Expert Interviews

National STD Curriculum Podcast

Challenging Cases of Mycoplasma Genitalium

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Dr. Ina Park, Professor at the University of California, San Francisco, and Principal Investigator of the California Prevention Training Center and Dr. Meena Ramchandani discuss current and future treatment options and resources for addressing *Mycoplasma.*

Topics:

- M genitalium
- M gen
- mycoplasma
- treatment failure

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Disclosures

Disclosures for Ina Park, MD, MS

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References

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introduction**[00:00] Introduction**

Hello, everyone. My name is Meena Ramchandani. I'm an infectious disease physician at the University of Washington in Seattle. This podcast is dedicated to an STI [sexually transmitted infections] review for health care professionals who are interested in remaining up to date on the diagnosis, management, and prevention of STIs.

So, we welcome back Dr. Ina Park. Dr. Park is a professor at the University of California, San Francisco, and principal investigator at the California Prevention Training Center. She's a national authority on sexually transmitted infections, and we're going to continue our discussion on *Mycoplasma genitalium*. Dr. Park, welcome back.

Dr. Park

Thank you, Meena.

doxycycline-moxifloxacin-timing**[00:42] Doxycycline and Moxifloxacin Timing**

Dr. Ramchandani

Let's take our audience through some specific, challenging clinical scenarios and have you guide us through your recommended approach. So, the first one I want to start out with: We have a male patient who comes in with urethritis and receives ceftriaxone and doxycycline. He returns to clinic after finishing the medication, and he has persistent symptoms despite not having any new sexual contacts. The clinician tests him for *Mgen* (or *Mycoplasma genitalium*), and the test results return positive. You don't have access to resistance testing. It's been about one week since he took his last dose of doxycycline. What would you do in this situation? Would you restart doxycycline before starting moxifloxacin?

Dr. Park

Typically, if someone's coming in within a week, we don't restart. At least that's not the practice in our clinic. We just go ahead and give them the week of moxifloxacin. But a lot of times, people have finished their doxycycline, and it's been several weeks, and therefore, we resume and start the doxycycline again and then

give them moxifloxacin on top of it. But if you're testing somebody, and some clinics do this, actually, they've just adopted an algorithm where they're testing people, actually, initially when they first present. And if you have the results and the patient has not completed their doxycycline, or it's been less than a week since they finished their doxycycline, they can go ahead and not take an additional week but just go ahead and take a week of moxifloxacin.

Dr. Ramchandani

So, what if a patient was taking DoxyPEP and maybe they had just taken DoxyPEP? Is that enough to reduce the organism burden that you wouldn't start doxycycline or how would you approach that?

Dr. Park

Okay, now you're trying to mess with me, Meena.

Dr. Ramchandani

I'm actually curious because I don't know what I'd do.

Dr. Park

We don't know the answer to that question. Do you need to have that daily, constant concentration of doxy to effectively lower your organism load? I don't think anybody knows the answer to that question. My gut feeling is that if they had just taken a dose of DoxyPEP, it's probably not enough. Do you know what I mean? But I really don't know.

Dr. Ramchandani

Yeah. I don't think there's good data. I probably in that situation would recommend taking the course of doxycycline because that's just where we have the best data, and not really sure the length of time of doxycycline needed to reduce that organism burden. But, if it works, then it might be worth it to try.

Dr. Park

Yeah. I mean, the half-life of doxy is around 20 to 24 hours, right? So, five half-lives... There's still going to be some doxy around, but I just don't know if it's enough. And so, I think we just go with what we have data for.

retesting-mgen**[03:25] Retesting for *Mgen***

Dr. Ramchandani

So, the patient takes doxycycline and then moxifloxacin—takes all their doses——and the urethritis symptoms temporally improve, but then they reoccur. Let's say just within a few days. Again, no new sexual contacts. Would you test him for *Mgen* again or when would you test again?

Dr. Park

This is such an important question. I'm so glad you're asking this. The way I want people to think about *Mycoplasma* is that it's a very slow growing bug, so it takes a long time for it to eradicate, and it takes a long time actually for the residual genetic material to clear. So, the way folks should think about it is after they finish that last dose of moxifloxacin, you should wait three weeks to retest them if you're looking for a test of cure. It can take that long for all the genetic material to be eliminated.

What you don't want is a false-positive that then makes someone think that they have a treatment failure

when they really don't. Now this patient is still symptomatic, so I highly suspect that they're going to have an *Mgen* treatment failure if that's where we're going with this right now.

Dr. Ramchandani

We are. Although I have seen that sometimes patients might have some mild symptoms that might be just irritation after having an their *Mgen* testing is negative, so they have been cured their infection. So sometimes that can take a little while to resolve, at least I've seen.

Dr. Park

Yes, the tingle. Some people come in and they say, "I'm still tingling, I'm still irritated," and yet all their repeat testing is negative. That absolutely happens. And I'm not sure if it's just taking the body some time to sort of calm down on the inflammation that occurred with the initial infection.

alternative-mgen-therapy**[05:07] Alternative *Mgen* Therapy**

Dr. Ramchandani

But in this patient scenario, you wait three weeks, and the test for *Mgen* returns positive. So, now what do you do? I'm going to go down that course where the patient is trying different antibiotics. And so, what would you pull out next for a different type of therapy?

Dr. Park

Let's talk about what we have that's easily available here in the United States. And, the next place I would likely go, obviously we're asking about possibility of reinfection or new exposure to sexual partners, but assuming that none of that has happened, the next place I'm probably going with this is minocycline. And I know we just got finished talking about how tetracyclines like doxycycline are not that effective against mycoplasma, but minocycline actually has decent in vivo activity against *Mycoplasma genitalium*.

Now your listeners are not going to be impressed by this, but based on two studies, both out of Australia, the efficacy for a microbiologic cure is about high 60s to low 70%. And that does not inspire confidence, I think, in many people who are listening, but anecdotally, and as well as in these studies that are not controlled, by the way, not randomized controlled trials, we certainly have seen people have successful treatment with minocycline.

Something I'd like to throw in the mix for folks to consider is that the Australians also put out, actually just last year in 2025, some additional data looking at adding metronidazole of all things on top of the minocycline (aka mino), so then you're having someone taking mino and metronidazole at the same time for 14 days. And so, if you can imagine the GI [gastrointestinal] and CNS [central nervous system] potential side effects that someone could have with that, but if you have a difficult-to-eradicate *Mycoplasma* infection, some people are very motivated to withstand some side effects. So, at any rate, the Australians did put out some data, and I have some additional data forthcoming that have shown in an uncontrolled study that you get slightly better efficacy, about 10% better. So maybe you get instead of 70% efficacy, 80% efficacy. So, in the study that's published by K. Htaik published in the *Journal of Antimicrobial Chemotherapy*, they found that, overall, less than 10% of the patients in the study actually had to discontinue for side effects.

And most of those were the CNS effects that you could imagine like dizziness or brain fog. And then of course some people on metronidazole had GI side effects like nausea. So just something to put out there for people. There's not a lot of data yet, but when you have a difficult-to-treat *Mgen* case, you could consider adding metronidazole to the minocycline. It may help.

Dr. Ramchandani

I'll be interested to hear more about that in years to come as they publish more studies with that. I've tried minocycline and had some good success.

Dr. Park

Me too. Yes, me too. And on a patient who had been having *Mgen* symptoms for six months, and they just hadn't tried minocycline yet, and then the patient did well. So, I think both anecdotally as well as in these smaller, uncontrolled studies, we've seen some efficacy, but we have so few drugs, Meena. And I know you studied one yourself actually, which I don't know if listeners are aware of because this drug lefamulin was actually approved for community-acquired pneumonia, but I thought that was a very interesting study that you and Lisa Manhart and the Australians did looking at the use of this drug lefamulin, which by the way, the company has announced should be re-released at the end of 2026. So, I think it could be something you may want to tell listeners a little bit about, I think you used it in combination with doxycycline and sometimes as monotherapy, but in your U.S. population saw some folks who did get a microbiologic cure with that regimen. I just want to put a pin in that, right, because we don't have that drug yet, but I do think when it is re-released, it's something for folks to consider as well.

Dr. Ramchandani

It was a study commissioned for this small study, and the patients were very treatment experienced, especially the ones in Australia. We saw about 50% efficacy, especially those who took doxycycline and then lefamulin. So, still not great and very low numbers, but if a patient has failed minocycline, that might be a potential option if it becomes available again.

Dr. Park

Yeah. But I just want to put things in perspective for your listeners for a second because when we talk about gonorrhea we're talking about—and for example, new alternative treatments—we're talking about efficacy of over 90, 95%. And for mycoplasma, we're talking about things like 60, 70, or even 50%, and saying, oh, well, maybe that's a possibility. So, I think it just points to how desperate we are for new therapeutics for this really common infection that is becoming more difficult to treat. I think anyone out there who's seeing STIs is going to be seeing this and is going to be dealing with treatment failure at some point.

mgen-treatment-options**[10:33] *Mgen* Treatment Options**

Dr. Ramchandani

I know that a lot of infectious disease physicians also get referrals for patients who have *Mgen* who have failed the doxycycline, moxifloxacin, and recommended treatment, and then it's like, now what? So, what other options do we have for *Mgen* treatment here in the U.S. and if not available in the US, what other options that are available abroad?

Dr. Park

We're recording in June right now, and I want folks to be aware that Chase Cannon and Tim Menza are going to be publishing a paper looking at these really difficult-to-treat cases of *Mycoplasma* where they also tried combinations that included minocycline plus tinidazole. So, it's interesting because we talked about metronidazole on top of minocycline—taking concurrently—which is what the Australians have looked at.

Doctors Cannon and Menza have looked at using sequential therapy with minocycline. And for these folks, they were using courses of 21 to 30 days of lead-in with minocycline and then following that with tinidazole 10- to 14-day courses. And so, when we're thinking about how much antibiotic therapy that is, we're talking about people having five, six weeks of antibiotic therapy. And as I told you, because this organism metabolizes slowly, it grows slowly, it can take very prolonged exposure to antibiotics to eradicate it, but they

have seen some success with sequential minocycline leading into tinidazole.

And, for the listeners, just so you know, nitroimidazoles do have great in vitro activity against *Mgen*. Tinidazole actually has better in vitro activity than metronidazole. But again, this is going to be a case series. It's going to be a very small number of patients, but that just points to the desperation. We have some folks in that case series who had six courses of antibiotics before they were clear and asymptomatic. So, it's serious.

Dr. Ramchandani

Yeah. I've never thought of giving tinidazole for long courses. Usually, it's one dose and that's it.

Dr. Park

Yeah. I have used it in longer courses for folks with resistant trichomoniasis, but I've never used it for *Mycoplasma* myself, although I have multiple colleagues who have tried that. And there is a case report actually, just one case report, of someone who had failed multiple therapies, and the provider used tinidazole monotherapy, used two grams a day for seven days and had successful eradication. But this is the realm that we're dealing with is case reports.

And, just for listeners, I just want to point out, there are many other drugs outside of the U.S. that we don't have access to here and I'm going to just name off a few of them. One of them is pristinamycin. That is actually also safe in pregnancy. That's used and available in Australia and Europe. And we've had some providers who I know have sent patients to France to receive the therapy and we're able to get that at a French urgent care, but hopefully we don't have to resort to that here in the U.S.

Sitafloxacin, which is a different fluoroquinolone, actually works in patients who have failed moxifloxacin and is used extensively in Japan. And then for those listeners who have been around a while, might remember when we had access to spectinomycin for gonorrhea, which was way back in the day before my time. And it has been used successfully both in Japan in combination with sitafloxacin, as well as this crazy case series published out of Belgium by Van Balen last year actually put people on four-drug therapy that included pristinamycin, minocycline, metronidazole, and methenamine at the same time. During that same time period, the Japanese put out a study that looked at spectinomycin with doxycycline. So, people are trying all types of novel combinations for these folks who've had many months of symptoms. In the Belgian case series, some folks had more than two years of symptoms from *Mycoplasma*.

Dr. Ramchandani

Wow, that's incredible.

Dr. Park

We *must* respect this bacteria.

Dr. Ramchandani

Sometimes it can be easy to treat and sometimes it can be extremely challenging.

future-mgen-treatment**[14:45] Future of *Mgen* Treatment**

Dr. Park

But can I give folks some hope?

Dr. Ramchandani

Please do.

Dr. Park

Well, okay. So yes, this is serious. Yes, we are concerned. Yes, it's really a challenge, but I'm so happy that there's some national attention being paid to this. The NIH [National Institutes of Health] is having a consultation in two weeks that's going to be going over two days to just discuss all of the different research priorities. And so, my hope is that this also will lead to increased funding for folks who are doing work in *Mycoplasmas*, many of them who are at your institution over at University of Washington. That's my optimistic thought for the day.

Dr. Ramchandani

I think that'll be helpful to see the new updated STI Treatment Guidelines, which you are writing this section on, on *Mgen* and the recommendations for the U.S.

Dr. Park

Lindley Barbee, who was at University of Washington, who's an *Mgen* researcher in her own right, decided to give me this section. I have typically worked on sections like HPV [human papillomavirus] and syphilis, which are much more straightforward, and I have developed a deep appreciation for the challenge that we're facing right now with *Mgen*. And so, I'm really excited that you're shining some light on it because I know that there are providers out there and patients who are suffering, and we all have to hold each other up.

And can I also give people a resource, which is the STD Clinical Consultation Network, stdccn.org. I would really encourage folks who are dealing with a challenging *Mycoplasma* case out there to submit your case. There was a publication, actually in 2026, and there were 300 cases submitted, and almost all of them were submitted after 2023, and about a third (1/3) of those are treatment failure cases. But there is someone on call. There's eight centers that are answering these consults, and so there is absolutely somebody paying attention, and you will get a response and get someone to be a thought partner with you as you're dealing with these challenging *Mgen* cases.

Dr. Ramchandani

Yeah, that's an incredible resource for clinicians to really think about that individual case that they're dealing with and how to approach the management.

Dr. Park

Yeah. And can I also invite providers who are dealing with a difficult case to put it into CDC's [Centers for Disease Control and Prevention] registry. CDC has a *Mycoplasma genitalium* Treatment Failure Registry, and the results of that registry were actually presented at the international STI meeting [STI & HIV 2025 World Congress] last year in Montreal. But they've had complete data on over 50 cases of treatment failure, and some folks out there who've received up to eight courses of antibiotics that are still symptomatic. But the sort of median number of courses that people have needed to eradicate their infection in that registry is somewhere between two and three courses of antibiotics needed.

But yeah, if you Google or put into any search engine CDC *Mycoplasma genitalium* Treatment Failure Registry , it'll pop up and it's a public form that you can enter your information. It does not include any patient identifiers, obviously, but it really helps the CDC keep track of what's being used out there for treatment failure and someone at CDC will get in touch with you to get more information on the patient.

Dr. Ramchandani

Yeah. It probably also helps to inform what's needed in the new guidelines as they get updated.

Dr. Park

That's right.

pregnancy-mgen**[18:01] Pregnancy and *Mgen***

Dr. Ramchandani

Right. Well, let's look at another very challenging scenario. So, we have a pregnant woman who's asking for full STI testing and goes to another provider and was tested by her provider for *Mgen* and then referred to you for counseling and treatment. She has no symptoms. How would you approach her case?

Dr. Park

Yeah. This is really difficult because I just got finished earlier in this podcast mentioning that we've seen some associations. These are not randomized controlled trials, by the way, but epidemiologic studies that are demonstrating an association with preterm labor or low birth weight, et cetera. With odds ratios usually of around two, so not astronomically high, but we've certainly seen some significantly increased odds of bad outcomes, but we have no idea whether screening and treatment in pregnancy actually reduces those outcomes.

We have seen an association with bad outcomes with the organism, but that next question of whether or not it actually helps to screen and treat people is really unclear. And so first of all, we've been encouraging people not to screen in pregnancy because out of all of the different drugs that I've talked about, pristinamycin is used in pregnancy, but it's not available in the U.S. And then azithromycin, which we have mentioned very briefly, is really not effective anymore against mycoplasma. And so generally speaking, I would counsel providers to reassure the patient as much as possible that we don't know what the meaning of this infection is, and essentially just to leave it alone.

Now, the thing that is really tricky is when you have someone who has evidence of cervicitis, for example, and then is discovered to have *Mgen* during the pregnancy. The only drug that we've mentioned that is safe in pregnancy or known to be safe in pregnancy is azithromycin. So, I have seen folks use azithromycin monotherapy with an extended course, but we're not routinely using doxycycline or moxifloxacin in pregnancy and therefore, generally speaking, I don't recommend their use. What I have seen happen is that sometimes folks who have some evidence of cervicitis are given azithro monotherapy, and then if that doesn't work, essentially just have to wait until postpartum to treat the infection. So, *Mycoplasma* in pregnancy is particularly challenging, and I would strongly encourage folks not to screen because we really don't know what the meaning of an asymptomatic infection is.

partner-management--mgen**[20:38] Partner Management & *Mgen***

Dr. Ramchandani

The patient also asks about her partner, and I think partner management is a question that comes up a lot for patients and providers. And when should a partner be treated and how would you counsel the patient and the partner about treatment?

Dr. Park

This is a little bit of a paradigm shift from what people are used to in terms of bacterial STI partner management, because when we think about—I'll use gonorrhea and chlamydia as easy examples—often if a partner comes in and says, "I've been exposed to chlamydia," we go ahead and treat them routinely. When

we have someone, whose partner has *Mycoplasma*, the recommendation from CDC is to actually test the person first. And I'll tell you why, Meena. We did mention that patients can clear *Mycoplasma* without treatment, and it's interesting in that the studies of couples that have been done of which there are about five or six I think total, the correlation between partners is not that high. It's about 30 to 40%. And so, we already mentioned that what you're buying someone from *Mycoplasma* treatment is two weeks of antibiotics. Generally speaking, in terms of being good stewards of antibiotics, we're trying not to treat folks unless it's absolutely necessary.

And so, what I would recommend is that if the patient walks in and says, "My partner has *Mycoplasma*, go ahead and test them with a nucleic acid amplification test." If that test is negative, they don't need to be treated, but if the test is positive, then I would encourage treatment, even if they are asymptomatic. That's the only exception in terms of when we're treating asymptomatic people is that if they're in a partnership where they could be then reinfecting each other with *Mycoplasma*, then I would recommend treating an asymptomatic partner, if they're positive.

Dr. Ramchandani

That's really helpful. So, the partner should come in for testing. So therefore, ETT (or expedited partner therapy) would not be recommended.

Dr. Park

No. It's not on the table for this particular infection, no. I mean, obviously, we use it for gonorrhea and chlamydia pretty frequently, but not for this infection.

mgen-clinician-resources**[22:36] *Mgen* Clinician Resources**

Dr. Ramchandani

Well, I know managing *Mycoplasma genitalium* can be really challenging for clinicians. You talked about some free resources, which is really helpful, including the *Mgen* registry on the CDC website. I do want to put in a plug for the National STD Curriculum because that does have a really nice chapter section for *Mgen* that clinicians can go through and get CME credit. Anything else that you would recommend?

Dr. Park

Yes. First of all, I wholeheartedly agree with the STI curriculum and also, I just want to plug one more time the stdccn.org website to put in your challenging case and then one of us could be me, actually could be Meena. We'll get back in touch with you and provide you support on managing your difficult-to-treat *Mycoplasma* case.

in-closing**[23:25] In Closing**

Dr. Ramchandani

And last, I always like to ask every person who's on this podcast, what's the most common question you get about *Mgen* and infection?

Dr. Park

The most common question I get about *Mgen* infection is the most common question I get about every STI because I have a lot of patients who have multiple partners, so they always want to know, “Can I figure out who gave this to me?” And I always tell them, “No.” I mean, I think when you have one partner and you're both in a monogamous relationship, in theory, then when an STI enters the partnership, it can be a sign of

infidelity. But, when there are multiple people in the mix, it's very difficult to pinpoint, especially because we know that people can live with this infection for more than a year before it clears sometimes. So, I think it's really hard to answer that question except in very rare cases where I can say, “Yes, your partner cheated on you,” but rarely am I able to say that.

Dr. Ramchandani

Yeah, that's a great question, especially because I'm not sure we know the length of time... I mean we absolutely know the natural history variables, right? So, if someone could be asymptomatic for a really long time and then be in a monogamous relationship. And so, it's not clear at what point did they acquire the infection before it became symptomatic.

Dr. Park

Right, and I think with *Mgen*, it's basically almost impossible. I think with something like gonorrhea, I've had patients who had not had sex for years because they were incarcerated, for example. They had sex as soon as they got out of prison, and then they got gonorrhea in two days. And I said, "Probably the person you had sex with right after you got out of prison gave it to you." So, then you can pinpoint. *Mycoplasma*, very hard to do. Same with trichomoniasis. Chlamydia can be challenging also.

Dr. Ramchandani

Well, Dr. Park, thank you for this great discussion about this very important topic. This has been incredible, educational session and we really appreciate your time. Thank you so much.

Dr. Park

Thank you, Meena.

credits**[25:30] Credits**

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