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ECHO: REVIEW OF COMMONLY PRESCRIBED ANTIMICROBIALS FOR SEXUALLY TRANSMITTED INFECTIONS: PHARMACY PEARLS AND CONSIDERATIONS

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ECHO: Review of Commonly Prescribed Antimicrobials for Sexually Transmitted Infections: Pharmacy Pearls and Considerations
[video transcript]

00:08
Now I will hand it over to Sarah. Thank

00:12
you very much. This afternoon I wanted to talk about a review of commonly prescribed anti microbials that are used for the treatment of sexually transmitted infections. And I wanted to highlight certain parts of pharmacy pearls as well as important considerations for patients. I do not have anything to disclose for the presentation. The learning objectives are to recognize mechanism of action for prescribing antimicrobials, as well as identifying potential side effects as well as mitigation or avoidance strategy of those side effects. For I'll specifically be talking about doxycycline azithromycin, and then a broadly in the broad sense fluoroquinolones. Starting with tetracycline, tetracycline, there are a class of anti microbials that have a really broad spectrum of activity on this includes gram positive and gram negative bacteria as well as atypical or organisms. They're used for a plethora of infections that they can utilize for infection SUTA Staph aureus, they're used in combination therapy for treatment of multidrug resistant gram negative infections. They're commonly used in rickettsia illnesses or non tuberculous mycobacterial infections. doxycycline in particular, has a large role in the treatment of sexually transmitted infections. And you can also see tetracycline be used for non infectious diseases issues like acne or Gingival Hyperplasia, but the point is wide use across across medicine. Starting off in the 1940s, the first members of the tetracycline class they were discovered from two species of strep and ICS. And from there that really catapulted the semi synthetic derivatives of tetracycline, which were then produced kind of around the 1950s throughout the 70s, focusing in on doxycycline. It is a semi synthetic tetracycline that first became available in 1967. It does have a broad spectrum of activity, including gram positive gram gram negative and a typical organisms, but it also has activity against hierarchies such as treponema pallidum also recut CA, it is also active against malaria and other parasites, although with increasing use. tetracycline resistance can kind of limit sometimes it's used and really wasn't until much later until further development occurred where tetracycline started to overcome some of those resistance mechanisms and expanded upon the spectrum of activity. So like I said, I wanted to focus specifically on doxycycline. Especially now it's becoming more and more used in the setting of the penicillin I am shortage, as well as with Doc CPAP. doxycycline is a second generation tetracycline, it does have improved bioavailability and tissue penetration compared to older tetracycline, and that's because of its lipophilic properties. If you look on the right side of the screen, it's a picture of a rhizome highlighted our three major active sites a P and an E, which is the exit site and all these sites are in some way shape or form involved in the binding of T RNA doxycycline x b, x bi allosteric ly binding to the bacterial 30 S sub ribosomal subunit, and it prevents the binding of new amino acids at the A site, which then presents prevents peptide elongation and ultimately preventing bacterial protein synthesis. So tetracycline is particular doxycycline. They're active on the 30 S ribosomal subunit. Prior to the 1950s, the majority of bacteria were actually susceptible to tetracycline, but as we know, with increasing Antimicrobial

Use, resistance can occur over time. And unfortunately, that's what's happening with tetracycline, doxycycline. And resistance to doxycycline. It does occur in a multitude of ways. So what I have highlighted here is just a gross figure of potential mechanisms of resistance. So the first mechanism of resistance as you just have decreased accumulation of doxycycline inside the bacterial cell, and this can be achieved through two different mechanisms. One is decreased influx. So if you see towards the left highlighted in purple is a foreign channel. So the outer membrane of a bacterial cell, it's really the first line of defense against toxic compounds and hydrophilic agents like tetracycline doxycycline they use porn channels to pass in and out or to pass through the bacterial cell. However, if you have changes or mutations in the porn channel that can affect how well or how easily are the amount of doxycycline that gets transported from the exterior through the cell membrane and into the cell. So you could have decreased in flux through poor internal mutations. Another way to decrease your concentration of drug inside the cell is to have increased efflux. So, the green green little box with an efflux pump, so tetracycline resistance can be manifested due to efflux mediated room mediated resistance or Tetra cycling efflux expel doxycycline. Using a proton exchange as an energy source, there's a lot of tetracycline genes present. A lot of times tetracycline efflux efflux pumps are found in gram negative organisms and they can be encoded by genes such as tech K or Tet owl. An interesting interestingly, a lot of these tetracycline efe lumps tend to be more specific to tetracycline and doxycycline, as opposed to minnow and Tyga cyclin. But there are, of course, other types of efflux pumps that expel not only tetracycline but other antibiotics as well. So it kind of contributes to that overall multidrug resistant phenotype. Other mechanisms is something called acquired resistance via plasmid. So there can be changes in target site where target side of the ribosomes via ribosomal protection and the production of ribosomal protection proteins, they displace drug from the target site, and that's mediated by Tet, oh and tight and as you see in the middle of the figure, essentially, there's a mutation that target sites of the ribosome camp or the antiviral antimicrobial camp binds, and then to lesser mechanisms of resistance not pictured you can have enzymatic degradation through a gene called to xx. And then you can also have reduced binding affinity via ribosomal mutation that changes the binding site. So the tetracycline doesn't bind efficiently to the ribosome. So, again, the point of this slide is it's multifactorial, a lot of things are happening at once, you can have mechanisms of resistance in in singlet or they can be a combination and unfortunately, a lot. It's not only chromosomally mediated, a lot of times these mechanisms can be transferred bacteria to bacteria via plasmid mediated resistance. This slide is an overview and general overview of doxycycline. In general, the dose is 100 milligrams either IV or PIO every 12 hours. There are some non ID indications that call for a 50 milligram every 12 hour dose. It's available in capsules, tablets, suspension solutions, so a lot of different dosage forms. It's highly that bioavailable, which is a good thing, in terms of absorption. For doxycycline. The average peak plasma concentration potentially can be reduced by 20%. If taken with a high fat meal or with dairy products, it does distribute widely into body tissues and fluids, which includes the notes and ovo plural prosthetic bronchial secretions. But of note, it does not concentrate very well into the CSF. It's highly protein bound. And due to the large volume of distribution, because it penetrates tissues really well, it does not concentrate in the serum at high enough concentrations to effectively treat a bacteremia. It does have a longer shelf life between 18 to 22 hours. It is not hepatic, ly metabolized, but it is inactivated by keylite formations in the GI tract, which we can get into because it does have some consequences on administration of the meds.

And there are no adjustments and hepatic or renal insufficiency. And then from an efficacy standpoint, how well the drug works. It is time and concentration dependent meaning from a dosage standpoint, we want to optimize the time that the concentration of the drug is above the NIC of the organism. But right now, there's not really an efficacy that's been linked with a total target exposure.

08:54
I've put together a slide that depicts currently available doxycycline products and formulations and there's a lot as you can see, there's two main formulations doxycycline monohydrate, and doxycycline. High cleat and both come in various tablets, capsules, delayed release formulations, suspensions at various strengths. And the point of the slide is really just to highlight that there's tons of products out there. But the question comes up is there really a difference between the doxycycline monohydrate formulation and the doxycycline hyclate formulation. So upfront, the two main differences are the salts. So mono hydrate and high plate are the two different salts and the purpose of a salt is to aid in drug dissolution and drug absorption. Starting with doxycycline monohydrate. In particular, it is more lipophilic and less water soluble and because of those properties, it does tend to dissolve slower in the GI tract compared to high plate and also specific to monohydrate. The absorption can be affected by the presence of ash Since depression medication, so there's actually data with coadministration OMAP, Rizal and doxycycline monohydrate together, and it was found to have an overall decrease in the doxycycline serum serum concentration. Specifically, their total concentration or the area under the curve was decreased by about 40%. And the peak or the C max was decreased by 56%. And if you recall on the previous slide, we talked about efficacy parameters of time and concentration dependency. So, the concern here is potentially decreasing serum concentration, therefore, decreasing efficacy of the antimicrobial. With doxycycline high plate this is highly water soluble and it also has a very acidic pH. There really no difference from an advocacy standpoint, both forms are considered equally efficacious. But there are subtle differences that could potentially have impact on patient compliance. And the next question that tends to come up is Why is one formulation more tolerable than the other? The short answer is there really hasn't been conflict true comparative data to support that one is better tolerated than another. But there's a bunch of hypotheses, hypotheses that support potentially, the doxycycline monohydrate form is more tolerable from a GI standpoint, the reasons cited include a slower dissolution time, so there may not be that dose dumping effect that you may get if everything dissolves at once, so leading to fewer gi side effects. Also, it's hypothesized that because doxycycline high cleat is an acidic molecule, that it potentially could exacerbate gi side effects. But again, really not true good comparative data showing that one certainly is more tolerable to the other. And then the final question that I'm sure a lot of people have ever received through communication with patients or through communication with their local pharmacies is cost is one more expensive than the other? And the answer is it depends. So a lot of times this is driven by the insurance companies, what what formulation, the insurance prefers, what dosage form the insurance prefers. But for patients who do not have commercial insurance or who are paying cash. Again, it does vary. When I looked at good RX last week, and I do know good RX is not a true representation of cash price. They seem to be relatively similar in pricing between the two formulate or the between the monohydrate and the high plate. But I do know that that can change unfortunately. So you know, a lot of times it depends, it's

driven by insurance, and then also what the set costs is at that point in time. So I wanted to then talk about some of the adverse drug effects that can affect patients as well as their ability to be compliant or finish their medication. The first one that's probably most prevalent is GI upset. doxycycline is known to cause nausea, vomiting, diarrhea, abdominal discomfort, and even in some cases of esophageal burning or esophageal alterations. The tolerability with the side effects that can be approved by administering these drugs with food. You know, we did talk about wanting to separate doxycycline from dairy due to the potential risk for decrease in their overall serum concentrations. Again, doxycycline has been associated with the Safa, giantess, and esophageal ulcers. So to reduce that risk, patients should be counseled to take it with some water and avoid laying down afterwards. So try to stay upright for at least 30 minutes to an hour following the dose. There are some data that maybe doxycycline monohydrate can cause a less esophageal burning or a lot esophageal ulceration in comparison to the doxycycline hyclate formulation. Another adverse effect that may not be prevalent in the winter in New York State, but definitely prevalent in other parts of the world or country as well as prevalent and more of the sunnier times is the phototoxicity. So doxycycline phototoxicity. It occurs as a result of direct splint exposure on exposed skin off patients who are receiving doxycycline and this reaction can really range from mild erythema to severe blistering the risk of phototoxicity. it's multifactorial, it includes the dose of doxycycline. The patients taking the UV wavelengths skin phototype, as well as the geographic location of the patients and patients should be made aware of these risks. They should be advised to use broad spectrum sunscreen a high SPF that has activity against UVA and UVB wavelengths. Patients should wear sun protective clothing that includes you know, long sleeves or long covering the hat if possible, and really trying to avoid direct sunlight when outdoors and to practice behavioral avoidance of the sun. If at all possible. The next I wanted to highlight certain adverse events that it's included in the drug label but newer data, or more, I should say more recent data, maybe shows that it's not as big as a concern as once thought, but I do want to bring it to your attention because it is included in Lexi COPPA, and it you know, it is included in the FDA and it is something that still gets taught in schools. So, first I wanted to talk about the risk of tooth discoloration. So, the use of tetracycline, older tetracycline, they were linked with cosmetic staining of permanent teeth when given to children under the age of eight. And this was right when tetracycline were first being used in the you know, in the 1950s. But as a result of that, in the 1970s, there's a blanket warning that was added to the tetracycline class essentially said to avoid in that age population because of teeth discoloration. And now we know that the risk of with the tetracycline not the class, the drug tetracycline seems to be associated with the amount of drug administered as opposed to the duration it's a cumulative drug risk. It seems to be the highest when tetracycline is are given to infants before their first dentition. But the risk is hypothesized to still be there in infants of two months to five years of age, while teeth are still being calcified. And again, risk factors are higher doses long term use pediatric course is greater than 21 days. However, this risk is controversial. Specifically, regarding doxycycline doxycycline does bind less readily to calcium and there it has not been shown to cause the same to staining risks or effects as tetracycline, or tetracycline. There have also been several studies that previously been published that showed a lack of staining of permanent teeth when doxycycline is used in children. But the warning is currently present in all tetracycline class antibiotics. And it continues to mention the concern of the risk for dental staining and again doxycycline has not been shown to cause to staining and validated studies and most recommend short term use of doxycycline you know, less than 21

days and children regardless of the age if you know there's a life threatening disease or if the treatment of choice for that infection is in fact doxycycline. Another rare side effect that can get included in you know in packaging or labeling is skin hyperpigmentation or blue gray discoloration. Honestly, this is uncommon with doxycycline. There are case reports out there, however, tends to be more common with mineral cycling. But with doxycycline. It's associated with higher doses and long tree longer treatment durations. It can be semi reversible after drug discontinuation and time reversibility time after discontinuation pled it to be anywhere from one month to actually 12 months. And then lastly, another one I wanted to include just because it is included in the label is bone growth suppression. Originally, it was reported in premature infants that who are treated with tetracycline, tetracycline does bind to calcium and growing bones, that and that can negatively affect the calcium oral phosphate metabolism. growth restriction is seen with tetracycline is up to 40%, but it can be reversible upon therapy. However, again, they're they're limited to no data with doxycycline specifically, but the risk for bone growth suppression is extrapolated off of the current data with tetracycline

18:32
and then I wanted to throw in some other considerations doxycycline is recommended to be avoided with di valen and travaillent cat ion. So those types of medications can be calcium carbonate, magnesium hydroxide, aluminum containing products, iron containing products for die Vaillant, travaillent cod ions, they can key late and reduce the absorption and the overall available drug for doxycycline. That leads to a reduced anti antimicrobial effect. Usually the recommendation is just to avoid coadministration. But specifically with oral iron preparations, it's recommended to give the oral iron or to take oral iron two hours before the dose of Doxy or four hours after the dose of doxycycline to kind of minimize that chelation risk. Again, it's traditionally avoided in patients less than eight but has recently been accepted for short courses when medically necessary. And then also traditionally avoided in pregnant and breastfeeding patients. So doxycycline counseling pearls, you know, to kind of whether it's conveying to the patient in clinic or conveying at their pharmacy. You know, we want to provide patients with education so they know what to expect with their medications. They know you know when to reach out to providers that something's concerning and also to try to, you know, the best antibiotic is one that somebody will take. So making sure that they can, you know, stay adherent to their regimen. And so, you know, doxycycline, it can be upsetting to the stomach, take it with food, it's important to set up right after the administration and to take with a full glass of water. And then again, trying to avoid taking supplements or vitamins with minerals at the same time of doxycycline because you want to maximize the amount of drug that gets absorbed, and also just reminding patients to protect themselves from sunlight. So that was the main part with macro or with doxycycline. I do want to briefly touch upon macrolides specifically is it through mice and so macrolides were discovered in the early 1950s, the first one being overthrown bison, again from a species of strep and ICS and, you know, similarly to doc to tetracycline, semi synthetic drugs were then derived thereafter. macrolides are also used for a wide range of infections, including community acquired respiratory infection, sexually transmitted infections, you know, H. Pylori eradication, the setting of Clarithromycin, and again on the right hand side you see another depiction of a bacterial ribosome. However, macrolides inhibit bacterial protein synthesis by binding to the 50 S ribosomes if you recall doxycycline it inhibits 30 as essentially, by binding to the bacterial 50s ribosomal subunit it stops bacterial protein synthesis and macrolides sort of

plug the exit tunnel that prevent further synthesis of the peptide chain. Mechanisms of resistance for macrolides are two multifactorial, you can have increased drug efflux out of the bacterial cell. There's also ribosomal protection by the IRM gene, which are essentially just methylation enzymes that modify a ribosomal target the 23 S ribosomal target, and it decreases drug binding and it actually potentiate mat macrolide cross resistance and entero vector rallies. They produce Aster aces which can degrade the macrolide. And there's also alteration of the ribosomal 50 s binding site which is a chromosomal mutation. That just decreases the affinity of binding to the ribosome. I did highlight increased drug efflux as well as erm genes because those are the two main mechanisms of resistance and gonorrhea against is it through Meissen. Another broad overview of this is a true myosin is the dose does vary by indication the dose can range from 500 milligrams daily to a single one gram or two gram dose really depending on the indication. There are both IV and Pio formulations compared to other macrolides is it there? Meissen does have the least drug interactions, but there is still considerable amount of drug interactions with azithromycin. Because of the metabolism pathway. It is a substrate of that three four was essentially it's just a very common metabolism pathway shared with a lot of other drugs, which can be upregulated or downregulated. So always important to run a drug interaction checker to consult with a pharmacist if your patients are on a lot of other drugs. From a PK PD standpoint as that's where my son is rapidly absorbed. It has extensive distribution into the tissues and it's often much greater in the tissues than it is in the serum. However, CSF concentration is also poor. azithromycin has a very long half life on you know on the level of like multiple days, and that sought to be due to the extensive tissue distribution and high concentrations that's achieved in the tissue. There are not dose adjustments for any hepatic or renal insufficiency and total exposure and the concentration is really what drives the efficacy of the drug. Despite its favorable PK PD properties, it does have some limiting drug events. Most notable for most notable for many patients, it can cause drug, gi intolerance and macrolides they're they're used as Pro motility agents, you know, erythromycin is one that's often used in that regards macrolides actually bind to a motilin receptor and that causes an increase in annual contract tility So that's linked to you know, the awful GI and tolerance and tolerance that's associated with azithromycin. You know, the increased contractility leads to nausea, vomiting, diarrhea, and unfortunately with azithromycin This happens to be dose dependent. So this is a lot more common in patients who are taking like a high dose a one or one gram or two grams single dose, patients can take the drug with food to sort of lessen those gi side effects. Another important risk of azithromycin or I should say adverse event of is that there Meissen is the risk of Qt see prolongation. So, is that your Meissen has been reported to cause cardiac arrhythmias including Qt prolongation. There's actually a large cohort study out of Tennessee that did find a small but statistically significant increase in the risk of sudden cardiac death with visits for Meissen therapy when it was compared to treatment with amoxicillin or compared to patients that were We're receiving no treatment at all. So because of this, it's you know, encouraged that is information should be used cautiously in patients who are on competent antiarrhythmic medications or those who are on multiple multiple drugs that do prolong the Qt C. And then another risk of adverse drug events is just drug interactions. Do the metabolism, you know is it through Meissen concentrations can be altered or azithromycin can alter other drug concentrations that can lead to either a lack of therapeutic events or toxic concentrations and side effects of other meds. So again, I'm born to do a drug interaction review on the patients are on other medications and they're receiving visits from bison. And then lastly, I wanted to briefly

discuss fluoroquinolones. I'm just for this presentation focusing on Ciprofloxacin levofloxacin moxifloxacin, I do acknowledge there are other ones out there. The first floor quinolone does date back to the early 1960s. Ciprofloxacin came to the market in the mid 80s. It had an improved PK profile, it also had an enhanced spectrum of activity. Other fluoroquinolones you know at around the same time were illegal Blakiston and moxifloxacin and all three are still use today. On fluoroquinolones, they do inhibit replication and transcription of bacterial DNA through the inhibition of DNA Gyrase. And DNA Gyrase is responsible for the relaxation of supercoiled DNA. So when you inhibit DNA Gyrase fluoroquinolones are all can be responsible for the breakage of double stranded DNA. You know, we've we've heard a lot about over the years, I'm sure in our clinical practice about the resistance to fluoroquinolones and how fluoroquinolones develop resistance quickly. It's spreadable, and that's really true resistance of these agents. it's multifactorial, it can be via one or a combination of targets like gene mutations, increased production of multi drug resistance, efflux pumps, modifying enzymes and target protection proteins. We have target site gene mutations, which alter fluoroquinolones binding affinity to the enzyme, multi drug resistant efflux pumps, you know selectively transport fluoroquinolones out of the cell. And then we also have changes in membrane permeability, leading to the decreased ability of fluoroquinolones to get inside the cell. Lastly, I did want to mention a Q and R gene. Again, this is planned and plasmid mediated meaning it can be transferred from bacteria back to bacteria. It's also chromosomally determined. It's a protein that protects DNA Gyrase and other enzymes from being inhibited by fluoroquinolones. So that does tend to be you know, a rapid spreader and a major issue of fluoroquinolone resistance in the community. On this slide, so highlight some of the PK PD considerations for the three fluoroquinolones all of these agents have oral and IV formulations. They do have good bioavailability they achieve high tissue and high serum concentrations, notably Ciprofloxacin levofloxacin do have renal dose adjustment considerations where moxifloxacin does not and all fluoroquinolones have the efficacy parameter of peak to MSC. So this is why sometimes when treating infections like pseudomonas, you want to push the doses a little higher to get higher serum concentrations.

28:22
In recent years, the FDA has put together several alerts regarding the use of fluoroquinolones you know this is range from really don't use fluoroquinolones unless you have no alternative treatment from on bringing to light the risk of tendinopathies psychiatric side effects and most recently, aortic dissection so ruptures really important to try you know to avoid patients who are at increased risk of these events or have existing or pre previous aneurysms. Just to try to, you know, limit limit the side effects from these medications. And the major theme of this slide is really just assess the risk versus benefit before initiating quinolones and patients. I've included common side effects, you know, fluoroquinolones can cause GI upset. It can cause a CNS disturbances like psychosis and the elderly, there's a risk of C diff. It's been known to cause high and low blood glucose as well as a risk of Qt prolongation, that can be amplified in the presence of other medications. I did touch upon some of these black box warnings in the previous slide but just want to include them here for complete for completeness sake. Other considerations, they can key late as well. So try to separate them from try Vaillant and die. Vaillant can ions, and there's a multitude of drug interactions, you know, so again, try to do a drug interaction review or consult with a pharmacist, and there's also the risk of photo sensitivity reactions. So again, counseling pearls. For patients, it's important to take with food they should

be aware to reach out if they have have excessive hair foul smelling diarrhea because of the C Diff risk, they should reach out if there's any type of tendon pain that's unexplained, and just counseling on the separation of the DI Valle and travaillent, cat ions as well as the protection from sunlight. And, you know, we try to empower patients by giving these information upfront, so they can take charge of, you know, being an advocate for their for themselves and, you know, give them the most success of taking their entire entire course or reaching out if any of these side effects happen. So, with that, that is my quick overview. And I'm happy to answer any questions that may arise at this time. Thank you.

30:39
Thank you, Sara. Thank you so much. That was a wonderful talk, a nice comprehensive review of these, these classes of antibiotics that we use a lot. We had a couple of questions. So while we're waiting for folks to enter there, you want to go first. So I

30:58
recently had a call about a patient who was taking doxycycline not for an STI, but for Lyme disease. And this was prescribed, like, a day before traveling to the Caribbean. And this, this was the most significant photosensitivity reaction I had ever seen. With really, pretty much near blistering and even some blisters, despite clothing and sunscreen. So one of the questions that came to me was, you know, if I stop it now, how long? How long is this going to go on? What's you know, what's the duration of this reaction? And I was really sure how to answer that.

31:42
That's a great question from what I was reading from case reports or published literature, it really depends on a lot of times, you know, this does not seem like, you know, mild erythema that can resolve in a few days, there are some cases of taking, you know, upwards of a week with the addition of steroids. And other you know, other what am I trying to say non pharmacologic events, but I wouldn't, you know, it's really unclear with how fast but it should resolve within drug discontinuation. And it shouldn't something it shouldn't be that they're now going to have an increased risk after the drug is stopped. But from the resolvement of those symptoms, I think it just really depends on if they need adjunctive treatment. Or if if it resolves kind of on their own. So you know, usually a couple of days, but I have read, it can take up to a few weeks to completely resolve.

32:38
So there was a comment that just came in, scrolled up, so I can't see the whole thing right now. But they're addressing is this a concern also for animals? Do you know when animals are prescribed doxycycline?

32:51
That's a great question. I do not know specifically with animals. I do know the mechanism in humans at least is that that that doxycycline undergoes some a chemical reaction when it's in the presence of certain UVA UVB wavelengths, so that chemical chemical reactions, manifests that is like a burning. So I'm not sure if that process is the same in animals as it is in humans. I

haven't seen any case reports and animals. But that's something I should look into. Because that's actually an interesting point.

33:32
There's another question here. The recent CDC Doxie, PEP draft guidance states, there's an interaction with oral contraceptives and doxycycline, decreasing the efficacy. But when I looked into this, it appears to be outdated information. Could you comment on that? That's

33:53
a great question. I do get that question a lot. And when I've looked into that before, it just says, reduce, like I couldn't find great data other than reducing the efficacy. I can look into that right now and get back to in the chat. I do agree it, the data isn't great. But I would have to look specifically to see where the older data came from, to be completely honest.

34:15
I also will just add that in that situation, oftentimes, and you may already do this. But the answer is to not not prescribe the Doxy. Right. It's just a really heavily Council on a backup method being needed. And the likelihood, especially if this is outdated information is that it still works probably just fine. And it might just be for I don't know. I'm going to take a look on the MEC as well to see while you're looking that up to Sarah

34:49
I one of the questions that we get a lot is about you know if somebody is on one of these other medications that has a Qt prolongation more Turning, and maybe you need to give them as a through Meissen for chlamydia or as part of their alternative gonorrhea treatment. Do you have to worry about the single dose of azithromycin and the Qt prolongation because of single dose but generally it's a high dose. So

35:18
right it is my understanding it is dose dependent. I think in that instance, if the Pay It should depend on patient specific factors if they have a baseline EKG if their electrolytes specifically potassium and magnesium are optimized, or if it's possible, and what the QC risk is what that other medication. So I think it is patient specific and dependent upon what other concomitant medications they are really to make that decision but from my understanding, with azithromycin, it can be a dose dependent risk.

35:58
In the in the study that looked at the alternative treatment for gonorrhea with gentamicin, plus two grams of azithromycin. Their entry criteria were only to get an EKG if the patient was on a baseline anti rhythmic, but they did not do EKGs for all comers. So the interesting so that was what they used as their screen for a significant risk. So thanks for joining us today. And thanks to our speaker. We are Sarah. Yeah. Thanks very much, Sarah. Really appreciate it.

[End Transcript]