Expert Interviews

National STD Curriculum Podcast

Mgen: Co-Occurring STIs & When to Treat

April 11, 2023

Season 3, Episode 11

Dr. Lisa Manhart, a University of Washington Epidemiology Professor and a *Mycoplasma genitalium* (Mgen) expert, discusses how Mgen may cause or co-occur with other diseases (nongonococcal urethritis, cervicitis, pelvic inflammatory disease, and bacterial vaginosis) and when and whom to test for Mgen in an interview with the National STD Curriculum Podcast Editor Dr. Meena Ramchandani.

Topics:

- Mgen
- M.genitalium
- NGU
- PID
- BV
- cervicitis

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Disclosures

Disclosures for Lisa E. Manhart, PhD, MPH

Research funding & research supplies: Hologic, Inc. and Nabriva Therapeutics
Consultant fee: Health Advances

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No Disclosures

Transcript

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In this episode:

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introduction**[00:00] Introduction**

Dr. Ramchandani
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 STD [sexually transmitted diseases] review for health care professionals who are interested in remaining up to date on the diagnosis, management, and prevention of STDs.

For this episode, it's a distinct pleasure to introduce Dr. Lisa Manhart. Dr. Manhart is a professor at the University of Washington in the Departments of both Epidemiology and Global Health. She is an internationally recognized expert on *Mycoplasma genitalium* and is on the editorial boards of journals *Sexually Transmitted Diseases* and *Clinical Infectious Diseases.* She has also served as an expert consultant for the Centers for Disease Control and Prevention. This is the first episode of two interviews that we are doing with Dr. Manhart on *Mycoplasma genitalium.* Lisa, thank you so much for being here today.

Dr. Manhart
Thank you, Meena. I'm really thrilled to be here. And, as you know, I love talking about *Mycoplasma genitalium*.

Dr. Ramchandani
So, I'm going to say "Mgen" for short. I want to first hear from you—how did you first get interested in researching Mgen, and what studies are you working on now?

Dr. Manhart
Yeah, that's such a great question, Meena. I wish I could take credit for it and say that I was clairvoyant and knew that this would be a great thing to study, but I got started studying *M. genitalium* because I did my dissertation on it at the suggestion of King Holmes [University of Washington Professor Emeritus]. And I have, throughout my career, really spent a lot of time researching many topics in the field of STI and HIV. But I kept coming back to Mgen because it's so interesting. And right now, I would say all of my current research is focused on Mgen. I have three ongoing research projects. One is a multisite surveillance study of Mgen and antibiotic resistance. I'm also doing a large serostudy of *M. genitalium* for NHANES. And, then, I'm involved in a couple of studies to test alternative antibiotics for treating Mgen.

prevalence**[02:20] Prevalence**

Dr. Ramchandani
So let's get an overview of Mgen. This comes from a lot of questions that patients ask me. How prevalent is Mgen? What is the reported prevalence in different populations?

Dr. Manhart
That's a great question, and like all questions that you ask about epidemiology, the answer is "it depends." So in your kind of typical general population, which is primarily low-risk individuals in nationally representative surveys, the prevalence of Mgen is about 1 to 3% globally. The most recent estimate we have in the United States is from the NHANES survey, which is our large, nationally representative population-based survey, and Mgen prevalence was 1.7%. That sounds really low, but the prevalence of chlamydia in that same population was only a little bit higher. And the prevalence of gonorrhea in population-based surveys is dramatically lower

than that. So that's really consistent with what we see in higher-risk populations attending sexual health clinics. Mgen prevalence in those populations ranges anywhere from 12 to about 30%. In our recent surveillance project, initial estimates suggest that in kind of overall combining symptomatic and asymptomatic cisgender males and cisgender females, the prevalence is about 16%.

mgen-ngu**[03:57] Mgen and NGU**

Dr. Ramchandani
And what percentage of NGU diagnosis, or nongonococcal urethritis diagnosis, is caused by Mgen? What about persistent or recurrent urethritis, and where does this data come from?

Dr. Manhart
There're multiple studies that have estimated the contribution of Mgen to NGU. Overall, NGU, it's about 20 to 30%, is usually due to Mgen; approximately 40 to 50% of persistent and recurrent NGU is due to Mgen. So a very high proportion. And there's actually a great study out of San Francisco that was recently published. This study in San Francisco implemented Mgen testing at the initial diagnosis of NGU and treated with moxifloxacin. And that, combined with the overall change in guidelines of using doxycycline as initial therapy, resulted in a 60% decrease in cases of persistent and recurrent NGU. So, it's responsible for a lot of persistent, recurrent NGU, and it looks like, by testing and effective treatment, that actually goes down.

Dr. Ramchandani
So it sounds like that by implementing Mgen testing in the initial management for NGU, they were able to diagnose quite a few Mgen infections that were responsible for the NGU diagnosis or persistent NGU.

Dr. Manhart
Exactly. By picking up Mgen initially and giving treatment that was effective against it, they eradicated the organism and prevented those cases of persistent or recurrent NGU that *would* have happened had they only been treated with doxycycline.

mgen-extragenital-oropharyngeal-infections**[05:51] Mgen and Extragenital and Oropharyngeal Infections**

Dr. Ramchandani
So, speaking of colleagues in sexual health clinics in different cities, one thing that has come up as a question is, can Mgen cause extragenital infections, for example, rectal infection or proctitis? And should everyone with proctitis be tested for Mgen as part of the initial workup?

Dr. Manhart
Mgen definitely is also an extragenital infection. It's been detected in both the rectum and the oral pharynx, although much less frequently in the oral pharynx. The prevalence of Mgen, particularly in gay and bisexual men who have sex with men, in the rectum is quite high, and there's really not great data on whether it causes proctitis. There are lots of studies showing you find Mgen frequently in the rectum, but some studies show a relationship with proctitis, and some studies don't. So given that uncertainty, I don't think everyone with proctitis should be tested for Mgen. I think if you have a patient with CT [*Chlamydia trachomatis*]-negative/GC [*Neisseria gonorrhoeae*]-negative proctitis, who doesn't get better, I would absolutely test for Mgen, but I probably wouldn't do it on the initial presentation.

Dr. Ramchandani
Now, Lisa, you mentioned oropharyngeal infections. Can Mgen in the rectal or oropharyngeal area lead to transmission of the organism?

Dr. Manhart
There's mostly cross-sectional data on oropharyngeal infections, and historically the prevalence of oropharyngeal infections has been really low. However, most of those studies also used older, less sensitive

assays. And Dr. Lindley Barbee has a really nice prospective study in men who have sex with men using a more sensitive FDA-cleared NAAT [nucleic acid amplification testing] and actually identified a pretty high incidence of oropharyngeal infection. So it definitely happens, but we don't know anything about the efficiency of transmission from either the pharynx or the rectum. I'd be surprised if it *didn't* contribute to transmission, but we just don't have any studies that have really carefully evaluated that.

Dr. Ramchandani
That's helpful.

mgen-cervicitis-or-pid**[08:16] Mgen and Cervicitis or PID**

Dr. Ramchandani
Is there any evidence for a role for Mgen to cause infection in women or those persons with a cervix or vaginal tissue?

Dr. Manhart
Yeah, there are a fair number of studies both of Mgen and cervicitis and pelvic inflammatory disease [PID]. The challenge with those studies is that most are cross-sectional, so only at one point in time. So, you can't really tell that the Mgen infection came before the cervicitis or the PID. The data—some studies show an association, and some don't. In my opinion, the balance of the studies is really that they more consistently do show an association, and I do believe that Mgen plays a role in cervicitis and PID. I also think that the data are fairly convincing for a role in female infertility. The data are a little conflicting, but the best-designed studies do show an association. We have almost no data, very little data on ectopic pregnancy, so really hard to tell. If it's causing infertility, pelvic inflammatory disease, I'd be surprised if it didn't also play a role in ectopic pregnancy.

Dr. Ramchandani
Per the 2021 STI treatment guidelines, should women with PID be tested for Mgen as part of the initial workup or treated empirically for Mgen if patients do have PID?

Dr. Manhart
The guidelines are a little vague on that point. They clearly state that Mgen testing in women should be done for cases of persistent cervicitis, but they indicate that Mgen testing can be considered in PID. So I really think it is probably up to clinician discretion.

mgen-bv**[10:13] Mgen and BV**

Dr. Ramchandani
Is there any data to support *M genitalium* infection associated with bacterial vaginosis?

Dr. Manhart
I think in the community of researchers, perhaps the biggest outstanding question is, does bacterial vaginosis [BV] in women play a role in M. *genitalium*? There really seems to be some synergy between Mgen and BV in women—in ciswomen, people with a cervix and a vagina—and I think that that is an area of really interesting future investigation. Teasing out those relationships and seeing how much of a role that synergy plays in cervicitis and pelvic inflammatory disease.

Dr. Ramchandani
Who is researching that area right now? What studies are going on to see what that synergy is like?

Dr. Manhart
I do not know. The comment is motivated by some really intriguing results that women with PID in a randomized trial comparing the addition of metronidazole to standard therapy for PID actually were much less likely to have an Mgen infection 30 days after therapy, which was really surprising because the general

thinking is that metronidazole is not active against Mgen. So, the result that the investigators observed is: either because there's some relationship with other organisms that the metronidazole is active against, or metronidazole does have efficacy against Mgen, or it was just random chance. I don't think it was random chance, though, because there are lots of other studies showing strong associations between Mgen and BV.

testing-treatment-pregnancy**[12:08] Testing and Treatment in Pregnancy**

Dr. Ramchandani
I heard from a clinician that some asymptomatic women, including those who are pregnant, are asking for Mgen testing as part of their routine STI screening. Tell us, what is your take on this? Is Mgen testing a recommended part of the routine STI screening in pregnant persons?

Dr. Manhart
The quick and easy answer is unequivocally no. Asymptomatic pregnant women should *not* be screened for Mgen. And that's for a couple of reasons. One, there are a little bit of data on adverse pregnancy outcomes as a result of Mgen infection, but not a lot. So we actually don't know if it causes harm. Kind of going back to that argument of weighing the benefits and the harms. And there are particular challenges with Mgen infection in pregnant women because we really have a single antibiotic that we can use in pregnant people in the United States, and that's azithromycin. And with all of the macrolide resistance, that is unlikely in many cases to be effective. And so then you are left with a patient with a diagnosed infection that you can't treat who's anxious about the diagnosed infection and few to no options for helping that individual.

Dr. Ramchandani
And it's not only the options, right? You also don't know the implications. So, if one has Mgen, like what does that mean? So, it's not necessarily that there are benefits in treating something that you're not sure is going to cause harm.

Dr. Manhart
Right. If you have a pregnant person who is symptomatic—who has cervicitis, some clinicians have counseled the patient to wait until after delivery and then treated with other antibiotics that are safe after pregnancy, but it's really challenging. There is, to my knowledge, a single other antibiotic worldwide that is safe in pregnancy, and that's pristinamycin. We do have reports of patients who actually travel to Europe to get pristinamycin, so that is one option if the patient is able to do that. Not many patients are able to do that. So, asymptomatic testing in pregnancy is *absolutely*not recommended. There's very little known benefit for that.

Dr. Ramchandani
That's really helpful, thank you.

testing-risks-benefits**[14:44] Testing Risks and Benefits**

Dr. Ramchandani
I want to turn to a recent article that you published in August of 2022 in *Emerging Infectious Diseases* with what I call the dream team of specialists in the field of Mgen infection. This article is titled "Weighing The Potential Benefits and Harms of *Mycoplasma Genitalium* Testing and Treatment Approaches," and I highly recommend our audience take a look at this article if they're interested in learning more because this manuscript reviews 398 full-text articles on Mgen. How would you summarize the risks and benefits of Mgen testing and treatment approaches for this infection? What would you say are the key messages or highlighted points from this review?

Dr. Manhart
My immediate thought is it's really frustrating because there's lots of data out there on Mgen, but it's not of what people would grade as "Grade A" evidence. We like to make decisions on testing and treatment based on results from randomized trials that *clearly* show that there is a benefit, and we just don't have those for Mgen. So I think the theme of the paper that my colleagues and I wrote, and I really want to acknowledge the

rest of the team, Will Geisler, Catriona Bradshaw, Jørgen Jensen, and David Martin, fantastic clinician epidemiologists.

The heart of that article really is that because of the lack of rigorous data or the weaknesses in the data, we're often left with doing exactly what the title says, weighing the risks and the benefits, and having to make choices based on imperfect evidence. So, I think we have great evidence suggesting that Mgen is associated with all of our reproductive tract syndromes; and testing in symptomatic persons, the benefits likely outweigh the harms. But we just don't know enough to be able to definitively say that the benefits of testing asymptomatic persons outweigh the harms. And the current thinking really is that the harm of increased antibiotic resistance outweighs the benefit of detecting an asymptomatic infection.

Dr. Ramchandani
That's really helpful. I'm so glad you and others are researching Mycoplasma genitalium because I think that there is just a lot more that we can know about this infection, and patients are understandably frustrated when they have this infection and have persistent symptoms that don't resolve with antibiotic therapy. So really appreciate your work and others in this field.

Lisa, thank you so much for being on this episode. I can’t thank you enough. I know that our audience is very grateful to learn about this topic because I think there’s a lot of questions that come up from both patients and public health and the clinical world. So, thank you for being here today.

Dr. Manhart
Thank you so much for inviting me, Meena. It was truly a pleasure.

credits**[17:56] Credits**

Dr. Ramchandani
This podcast is brought to you by the National STD Curriculum, the University of Washington STD Prevention Training Center, and is funded by the Centers for Disease Control and Prevention. Transcripts and references for this podcast series can be found on our website, the National STD Curriculum at www.std.uw.edu.