

TPWKY

This is Exactly Right.

Erin Allmann Updyke

Okay so this is a small disclaimer for this episode since a lot of you either are kids - hi kids - or you listen with your kids - hi parents and kids. We are discussing a sexually transmitted disease today which means we're going to be talking about sex and genitals. So if you want to veto that for your 5 year old that's listening, put your earbuds in now. (laughs)

Erin Welsh

"January 18th, 1763. I this day began to feel an unaccountable alarm of unexpected evil. A little heat in the members of my body sacred to Cupid, very like a symptom of that distemper with which Venus, when cross, takes it into her head to plague her votaries. But then I had run no risks, I had been with no woman but Louisa and sure, she could not have such a thing. Away then with such idle fears, such groundless, uneasy apprehensions."

"January 19th. The evening was passed most cheerfully. When I got home though, then came sorrow. Too, too plain was Senor Gonorrhoea."

Erin Allmann Updyke

(laughs)

Erin Welsh

Wait, there's more. (laughs)

Erin Allmann Updyke

I can't.

Erin Welsh

"Thus ended my intrigue with the fair Louisa which I flattered myself so much with and from which I expected at least a winter's safe copulation. It is indeed very hard. I cannot say, like young fellows who get themselves clapped in a body house, that I will take better care again for I really did take care. However since I am fairly trapped, let me make the best of it. I have no got it from imprudence. It is merely the chance of war."

TPWKY

(This Podcast Will Kill You intro theme)

Erin Allmann Updyke

(laughs)

Erin Welsh

I mean it goes on and on, like there's much more but that's just...yeah.

Erin Allmann Updyke

Oh my gracious.

Erin Welsh

Isn't it so good?

Erin Allmann Updyke

What is that from?

Erin Welsh

Okay, so that is from James Boswell. So James Boswell was the biographer of Samuel Johnson who's a literary figure.

Erin Allmann Updyke

Okay.

Erin Welsh

Yeah. James Boswell throughout his life, throughout his journal entries at least became infected with gonorrhoea at least 19 separate times.

Erin Allmann Updyke

(laughs)

Erin Welsh 19. So this is merely one of them. I just... You should take some time and just go and seek out the entirety of-

Erin Allmann Updyke Read his whole journal entries?

Erin Welsh Yeah. Yes.

Erin Allmann Updyke Man.

Erin Welsh (laughs) Hello.

Erin Allmann Updyke Hello!

Erin Welsh I'm Erin Welsh.

Erin Allmann Updyke And I'm Erin Allmann Updyke.

Erin Welsh And put your hands together for-

Erin Allmann Updyke Put your hands together!

Erin Welsh For gonorrhea, the subject of today's episode of-

Erin Allmann Updyke This Podcast Will Kill You.

Erin Welsh Welcome.

Erin Allmann Updyke Welcome. We're gonna have fun today, I can tell.

Erin Welsh Oh yeah. I mean if that journal entry is any indication.

Erin Allmann Updyke Right.

Erin Welsh Okay. So what are we drinking to talk about gonorrhea?

Erin Allmann Updyke We're drinking of course Burning Love.

Erin Welsh And it is burning because it does contain jalapeno simple syrup and tequila, lemon juice, and a cucumber slice.

Erin Allmann Updyke Just for freshness.

Erin Welsh It's pretty delicious I gotta say.

Erin Allmann Updyke It is delicious, I'm really enjoying it. And as always we'll post the full recipe for this quarantini as well as our placebo, our nonalcoholic version on all of our social medias. You can find us on Twitter @TPWKY, on Instagram and Facebook @thispodcastwillkillyou and on our website thispodcastwillkillyou.com.

Erin Welsh	And if you ever feel like reaching out to us you can email us at <a href="mailto:thispodcastwillkillyou@gmail.com">thispodcastwillkillyou@gmail.com</a> or go to our website for a contact form.
Erin Allmann Updyke	Yep. Cool.
Erin Welsh	All right. Let's do it.
Erin Allmann Updyke	Right after this short break.
TPWKY	(transition theme)
Erin Allmann Updyke	All right, gonorrhoea.
Erin Welsh	Gonorrhoea.
Erin Allmann Updyke	Let's get into it. So gonorrhoea is caused by a bacterium, it's called <i>Neisseria gonorrhoeae</i> . I never know how to pronounce all those vowels.
Erin Welsh	There's so many vowels at the end of that word.
Erin Allmann Updyke	I know. It's a lot. <i>Neisseria gonorrhoeae</i> is closely related to another bacteria that some listeners and you, Erin, will definitely have heard of. Do you remember what it is?
Erin Welsh	Meningitis?
Erin Allmann Updyke	Yes, <i>Neisseria meningitidis</i> which causes meningitis. So all the <i>Neisseria</i> are gram-negative diplococci which means that they stain pink when we use stains to look at them under a microscope and they're just these two little balls. (laughs)
Erin Welsh	(laughs) It's gonna be a lot of that, isn't it?
Erin Allmann Updyke	Yeah. Okay so really we're gonna get right into how all this goes. So we all know how gonorrhoea is transmitted I think, right?
Erin Welsh	Well maybe you should just do a refresher just in case.
Erin Allmann Updyke	I mean, okay. So gonorrhoea is transmitted via sexual relations. So you can get it from all the kinds of sexual intercourse, vaginal, oral, anal, and in any direction, giving, receiving, doesn't matter. And for adults that's pretty much the only way that you're going to get gonorrhoea is via sexual intercourse of some design.
Erin Welsh	Okay.
Erin Allmann Updyke	In neonates, so in tiny baby infants, it can be passed from mother to baby during delivery, during birth, during passage through the birth canal.
Erin Welsh	Right.

Erin Allmann Updyke So in general in this country and in most other countries we screen pregnant people for gonococcal infection. This is often called gonococcus or gonococcal infection or just gonorrhea. So I'll probably use all those words interchangeably. But yeah, infection in a newborn is actually pretty serious and so you screen for it during pregnancy and then you treat it and that reduces the risk of neonatal infection.

Erin Welsh Cool.

Erin Allmann Updyke Okay, so cool. So what happens when you get exposed after a fun night to gonorrhea? Basically the bacterium which has been deposited into your body will adhere to your epithelial cells.

Erin Welsh Okay.

Erin Allmann Updyke Either along the vaginal canal or on the endocervix or in the anal canal or - I wrote penile canal and then I realized that's just called your urethra.

Erin Welsh (laughs)

Erin Allmann Updyke You urethra. And it attaches to these epithelial cells using pili which are basically... Isn't that fun? I didn't know that until I started researching this.

Erin Welsh It's really interesting, yeah.

Erin Allmann Updyke Yeah. So pili are basically these long, stringy protein bits that bacteria have. They're kind of like, you remember those sticky hands that you used to get from the 25 cent machines?

Erin Welsh Oh yeah.

Erin Allmann Updyke You'd like throw them out and stick them on your wall and then your mom gets mad at you cause you ruined her white walls?

Erin Welsh Well and then they get covered in fuzz and they don't stick anymore?

Erin Allmann Updyke Yes! Just like that.

Erin Welsh Okay.

Erin Allmann Updyke But you know like if you throw that out and stick it and then you let it go, it like flings towards the wall, right? So that's kind of what these pili do. They reach out, they grab onto the epithelial cells and then they contract and that sucks the bacteria up against the epithelial cells.

Erin Welsh That's so cool.

Erin Allmann Updyke It's very cool. And it's great if you're in something like a urethra or up against the cervix because you're probably gonna have fluid rushing through those tubes and so you wanna be able to stick on and grab on real tight.

Erin Welsh Yeah.

Erin Allmann Updyke So gonorrhea's good at that. And once it sticks on, it starts to replicate basically right then and there. It's not a virus so it doesn't have to infection your cells, it just grabs a hold and then starts replicating.

Erin Welsh Whoa.

Erin Allmann Updyke It's pretty fun.

Erin Welsh Yeah.

Erin Allmann Updyke And then once it colonizes, once it starts growing, it stimulates the release in your body of a whole bunch of pro-inflammatory molecules. So this basically stimulates your immune response, so then a whole bunch of immune cells, especially neutrophils and macrophages which are kind of the first line defense against bacteria, they come in and in normal bacterial or other bacterial infections they'd be able to phagocytize which means swallow up essentially, eat the bacteria and then help clear the infection. But gonorrhea are sneaky little suckers and they can actually survive inside of neutrophils.

Erin Welsh Oh that's amazing.

Erin Allmann Updyke I know! So when you look at a swab from someone who has a gonorrhea infection, if you stain it you'll actually see neutrophils just full of gonorrhea bacteria.

Erin Welsh Oh my gosh.

Erin Allmann Updyke It's very cool.

Erin Welsh Like a Trojan Horse.

Erin Allmann Updyke Yes. Yes!

Erin Welsh Maybe, I don't know. (laughs)

Erin Allmann Updyke (laughs) Sure! The neutrophils normally kill bacteria by using reactive oxygen species but the Neisseria can actually - what's the word I'm looking for - neutralize those because they have an enzyme called catalase which helps to neutralize that. So they can just survive inside of the neutrophils which I think is very cool.

Erin Welsh That's awesome.

Erin Allmann Updyke And because they're recruiting a bunch of neutrophils and macrophages, that is also what kind of results in the symptoms that we see. So if you get a genitourinary infection, let's talk about what kind of symptoms you'll actually have. First of all, most of the time you won't have any. Most infections are straight up asymptomatic which is part of why it can spread so easily because anything that's spread by sexual contact, like in certain populations it's gonna be pretty easy to spread, and if it's asymptomatic then it never gets detected or treated so you just keep sharing the burning love. So for a genitourinary infection, if you get infected in the urethra, you're gonna see dysuria, so that means painful urination because you've got basically inflammation going on along the lining of your urethra and then you'll also get a discharge and that discharge will be either white or yellow or greenish.

Erin Welsh: Okay.

Erin Allmann Updyke: Gross. And it's mostly neutrophils, it's mostly neutrophils, dead cells, and bacteria and then even though neutrophils are often full of gonococcal bacteria as well.

Erin Welsh: So all of the stuff that you are secreting is packed with gonorrhoea bacterial cells?

Erin Allmann Updyke: Absolutely, yeah.

Erin Welsh: Okay.

Erin Allmann Updyke: Yeah so that discharge is super infectious.

Erin Welsh: Okay.

Erin Allmann Updyke: You also can get infection of the epididymis. So if it travels through the urethra and back down into the epididymis which is the tubes that surround the testis where the sperm actually have to travel through, then you can get what's called epididymitis which is infection, inflammation of the and that can be very, very painful. So you can have testicular and scrotal pain on top of painful urination and urethral discharge. If you get an endocervical infection, so an infection of the vaginal canal and the cervix at the top there, it's even more likely to be asymptomatic than a urethral infection.

Erin Welsh: Okay.

Erin Allmann Updyke: If you do get symptoms, they're often mistaken for a bladder infection or a vaginal infection, like a yeast infection or a bacterial vaginosis or something. So you might have some dysuria, you might have some vaginal discharge or some bleeding inbetween periods but more often there are no symptoms in people with an endocervical or a vaginal infection.

Erin Welsh: And when you say more often like can you put a number to the percentage of cases?

Erin Allmann Updyke: I don't have a number. I was trying to find solid numbers and it's just like most of the time in endocervical infections it's asymptomatic.

Erin Welsh: Okay.

Erin Allmann Updyke: And most of the time in urethral and penile infections it is symptomatic or it's more likely to be symptomatic.

Erin Welsh: Okay. Yeah.

Erin Allmann Updyke: Though in both cases it can be asymptomatic. The problem with endocervical infections is that they can spread. They're asymptomatic so they're less likely to be detected and they can spread from the endocervix to the uterus or the fallopian tubes which causes what's called pelvic inflammatory disease or PID. PID is a very serious disease, it can cause abdominal and pelvic pain, fever, abscesses, it kind of is considered a more systemic infection. And it can lead to infertility because it can really severely damage the fallopian tubes and the uterus itself. And it also can cause scarring on the fallopian tubes that can increase the risk for future ectopic pregnancy which is when an embryo plants outside of the uterus and that can be very dangerous.

Erin Welsh: Yeah. Very bad.

Erin Allmann Updyke: In rare cases epididymitis can also lead to infertility but it's more common that in people with a uterus or ovaries you end up with infertility as a complication of a gonococcal infection. You can also get rectal infection, all holes here. It's usually asymptomatic but you kind of do have the same symptoms. Discharge, anal itching, soreness, bleeding. You can also get a pharyngeal infection, an oral infection.

Erin Welsh: (laughs)

Erin Allmann Updyke: So I have heard stories from people who work at the student health clinics of kids coming in and they think they've got sore throat and it turns out it's gonorrhea in your throat.

Erin Welsh: Oh my gosh.

Erin Allmann Updyke: I got a kick out of it.

Erin Welsh: So it causes the same symptoms as sore throat?

Erin Allmann Updyke: Yeah it's basically just a sore throat, it's a pretty minor infection. And even in your throat it's usually asymptomatic.

Erin Welsh: Okay.

Erin Allmann Updyke: So that's why gonorrhea is so easily spread is because in so many cases it's just completely asymptomatic. So yeah. But gonorrhea, while it can cause these symptoms and this time of infection just kind of right away, right after it attaches and starts to colonize, it can also pass through that epithelial cell border which is essentially your body's protection against bacteria, it's like first line of defense. So it can make its way past that epithelial cell border and then make it into your bloodstream.

Erin Welsh: Yikes.

Erin Allmann Updyke: Yeah. And if Neisseria makes it into your bloodstream it's very, very bad, it's called a disseminated gonococcal infection because it's disseminated amongst your whole body through your bloodstream and it most often will then go to your joints and your synovial fluid around your joints and your skin and it'll cause dermatitis and arthritis. And in very rare cases it can infect your meninges just like its cousin - I don't know, do you call bacteria in the same genus cousins?

Erin Welsh: Relative.

Erin Allmann Updyke: Just like its relative Neisseria meningitidis which is a very common cause of meningitis, Neisseria gonorrhoeae can also cause meningitis if it infects your meninges, your spinal cord, or your brain.

Erin Welsh: Wow.

Erin Allmann Updyke: Yeah.

Erin Welsh: Yikes.

Erin Allmann Updyke: So that's bad. Bad news bears. In neonatal infections when an infant gets infected it most commonly results in an ocular infection, it'll get into their eyes as they pass through the birth canal and this can cause blindness, it's really, really, really bad.

Erin Welsh: Yeah.

Erin Allmann Updyke: So that's why we screen pregnant women and most neonates when they come out they give them erythromycin eye drops just in case.

Erin Welsh: Yeah.

Erin Allmann Updyke: So that's just to cover all the bases because that would be terrible. It also can infect babies, it can pass through their eyes and because that's a mucus membrane where there's a lot of blood flow, it can get into their bloodstream and cause disseminated infection in babies as well which can be life threatening, especially because babies have basically no immune system to help protect them.

Erin Welsh: Also bad, yeah.

Erin Allmann Updyke: Also bad. It's not a great disease.

Erin Welsh: No, no. They never are.

Erin Allmann Updyke: (laughs) They never are. It is preventable though, which is cool. Condoms work.

Erin Welsh: Right.

Erin Allmann Updyke: So that's great.

Erin Welsh: What about treatments?

Erin Allmann Updyke: Treatment? Great question. It is still treatable today. So yeah, as of now there is one recommended treatment and that's recommended by the CDC and the WHO. If you get diagnosed with gonorrhea you will get an injection of ceftriaxone which is an extended spectrum cephalosporin antibiotic. You get an injection of that and then you also get a single dose, a whole gram of azithromycin and you pop that oral. And that will take care of the gonorrhea, it also takes care of chlamydia because it's extremely common to have co-infection. I was trying to find one solid number on how common gonorrhea and chlamydia co-infections are and I couldn't find one solid but in some studies I found it was like up to 40% of people who were diagnosed with gonorrhea were also diagnosed with chlamydia.

Erin Welsh: That's really interesting. Do they colonize the same areas? Is there competition or is it facilitation or what?

Erin Allmann Updyke: That's a really good question. I don't know specifically. I don't know if it's just because they're transmitted in exactly the same way and have the exact same risk factors, so if you have one it's really likely to have the other.

Erin Welsh: Yeah.



Erin Allmann Updyke Or if there is any kind of interactions that go on between the two bacteria, I'm not sure.

Erin Welsh Interesting.

Erin Allmann Updyke It's a great question though, yeah. But it's super common. Azithromycin will clear both a resistant gonorrheal infection that's resistant to the ceftriaxone but it will also additionally take care of the chlamydia. So that's why we give both.

Erin Welsh Okay. Cool.

Erin Allmann Updyke So if you've ever been diagnosed and been like, 'Why do I need this giant horse pill and a shot in my butt?' I assume they put it in your butt, I'm not positive though. That's why.

Erin Welsh Yeah. Okay.

Erin Allmann Updyke (laughs) So yeah, that's the biology. It's a pretty straightforward bacteria as far as they go, I feel like.

Erin Welsh Yeah.

Erin Allmann Updyke Yeah.

Erin Welsh It seems like it goes there to do the job that it came there for, it does the job, and then you treat it hopefully.

Erin Allmann Updyke Yeah. Hopefully, yeah.

Erin Welsh Okay.

Erin Allmann Updyke So how did we get here, Erin? Where did this bacteria come from?

Erin Welsh Okay.

Erin Allmann Updyke And oh my gosh, tell me how it got its name. I can't wait.

Erin Welsh Okay. (laughs)

Erin Allmann Updyke (laughs) Right after this break.

TPWKY (transition theme)

Erin Welsh Gonorrhea is an oldie and we've got the holy trinity of Ancient Egypt, the bible, and Hippocrates to back that up.

Erin Allmann Updyke The holy trinity, I like that.

Erin Welsh (laughs) There's a papyrus from 3500 BCE in Ancient Egypt that recommends some certain plant extracts for painful urination, there's a passage in Leviticus in the Old Testament that declares that men with runny penises are unclean, not in those words but more or less in those words, and Hippocrates describes genital ulceration and how it is sexually transmitted. We've also got Abu Bakr Muhammad ibn Zakariya al-Razi.

Erin Allmann Updyke Again!

Erin Welsh Again.

Erin Allmann Updyke Yeah.

Erin Welsh He's everywhere. And Ibn Sina, so Avicenna also is the latinized name.

Erin Allmann Updyke Okay.

Erin Welsh They seemed to describe urethral discharge and urine retention both of which are characteristics of gonorrhoea. Now any one of them could be referring to many other sexually transmitting infections but gonorrhoea is definitely old. As its name which was given by the Greek physician Galen in the 2nd century CE.

Erin Allmann Updyke That's a long time ago.

Erin Welsh It's a long time ago. For a long time it was tied in with syphilis and it went by many different names in different places and so on, so it's interesting that this one was the one to make it through the whole way. But gonorrhoea is from 'gonos' for seed and 'rhoa' for flow. So it just sort of-

Erin Allmann Updyke Seed flow?

Erin Welsh Seed flow. Yeah.

Erin Allmann Updyke Ugh, that's kind of yucky.

Erin Welsh I mean... (laughs) By at least the 10th and 11th centuries, gonorrhoea seemed to be pretty prevalent or at least prevalent enough to lead to the creation of laws that were to prevent any activity that spread the disease of burning pee. It also may have had a hand in secularizing medicine in some places because physicians were ordered to treat everyone with the disease without being able to refuse based on moral objections.

Erin Allmann Updyke Oh, interesting.

Erin Welsh So yeah. Along with like leprosy and some other sort of more stigmatized diseases.

Erin Allmann Updyke Yeah.

Erin Welsh But even so no one really paid much attention to gonorrhoea alone for another few hundred years. But before I get into that, where did it come from?

Erin Allmann Updyke Yeah.

Erin Welsh: And I couldn't find a ton of good info on its evolutionary origins but according to one of my sources there are two possibilities and neither of which is particularly exciting. But one is that it came from a avirulent strain in the vaginal and rectal mucosa which mutated into a virulent strain. Okay? Another is that it came from the nasopharynx and mutated into a virulent strain via oral sex. So yeah. I don't know when this occurred or where but it would have required a decent population density to be sustained and then spread throughout medieval times, though not as big of a population as something like measles and that's because of the long duration of infectivity and the possibility of sort of these latent infections, yeah.

Erin Allmann Updyke: Asymptomatic.

Erin Welsh: Yeah. Okay. Around the 1500s is when it began to be called the clap.

Erin Allmann Updyke: Yes!

Erin Welsh: Which is one of its colloquial names.

Erin Allmann Updyke: I had no idea that it was gonorrhoea that was called the clap.

Erin Welsh: Oh yeah. Because I think a lot of people think it's chlamydia because 'C'.

Erin Allmann Updyke: Yeah, that's what I thought.

Erin Welsh: That makes sense.

Erin Allmann Updyke: Chlamydia, yay!

Erin Welsh: Yeah.

Erin Allmann Updyke: No, gonorrhoea. (laughs)

Erin Welsh: Okay so why was it called the clap? There are a couple of hypotheses. One, which is the most likely one, is that it refers to 'les clapiers'.

Erin Allmann Updyke: (French accent) Les clapiers?

Erin Welsh: Yeah, there you go. Which is the french word for brothels, a possible source of infection.

Erin Allmann Updyke: Really?!

Erin Welsh: That's what they were called, yeah.

Erin Allmann Updyke: I never knew that.

Erin Welsh: Another I read somewhere is that it causes a clapping sensation when you pee. And the most horrifying one I found was that it refers to a common treatment for gonorrhoea infections in men where you are supposed to clap the penis hard to get the pee flowing again, maybe using your hands, maybe using a book and a hard surface. (laughs)

Erin Allmann Updyke

Oh no.

Erin Welsh

Yikes, yeah. But for much of its history, gonorrhea was overshadowed by syphilis which we will definitely be doing an episode on.

Erin Allmann Updyke

Oh, big time. Absolutely. Syphilis is major.

Erin Welsh

It's huge, yeah. But syphilis had settled down enough around the 15th-16th century for people to start taking note of this other disease and describing it. And one of the hurdles to tracing this early history of course relates to that where gonorrhea and syphilis were assumed to be the same disease with gonorrhea to be more the mild precursor to full-blown pox of syphilis.

Erin Allmann Updyke

That makes sense.

Erin Welsh

One guy in the 1700s decided to settle this once and for all.

Erin Allmann Updyke

Oh no.

Erin Welsh

He wanted to prove that they were the same and that gonorrhea was the secreting form and syphilis was the skin form. So he took the pustular discharge from an infected person and then smeared it onto himself.

Erin Allmann Updyke

Onto his...

Erin Welsh

Yeah, onto his penis. Unfortunately he came down with syphilis. So he didn't really prove anything. But I guess, yeah.

Erin Allmann Updyke

So he swabbed somebody's ulcer or something and then...or what did he...?

Erin Welsh

What it seemed like is that he took the discharge. So the direct quote was "pustular discharge".

Erin Allmann Updyke

Okay.

Erin Welsh

So I don't know if it was from the urethra or if it was from a sore, a pox.

Erin Allmann Updyke

A sore.

Erin Welsh

Yeah. In any case-

Erin Allmann Updyke

I mean yeah, you get discharge with... Ugh, that's so yucky.

Erin Welsh

Yeah, yeah. Well anyway. The pathophysiology of gonorrhea was still under debate. Maybe the discharge was caused by ulcers in the urethra, maybe it was from the seminal vesicles, no one really knew but as was the route of transmission. One popular view as you might imagine is that it came from women.

Erin Allmann Updyke

Of course.

Erin Welsh

Originated in women, I should say.

Erin Allmann Updyke: It would only originate in women, that's the only logical explanation.

Erin Welsh: Yep. One surgeon said, quote: "This thing resteth in their secret places, forming therein pretty little sores full of venomous poison, being very dangerous for those who unknowingly meddle with them."

Erin Allmann Updyke: That's our title, 'Resteth in In Your Secret Places'. (laughs)

Erin Welsh: (laughs) Other theories acknowledge that intercourse was a likely source of infection along with nonsexual things like gout or rheumatism. Eventually though gonorrhea and syphilis got their separate entries and as a result separate cures. I think you know that one of my favorite parts of doing this research for the history is coming across the old treatments that were used before-

Erin Allmann Updyke: I think this is one of everyone's favorite parts.

Erin Welsh: (laughs) Okay, are you ready for gonorrhea?

Erin Allmann Updyke: I can't wait.

Erin Welsh: Let's start with the easy ones. Rest, avoid alcohol, avoid sex.

Erin Allmann Updyke: Okay.

Erin Welsh: Yeah, okay.

Erin Allmann Updyke: Seems reasonable.

Erin Welsh: Inject some mercury into the head of your penis.

Erin Allmann Updyke: (laughs)

Erin Welsh: It worked for syphilis, why not gonorrhea? It didn't work for gonorrhea, it did not. (laughs) Atropine, throwback to belladonna, yeah, widened that urethra. Let's take it up a notch.

Erin Allmann Updyke: Okay.

Erin Welsh: Maybe some bleeding and purging, maybe some leeches, yep.

Erin Allmann Updyke: Seems right. On your ween or what?

Erin Welsh: Uh huh, yeah.

Erin Allmann Updyke: Okay.

Erin Welsh: Yeah so let's see, where's another one. Take the milk of a woman, like breast milk I assume.

Erin Allmann Updyke: Breast milk, yeah.

Erin Welsh: A little sugar, oil of violets, and barley water and administer it with a syringe. I mean that could've been our quarantini but...

Erin Allmann Updyke: (laughs) Good god. I don't have any source of breast milk around here.

Erin Welsh: Sure, isn't that why Craigslist exists? And if that doesn't work you can always resort to urinating with your penis in warm cow's milk.

Erin Allmann Updyke: (laughs) Just plop it into cow's milk and then pee. That's a very interesting idea you know, I'm not opposed to that idea in concept.

Erin Welsh: No, yeah. Well eventually the treatments became a bit more tame with lavage or washing out of the urethra as the most common treatment. Often the symptoms of virulent gonorrhea would disappear after a few weeks, can't really say 'cured' because microbial confirmation was not possible. And something called gleet was left in their place. New word for me too.

Erin Allmann Updyke: What is gleet?

Erin Welsh: Gleet is basically the post-gonorrhea clear or cloudy discharge without any other symptoms such as pain or urination problems.

Erin Allmann Updyke: Ugh.

Erin Welsh: It's also probably what gave gonorrhea its other nickname, the drip. Yeah.

Erin Allmann Updyke: Gleet. That's a good word for that.

Erin Welsh: Gleet.

Erin Allmann Updyke: I can imagine exactly what it is.

Erin Welsh: Yeah, yeah. I'm never gonna forget it. (laughs) Gleet was usually treated with astringents which probably didn't do anything because gleet usually disappeared around the same time that the person stopped using the astringents, it's probably just irritating your penis more.

Erin Allmann Updyke: Yeah.

Erin Welsh: But wait, there's more.

Erin Allmann Updyke: Of course there is.

Erin Welsh: Okay. So the word 'bogie'. Have you come across bogies in med school?

Erin Allmann Updyke: I don't know how to answer this question.

Erin Welsh: (laughs) Okay then so doesn't sound like you have. Okay, bogie didn't always mean bourgeois.

Erin Allmann Updyke: Okay.

Erin Welsh  
No. No, no. Sometimes after a male became infected with gonorrhea and recovered, his urethra would remain obstructed and urination was difficult, maybe from the gonorrhea itself, maybe from the treatment, physicians didn't really know. But to treat this, bougies were used. Bougie meaning a thin, flexible instrument made of silver, lead, or wax. They're still used today, by the way, like bougies are still around. Sort of like a sound but not really a sound. Anyway. After giving the person a painkiller the bougie would be inserted into urethra, sometimes it would be left there for days, only removing it when you needed to pee. Other times-

Erin Allmann Updyke  
I'm sorry.

Erin Welsh  
(laughs)

Erin Allmann Updyke  
I'm sorry so this is like... You said silver, lead, or wax?!

Erin Welsh  
Yeah it's gotta be a little flexible.

Erin Allmann Updyke  
Okay. And it's like a rod.

Erin Welsh  
Yeah.

Erin Allmann Updyke  
A flexy, wire rod.

Erin Welsh  
Uh huh.

Erin Allmann Updyke  
And you just poke it up there.

Erin Welsh  
Yeah.

Erin Allmann Updyke  
And leave it.

Erin Welsh  
Yeah. We will post some pictures of bougies.

Erin Allmann Updyke  
Excellent.

Erin Welsh  
Oh yeah, there are some great old illustrations of the variety of bougies, especially once they became more popular throughout the 1800s and things. And then there was like electro-something bougie.

Erin Allmann Updyke  
Oh no.

Erin Welsh  
And then there were ones that were like linked together with tubing and yeah.

Erin Allmann Updyke  
Okay.

Erin Welsh  
But one of the most horrific ones is that there were some bougies that would have a corrosive crystal at its tip which was designed to clear the passage by eroding whatever the inflammation was. So people actually died from that.

Erin Allmann Updyke  
Uh yeah.

Erin Welsh	Yeah. But a surgeon's reputation could be made or destroyed on how well he could work his way around a urethra with a bougie. (laughs) Yeah.
Erin Allmann Updyke	Awesome.
Erin Welsh	And so we don't really see throughout history, we don't really see a lot of descriptions of gonorrhea in females, we just get sort of this male-specific thing and as such we also don't get very many women-specific treatments.
Erin Allmann Updyke	Right.
Erin Welsh	Treatments for female patients, the ones that are listed, weren't much better. Most included a frequent and thorough cleaning of the vulva and vagina and treatment with silver salt or other chemicals.
Erin Allmann Updyke	Ugh.
Erin Welsh	Irrigation of the urethra was also done, sometimes with a treated solution. And finally sometimes the cervix was cauterized with silver nitrate or a medicated wick was inserted. Yeah, more often than not though, the prescribed treatment was just wait it out which often led to infertility. Yeah. If these early venereologists had anything to say about gonorrhea in females it was that they were surprised at how much milder the infection seemed. Diagnosing gonorrhea in females was more difficult because physicians had a tough time distinguishing between normal vaginal discharge and gonorrhea discharge so doctors often relied on the next best thing, patient history. But not firsthand, no.
Erin Allmann Updyke	Oh no.
Erin Welsh	Doctors took the word of quote, "those whom we look upon as men of veracity." Meaning a dude could say, 'I slept with her and now I have gonorrhea, so she must've given it to me' and that would be basically the diagnosis.
Erin Allmann Updyke	Wow.
Erin Welsh	Yeah.
Erin Allmann Updyke	Awesome.
Erin Welsh	Cool. In the case of gonorrhea, it was pretty much always a one-way street from vagina to penis, that was how it was perceived throughout most of history. Some physicians did note other signs of gonorrhea infections in females including inflammation of the labia and clitoris but there wasn't a lot of attention paid to any internal indications of the disease.
Erin Allmann Updyke	Shocking.
Erin Welsh	Right? The cervix which is recognized today as a principal site of infection was rarely mentioned and that's because up to the 19th century, physicians who were almost without exception male pretty much never performed vaginal exams.
Erin Allmann Updyke	Right, they're never gonna be looking up there.



Erin Welsh

No. No, god forbid they take a speculum and peek inside. And if the woman was unmarried, forget about it.

Erin Allmann Updyke

Right.

Erin Welsh

In the 1800s people finally started talking about where gonorrhea came from and how to prevent it. Was it a specific infectious particle? Was it just random inflammation? According to someone named Swediaur it was the latter and he set to prove this by injecting an aqueous solution of ammonia strong enough to give it a quote "burning taste" into his urethra twice.

Erin Allmann Updyke

What?

Erin Welsh

Yeah. He said that the second injection caused the most pain he had ever experienced. So the next morning, no surprise, he had some seepage. "A considerable evacuation of purulent matter of the same yellow-green color as that of a virulent chaude-pisse." Aka hot pee gonorrhea. So he concluded, his conclusion was that gonorrhea was nothing more than simple irritation of the urethra.

Erin Allmann Updyke

Oh dear.

Erin Welsh

Uh huh.

Erin Allmann Updyke

And he did this by...

Erin Welsh

To himself.

Erin Allmann Updyke

What a weirdo, man.

Erin Welsh

I mean do you not... I am amazed at the self-experimentation that went on.

Erin Allmann Updyke

Yeah that's bold.

Erin Welsh

These are precious parts. I mean and don't worry, there is some human experimentation for prisoners and people who can't advocate for themselves.

Erin Allmann Updyke

(laughs) Don't worry. Just wait for our syphilis episode for plenty of that.

Erin Welsh

Yeah. Others attribute it to something female-specific like if you had sex with a woman who had certain vaginal discharge or maybe she was on her period. And then there were predisposing factors, too much sex, sex that goes on too long, an unnatural size of the male organ, I don't know which direction.

Erin Allmann Updyke

Which direction, yeah.

Erin Welsh

Alcohol, a rich diet, etc, etc. By the late 1800s we're finally getting to the age when the mysteries of so many infectious diseases are revealed, the age of microbiology or the beginning. And gonorrhea is no exception. And the name that you might most associate with gonorrhea is Neisser, *Neisseria gonorrhoeae*, but there was another mostly forgotten physician who made huge contributions to the understanding of the disease. His name was Emil Noeggerath and he was a German physician who was especially interested in pelvic inflammatory disease. I wanted to put this tidbit in here, he was a workaholic who spent hours and hours at his desk keeping himself awake with tons of coffee and putting his feet in a bowl of cold water under his desk.

Erin Allmann Updyke

Just to keep him awake?

Erin Welsh

Yeah.

Erin Allmann Updyke

That's so funny.

Erin Welsh

I feel like we could've used that when we were finishing our dissertations. Anyway after many clinical examinations of which the majority of subjects were female, he announced his findings that 1) gonorrhea was likely a latent infection and that gleet could still cause infection in women, 2) gonorrhea did affect females and that it was a common cause of infertility in both sexes, and 3) gonorrhea was extremely prevalent. He estimated that 60% of men in large cities in the U.S. had had gonorrhea at some point and that 60% of those men would infect their wives. And that men could give the disease to women was itself kind of a revolutionary thought. But unfortunately his conclusions were not well received at the time primarily because American physicians took those prevalence estimates as a direct attack on the morality of American males.

Erin Allmann Updyke

(laughs) Oh dear.

Erin Welsh

But the suggestion of gonorrhea as a latent infection made it more difficult to treat clinically. How could you tell when an infection was over if you couldn't use gleet to guide you? Fortunately in 1879, just a few years after Noeggerath announced his findings, Albert Neisser, the namesake of *Neisseria gonorrhoeae*, isolated the bacterium making it possible to identify exactly when a person was no longer capable of transmitting the infection.

Erin Allmann Updyke

Whoa.

Erin Welsh

Which is pretty cool.

Erin Allmann Updyke

Yeah.

Erin Welsh

Gonorrhea had been fairly well described in adult males and very poorly described in adult females but as you mentioned there's another group that is commonly affected by the disease: infants. Gonorrhea can cause this conjunctivitis in newborns which can lead to blindness if left untreated, like you said, and despite the fact that gonorrhea in females was so poorly characterized, the link between the infection and this outcome in infants was discovered in the early 19th century, helped along by more horrific experiments in which the eye pus of one of these infants was inserted into a male urethra, producing gonorrhea within a few days.

Erin Allmann Updyke

Whoa.

Erin Welsh: Yeah. Still it wasn't necessarily conclusive because sometimes babies were born to mothers who did not appear to have gonorrhea but the discovery of asymptomatic infections would clear that up over time. But even though the link between gonorrhea infection in a mother and eye infection in the newborn was discovered, it was still not able to be treated and that was a huge problem because cases were growing. So by the mid 1800s up to 12% of neonates in European hospitals developed the eye infection.

Erin Allmann Updyke: Whoa.

Erin Welsh: 20% of those developed corneal ulceration and 30% of those became blind.

Erin Allmann Updyke: Oh my goodness.

Erin Welsh: So that's huge numbers.

Erin Allmann Updyke: That is huge numbers. 12% of babies infected, good gracious.

Erin Welsh: Yeah. Okay so let me introduce you now to a German obstetrician named Carl Sigmund Franz Credé who in the 1850s founded one of the first gynecology departments in Europe at one of our favorite historical hospitals, Charité.

Erin Allmann Updyke: Oh!

Erin Welsh: Still in existence today and featured on that amazing show that we have talked about. So when he was at this hospital he noticed the high rate of eye infections born to mothers infected with gonorrhea and he tried all manner of things to try to lower the cases. He tried to douche the vagina prior to delivery, didn't work. He tried to wash the eyes of the infant with a borax solution, didn't work. Yeah. Finally he tried wiping the eyes with cotton wool and plain water and then adding a drop of 2% silver nitrate and that worked like a charm and the technique was picked up all over the continent. Okay. And then we've got finally the isolation of the bacterium itself which happened in 1879 by the 24 year old Albert Neisser. Unfortunately there was no suitable animal model for gonorrhea because this is an exclusively human bacterium, so what remained but to conduct human experiments?

Erin Allmann Updyke: Oh dear.

Erin Welsh: Human volunteers were produced, inoculated, and subsequently found to have gonorrhea.

Erin Allmann Updyke: Volunteers.

Erin Welsh: Volunteers.

Erin Allmann Updyke: In quotes.

Erin Welsh: Yes, in quotes.

Erin Allmann Updyke: Yeah.

Erin Welsh

So finally it was accepted that this bacterium caused gonorrhoea. Even though a lot of progress had been made towards identifying the causative agent of gonorrhoea and describing its clinical symptoms, treatment still had a really long way to go and this was a problem because gonorrhoea can be fatal and frequently was in the 1800s as a result of bacterial endocarditis. But fortunately gonorrhoea reached a turning point when antibiotics were developed. In 1937 clinical trials of sulfonamides were shown to be moderately effective against the disease but the victory was short-lived. By 1944, only 7 years later, only 25% of people with gonorrhoea were being cured due to the emergence of resistant strains and doctors had to dust off their bougies.

Erin Allmann Updyke

(laughs)

Erin Welsh

Fortunately penicillin took over as a primary and very effective treatment for the disease and by the late 1940s was widely used. Initially because gonorrhoea was so sensitive to penicillin, doctors were like, 'Well we don't foresee any resistance occurring.'

Erin Allmann Updyke

Oh dear.

Erin Welsh

Right? I mean, come on. History repeats itself, people. But within 10 years resistant strains had emerged and become obviously a major problem.

Erin Allmann Updyke

Yeah.

Erin Welsh

Then streptomycin was introduced and resistant strains emerged once again, blah, blah, blah. It's been this continuous struggle to find one drug to effectively treat gonorrhoea. And I'm sure you'll tell me all about the horror show that's going on today.

Erin Allmann Updyke

Oh yeah.

Erin Welsh

You might expect that the prevalence of gonorrhoea would decline over the 20th century with the availability of antibiotics but if you look at a figure of rates over time for certain countries, you actually see a huge increase starting in the 60s. And that increase actually represents what is called a gonorrhoea pandemic that peaked in the mid 1970s, occurring in places like the U.S., Sweden, Canada, and the U.K.

Epidemiologists point toward a few things that could've caused a huge increase and it was probably a combination of things like changing perceptions and sexual practices. People were having a lot more sex with a lot more partners. A huge population boom as the baby boomers became sexually active young adults, and the greater availability of contraceptives such as the birth control pill which did not protect against STIs. In any case the disease began to decline again and I don't really know why, I don't know if there were certain public health campaigns that went on but gonorrhoea today continues to make headlines as these superbug resistant strains have totally gotten out of control. So, Erin. Tell me more about those guys and about where we stand with gonorrhoea today.

Erin Allmann Updyke

I can't wait to.

TPWKY

(transition theme)

Erin Allmann Updyke

So let's talk quickly just about the status or how many people are we talking when we talk about gonorrhea and then we'll talk a little bit more in depth about the antibiotic resistance cause that is sort of the main part of the current story of gonorrhea. Okay? Okay. So in the U.S. according to the CDC, they estimate about 820,000 new infections of gonorrhea every year. 820,000.

Erin Welsh

Wow.

Erin Allmann Updyke

It is the second most commonly reported communicable disease in the U.S. after chlamydia.

Erin Welsh

Wow.

Erin Allmann Updyke

Which is the number one.

Erin Welsh

Well goes hand in hand, seems to make sense.

Erin Allmann Updyke

Yeah. So in 2017 there was over 555,000 cases that were actually reported and so the number 820,000 is the estimate. So that means that it's estimated that 270,000 people each year are getting infected with gonorrhea and just don't know it. So that's a bummer.

Erin Welsh

That's a lot of people.

Erin Allmann Updyke

It's a lot of people. Worldwide the World Health Organization estimates 78 million people are newly infected with gonorrhea every year. 78 million.

Erin Welsh

Wow.

Erin Allmann Updyke

That's a lot.

Erin Welsh

This is much more prevalent than I realized.

Erin Allmann Updyke

Me too.

Erin Welsh

People don't really talk about it that much, yeah.

Erin Allmann Updyke

I knew that it was one of the most common STIs.

Erin Welsh

Sure.

Erin Allmann Updyke

But I have no idea that it was...yeah. So the U.S. Public Health Taskforce currently recommends screening only for certain populations of people. So it recommends screening for any women with vaginas who are sexually active under the age of 25 in any kind of sexual relationship, women who are over the age of 25 if they have multiple partners every year, and any men who have sex with men. That is the U.S. Public Health Taskforce recommendations. And a study that I found that looked at whether this type of screening protocol, so screening every year regardless of if your in a monogamous relationship or not, just if you're sexually active. I found a paper that looked at from 2000-2015 whether this type of screening actually reduced the incidence of gonorrhea and it found that it did but what's interesting is that they also looked at other screening scenarios. So what if we did universal screening of everyone of a certain age group regardless of their sexual practices, just whether or not they're sexually active? And you can actually reduce incidence even more is what they found if you did more universal screenings.

Erin Welsh

Well yeah, that makes complete sense. People who are in monogamous relationships, maybe one person doesn't realize they're in a monogamous relationship or...

Erin Allmann Updyke

Exactly.

Erin Welsh

One person assumes they are.

Erin Allmann Updyke

Right, yeah. So yeah, so overall it's a very common disease so screening in general makes a lot of sense especially because there's such high rates of asymptomatic infections. But the big story with gonorrhea is antibiotic resistance, it's definitely the most important part of the story. Antibiotic resistance has been detected in basically every country that has gonorrhea on its reportable disease list. So everywhere where there is gonorrhea, there is antibiotic resistance. There's resistance to all of the drugs that you mentioned that used to be used to treat gonorrhea, so the penicillins or the beta-lactams, streptomycin and all of the fluoroquinolones as well. In addition there's also resistance to some cephalosporins which is why now the only drug that's recommended that is still considered effective are the extended spectrum cephalosporins like ceftriaxone which is what we treat with. The scary thing is that in over 50 countries they have reported resistance to these drugs as well.

Erin Welsh

Ooh.

Erin Allmann Updyke

Yeah. That's bad.

Erin Welsh

I mean it's what you'd expect.

Erin Allmann Updyke

Right. And we're also seeing increasing resistance to azithromycin which is what we give as a backup in case gonorrhea is resistant to ceftriaxone.

Erin Welsh

Yeah.

Erin Allmann Updyke

So now it's our main line of defense and our backup line of defense that is becoming resistant. So the reason or one of the reasons that we see such high rates of antibiotic resistance is that there's a lot of different mechanisms by which bacteria can evolve antibiotic resistance. They can evolve ways to inactivate drugs, so just sort of attacking the drug itself and inactivating it. They can alter their cell membranes that the antibiotics use as targets so that the antibiotics can no longer bind and actually do their job. They can also evolve new mechanisms to export the drugs out of the bacteria once they make it in or to prevent the antibiotic from getting into the bacteria to begin with. And all different classes and groups of antibiotics that we've developed so far have different mechanisms of action and some bacteria are good at developing resistance against maybe one class of antibiotics, so they can change their cell membrane so that penicillins can't bind as well but then maybe they can't figure out a way to export it so they can't be resistant to all antibiotics.

Erin Welsh

Gotcha.

Erin Allmann Updyke

It turns out the *Neisseria gonorrhoeae* has shown the ability to develop resistance in basically all of the ways that bacteria can develop resistance.

Erin Welsh

Cool!

Erin Allmann Updyke

Yeah. So it's really good. They're really good naturally at uptaking and recombining, so shuffling around DNA from the environment and because they have those pili which they use to grab onto the walls, they can also use pili for what's called conjugation which is kind of like bacteria sex where they transfer DNA from one bacteria to another.

Erin Welsh

Right.

Erin Allmann Updyke

And what they often transfer are plasmids which are those little round pieces that usually or very often have antibiotic resistant genes on them.

Erin Welsh

Yep.

Erin Allmann Updyke

So *Neisseria* are really good at that. So that's why we see such high rates of antibiotic resistance. And very quickly because you can have a single *Neisseria* bacterium just giving its genes to all of the other bacteria around them.

Erin Welsh

Yeah.

Erin Allmann Updyke

It's great. It's really great.

Erin Welsh

That's amazing.

Erin Allmann Updyke

Yeah. So obviously there's a lot of interest in developing better methods of treatment. Unfortunately from what I found on the World Health Organization website there's only 3 candidate drugs in the pipeline in development for treatment of resistant gonorrhea.

Erin Welsh

Uh oh.

Erin Allmann Updyke

Yup. There's like 3 new drugs in the pipeline, one of them is I think either in or just finished phase 3 trials, I don't know if those trials went well. And then the other 2 are still in phase 2 clinical trials, so they've still got a long way to go before they're on the market.

Erin Welsh

Okay.

Erin Allmann Updyke

So then the next natural question is if we can't develop better antibiotics-

Erin Welsh

Vaccine.

Erin Allmann Updyke

What about vaccines? There's a lot of discussion about this. There's nothing very close on the horizon.

Erin Welsh

Okay.

Erin Allmann Updyke

Progress for a gonorrheal vaccine in general has been very, very slow. So we have seen development of vaccines for other STIs like HPV which is excellent, there's also a vaccine in development for HSV so herpes simplex virus. Gonorrhea not so much. Gonorrhea and syphilis are proving to be very, very difficult to try and develop vaccines for. However I did find one paper that was very interesting that was just looking at a mouse model that suggests that at least in theory it should be possible to stimulate the right kind of immune response that you would need to even be able to develop a vaccine. Because we'll talk more about this in the vaccines episode but basically for a vaccine to be able to work, whatever bacteria or virus you're trying to fight has to stimulate an immune response that creates a memory response.

Erin Welsh

Right.

Erin Allmann Updyke

And so if the bacteria don't do that to begin with, then your body never develops memory and so your body can't just fight them off every time you get infected.

Erin Welsh

Right.

Erin Allmann Updyke

So it does seem that at least in theory it's possible to generate that type of response with some gonorrhea antigens which are the surface proteins of gonorrhea.

Erin Welsh

Why does it not create a memory?

Erin Allmann Updyke

Gonorrhea have a huge amount of antigenic variation, like massive antigenic variation. So there's tons of different strains and there's tons of variation in those cell membrane proteins and so they're really good at evading our immune system. And then on top of that, they're really good at fighting off our body's first line defenses which are those neutrophils and macrophages cause they can just live inside of those cells.

Erin Welsh

Okay, okay. That makes sense.

Erin Allmann Updyke

Yeah. So people are working on it it seems, it's definitely far in the future, it's nothing that's going to be happening in the next few years or anything like that. Yeah, that's gonorrhea.

Erin Welsh

Wow.

Erin Allmann Updyke

Yeah.

Erin Welsh

That was a good one.



Erin Allmann Updyke

Yeah it was. I had fun.

Erin Welsh

I did too. I learned a lot on this one.

Erin Allmann Updyke

Me too. Clap, clap, clap.

Erin Welsh

Let's give ourselves a round of applause. (laughs)

Erin Allmann Updyke

That's another good title. (laughs) I really like that. I like that a lot. Well should we do sources?

Erin Welsh

Yeah, sources. Okay. I read sections of a book called 'The Scars of Venus: A history of Venereology' by J. D. Oriel and I'm sure I'll be going back to that for future episodes. I also used the Cambridge World History of Human Disease edited by Kenneth Kiple and some papers that I will put on the website.

Erin Allmann Updyke

Awesome. And I have several really interesting papers mostly about the current epidemiology of gonorrhoea. So as always we will post our full source list on our website [thispodcastwillkillyou.com](http://thispodcastwillkillyou.com), just go to the EPISODES tab and you can find every source that we used in all of our episodes.

Erin Welsh

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

Erin Allmann Updyke

And thank you guys for listening! We love making this podcast and we love that you listen to it. And if you haven't heard already, we have merch!

Erin Welsh

We have merch!

Erin Allmann Updyke

So go check that out. You can get to it from our website [thispodcastwillkillyou.com/merch](http://thispodcastwillkillyou.com/merch), you can also get to it from the Exactly Right media website [exactlyrightmedia.com/merch](http://exactlyrightmedia.com/merch). So yeah.

Erin Welsh

All right. Wash your hands.

Erin Allmann Updyke

You filthy animals!