very location-specific.
Erin Allmann Updyke	Exactly. So some studies have shown with math modeling and things like that that it's very possible that the distribution of malaria could change going forward because of climate change.
Erin Welsh	Mm-hmm.

Erin Allmann Updyke	So we might see these mosquitoes and in some cases we already are seeing these mosquitoes move up to higher altitudes where they were never previously able to live because it would get too cold.
Erin Welsh	Right.
Erin Allmann Updyke	We could also see a shift from coastal regions to more inland regions. And so all of this could very dramatically affect the malaria burden that we actually see in humans. So then the question becomes what do we do moving forward?
Erin Welsh	It's a really tricky question.
Erin Allmann Updyke	Yeah, there's not a clean answer for this.
Erin Welsh	No.
Erin Allmann Updyke	So I just wanna talk about something that I'm into. Cause I can.
Erin Welsh	Okay. Let's do it.
Erin Allmann Updyke	It's our podcast. (laughs)
Erin Welsh	(laughs) Again, why we're here.
Erin Allmann Updyke	Right? So one thing that I am super interested in is the possibility of transgenic mosquitoes.
Erin Welsh	Oh yeah.
Erin Allmann Updyke	I know people are gonna hate me for... Maybe we'll get our first hate mail for this.
Erin Welsh	Some GMMs?
Erin Allmann Updyke	I would love it if we got some GMMs.
Erin Welsh	(laughs) You would love hate mail?
Erin Allmann Updyke	Yeah, yeah. GMMs. Yeah, I mean kind of. I think it'd be thrilling.
Erin Welsh	I don't want hate mail.
Erin Allmann Updyke	Okay, don't send us hate mail. So there's a lot of really cool research that's being done on how to make these mosquitoes less permissive to malaria infection.
Erin Welsh	What does that mean?
Erin Allmann Updyke	So basically it means that instead of focusing on stopping these mosquitoes from biting you or curing everyone with the parasite or removing mosquitoes from the ecosystem, this looks at blocking the cycle of reproduction of the malaria parasite within the mosquito.

Erin Welsh	Okay. How?
Erin Allmann Updyke	So there's a few different groups and a few different ways that people are looking to do this. Actually what I think is cool is that there were two different groups that published two different papers in the same issue of Science in September of this year that were looking at two different strategies to do this.
Erin Welsh	Oh man I bet that they were racing to both get it ready in time.
Erin Allmann Updyke	I'm sure that Science was like, 'Hey guys, we're gonna do this on purpose, like just put them both in one.'
Erin Welsh	(laughs)
Erin Allmann Updyke	I just hope that these two groups are less like Salk and Sabin and more like Erin and Erin.
Erin Welsh	(laughs)
Erin Allmann Updyke	Get it? Like they work together?
Erin Welsh	Collaborative, cool.
Erin Allmann Updyke	Hilarious. Anyways. So one of these groups was looking at using a genetically modified bacteria that's found in the gut of mosquitoes that can help to fight off the Plasmodium infection.
Erin Welsh	Whoa.
Erin Allmann Updyke	Yeah so it's this bacteria that's normally present in the gut of all mosquitoes but they basically genetically modified it to produce more compounds that would help the mosquito fight off this infection. Cause don't forget that this Plasmodium, this malaria parasite is bursting through the gut wall of these mosquitoes and traveling through their body to get to the salivary glands. So the mosquitoes generally have some sort of immune response to this, it's not like a totally benign infection necessarily in the mosquito.
Erin Welsh	Oh, okay. So you can kinda jump on that train with this bacterium to try to stop the infection overall.
Erin Allmann Updyke	Exactly, yeah. Exactly. And the other study was looking at genetically modifying the mosquitoes themselves to basically produce more immune compounds to fight off the infection itself.
Erin Welsh	That's cool.
Erin Allmann Updyke	It's very cool. And that study was really interesting because they actually found that genetically modified males were more likely to mate with unmodified females. So they basically, they were good at sending this gene forward which is one of the big challenges of genetically modifying mosquitoes is how do we get this gene into the population of mosquitoes that already exists.
Erin Welsh	Mm-hmm.
Erin Allmann Updyke	I love this stuff.

Erin Welsh	So is that the state of malaria today?
Erin Allmann Updyke	That's the state of malaria today.
Erin Welsh	That is a... It's depressing.
Erin Allmann Updyke	It's depressing.
Erin Welsh	It's a little bit uplifting because it seems like there's work being done but it's really disheartening that there are still so many, over 200 million people infected every year!
Erin Allmann Updyke	Every year.
Erin Welsh	Wow.
Erin Allmann Updyke	Yeah. And it was actually a little higher in 2016 than it was in 2015. We are definitely not seeing the decline that we've seen in other diseases that we've talked about. So yeah.
Erin Welsh	All right well, sources?
Erin Allmann Updyke	Sources.
Erin Welsh	All right. Okay. I read a few books. One is called 'The Fever' by Sonia Shah and this is a really great overview, it's really written well, it's interesting, I really liked it. Take a look, she's a great science writer. The other is called 'The Making of a Tropical Disease' by Randall Packard and that's a more... It's a less accessible take on the history of malaria, it focuses largely on the role that agricultural practices have played in the transmission of malaria and I wish I had more time to talk about it because it was really interesting to see how small scale farming vs large scale farming, etc.
Erin Allmann Updyke	Wow.
Erin Welsh	Anyways take a look if you're interested. And the final one is called 'The Fever Trail' by Mark Honigsbaum and it was interesting, I don't necessarily highly recommend just because the readability was a little bit less. But it was very cool, it mostly focuses on quinine and the discovery of the cinchona tree.
Erin Allmann Updyke	I've got several papers I wanna cite today. I always cite the WHO but at least three other papers today. So one was by Bhatt et al in Nature published in 2015 and that was the paper on the effect of malaria control on P. Falciparum in Africa between 2015. And then the other two were the two papers about genetically modified Anopheles and genetically modified bacteria. Those were both published in the September 2017 issue of Science, so you can find those. The first one is by Wang and the second one is by Pike.
Erin Welsh	Hot off the presses.
Erin Allmann Updyke	Hot off the press, September 2017. There was a bunch of others so if you're interested in any specific aspects of malaria, shoot us a message or something.

Erin Welsh	And also just as a reminder, we do have a Goodreads list which has all of these books and we're working on getting a Google Docs up for the different articles that Erin mentioned so you can take a look at those if you're interested in reading further.
Erin Allmann Updyke	Yeah.
TPWKY	(transition theme)
Erin Welsh	Well I think that that about wraps up our episode today.
Erin Allmann Updyke	It does.
Erin Welsh	Thanks again to Ummat for providing his firsthand account of malaria, super interesting. And also thank you again to Bloodmobile for providing the music in this episode and for all of the bird people out there, one of the songs features a bird native to the Andes. So see if you can pick it out.
Erin Allmann Updyke	Rate, review and subscribe please.
Erin Welsh	Please. Follow us on social media.
Erin Allmann Updyke	And thanks for listening!
Erin Welsh	Thanks so much. Now wash your hands.
Erin Allmann Updyke	Ya filthy animals!