

Expert Interviews

National STD Curriculum Podcast

Antimicrobial Resistance in Neisseria Gonorrhoeae: Surveillance Programs

July 15, 2025

Season 5, Episode 11

Microbiologist and Associate Professor at the University of Washington Dr. Olusegun Soge reviews four U.S. based surveillance programs: GISP, eGISP, SURGG, and CARGOS - the umbrella program rolled out in August 2024. Dr. Soge and National STD Curriculum Podcast Host Dr. Meena Ramchandani also discuss a vaccine and another STI pathogen developing resistance.

Topics:

- Gonorrhea
- antimicrobial
- vaccine
- MenB
- GISP

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[Disclosures](#)

Disclosures for Olusegun O. Soge, PhD

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Consulting Fee: Innoviva Specialty Therapeutics

Transcript

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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 infection] review for health care professionals who are interested in remaining up to date on the diagnosis, management, and prevention of STIs.

We are very excited to have back Dr. Olusegun Soge, who also goes by S.O., and is an associate professor at the University of Washington. Dr. Soge is a microbiologist with expertise in molecular diagnostics and antimicrobial resistance of sexually transmitted pathogens. We are very excited to have him on this episode to talk about antimicrobial-resistant *Neisseria gonorrhoeae* and surveillance for this organism.

Dr. Soge

Well, thank you. Thank you so much for having me.

[continued-evolution](#)[00:50] Continued Evolution?

Dr. Ramchandani

Do you think antimicrobial-resistant *Neisseria gonorrhoeae* will continue to evolve in the future?

Dr. Soge

Oh, well, that's an excellent question. I remember there was a time that I talked to someone, and I was like, "What do you think would be a very great project to propose to submit to the NIH [National Institutes of Health] that you are sure will have the highest likelihood of success? And this was someone from NIH, which I'm not going to mention the name. And then they told me, "If you can figure out how to stop *Neisseria gonorrhoeae* from developing resistance, guaranteed you're going to be funded." And I'm like, "Okay, so wow!" So that's the question you're asking me, do I think it's going to continually evolve resistance? Yes, it would do it because that's just a normal evolutionary phenomenon for *Neisseria gonorrhoeae*. It's just a way of survival. You want to kill *gonococcus*; *gonococcus* wants to survive. And over the years, it's actually developed several mechanisms to be able to do that over, and over, and over again.

So, I think we are going to be in denial if we are going to say we are going to be able to stop the development of resistance in *Neisseria gonorrhoeae*. We've seen that with the rapid evolution of resistance, from the sulfonamides to the penicillin, to the tetracycline, to the macrolides, to the ciprofloxacin. Do you think all of a sudden, it's just going to change itself and say, "Hey, no, I'm just happy; I'm not going to develop resistance, just kill me with a new drug?" It's going to continually develop resistance. That's why the most effective tool that we need is a vaccine because if you don't get gonorrhea, you're not going to develop resistance. So, being able to develop effective vaccine for gonorrhea will be the game changer.

Dr. Ramchandani

Do you think that's possible when the pathogen changes its antigens or its surface?

Dr. Soge

That has been the greatest challenge, but now there's a study that's shown that the MenB vaccine, which is for meningococcal infections, works. So, the goal is using the same technology to see whether we can get a very effective vaccine for gonorrhea. To my knowledge, there's actually been some trial to see whether the MenB vaccine will work to prevent gonorrhea to some extent, at least reduce cases of gonorrhea. And I'm also aware there's going to be a clinical trial to look at gonorrhea-specific vaccine, so it's not completely bleak like it was decades ago that due to antigenic variation and all those changes in the surface antigen, there has been challenges developing a vaccine against *Neisseria gonorrhoeae*. So, I'm hopeful maybe in the future, but it's not going to be tomorrow. And sorry, it's not going to be probably next year to have a vaccine, but that will be the game changer. That will be the most effective strategy to control antimicrobial resistance in *Neisseria gonorrhoeae*.

Dr. Ramchandani

That's reassuring that we have the tools that a vaccine is even possible, and some data that we can get protective immunity, at least to some degree, to *Neisseria gonorrhoeae*.

[new-antibiotics](#)**[04:15] New Antibiotics**

Dr. Ramchandani

We probably need to invest a lot more also into antibiotics because if it is going to continue to evolve, zoliflodacin might not be the end.

Dr. Soge

There's a second antibiotic that also did well in phase 3 clinical trials. So we're hopeful maybe in the coming years there will be two new antibiotics that we can use to treat *Neisseria gonorrhoeae*. Being able to monitor development of resistance in those new drugs I think would be the best way to actually introduce them for treatment, especially in places of the world where resistance develops first. We can have good surveillance to monitor development of resistance to the new drugs, and we can prevent the spread of that resistance globally will be a very effective strategy to use.

And you're totally correct, we need to invest more into the development of antibiotics. But you know it's very expensive and pharmaceutical companies are reluctant to put in a lot of money when the return on investment is not guaranteed because *Neisseria gonorrhoeae* is an amazing troublemaker when it comes to developing resistance. That's why it's so fascinating.

[gisp-egisp-surrq](#)**[05:32] GISP, eGISP, and SURRG**

Dr. Ramchandani

Tell us about the surveillance in place for antimicrobial resistance in the U.S. on either a national or even a local level for *Neisseria gonorrhoeae*.

Dr. Soge

Well, thank you. That's a very good question and that's actually the program that supports my lab and the University of Washington *Neisseria* Reference Lab has been a regional lab for gonococcal antimicrobial resistance surveillance since the establishment of the Gonococcal Isolate Surveillance Project (GISP) under the leadership of the late Dr. King Holmes who recently passed away. I took over the lab from Dr. King Holmes in 2010. We have local surveillance in Seattle for instance. So, the first one, the national surveillance in the U.S., is the GISP that was established in 1986. But the limitation of that program, even though for many,

many years, was that they collect only male urethral isolates from the first 25 patients. And so, for many years, that was what we used to inform revisions to our treatment guidelines and making changes to our treatment guidelines. The data that is generated by the regional lab doing all the testing and the clinic side collaborating, providing clinical and demographic data, that's what has been used to revise treatment guidelines.

And it worked, it worked great. But the limitation is we don't have extragenital isolates data, so there's no pharyngeal isolate being collected and there's no rectal, and then we're also not collecting specimen from women. In 2017, in recognition of that limitation, there was a new program that was started called the eGISP, Enhanced Gonococcal Isolate Surveillance Project. And at the same time, they started this rapid *Neisseria gonorrhoeae* detection project which was called Strengthening the United States Response to Resistant Gonorrhea (SURRG). And the goal of that is to fund nine jurisdictions, give them a ton of money and see how they can control gonorrhea. So, they are now going to use agar dilution testing. You now, the agar dilution testing is performed by a specialized lab, like my lab, which isolates are batched.

So, the methodology for GISP is that they call it isolate, *Neisseria gonorrhoeae* isolate, has to be urethral, has to be from men, first 25, and then they put it in their freezer. At the end of the month, then they send it to the reference lab, and some reference lab would take months to do the testing, so it's not meant to be actionable. So, by the time you get the result back that someone has resistance to cipro, that was like maybe two months after the person has been treated, you're not going to call the person back and say, "Hey, by the way, we saw you two months ago and the gonorrhea you had is actually resistant to cipro. Are you okay? Are you going to come back and make sure?" No, they're not going to do that. That's not the goal. It's not meant to be actionable. It's surveillance. It's meant to contribute data that would help to guide the selection of effective therapies for *Neisseria gonorrhoeae* treatment, which means we only need the data when they're actually looking at the treatment guidelines to say, "Hey, the percentage of resistance to this drug is still below 5%. Oh, we're still having 95% efficacy to this drug, so we're good." And once you see the resistance above 5%, it's 10%, it's 20%, it's 70%, you know the world is coming to an end. That's not a good drug to use.

So, what SURRG did was to expand the collection of isolates to extragenital. So, we collect rectal, we collect pharyngeal, we collect isolate from women, and then we don't wait, we don't just put the isolate in the freezer. We rapidly test them using what is called the *Etest* [Epsilometer test]. The *Etest* is just like a strip which you put on the plate. You say, "Oh, it's susceptible. It's resistant." You can get the minimum inhibitory concentration (the MIC), which is the lowest concentration of the antibiotic that will inhibit the growth of the *gonococcus*, *Neisseria gonorrhoeae*. And so, SURRG was introduced at the same time that eGISP was introduced.

So, there are some sites that have been part of the GISP for decades, but all they collected was urethral. So, they gave them just a little bit more money. Why not just collect pharyngeal, collect rectal? It's the same patient, they got both, right, and they got a pharynx. So, you can just culture it and if you have anything growing, they do not do *Etest*. That's the difference. The eGISP, they collect those isolates, they put it in the freezer, they wait until the end of the month, then they send it to the regional lab. So that's the difference between eGISP and SURRG. And just know that you must have been eGISP collecting urethral and they give you just a little bit more money to collect rectal, to collect pharyngeal isolates, and send it to the regional lab for testing. But if you're a SURRG, you are doing *Etest*, rapid testing, antimicrobial susceptibility testing using a faster method, which will give you MIC.

And if you find anything that is an alert to when we started the program, anything that is an alert to azithromycin because it started in 2017. That was when they were still recommending dual therapy of azithromycin and ceftriaxone for gonorrhea treatment. So, anything that is an alert to azithromycin, to ceftriaxone, as well as cefixime, then you have to call the patient and you do investigation, and you do partner notification. And then you call the patient back, and then you do test-of-cure, and then you want to make sure, and you do first-generation, second-generation, all those DIS [disease intervention specialist] tracing just to make sure that we are catching *Neisseria gonorrhoeae*, resistant gonorrhea, before it spread in our local jurisdiction. And when CDC dropped azithromycin as a component of the dual therapy, then we stop

doing any follow-up on any alert. We stop doing any case investigation of azithromycin alert. We only do it for cephalosporin.

[cargos](#)[12:10] CARGOS

But guess what happened? In 2017, eGISP and SURRG. And what happened last year in August 1, 2024? All GISP sites were all combined. SURRG, GISP, eGISP now became a program under one umbrella of CARGOS: Combating Antibiotic Resistant Gonorrhoea and Other STIs. And whereas we used to have 32 states, those 32 now got reduced to only 20 CARGOS sites. So, we reduced the number of sites that are participating in our surveillance from 32 to 20, because if you're a SURRG site, you still have to be part of the GISP. So now, we have only 20 clinic sites and the good news is Seattle is also one of those 20 sites that are CARGOS sites.

So, you could see the evolution, the difference, what is happening in our surveillance of antimicrobial resistance in *Neisseria gonorrhoeae*. We did that for decades where we're only collecting urethral isolates (GISP), and the data was being used to revise gonorrhoea treatment guidelines and to revise, and then we addressed the limitation of not having extragenital isolate and female isolate by introducing eGISP and SURRG.

And then the question is the SURRG site, they were doing rapid testing, rapid susceptibility testing using *Etest*. So, it can be actionable. You are not just collecting isolate and putting it in the freezer. However, the concern was only nine jurisdictions were being funded to do that work. And they're like, "Can we expand that? Make it more representative as in Seattle, San Francisco? I mean, they're on the West Coast, we know what is going on there. Can we make sure we are more inclusive?" I'm not going to speak for CDC, how they made the decision, but they expanded all the CARGOS site that have not been doing *Etest*, that were not part of SURRG. They are building the capacity to be able to do that, to be able to do actionable testing, to have collaboration between epi (epidemiology) and labs so that you can follow up, you can respond when there's emergence of resistance. And then they are also supporting molecular testing, the development of molecular assays so that you can do some population-level surveillance.

However, I don't know how you will feel if you've participated in GISP since the inception, and now you get cut, and you cannot continue. So, we went from 32 to only 20 sites that are contributing data to the Gonococcal Antimicrobial Resistance Surveillance.

Another point I want to mention, *Neisseria gonorrhoeae* culture is not available in all labs. Most clinical labs do not do culture. And so, some of those culture capacity we've actually lost because if they're not part of GISP and they're already doing that and they don't have the funding, they're no longer going to be doing the culture. So, that's valuable isolate that we're not getting to contribute to our monitoring antimicrobial resistance surveillance. But I knew for sure CDC looked at the pros and cons, and I'm sure the pros did outweigh the cons, but I cannot speak for that.

Dr. Ramchandani

Can other sites send samples to the sites that are participating in the new program?

Dr. Soge

No, because there's no funding to support that. And one of the things that happened with the first year of CARGOS actually was the rectal culture and female culture became an optional activity. And so, you're only required to culture urethral and pharyngeal from the first 25. So, a site like Seattle, we continue doing that and we are able to justify it. But some CARGOS site, they only culture the urethral and the pharyngeal, the pharynx. And the reason, the justification was, one, pharyngeal gonorrhoea is much more difficult to treat because of other things like availability, bioavailability, and penetration. Also, because of commensal *Neisseria* species that are in the pharynx, the isolate from the pharynx tends to be more resistant than those from the rectum and from the genital site. So those sites do not have enough money to even culture rectum.

I don't see why they would take samples plus that data will not go to CDC because the CDC funds you as a jurisdiction and you can't just take specimen from a former GISP site that is no longer being supported. So, you will think that will go to CDC for testing or it will go to the regional lab for testing, but they use agar dilution. And CDC did support Maryland and Washington State to do *Etests* for treatment-failure cases. And that funding did not continue in this new cycle of funding. So, there's a lot going on, which I think it has to do with funding that was available and they didn't have enough funds to support all the CARGOS sites to do that or to keep all the GISP sites, all the 32, to continue as a CARGOS, but that will be a very good question for the [CDC] Division of STD Prevention. Whenever you interview them, you can ask question about CARGOS.

Dr. Ramchandani

So that was really helpful in understanding how surveillance has changed over time in the U.S. and how it seems like the type of testing that's done for *Neisseria gonorrhoeae* resistance is more actionable to help treat the patient as well as prevent transmission of potentially resistant organisms.

[cargos-first-year](#)**[18:20] CARGOS: First Year**

It seems like the data that we're getting is less because the number of sites potentially have decreased, although we're now using extragenital sites to evaluate as well.

Dr. Soge

That's a good summary, but I have to be cautious to say that. The reason is because this is just year one of CARGOS. You don't know what will happen in year two because CDC got all the comments, all the feedback, especially from the SURRG sites. Another thing with CARGOS, the clinics with SURRG you were required to partner with non-STD clinics. And so, we partner with like eight non-sexual clinics, not categorical STI clinics. With CARGOS, they only funded us to work with the sexual clinics, so we had to terminate all our collaboration with the non-sexual health clinics that we built over time. And so, CDC had all the feedback. And, if funding becomes available, I think they probably will support collection of rectal specimens, as well as collection of isolate from women.

However, I don't know whether they will go back to the 12 sites that were discontinued and say, "Hey, we want to hire you to become a CARGOS." I don't know how that will work, but I think the decision probably was taken due to concerns about funding. But, definitely yes, the isolate we're getting are reduced. And the reason why I can say that is because I'm also the lab doing the agar dilution testing. I'm part of the AR, Antibiotic Resistant Lab Network, that performed the regional lab that performed the antimicrobial susceptibility testing using agar dilution for the Washington State. So, Washington State Public Health Lab[oratories] is the grantee and I'm like a subcontractor to them, so I work with them. So, I've seen that there's been a reduction in the number of isolate we're getting. You expect there will be reduction because such sites stopped doing rectal culture, and they stopped doing female culture, and also you tell them no more than the first 25 is what they should be collecting.

So, there's been reduction, but I think CDC made a decision with the understanding that they will still get enough data to continue to systematically guide the selection of the most effective treatment for gonorrhea. So, I'm sure they've talked about this and the decision they have made is in the best interest of the field and also in the best interest of "Well, we'll make sure we have good evidence to select effective therapies." But actually, I would hope that we have more funding to be able to keep all the GISP sites and to be able to get the same data that we were getting before and not reduce the number of sites that are participating in CARGOS, so I want to wish CDC well and hope they get more money.

[global-antimicrobial-resistance-surveillance](#)**[21:25] Global Antimicrobial Resistance Surveillance**

Dr. Ramchandani

Tell us a little bit about surveillance for antimicrobial resistance for *Neisseria gonorrhoeae* in other countries. How do they compare to what we're doing here in the U.S.?

Dr. Soge

I'm not biased. I think we're leading in terms of surveillance of antimicrobial resistance, the way we are systematically collecting isolate, collecting data. And we've actually addressed the limitations of not having extragenital isolates and data from the rectum specimen as well as pharyngeal. So, there are other surveillance programs in other countries. How do they compare? Every country is different. Like the United States, we're a big country. We're not going to compare ourselves to Australia, but the goal of surveillance is to have useful data that will guide the selection of effective treatment for your country. And so, it's the same goal wherever you go where they have the surveillance program is to be able to generate data that will guide them to select effective therapies.

WHO has been doing a great job trying to expand surveillance to low-resource countries where they don't have the resources, they don't have the tools. They're not like the United States, they're not like the United Kingdom, they're not like Australia. They're not like Europeans because Europeans have their own surveillance program, UK has its own surveillance program, Australia has its own surveillance program, Canada has its own surveillance program, which there's some similarities, but they are not exactly the same.

For instance, in United Kingdom, they only will collect isolate from July to September. And then they collect urethral, they collect rectal, they collect pharyngeal, and then they send it to the regional lab, and that's what they do. It's just during that period. Whereas, in the U.S., throughout the year we collect, and we've been doing that since 1986. So, we spend more on that surveillance and I'm hoping that we will continue to do that. So, I think our own surveillance is more robust because even with the designation of *Neisseria gonorrhoeae* antimicrobial resistance as an urgent threat, we got more money to do more because what we were doing before then wasn't as robust. And now we're doing all genome sequencing of a subset of all the isolate that we collect just to understand the genomic evolution of antimicrobial resistance.

So, WHO has been working with CDC and that collaboration has been pushed right now. And that's what allowed us to get data from Cambodia, to get data from Vietnam, from Thailand. And the EGASP, which is the Enhanced Gonococcal Antimicrobial Surveillance Programme, spelled in the British way, with the double *m* and *e*. The goal of that project, they are not doing any extragenital collection. It's all urethral from male. And then the goal is that from each country in a year, you collect 100 isolates. And as you can tell, it has to do with investment, it has to do with amount of money that is available to do that, and that is being useful to actually get data from Philippines, from Cambodia. So, they're not looking at their neighbor, "Oh, no resistance. So, there's no resistance here." They're not extrapolating. It's allowing us to get data from individual countries that can be used to guide the selection of effective therapy for gonorrhea treatment.

So, regardless of where the program is, the overall goal of a gonococcal antimicrobial resistance surveillance is to generate data that would let us know the trends in antimicrobial susceptibilities of *Neisseria gonorrhoeae*. Which will be used to guide the selection of effective therapy for gonorrhea, and whether you need to revise the treatment guidelines or whether the treatment guidelines works just fine or not.

Dr. Ramchandani

Yeah, and also help with prevention too.

Dr. Soge

Yes.

Dr. Ramchandani

Right, especially in terms of the dissemination of those resistant isolates in the future?

Dr. Soge

Yeah, I agree. Exactly.

[m-genitalium](#)[25:37] **M. Genitalium**

Manhart LE, Leipertz G, Soge OO, et al. *Mycoplasma genitalium* in the US (MyGeniUS): Surveillance data from sexual health clinics in 4 US regions. Clin Infect Dis. 2023 Nov 17;77(10):1449-1459. [PMID]

Dr. Ramchandani

Has there been an increase in antimicrobial resistance and other STI pathogens besides *Neisseria gonorrhoeae* that we need to be aware of?

Dr. Soge

I think we should be aware of resistance in *Mycoplasma genitalium*, and it would be nice for you to have a podcast on that because *Mycoplasma genitalium* infection is not a notifiable infection in the U.S. But, right now, CDC is actually putting it on a watch list that is something we should be looking out for because right now there's been high percentage of resistance to azithromycin. It's not a good drug and it's difficult to culture *Mycoplasma genitalium*, it's not like *Neisseria gonorrhoeae*, so only specialized labs, few labs can actually culture it. And for many years there were no FDA-cleared assay to do the test. So, we didn't have a nucleic acid amplification test, but now we do, going into 10 years now. I don't know exactly when it was approved.

So now we know there's a lot of *M. genitalium* infections, and now there are lab-developed tests to look at resistance. There have been some commercially available tests, which none of them is FDA-cleared to look at resistance. Some of them are CE [Conformité Européenne (European Conformity)]-marked. In Europe, you get approval and then you can use it, but in the U.S. none of them is being approved by FDA. So, we've seen a lot of macrolide resistance, there's some fluoroquinolone resistance. And what happened was there was a surveillance that was started, which Hologic supported, called MyGeniUS, and the University of Washington with Dr. Lisa Dr. Manhart and Dr. Mark Goldin as the Co-PI [Co-Principal Investigator], and I'm a co-investigator on that, surveillance to look at *M. genitalium* infections in the U.S., which a few sites that were included. And we have used the Hologic ASR, Analyte-Specific Reagents, to look at resistance. So, there's a ton of macrolide resistance, and now we're doing PCR [polymerase chain reaction], doing sequencing, looking at fluoroquinolone resistance as well. We should worry about *M. genitalium* infections becoming untreatable.

Dr. Ramchandani

I just want to say, thank you, S.O. That was an incredible review of antimicrobial-resistant *Neisseria gonorrhoeae* and the surveillance that's being done for this pathogen.

Dr. Soge

Well, thank you so much for having me. I surely did have so much fun, and I would love to come back anytime. Thank you.

[credits](#)[28:10] **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. Thank you for listening and have a wonderful day.

