

Erin Welsh

"In high school I heard the rumors and saw the writings on bathroom walls of the quote 'dirty' people who slept around and got STIs like the clap. I never wanted to be like them and I thought I was better than them for being quote 'cleaner' and selective about whom I was seeing. I thought I was doing everything right. So you can imagine my surprise when my senior year of high school my then partner and I tested positive for chlamydia. I was shocked and confused wondering how it had happened. I felt ashamed and dirty, angry both at myself and my partner. Thoughts like 'I'll never have sex again' and 'my life is over' flashed through my head. I even blamed the person my ex contracted it from. I felt betrayed by my partner, thinking how could you do this to me? But after a conversation with my doctor who was very familiar with these cases, my assumptions about the disease were thrown out the window and replaced with a new understanding. A simple round of antibiotics and we'd both be fine.

I felt the stigma had dropped and I wasn't shy to tell my story to let others in the same boat know that it isn't the end of the world and that you are not defined by a diagnosis. I was proud to handle it the way I did. Then college came and it followed me. I hooked up with a person who turned cold towards me days later. I knew something was off and I asked them about it. They told me they heard about my past. They said that they had heard quote 'something about chlamydia' and it scared them. They were ashamed for being intimate with me as someone who was once diagnosed with this infection. They thought I was dirty and that it made them dirty too. The feeling of rejection cut deep and I begged him to keep his voice down. Doing what I could, I told him some of the facts I knew. How men are usually asymptomatic, how antibiotics are used to treat it, condoms are one method of prevention, and how it can increase the risk of pelvic inflammatory disease in women.

Still I was so angry and shocked that this had happened. Of course they didn't know better but maybe they should have. I was upset both for the judgments they made about me but also anyone who had been diagnosed with an STI. I thought to myself why am I to blame? Why not my male partners? Why not the disease itself? What blame is there to be had anyway? I have learned my lesson that what matters in sexual intimacy is not rumors and history but who someone is at their core and whether or not their values and understanding of the world aligns with yours. What's important is mutual respect and open and healthy communication. STIs can happen to virtually anyone and your value as a person has nothing to do with your sexual health. You are not a diagnosis."

TPWKY

(This Podcast Will Kill You intro theme)

Erin Welsh

I feel like that is just such an important message, right? You are not a diagnosis.

Erin Allmann Updyke

You are not your diagnosis. It's my favorite. I had a whole paragraph at the beginning of my notes that's all about why it's so important that we talk about chlamydia because it is so common and we need to reduce the stigma. So I love that firsthand account. Thank you.

Erin Welsh

Yeah. So that story was sent in by one of our listeners and yeah, I just want to say a huge thank you to both this listener and also to everyone who has ever submitted a firsthand account because it is a really vulnerable position to be in, right. You're kind of baring your soul talking about your experiences, something very personal to you. And that's difficult to do and I just want to acknowledge that and say thank you. And also that it's so wonderful and impactful because I feel like it really drives home that these diseases do happen, these things happen to people who are living their everyday lives. And yeah, I think it just sort of reinforces once again you are not a diagnosis.

Erin Allmann Updyke

Yeah, yeah.

Erin Welsh

Hi, I'm Erin Welsh.

Erin Allmann Updyke: And I'm Erin Allmann Updyke.

Erin Welsh: And this is This Podcast Will Kill You.

Erin Allmann Updyke: Welcome to chlamydia.

Erin Welsh: Welcome. Yeah. This is an interesting one because it's sort of a two for the price of one episode.

Erin Allmann Updyke: I would call it even 2.5 as you'll hear in the biology. Yeah.

Erin Welsh: I'm very intrigued by that. So is it a certain time of evening? What time is it?

Erin Allmann Updyke: It's quarantini time according to - I'm actually wearing a watch today.

Erin Welsh: You are! What are we drinking this week Erin?

Erin Allmann Updyke: We're drinking Happy as a Chlam. Get it? Cause chlamydia.

Erin Welsh: C-H-L-A-M, yep. And in Happy as a Chlam is of course Clamato, we had to.

Erin Allmann Updyke: Clamato!

Erin Welsh: How could we resist? Tequila and basically it's your standard Bloody Mary but with tequila instead of vodka. And yes, we do know that we made a Bloody Mary for typhoid.

Erin Allmann Updyke: But it's with Clamato so it's different.

Erin Welsh: It's with Clamato and it's with tequila instead of vodka. So hopefully that's different enough.

Erin Allmann Updyke: And in any case we'll post the full recipe for the quarantini and the nonalcoholic Clamato-based placeborita on our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com) and all of our social media channels.

Erin Welsh: On our website you can find all sorts of things like transcripts, sources for all of our episodes, you can find links to music by Bloodmobile, you can find links to our bookshop.org affiliate account, you can find links to merch and Patreon. Probably a few more things that I'm forgetting. But you know, that's enough.

Erin Allmann Updyke: Check it out. Go there.

Erin Welsh: Check it out. And just real quick I wanted to mention again that if you have a firsthand account that you might be willing to share on the podcast, please shoot us a message on the Contact Us form on our website or send us an email at [thispodcastwillkillyou.com](mailto:thispodcastwillkillyou.com). I'm also putting it on my to do list to create like a FAQ or a firsthand account link so that maybe things will be set up more easily on the website and you can get more information.

Erin Allmann Updyke: Oh that's nice. Well then shall we dive into this episode?

Erin Welsh: Let's do it right after this short break.

TPWKY

(transition theme)

Erin Allmann Updyke

Chlamydiae. Is that how you would say that? Chlamydia, chlamydiae with an E at the end?

Erin Welsh

Yeah.

Erin Allmann Updyke

Sure. Chlamydiae are gram-negative obligately intracellular bacteria of which there are several different species. And they infect a pretty wide range of hosts and within those hosts a wide range of body sites. So we'll talk in this episode about different tissue tropisms which we've talked about before but that essentially just means which cell types these intracellular bacteria like to infect. There are two major species of chlamydia that infect humans primarily. That is Chlamydia pneumoniae which causes pneumonia, so it infects our respiratory tract, and Chlamydia trachomatis which is really the subject of today's episode. But other species can cause respiratory or urogenital or cloacal or conjunctival infections in mice, birds, cats, pigs, marsupials, snakes, turtles, guinea pigs, koalas, and probably other animals that I didn't mention. And some of these other species, just as a fun side note, for example Chlamydia psittaci, if I'm saying that right, is often a zoonotic pathogen that can cause disease in humans. It causes a disease called psittacosis but it's primarily a bacteria of I believe birds.

Anyways, all of that to say that today we're focusing on one species of chlamydia and that is Chlamydia trachomatis. This is a human-specific bacterium but there are at least 13, maybe 19 different serovars. And these serovars cause different diseases. Kind of a number of them. Let's get into it. Serovars A, B, and C cause an infection of the eyes that's called trachoma which can lead to scarring and blindness and is a really important major cause of blindness in many parts of the world. Serovars D through K cause what most of our listeners are probably familiar with as chlamydia, the sexually transmitted infection. And then the L serovars of which there are several cause another sexually transmitted infection called lymphogranuloma venereum.

Erin Welsh

Oh.

Erin Allmann Updyke

So it's like three different serovar groups that cause three different types of diseases more or less, there's some nuance there. So what I'm going to do here is take a pretty big picture view and talk about what all Chlamydia trachomatis has in common and then we'll go over the kind of different presentations of those diseases. Because it turns out even though each serovar infects different tissues and maybe causes slightly different diseases, there's a lot of similarities in terms of the basic biology of how this pathogen works.

Erin Welsh

That's so interesting that there are like distinct serovars.

Erin Allmann Updyke

Yeah.

Erin Welsh

The differences among these serovars, are they genetic? Is it just how they act? Is it expression? What is the origin of those differences? Yeah.

Erin Allmann Updyke

Oh it's a good question Erin, I wish I had a good answer for you. I don't. And that's not to say that it might be that a good answer exists out there better than what I can explain it but what it really comes down to at a very basic level is differences in tropism. So the different serovars have a tendency to infect different tissue types and that probably is based on some specifics of their genetics.

Erin Welsh

Okay.

Erin Allmann Updyke

But as we'll see especially the classically sexually transmitted serovars, D through K, actually have a fairly wide tropism. So it's also differences in just the kind of epidemiology of where you find them and who tends to be infected and things like that.

Erin Welsh

Fascinating.

Erin Allmann Updyke

Yeah.

Erin Welsh

I want to know so much more about tissue tropism. So let's get started.

Erin Allmann Updyke

Wouldn't that be fun? So chlamydia, like I said, it's an obligate intracellular bacterium. So it can't replicate without entering a host cell. Chlamydia bacteria are kind of fun, they have two different parts to their life stage. One is a kind of spore-like infectious form called an elementary body and that's what actually infects our cells. And once these bacteria actually enter our cells they actually differentiate into an active form that replicates prolifically and then will transition back into the infectious elementary body to leave our cells and go on and infect more cells.

Erin Welsh

Interesting.

Erin Allmann Updyke

Yeah.

Erin Welsh

So you mentioned that this was a spore-like condition. What does that mean exactly?

Erin Allmann Updyke

It means that they are hearty and they are not extremely metabolically active. They're not completely inactive but they don't replicate and they're not very active and they're a little bit heartier than most bacteria.

Erin Welsh

How hearty are we talking? What's the environmental durability of it?

Erin Allmann Updyke

Good question. I didn't see how long the environmental durability is. It's not like a true spore, it's not like drying out and surviving on surfaces.

Erin Welsh

Okay. It's not anthrax.

Erin Allmann Updyke

It's not anthrax. No, no. Good question. So chlamydia, all of the different serovars of Chlamydia trachomatis is transmitted generally by direct contact with secretions. And what secretions depend on what tissue we're talking about. But in general Chlamydia trachomatis has the ability to infect any of our mucous membranes. So anywhere that you have wet vulnerable epithelial cells you could get infected. That means eyes, nose, throat, penis, vagina, anus primarily and associated structures. And like I kind of touched on a lot, the different serovars have different tissue tropisms. So serovars A, B, and C tend to like the epithelial cells of our eyes and our nose, that's their preferred tissue tropism, that's where they do the best. D through K most often infect our genital tract but can also absolutely cause infection in eyes or throat. And then the L serovars, the ones that I think we think of the least often, they also tend to be sexually transmitted. So primarily infect the anogenital region. But what's really different about the L serovars is they have a tendency to invade past just that epithelial cell layer and cause a much deeper infection, which I think is fascinating and really does set them apart from the other serovars.

Erin Welsh

Interesting. And so the deeper tissues that it invades, what are those deeper tissues made of?

Erin Allmann Updyke

Oh, great question. It tends to invade into the lymph nodes and we'll talk a little bit more about that when I talk specifically about lymphogranuloma venereum. I know, I can see your face.

Erin Welsh

Interesting. Yeah, okay.

Erin Allmann Updyke

But despite those differences, at pretty much all of the sites of infection, one thing that claim media does across all serovars is it induces a pretty intense inflammatory reaction from us. And so what we'll see when we talk about the different symptoms is that while those symptoms are going to vary of course depending on what tissues infected, depending on which mucous membrane is exposed, the inflammatory reaction itself is universal. And as we talked about in our endometriosis episode, that inflammatory reaction that our body generates can often result in scarring. And this scarring can have chronic or long term consequences and that's across the board regardless of tissue type. So when we talk about chlamydia there's always the acute initial infection but then there's also the potential for this inflammation to cause scarring that can cause more permanent or progressive damage.

Erin Welsh

I find that really intriguing because as I'll briefly touch on these microbes have been evolving with humans forever. Forever.

Erin Allmann Updyke

Yeah.

Erin Welsh

So it seems like it would be selected for to have not so much of an inflammatory response or not cause so much inflammation, either from the human side or the bacterial side.

Erin Allmann Updyke

Well what's interesting is that yes, this is a pathogen that's been with us for a very long time. This is a pathogen that actually has a really intimate relationship with our cells and with our immune response. So what it actually tends to do is block a lot of proapoptotics, so it blocks a lot of processes that just straight up kill infected cells because that's what our body usually does when it recognizes an infected cell is just kill it. And instead what chlamydia tends to do is modulate progression through the cell cycle in a way to try and promote chlamydia's own growth and survival for as long as possible. So I suspect that the inflammatory response is more of a last ditch let's do what we can, so it's this constant battle between this bacteria that's inside of ourselves and our body trying as best it can to fight it off but then causing damage in the process.

Erin Welsh

Gotcha.

Erin Allmann Updyke

Yeah.

Erin Welsh

Do our bodies clear chlamydia infection on their own?

Erin Allmann Updyke

Excellent question. They absolutely can, yes.

Erin Welsh

Okay. And so does the inflammatory response then very substantially from person to person and the tendency to scar and stuff like that?

Erin Allmann Updyke

Probably yeah.

Erin Welsh

Okay. What factors might contribute to that?

Erin Allmann Updyke

Oh Erin, whenever we ask about host factors my answer is great question.

Erin Welsh

Fair, yeah.

Erin Allmann Updyke

We've got to have Angie Rasmussen back on to ask her. No that's a really good question though. But yes it presumably definitely would vary person to person. What those factors may be is probably the subject of an intense amount of research. All right. So that was chlamydia in general. So now let's kind of go through the different serovars and sites of infection to understand what these diseases actually look like. So serovars A, B, and C cause trachoma. A lot of listeners may have never heard of trachoma even though it is one of the most common causes of infectious blindness worldwide. But these serovars are generally transmitted from person to person by direct contact from eye and nose secretions. So think rub your eye on your hand and then touch somebody else or you're nuzzling with your baby, snuggling with your kid and you get these goopy eyes and nose all over you, or you're sharing a towel. It can also be transmitted by eye-seeking flies although the relative importance of eye-seeking flies and all of these various modes of transmission, it's a little bit like we don't know which is the most important.

But anyways. As an acute infection, an initial infection, these serovars of Chlamydia trachomatis cause a mucopurulent conjunctivitis, so an infection of the eye and the conjunctiva. And it generally is self limited. Like you asked Erin, it usually resolves. However reinfection especially in children is incredibly common in endemic areas and so trachoma, the disease that results, is the result of either longitudinal continued active infection which can also occur if you don't completely clear it or chronic inflammation that results because of repeated infection. And this inflammation can actually persist even after infection is resolved. And in either case whether it's a continual infection or continual reinfection with inflammation, it results in significant scarring to the eye and to the cornea.

Erin Welsh

Right.

Erin Allmann Updyke

So it tends to be young children who are infected frequently and recurrently but the scarring takes place over the course of decades. And what really happens is that the scarring, it causes the upper eyelid to kind of turn inward which then eventually progresses to something called trichiasis which is when the eyelashes inturn and begin rubbing against the eye. Sorry, I know eyes are difficult.

Erin Welsh

Eyes are difficult. Yeah, I saw a lot of pictures and descriptions in the books that I read and it sounds so painful.

Erin Allmann Updyke

So painful.

Erin Welsh

And horrifically uncomfortable. Yeah.

Erin Allmann Updyke

Yeah, exactly. I think we've all had the sensation of having an eyelash stuck in your eye.

Erin Welsh

Right. Imagine all of them.

Erin Allmann Updyke

All of them and always. It's not like you can just take it out. It's the way that your eyelid has turned. And so this in addition to being incredibly painful, incredibly uncomfortable, this constant rubbing actually leads to additional scarring of the cornea and this is what leads to blindness.

Erin Welsh

Gotcha.

Erin Allmann Updyke

And so the prevalence of scarring and blindness in adults relates to their exposure as children which is kind of an important public health concept because it's an acute infection that then causes this chronic disease and chronic scarring.

Erin Welsh

Right. It helps with who to target to disrupt this cycle of transmission or this chain of transmission. Yeah.

Erin Allmann Updyke

Right. Exactly. And it really has to be a kind of multi-tiered approach because you have to both prevent the disease in children and treat the disease in children. But then you also have to be able to deal with the after effects of the chronic infection in adults. So that's trachoma. Next to go into the chlamydia that everyone is probably more familiar with and that is serovars D through K, sexually transmitted chlamydia. So these are the serovars that tend to cause anogenital infections. So in people with a penis, chlamydia loves to infect the cells that line the urethra. Inflammation in this area is going to cause urethritis, inflammation of the urethra. Often it's called nongonococcal urethritis which I think is just so silly because it just means well it's not gonorrhea.

Erin Welsh

I have a little section about that.

Erin Allmann Updyke

I can't wait.

Erin Welsh

You'll understand where it came from and why people started using it in the first place.

Erin Allmann Updyke

I can't wait. In people with a penis, this your arthritis can also be complicated by epididymitis which is inflammation of the epididymis which is where sperm are stored and transported in the testicles. And one thing that's really important to know is that even in this population when it's a penile infection, 30%-50% of the time it's completely asymptomatic. So someone is not going to know that they're infected and potentially infectious.

Erin Welsh

Right.

Erin Allmann Updyke

If someone is going to become symptomatic, then the symptoms usually are like a pain or burning when you pee because of that inflammation or maybe a little bit of clear or white discharge. In people with a cervix, 70%-90% of the time infection is entirely asymptomatic.

Erin Welsh

It's so interesting that it's a different rate of asymptomatic. Why is that?

Erin Allmann Updyke

Well I think it's largely because the symptoms that you're having from urethritis are the pain and burning with urination because you have urine passing over these inflamed cells. But with cervicitis which is inflammation of the cervix which is the most common place that you're going to have infection in someone with a cervix in a sexually transmitted chlamydia infection, the cervix is pretty high up in the vagina. And so even if you do have that mucopurulent discharge which is what you may have, you might not notice it, it might not be painful, you might not have any other symptoms. And so you can have things like a little bit of bleeding after intercourse or if you did a speculum exam you might see the cervix look a little bit swollen or have a little bit of bleeding if you did a swab. But you might not feel that necessarily or notice it in terms of symptoms. That make sense?

Erin Welsh

That makes sense, yeah.

Erin Allmann Updyke

Yeah.

Erin Welsh

Interesting.

Erin Allmann Updyke

Now a person with a cervix can also have urethritis, right, because the urethra is really, really close to the vaginal opening and that might be more likely to be symptomatic but you might think it's a UTI or a bladder infection, right, because the symptoms are going to be similar.

Erin Welsh

What about the anus?

Erin Allmann Updyke

The anus absolutely can be infected and it may or may not be symptomatic. We'll talk more about the anus in a little bit. Don't worry, I won't leave out the anus.

Erin Welsh

Perfect, good. I'm relieved.

Erin Allmann Updyke

Now I want to focus on the cervix for a little bit longer because one of the things that makes chlamydia infection especially dangerous considering how often it's asymptomatic is that with a cervical infection, if it's untreated, about 20%-40% of the time that infection can progress upwards through the endometrial canal. Because this is a bacteria that's spreading from cell to cell, it can spread through the uterus and up into the cells that line the fallopian tubes. So it can cause an endometritis which is inflammation of the endometrium, the cells that line the uterus, or a cell salpingitis which is inflammation of those fallopian tubes. And if an infection ascends into the uterus and the fallopian tubes, that can become a persistent infection known as pelvic inflammatory disease. And that inflammation, just like it can happen in the eyes with the trachoma serovars, can cause a lot of scarring over time. And this scarring is a big risk factor for both infertility as well as ectopic pregnancy which can be a life threatening emergency.

Erin Welsh

So I have a few questions. Number one, can you talk a little bit more about pelvic inflammatory disease? What that is?

Erin Allmann Updyke

Yeah. Pelvic inflammatory disease is when a bacterial infection spreads up into the uterus and the fallopian tubes. So it's very often caused by chlamydia but it can also be caused by gonorrhea which I think we talked about in our gonorrhea episode or it can be caused by a number of other bacteria.

Erin Welsh

Just bacteria.

Erin Allmann Updyke

Generally bacteria, yeah.

Erin Welsh

Okay, okay. And then another question is about ectopic pregnancy. Why is that associated with chlamydia infection that has ascended?

Erin Allmann Updyke

Great question. Because that inflammation can cause scarring in the fallopian tubes such that even though sperm might be able to make it through the fallopian tube to fertilize the egg, the egg can't make it back through the fallopian tube to be able to implant or all the way through the fallopian tube to be able to implant safely in the uterus. So it implants ectopically which just means outside of the uterus.

Erin Welsh

Okay.

Erin Allmann Updyke

Yeah.



Erin Welsh: So in terms of infertility, what is the process by which this inflammation from chlamydia causes infertility? Is it sort of certain steps or is it multiple steps or is it just like the general inflammation?

Erin Allmann Updyke: Yeah, it's the general inflammation and the scarring that occurs because of that inflammation.

Erin Welsh: Gotcha.

Erin Allmann Updyke: It's not something that happens overnight or over the course of even a few days. This is the result of a longstanding untreated infection or repeated infection that's untreated in general, similar to trachoma in that way.

Erin Welsh: Right, right.

Erin Allmann Updyke: Chlamydia can also lead to infection in a newborn during delivery, most commonly affects the eyes and causes a conjunctivitis or can descend the respiratory tract and cause a pneumonia. So this is really a very versatile bacteria.

Erin Welsh: So the one that can cause pneumonia in newborns is not *Chlamydia pneumoniae* but *Chlamydia trachomatis*?

Erin Allmann Updyke: Right. *Chlamydia pneumoniae* could also cause pneumonia in newborns.

Erin Welsh: Sure.

Erin Allmann Updyke: But normally yeah, *Chlamydia trachomatis*, if someone is infected during delivery and delivers vaginally then the baby could become colonized and therefore *Chlamydia trachomatis* pneumonia.

Erin Welsh: Wow, okay.

Erin Allmann Updyke: Yeah.

Erin Welsh: Very versatile.

Erin Allmann Updyke: It really is. Now the L serovars we haven't even touched on so I'll breeze through it really quickly. But these are the ones that cause lymphogranuloma venereum. This is a disease that tends to be more deeply invasive than the other serovars. So they establish an infection not just in the epithelial cells of say the cervix or the urethra or the anus but they infect cells deeper in our submucosa and then are able to disseminate through our lymphatic to our lymph nodes and cause a more systemic infection. Now what's interesting about this especially is that it used to be considered a relatively rare disease in high income countries and classically was described as a painless ulcer followed by lymph node swelling, etc. But over the last few decades has become a much more common pathogen that more predominantly affects the anogenital region and can cause significant inflammation in the rectum in people that are having receptive anal sex.

Erin Welsh: Interesting.

Erin Allmann Updyke

Yeah. And of course the other serovars of Chlamydia trachomatis can also infect the anal region but this specific serotype seems to really like the anal region and can cause a more disseminated infection. So it can cause things like rectal bleeding, pain, a mucoid discharge. It can cause something called tenesmus which is this horrible sensation that you have to have a bowel movement even when your rectum is empty. So it can cause a lot of muscle spasm and be really painful. So the symptoms can actually be confused with inflammatory bowel disease because the symptoms really overlap.

Erin Welsh

And is this just because it has a tendency to invade more deeply and so the infection itself is just more exactly intense and almost systemic kind of?

Erin Allmann Updyke

It is and it is harder to treat. It needs a longer course of antibiotics.

Erin Welsh

Okay.

Erin Allmann Updyke

Exactly, yeah. I swear I'm almost done but there's one more thing I can't not talk about. And that is that chlamydia infection can also cause what's known as a reactive arthritis which happens weeks later after an infection and it can cause arthritis, so pain in the joints and inflammation in the fluid in your joints and also a conjunctivitis which is fascinating. How did the inflammation make it all the way up to your eye after just a urethral infection? I don't know the answer to that, we don't know the answer to that. It's really unclear if this reactive arthritis is caused by a persistent chlamydial infection or if it's caused by just our immune response causing this inflammation that then becomes more widespread. Chlamydia is not the only cause of reactive arthritis, salmonella, campylobacter, yersinia, a lot of other bacteria are also associated with reactive arthritis. But one of the papers that I read said that up to 4% of people with an acute chlamydia trachomatis infection go on to develop reactive arthritis which is way higher than I thought.

Erin Welsh

Yeah. Okay, questions.

Erin Allmann Updyke

Okay.

Erin Welsh

This is for all serovars of Chlamydia trachomatis?

Erin Allmann Updyke

I think it's mostly D through K but I don't think that it's impossible that any of the serovars could potentially cause this.

Erin Welsh

Okay. And would this happen even if you go on a course of antibiotics and clear the infection that way?

Erin Allmann Updyke

Great question. I think yes potentially.

Erin Welsh

Okay. So this is like the Chlamydia trachomatis is no longer there but your body is still reacting to something.

Erin Allmann Updyke

Well yes but the bacteria are often able to be recovered from synovial fluid in people with reactive arthritis but it's unclear whether they are active infectious bacteria or not. Remember there are multiple stages of the life cycle of chlamydia.

Erin Welsh

Yeah.

Erin Allmann Updyke: And whether or not antibiotics are effective in treatment is really up for debate right now. So it's unclear, it's one of these areas that much like so many chronic and autoimmune inflammatory conditions again is ripe for research because we just don't really understand this reaction.

Erin Welsh: How long does it last?

Erin Allmann Updyke: I think it tends to resolve even without treatment within at least a few months.

Erin Welsh: Okay.

Erin Allmann Updyke: Yeah.

Erin Welsh: Wow. Fascinating.

Erin Allmann Updyke: It is really interesting. And I mean that's *Chlamydia trachomatis* in not quite a nutshell but maybe several like a whole tree.

Erin Welsh: A bag of peanuts.

Erin Allmann Updyke: Yeah, a bag of peanuts.

Erin Welsh: (laughs) Or like hot boiled peanuts where you have five sometimes in a shell.

Erin Allmann Updyke: Yeah. You know I don't eat hot boiled peanuts.

Erin Welsh: That's true.

Erin Allmann Updyke: When have I eaten peanuts?

Erin Welsh: Hot boiled peanuts are the best though.

Erin Allmann Updyke: Yeah well anyways. It is still a treatable infection. All of the different serovars are treatable which is great and it's all with the same antibiotics, either doxycycline or azithromycin. Of course longer for the more deeper infection like I mentioned.

Erin Welsh: Antibiotic resistance.

Erin Allmann Updyke: It's a thing, it's a thing. And that is part of why it used to be that in the US sexually transmitted chlamydia was treated with a one time dose of azithromycin but now there's more data that shows that actually cure rates are better with doxycycline even though it's a longer course, it's 7 days. So yeah. Antibiotic resistance is definitely a thing. I think it's not yet as severe as say with gonorrhea but let's hope we don't get there.

Erin Welsh: Yeah I was gonna say just wait, just wait.

Erin Allmann Updyke: So yeah, any other questions? I don't know if I answered any of your questions adequately.

Erin Welsh: You did. No, I feel like I'm all set for now but I'm gonna keep thinking in the back of my head as I tell you the history.

Erin Allmann Updyke

Can you please? I want to know all about it.

Erin Welsh

Yeah. We'll take a quick break and then I'll get into it.

TPWKY

(transition theme)

Erin Welsh

Just like with the biology section I feel like we can split the history of *Chlamydia trachomatis* into multiple parts as well. But in this case I'm going to do it in two parts based on its name. So there's what we can think of as the chlamydia part of the story, so that's what I'm calling the disease as an STI, the pathogen as an STI.

Erin Allmann Updyke

Right. Yeah.

Erin Welsh

And then there's the trachomatis or trachoma part of the story, so the bacteria as the cause of this eye infection, this severe chronic eye infection.

Erin Allmann Updyke

Yeah.

Erin Welsh

And that's kind of how I decided to approach this history except for the fact that I am going to be giving trachoma more airtime than chlamydia as an STI, partly because, and I was a bit surprised to find this, that trachoma has a much deeper and much more extensive history than chlamydia as an STI. Because that was really only recognized as an STI fairly recently.

Erin Allmann Updyke

Really?

Erin Welsh

Yeah. Which of course it doesn't mean that it only emerged as an STI recently but in terms of clinical recognition, yes. Yeah. So kind of like you did I'm going to start with the evolutionary history overall and then I'm going to go into trachoma and then talk a bit at the end about chlamydia. So I'm going to call this the trachomatis-chlamydia approach.

Erin Allmann Updyke

I love it.

Erin Welsh

Thank you. For quite a while, people thought that chlamydia were mainly mammalian pathogens infecting mammals and a few other animals intracellularly. But then in the late 1990s some researchers observed chlamydia acting as endosymbionts inside free-living amoebae. They're not in the same genus, like for instance one is called *Parachlamydia*, but they are related to these intracellular pathogens.

Erin Allmann Updyke

Okay, okay.

Erin Welsh

Yeah. And this showed that not only are chlamydia way more diverse than people previously thought but also much older, like 700 million years old. Yeah. But we're not going to go through all 700 million years of history. Let's kind of get to where the human chlamydia-specific strains or species that we're interested in, right. So *Chlamydia trachomatis* essentially. The strains of chlamydia that cause eye infections apparently diverged from the strains that cause genital infections around 2 million to 5 million years ago which is around the time that *Homo habilis* and *Homo erectus* evolved. So these guys have been with us for like we said as long as we've been human.

Erin Allmann Updyke

Yeah.

Erin Welsh	Forever.
Erin Allmann Updyke	Forever.
Erin Welsh	And ancient writings further confirm that. So now is where I switch to focus on trachoma.
Erin Allmann Updyke	Okay.
Erin Welsh	So even though trachoma has probably always impacted humans, the transition to larger settlements and increased mobility would have provided more opportunities for the infection to spread to more people both within communities and also along trade routes. And its widespread prevalence is evident in the fact that trachoma is described in so many ancient texts, so many.
Erin Allmann Updyke	Really?
Erin Welsh	Yeah. Let's go through a few of these early mentions starting with the more vague mentions and then getting more specific.
Erin Allmann Updyke	Okay.
Erin Welsh	There's a description from sometime during 2600-2700 BCE about an emperor in China undergoing surgery for a trichiasis. And there are inscriptions of eye disorders found on animal bones and tortoise shells from around 1100-1600 BCE and there are also Bronze Age epilation forceps used for removing eyelashes found in Sumeria from around 2600 BCE.
Erin Allmann Updyke	Wow.
Erin Welsh	Yeah. The first specific references to trachoma come from around 420-581 BCE in China and in these references trachoma is described with terms including quote "pepper seed-like lesions" and quote "millet-like granules". And copper, octopus, and garlic rubbed on the eyelids was a commonly recommended treatment. Then we have writings from Sushruta from the 700s BCE who is an ancient Indian physician and surgeon that I've mentioned on the podcast at least a few times, I think many times. Specifically, I actually look this up, in our diabetes, rabies, and organ transplantation episodes for example.
Erin Allmann Updyke	I love that you looked it up.
Erin Welsh	I did. So Sushruta wrote about how the inner eyelid gets rough and thick and how the eyelashes can grow inward and how your eyelid can also turn inwards and cause the lashes to rub against your eye. It's pretty spot on trachoma, right?
Erin Allmann Updyke	Yeah.
Erin Welsh	The early history of trachoma honestly reads like a who's who of the early medical texts. Because up next is our old friend the Ebers Papyrus.
Erin Allmann Updyke	I was hoping you'd say that.

Erin Welsh	Of course I was going to say that. So in this classic text, which is from around the 1550s BCE or so, we've got lots and lots of different treatments for eye disorders including onions, gazelle excrement applied to the eye with a vulture feather.
Erin Allmann Updyke	Wow, specific.
Erin Welsh	And epilation followed by the application of lizard or bat blood.
Erin Allmann Updyke	Okay.
Erin Welsh	Interestingly both Plato and Aristotle suggested that trachoma was contagious with Aristotle going so far as to suggest that you could get it just by looking at someone who had it. But it would take quite a long time of course before they were vindicated in this belief. And we have another friend yet who is joining us which is Hippocrates and the Hippocratic texts. Yep. And in these texts there are descriptions of the fig-like appearance of the upper lid and inturned lashes and also some suggestions that the condition could be prevented by avoiding the cold winds from the north and the warm winds from the south. Which what winds are you left with?
Erin Allmann Updyke	Just avoid all winds.
Erin Welsh	Avoid all winds.
Erin Allmann Updyke	You can have an easterly breeze that would be fine.
Erin Welsh	Okay, yeah. Yeah. But also I really love these treatments, drinking wine, bathing, I'm down for that, purging, nope, bloodletting, nope, or applying a cleansing medication to the affected area.
Erin Allmann Updyke	Okay, yeah. We've got some decent ones in there.
Erin Welsh	Yeah. And of course there were also surgical procedures that were recommended to treat trachoma in these texts. In the 1st century CE, the Ancient Greek physician Dioscorides was the first to use the word trachoma, meaning roughness, to describe the condition. And a little over 100 years later, Galen described the four stages of trachoma. I could honestly go on and on this entire episode just listing these other ancient texts that have references to trachoma, like those by Avicenna and al-Kahhal the ophthalmologist, among others. And also you know that I would love to get into some of these incredibly varied treatments used, egg white, mouse ear, frog's blood, the bile of a goat, etc. But even without doing that, even without going further down this rabbit hole of ancient texts and trachoma, I feel like it has given us a pretty good sense of how widespread and devastating a problem this was.
Erin Allmann Updyke	Yeah, I honestly had no idea. It makes sense even now looking at the distribution and how many people are still at risk and affected, it makes sense. But I never realized that.
Erin Welsh	Yeah, me either at all. I really thought before researching this episode this is going to be an STI history where I'm going to talk about when people realized chlamydia was different than gonorrhea etc, etc. And then I realized this is really fascinating and important and it just gets more so. Because if you thought it was widespread in the ancient world, of course it's only going to get more widespread as global population increased, mobility increased, and so on.
Erin Allmann Updyke	Yeah.

Erin Welsh

So I'm going to mention one more thing in kind of olden times before jumping all the way ahead to the 1800s.

Erin Allmann Updyke

Olden times, okay.

Erin Welsh

So during the crusades in 1100-1200 CE you had a ton of crusaders and pilgrims that were venturing to the holy lands and many of them came back with trachoma, one of them possibly being St. Francis of Assisi who was actually blind at his death in 1226.

Erin Allmann Updyke

I'm loving this.

Erin Welsh

All right so now let's get to the 1800s. And why the 1800s you might ask? So from the ancient times to then, of course Trachoma was around, it was written about, it was described, it made an impact but also it was kind of used sometimes as a catch all term, as this umbrella term to describe both the acute phase and the chronic phase, more eye infections caused by other pathogens. It was not really featured as sporadically or studied very intensively. But all of that would change around the early 1800s. And the reason for that change is of course war, specifically the Napoleonic wars. Poor Napoleon has been featured on this podcast for so many times for all of the disastrous campaigns where his army was wiped out by various diseases, right. All the way back in Season 1 we talked about him and yellow fever. In our typhus episode we talked about how an unbelievably huge number of his soldiers died from typhus while trying to march up to Russia.

But with trachoma and Napoleon, we find ourselves not in Russia or Hispaniola but rather in Egypt. From 1798-1815, Napoleon decided to wage a series of campaigns basically all over the place to try to gain more control over the European continent, largely by disrupting British colonial and economic rule, that was his aim. In July 1798, Napoleon landed near Alexandria, Egypt and then he and around 40,000 French troops marched to Cairo. And the purpose of the Egypt invasion from what I can tell was essentially to establish a foothold in the region so that they could try to disrupt one of the main sources of British economic power, India, by driving the British out of that subcontinent. So they were like, 'All right, we're going to set up shop in Egypt and then from here we're going to defeat the British.'

Erin Allmann Updyke

Okay.

Erin Welsh

It also came with the plus of establishing French trade in the region. Not long after they arrived in Egypt however, Napoleon's troops began to experience many of the illnesses you'd expect a traveling army to. Dysentery, excessive dehydration, and also eye infections. By late September the prevalence of eye infections or inflammation had grown enormously. For example in one battalion of 300 soldiers, 125 had eye inflammation severe enough that they were effectively blind.

Erin Allmann Updyke

Wow.

Erin Welsh

And had to rely on their unaffected comrades to point their guns in the right direction from the trenches.

Erin Allmann Updyke

Oh dear.

Erin Welsh

And the high prevalence in this battalion doesn't really seem like a one-off because in an expedition in October 1798, 1400 French soldiers developed ophthalmia out of 3000, so nearly half.

Erin Allmann Updyke

Wow.

Erin Welsh

And the condition was not restricted to just the French soldiers fighting but also the people they were fighting against, namely Turkish and British troops, although Turkish troops later switched sides and fought against the British. So everyone was affected essentially is what I'm trying to say. And the British Army seemed especially affected by eye inflammation after around March of 1801. One report from the time described how out of an 8000 person division, 1600 soldiers developed ophthalmia in September and October and 158 became blind. Which is a lot.

Erin Allmann Updyke

Yeah.

Erin Welsh

That's a lot of people. Napoleon's invasion of Egypt marked a turning point in the history of trachoma because it led to a huge amount of interest in the disease, especially from military physicians. And it also led to the infection spreading much more widely. When these British and French troops returned to Europe from Egypt, many of them brought trachoma back with them and basically everywhere they traveled on their journey home, trachoma followed. For instance, French troops landing in Sicily in 1801 on their way back from Egypt kicked off an epidemic of trachoma that didn't peak until 12 years later.

Erin Allmann Updyke

Whoa.

Erin Welsh

It just rose and rose and rose. Yeah.

Erin Allmann Updyke

Oh my gosh.

Erin Welsh

This time of the Napoleonic Wars and really in the years after was a period of great upheaval and mobility across huge parts of Europe and trachoma was not alone in this, it was just one of the diseases that took advantage of this disruption and widespread travel. Trachoma moved from Sicily to Hungary, France, the Netherlands, Germany, Russia, and on and on and on, essentially everywhere. And it especially became a fixture in armies. Ophthalmia first showed up in the Russian Army in 1818 and within 20 years, nearly 80,000 Russian soldiers had been affected, thousands of soldiers in the Dutch and Belgian armies became blind or partially blind, and during the Crimean War, so 1861-1867 or so, quote "4% of all disability in the army was due to ophthalmia and 5% of the total discharges were because of blindness, although these rates were approximately half what they had been in the 1830s."

Erin Allmann Updyke

Wow.

Erin Welsh

Yeah. So 10% of the discharges being due to blindness in the army.

Erin Allmann Updyke

Wow.

Erin Welsh

Yeah. And so doctors, military doctors and also civilian doctors, had plenty on their hands in terms of trachoma. And as you might expect, one of the things in the front of everyone's mind was how to control or prevent this disease which in the years before germ theory was tangled up with the debate on whether trachoma was contagious or not. Was it warm rains or cool nights? Was it a dusty atmosphere or cold wind that led to outbreaks? Or was it the sharing of hand basins, not washing regularly, sharing towels, not cleaning bedding, or not using pillowcases, etc? And in reality it was kind of a little bit of both because having access to clean your face or not sharing towels one big part of it and some environmental factors playing another part through seasonal changes in fly prevalence for instance.



While some doctors continued to work on the control aspects of trachoma, others begin to concentrate and specialize on how to treat the condition. The author of the book that I read for this compared trachoma to Helen of Troy. But rather than ships, trachoma was the disease that launched 1000 hospitals. I loved that. By the mid to late 1800s, trachoma was a pervasive problem everywhere and it wasn't limited to just the military. Entire hospitals and medical divisions were created to treat it and trachoma also played a big role in making ophthalmology a specialization and profession in itself, rather than it being just a part of generalist care, like generalists who have an interest in ophthalmology.

Erin Allmann Updyke

Wow, I had no idea.

Erin Welsh

I know. The history of trachoma is so much deeper than I realized.

Erin Allmann Updyke

Yeah.

Erin Welsh

And also I really find it interesting to think about the origins of different specialties and specializations in medicine.

Erin Allmann Updyke

Oh my gosh, I know.

Erin Welsh

Yeah. Governments established trachoma schools attended by children who had trachoma or other eye conditions because like you said, it was so prevalent among children and it also became a notifiable disease in many places. By the second half of the 1800s, researchers had fully established that trachoma was indeed contagious even if they wouldn't discover the causative agent until 1907. But knowing that trachoma was caused by an intracellular bacterium didn't stop people from characterizing the epidemiology of the disease. Familial transmission was common, children under 7 had the highest prevalence, it seemed to be strongly correlated with access to sanitation and clean water, and it seemed to be most prevalent among low income households. And of course these last two characteristics, so low income households plus lack of access to sanitation or hygiene practices, these marked the disease as a social status indicator. Similar to many other diseases that we've talked about on the podcast before, tuberculosis, hookworm, trachoma, these were the diseases that the poor brought upon themselves just by being poor. That was the narrative, right. These diagnoses became wrapped up in a person's identity, labeling them unclean.

Erin Allmann Updyke

I feel like that's still the problem with trachoma and why we don't know anything about it.

Erin Welsh

Absolutely, absolutely. Although some control strategies for trachoma involved providing care to people who had the disease, many of them focused more on limiting the spread of the disease to wealthier populations, right. It wasn't so much let's manage and stop the cycle of transmission, it was like let's keep the cycle of transmission over there and not let it spill into here.

Erin Allmann Updyke

Yeah. Which is not only cruel, it's also ineffective.

Erin Welsh

It truly, truly is. So it seems unclear whether or not trachoma had been present in the US prior to the arrival of Europeans in the 1400s and 1500s but in any case the late 1800s saw a similar increase in trachoma in the US that the rest of the world was experiencing. And this rise in cases was blamed on immigration. Throughout this time period and into the early 1900s, millions of people were leaving their homeland which was often somewhere in Europe to travel to the US and try to find more opportunities or be with their family or escape some of the horrible situations that were happening like famine. Many, many, many different reasons. And I'm not going to go in depth about the immigration politics of this time because I don't know enough about it and there's probably better podcasts and resources out there but I will say that as immigration increased in the late decades of the 1800s, so did resentment and anti immigration sentiments which eventually led to policies aimed at reducing immigration by especially targeting people that they didn't want to admit into the country.

For instance the Chinese Exclusion Act of 1882 or other laws or acts that prevented people from being admitted if they had certain diseases including but not limited to epilepsy, quote "insanity", tuberculosis, cholera, typhus, ringworm, and trachoma. In 1897 the US Surgeon General called trachoma quote "a dangerous, contagious disease" and instructed medical officers to examine all immigrants. The examination process itself was painful and not at all sanitary which probably led to further spread of trachoma. They're like, 'Let me check your eyes. Okay, next. Let me check your eyes. Oh you have trachoma. Oh let me check the next person's eyes.'

Erin Allmann Updyke

Right.

Erin Welsh

And if you were suspected to have trachoma, the officer would mark a big chalk T on your shirt and you were sent to the contagious disease hospital to wait it out to see whether you had acute conjunctivitis or if it was trachoma. And if it was trachoma, that was bad news. Over 95% of those with trachoma were deported.

Erin Allmann Updyke

Whoa.

Erin Welsh

And if you were fortunate enough to be in the 5% not deported, you could remain in the US in the hospital for treatment but that usually took about six months.

Erin Allmann Updyke

Whoa.

Erin Welsh

Because remember this is all pre any sort of effective antibiotics.

Erin Allmann Updyke

Right, no antibiotics. Yeah.

Erin Welsh

In 1902 the US ramped up their restrictions against trachoma by placing a \$100 fine on every shipping company per trachoma case brought to the US. So then these companies started to do port of origin screening sites and these additional restrictions led to trachoma becoming one of the main reasons that prospective immigrants were rejected.

Erin Allmann Updyke

What?

Erin Welsh

Let me read you some numbers to give you a sense of just how much trachoma played a role in immigration. Quote: "Between 1897 and 1924, some 21,758,875 immigrants were examined and 33,847 were debarred because of trachoma." So it would be 0.16%.

Erin Allmann Updyke

Wow.

Erin Welsh

Another quote: "It was common to have 2%-5% of prospective immigrations rejected, 85% of those rejections were due to trachoma."

Erin Allmann Updyke

Wow.

Erin Welsh

I know. You would think that based on how seriously the US was taking trachoma in the context of immigration stuff that there would be almost no trachoma in the country, right?

Erin Allmann Updyke

Oh you'd think, right? That's logical.

Erin Welsh

Of course that's not true though.

Erin Allmann Updyke

No, no.

Erin Welsh

The first detailed look at trachoma in the US came out around 1911. That year a physician from Lexington, Kentucky released a report that showed just how prevalent trachoma was especially in eastern Kentucky and across rural Appalachia through to Kansas and Oklahoma. Rates of trachoma in these regions were comparable to or greater, much greater than many of the countries from which people were emigrating. For instance Native Americans were among those most impacted with an average prevalence rate of 23%. But it gets worse. In some Native American boarding schools in Oklahoma, that number would shoot up to a horrific 92%. 92%, yeah.

Erin Allmann Updyke

Oh my.

Erin Welsh

This report did kind of awaken public health officials to the tremendous issue that trachoma already posed in parts of the US and so they created trachoma hospitals and state-specific control programs and over the early 1900s, especially the 1930s and the 1940s, trachoma did sharply decline in the US and in many countries in Europe where it had been prevalent, essentially countries that were higher income countries. And I think it's not the easiest thing to tease out exactly why this decline occurred and how much these treatment centers contributed vs infrastructural improvements in things like sanitation and clean water that made it possible for people to regularly practice these hygiene practices that would help them keep their face clean, etc. Based on the timing of the declines, it's possible that antibiotics like sulfonamides played a role but if they did I have to feel like it was a fairly minor one since the decrease seemed to happen in many places long before the widespread introduction of these antibiotics.

Erin Allmann Updyke

Yeah. Which is really interesting in the context of current events.

Erin Welsh

It certainly is, yeah. I feel like this is such a good illustration of how disease prevalence can be reduced through changes in infrastructure rather than just treatment alone. And I think it also shows that treatment alone is never going to be sufficient.

Erin Allmann Updyke

Nail, head.

Erin Welsh

But as usual this decline in trachoma was not universal nor did it happen evenly across the landscape. In the US for example, trachoma persisted in many Native American communities through the 1980s and in Australia it continues to be a problem in indigenous communities. And there are many regions around the world that still have high rates of trachoma which I know you'll talk more about, Erin. It wasn't really until the mid 1900s that international organizations like the WHO started trachoma control programs for some low and middle income countries and they set an elimination goal only in the mid 1990s. Which honestly it really surprised me after reading about this history where I was like wait it's preventable, it's treatable, and it also has an absolutely enormous impact on quality of life.

Erin Allmann Updyke

Yep.

Erin Welsh

So I've almost gotten all the way to the end of the trachoma history part without even talking about the causative agent really and how it was identified and who discovered it and so on. And one of the reasons for that is, like I said earlier, knowing exactly what caused this condition didn't seem to be necessary to stop the cycle of transmission and reduce prevalence in some places. But what the identification of *Chlamydia trachomatis* did was allow people to distinguish trachoma from other acute types of eye inflammation, enable them to see which treatments might work best, and also let them look for other ways that this bacterium could infect humans such as genitally.

Erin Allmann Updyke

Genitals.

Erin Welsh

So let's go back in time to when *Chlamydia trachomatis* was first identified. The late decades of the 1800s could be considered the heyday of germ theory. People were identifying bacterial or parasitic causes of diseases left and right. I mean really can you imagine the dissertation would be like I looked in this person's boogers and I found this. Boom.

Erin Allmann Updyke

You're done.

Erin Welsh

Give me a Science or Nature paper. I don't think they existed back then but...

Erin Allmann Updyke

In theory.

Erin Welsh

In theory, yeah. And so when a disease existed that a bacterium or parasite wasn't easily or readily identified, it wasn't like oh this must not be infectious, it was often assumed that it was a transmissible filtering agent, aka a virus. And trachoma fell into this category at first.

Erin Allmann Updyke

Natural.

Erin Welsh

Of course. Until 1907 when Halberstädter and von Prowazek used a special stain to visualize the bacteria in trachoma. But they didn't realize at that time that it was bacteria they were seeing, they thought it was intracellular protozoa that appeared to cloak the nucleus of the cells they infected which gave rise to the name Chlamydozoa after the Greek word for cloak.

Erin Allmann Updyke

Oh that's fun.

Erin Welsh

Yeah. And of course it was later changed to chlamydia once people realized that they were not protozoa but bacteria. So now that people had found what caused trachoma, did that mean that they would also be able to link it to the genital infection? Not exactly. If you think back to our gonorrhea episode, I think I mentioned how, I didn't check my notes, prior to the identification of the gonorrhea bacterium, it's hard to tease apart which historical descriptions of genital infections are actually gonorrhea vs something else based on symptoms alone.

Erin Allmann Updyke

Right.

Erin Welsh

And the identification of *Neisseria gonorrhoeae* allowed people to finally say this is definitely gonorrhea, which also meant that they could say well I don't know what this is but it's certainly not gonorrhea and we can't treat it with the same things as we do gonorrhea.

Erin Allmann Updyke

Right.

Erin Welsh

And so this is how nongonococcal urethritis or non specific urethritis became a diagnosis. It was this diagnosis of exclusion.

Erin Allmann Updyke

That makes sense.

Erin Welsh

People did look for the cause of nongonococcal urethritis which I'm just going to call NGU moving forward. But one problem was that it wasn't just one thing causing it.

Erin Allmann Updyke

Right.

Erin Welsh

Later research has shown that it can be caused by *Chlamydia trachomatis*, *Mycoplasma genitalium*, *Trichomonas*, among others. But people didn't know all of these things could cause it at that time.

Erin Allmann Updyke

Right.

Erin Welsh

Yeah. So if you're a researcher, let's say you're digging in some secretions and trying to find out what the cause of this infection was and you're like I think I found it, I got it. And then you go over to a friend, take your little horse and buggy, go over to a friend and you say, 'I think I found it. Do you see it in your secretions?' And he goes, 'No, I don't. This is something totally different. So you didn't get the right one.'

Erin Allmann Updyke

Right, right. You just feel really bad about yourself. You're like my experiment failed.

Erin Welsh

Right. And you're like I'm leaving academia and I can't do this anymore.

Erin Allmann Updyke

I quit. I'm going to make a podcast. (laughs) Sorry that was funny.

Erin Welsh

That was really good.

Erin Allmann Updyke

Thanks.

Erin Welsh

But researchers did try to minimize this confusion about what caused NGU by seeing if they could distinguish among different types of NGU.

Erin Allmann Updyke

Okay.

Erin Welsh

How long was the incubation period? What were the symptoms? How long did they last? Things like that. And one of these people who was trying to characterize NGUs was named Ludwig, and I don't know how you pronounce this name but I'm very excited about it because it is spelled Waelsch which is very close to Welsh. And so I'm just going to call him Ludwig Waelsch. And he described a quote "rare form" of NGU that had an incubation period of 10-14 days. The course of the disease was mild but long and it was difficult to treat using the antibiotics of the day.

Erin Allmann Updyke

Okay.

Erin Welsh

Additional work also showed that the mucous membrane in cases Waelsch urethritis, as it would be called, was reddened with soft multiple infiltrates, quote "like the nodules in trachoma".

Erin Allmann Updyke

Interesting.

Erin Welsh

People had made a possible connection with the trachoma agent and genital infections before this. One gruesome experiment even involved taking material from people's genitals who had NGU and then applying that to the eyes of monkeys. And sure enough they developed an eye infection. There's definitely no IACUC approval on that one for sure.

Erin Allmann Updyke

No.

Erin Welsh

But it seems like the trachoma agent was just a tricky bug to work with and it was hard to know what it was or what it wasn't responsible for, including trachoma. Because there was still some debate about that and also there was no ability at the time to culture it. And even with Waelsch urethritis, sometimes people saw chlamydia in the scrapings of infected tissue under the scope and other times they didn't. But the link seemed strong enough for at least one researcher to suggest that this Waelsch urethritis was quote "a genital trachoma". The debate continued for decades but in the 1930s American ophthalmologist Phillips Thygeson drew a link between neonatal ocular infection and being exposed to genital infection during birth. And later that decade he also showed that trachoma could be treated with sulfonamides which was actually a pretty huge deal at the time. After the introduction of penicillin in the 1940s which could be used to treat gonorrhea but not NGUs, interest in NGU and the possible link between trachoma and genital infection increased even more. But the real turning point for both trachoma and chlamydia would come about in 1957. Earlier when I said that scientists thought that trachoma could be caused by a virus, they weren't actually that far off, right.

Erin Allmann Updyke

Right.

Erin Welsh

Chlamydia trachomatis acts like a virus in many ways, right.

Erin Allmann Updyke

Right.

Erin Welsh

And this similarity to viruses where they have to basically hijack a host cell's machinery to replicate, it kept researchers from being able to culture them for 50 years after their initial identification.

Erin Allmann Updyke

Wow. 50 years.

Erin Welsh

Yeah. It's a long time. And that made it really difficult to fully characterize the bacterium, see its life cycles, and see where it was involved.

Erin Allmann Updyke

Right.

Erin Welsh

In 1957, Tang Feifan along with a research team was able to culture the bacteria in a chick embryo. This was a huge breakthrough because it allowed people to culture large amounts of these bacteria which led to careful characterization of its infection cycle, diagnostic tests, exploration into vaccines, antibiotic sensitivity testing, and so on. And two years after chlamydia could finally be cultured, it was isolated after delivery from both the cervix as well as the eyes of the infant who had inclusion conjunctivitis. People were finding more and more chlamydia in genital infections and by 1965 the number of cases of NGU, many of which were chlamydia, possibly most of which, finally surpassed that of gonorrhea in the US, really illustrating how important it was to be able to distinguish among these NGU infections, right. It was no longer enough to just say they're NGU, that's NGU. Finally Chlamydia as an STI became a clinical entity in the 1970s.

Erin Allmann Updyke

What?

Erin Welsh

I know. And even then it would be another 10 or more years before it became a notifiable disease in some places. In the 1980s is when people started to discuss the possible ties between chlamydia and public inflammatory disease and infertility. And it seems like around the time of that research is when chlamydia began to be labeled as a disease of promiscuity, especially promiscuous women. Which is really no different from how women were viewed historically as the sources of STIs but not people who needed to be treated themselves, right.

Erin Allmann Updyke

Which is I can't even tell you how frustrating especially in the context of chlamydia today. But anyways, that's my personal high horse and I'll step off.

Erin Welsh

No, it is really frustrating especially when you read these descriptions of treatment that were not that old right from the 70s, the 80s. And the way that they described treatment is that in order to reduce chlamydia in men, we should prescribe antibiotics in women. Oh and I guess it'll treat them too.

Erin Allmann Updyke

That's fascinating. Because I literally just read a paper that was like what if we actually screen men? Can we reduce the rates in women? Because we still aren't screening.

Erin Welsh

We still aren't screening, are you serious?

Erin Allmann Updyke

Yeah. In people with a penis it is still not recommended for general screening.

Erin Welsh

Wow.

Erin Allmann Updyke

Yeah.

Erin Welsh

And the link between infertility and chlamydia seemed to be used to push this judgmental moralistic narrative where infertility was the punishment for being promiscuous, the world was witnessing a silent but deadly epidemic of infertility.

Erin Allmann Updyke

Oh god.

Erin Welsh: Things like that. And all during this, cases of chlamydia did seem to be on the rise although it was only routinely included in STI statistics in the US and Europe starting in 1990. So I realized this was kind of just a brief foray into these two different diseases with very distinct histories and social impacts and I could have probably spent an episode on each of them.

Erin Allmann Updyke: Had we known.

Erin Welsh: Had we known. But I think that what they both show us going back to kind of the theme I feel like for this episode is how easy it can be for a diagnosis to become wrapped up in someone's identity and how important it is that we don't let that happen.

Erin Allmann Updyke: Yeah.

Erin Welsh: So Erin, I would love for you to tell me more about where we stand with chlamydia and trachoma today.

Erin Allmann Updyke: I can't wait to right after this break.

TPWKY: (transition theme)

Erin Allmann Updyke: When it comes to trachoma this remains the most common infectious cause of blindness worldwide.

Erin Welsh: Yeah, it's really common.

Erin Allmann Updyke: It's really common. It's responsible for blindness or visual impairment in almost 2 million people which is about 1.4% of all blindness worldwide. And globally an estimated 136 million people in 44 countries across the globe live in trachoma endemic areas and are therefore at risk of infection which is a lot of human beings.

Erin Welsh: Yeah.

Erin Allmann Updyke: Yeah. And like you kind of mentioned Erin, the World Health Organization and the World Health Assembly has targets for global elimination which sounds so great but the initial target date was 2020. Womp-womp.

Erin Welsh: Womp-womp.

Erin Allmann Updyke: So the new target is 2030.

Erin Welsh: How are we doing with that target by the way?

Erin Allmann Updyke: Well I actually have some great news on that front, thanks for asking. As of March 7, 2022, 14 countries have newly reported achieving elimination goals. So I feel like that's something worth celebrating.

Erin Welsh: That's huge.



Erin Allmann Updyke

Yeah, that's very big. Unfortunately the COVID pandemic put a very big damper on public health efforts in 2020, half as many people received corrective surgery to treat trichiasis and reduce the progression of visual impairment and way less than half as many people as in 2019 received antibiotic prophylaxis or treatment. So that's a big bummer. But we're still at least seeing progress in a lot of places. So that's really good.

Erin Welsh

That's great.

Erin Allmann Updyke

Yeah. And like we kind of talked about before the strategies to kind of treat this, I'll post the World Health Organization's information for people who want to read more but it is a very multi-tiered approach which I think is important. Not only do they target infrastructure to be able to increase access to clean water and sanitation which is going to be able to reduce the spread of infection, it also includes antibiotic treatment in mass antibiotic campaigns especially in hyper endemic areas because this does tend to be a disease that in certain areas will be at really, really high prevalence and then in other areas will be at much lower prevalence. So mass antibiotic campaigns and then also surgical correction to be able to reduce the progression of disease in people who already had it as children.

Erin Welsh

Where are some of these hyper endemic regions? How is this distributed across the globe?

Erin Allmann Updyke

Great question. So across the globe it's the most economically disadvantaged and rural areas of Africa, Central and South America, Asia, Australia, and the Middle East. So the kind of most economically disadvantaged, poorest, most rural regions that tend to be the most hyper endemic.

Erin Welsh

Gotcha.

Erin Allmann Updyke

In terms of the STI chlamydia, we're talking about the most common bacterial sexually transmitted infection.

Erin Welsh

Yeah.

Erin Allmann Updyke

The most common one. The most recent studies that I read estimated a global incidence of 131 million new cases every year.

Erin Welsh

That's a lot of cases.

Erin Allmann Updyke

That's a lot of humans. With an estimated global prevalence of around 4% or so, 3.8%-4.2% of people with a cervix, so cervical infections, and anywhere from just under 3% to about 7% were the estimates that I saw of people with a penis. Surprisingly to no one we don't have as good of data on penile urethral infections because most countries do not universally screen people with a penis for infection the way that they do screen young adults people with a cervix universally. Which is again something that I hope will change in the next coming years. And importantly it does tend to be young adults aged 18-26 tend to have the highest prevalence. So overall it's probably close 3%-4% of the population, adult population infected at any given time.

Erin Welsh

Gotcha.

Erin Allmann Updyke

What? That's a lot of humans. And in the US as of 2019 there were over 1.8 million cases reported annually. And if you look just at the highest risk group that we screen, that we have good data on, that is people aged 15-24 with a cervix, the annual incidence is over 3700 cases per 100,000 people.

Erin Welsh: Okay, yeah.

Erin Allmann Updyke: That is incredibly common.

Erin Welsh: It's very common.

Erin Allmann Updyke: So I feel like one of the things that I hope that these numbers really highlight and kind of going back to what you were talking about Erin about how chlamydia infection has been used in the past to have a lot of shame and stigma specifically associated with it. This is an incredibly common infection. It is not something that only a certain type of people can have or only a certain type of people are going to be at risk for. When we're talking about sexually transmitted bacterial infection as common as this, anyone having sexual contact of any kind is going to be at some risk of infection. People having multiple different kinds of sex or sex with multiple people of course are going to have a higher risk but whether you're having any type of sex with one person or multiple people, things like using condoms can decrease our risk. Getting tested, getting treated, talking about this infection and making it less shameful so that we have an awareness about it is the way that we reduce this infection because it's not that it's inherently bad or shameful to get a sexually transmitted infection but they can be really serious and we have ways to reduce the risk and to be able to treat these infections. So I think that's really important.

Erin Welsh: That was really well said. I agree with that.

Erin Allmann Updyke: Thanks. And speaking of prevention, what about vaccines, Erin?

Erin Welsh: What about vaccines, Erin?

Erin Allmann Updyke: Yeah. We don't have one.

Erin Welsh: Yet.

Erin Allmann Updyke: Yet. I read a really interesting paper that I was looking at all chlamydias and over the last 70 years there have been at least 220 different vaccine trials. And in the last 10 years alone there's been an average of 12 vaccine studies per year on chlamydia which is like one a month. So that's thrilling. Not all of these studies have been on our friend *Chlamydia trachomatis*, a lot have also been on species affecting koalas. That's a spoiler. So far still no vaccine but of course lots of people doing fantastic research to get us closer.

Erin Welsh: Speaking of fantastic people doing research to get us closer to a chlamydia vaccine, I am very excited for next week's bonus episode when I get to chat with not one but two researchers working on chlamydia in domestic animals and wildlife including koalas. Dr. Martina Jelocnik and Dr. Sam Phillips, both from the University of the Sunshine Coast in Queensland, Australia will be joining me to talk about other chlamydia species of wildlife or veterinary health importance. We'll be talking about how these infections have led to declines in certain animal populations as well as the latest news regarding a chlamydia vaccine for koalas. So make sure you don't miss it because it's going to be great.

Erin Allmann Updyke: I really can't wait. Well that's chlamydia and trachoma.

Erin Welsh: Yeah, this was a very packed full episode.

Erin Allmann Updyke

Yeah, yeah. It's a good way to say it.

Erin Welsh

Should we round it out with some sources?

Erin Allmann Updyke

We sure ought to.

Erin Welsh

I had a few but what I really want to highlight our two. One is a book called 'Trachoma' By Hugh Taylor and that is a fantastic overview of everything trachoma. And then for chlamydia there is a chapter by Worboys from 2019 called 'Chlamydia: A Disease Without A History'.

Erin Allmann Updyke

I read a lot of papers for this since there were so many different aspects of it. So I'm not going to specifically shout out any in particular but suffice to say if you want more details on the specific immunology and cell biology, pathophysiology of Chlamydia trachomatis, I've got papers for you. If you want more details on reactive arthritis, got a couple of papers for you. You want more on those 70 years of vaccine research? Oh, I got it. More on trachoma? It's there. Check out our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com) and you'll find a list of every single source from this episode and all of our episodes. There's like 90 something.

Erin Welsh

Yeah, there's 90 something. Thank you again so very much to the listener who sent in their firsthand account for this episode. Again, we really appreciate your willingness to put yourself out there and be vulnerable.

Erin Allmann Updyke

Yeah, thank you. And thank you also to Bloodmobile for providing the music for this episode and all of our episodes.

Erin Welsh

And thank you to Exactly right. Listen, follow, and leave us a review on Amazon Music, Apple Podcasts, or wherever you get your podcasts. And don't forget you can listen to new episodes one week early on Amazon Music or early and ad free by subscribing to Wondery Plus in the Wondery app.

Erin Allmann Updyke

And thank you to you, listeners. We really appreciate you listening and we hope that you liked this episode.

Erin Welsh

We do. And a special thank you also to our wonderful generous patrons. We love you. Well until next time, wash your hands.

Erin Allmann Updyke

You filthy animals.