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9TH ANNUAL NYS SEXUAL HEALTH CONFERENCE: EMERGING ISSUES AND PRACTICE UPDATES - DAY 1

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[video transcript]

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Today's topics is antimicrobial resistance and cockle infection. And I'd like to introduce our three speakers. We wanted to approach this with a 90 minute panel discussion, focusing on the epidemiology of gonococcal infections, a clinical take on antimicrobial resistance and gonococcal infections, and also emphasis on laboratory methods and we are really delighted to welcome our three speakers include Dr. Wilson, Miranda, who has worked in public health for over 18 years, with a primary focus on communicable diseases, particularly TB, HIV and STIs. He currently serves as the head of surveillance and special projects in oshi, the Office of sexual health and epidemiology at the New York State Health Department's AIDS Institute. In this role, he is responsible for the oversight of statewide STI surveillance and research, partner services related surveillance, collaborations and system enhancements and efficient efficiencies. Our second speaker focusing on the clinical aspects of this topic is Dr. Michael ag Aachen from Dr. Obregon Ogden brown upon graduation from medical school at the University of Rochester pursued his residency at the North Shore University Hospital and then an infectious disease fellowship at SUNY Downstate is currently the Director of the Division of infectious diseases and the program fellowship director at SUNY Downstate Kings County. He is also professor of medicine and Epidemiology at SUNY Downstate and Vice Chair of the Department of Internal Medicine. In addition, he has been directed for the Kings County Hospital centers STD clinic for many years, has served in an advisory capacity for both the CDC STI treatment guidelines, and the New York State Department of Health AIDS Institute guidelines. And finally focusing on migratory infections. Dr. Karen Mitchell joined the Wadsworth center in 2010. As a Wodsworth center, emerging infectious disease postdoc fellow postdoctoral work at the Center include a training in the blood borne viruses laboratory, the bio defense laboratory and the micro bacteriology laboratory. In 2013, Dr. Mitchell joined the bacteriology laboratory, and is currently the director of bacterial reference and special projects. Wadsworth center, bacterial bacteriology laboratory serves as New York State Public Health reference laboratory, providing bacterial identification and characterization. So with that, I'll turn it over to Dr. Miranda, to review the session learning objectives and begin his focus on epidemiology.

02:53
Good afternoon. Thank you very much, Dr. Urban. First, can I get confirmation that my screen is visible? Looks good. Thank you so much. So thank you. Again, this is quite a privilege. I'm very honored to join my two esteemed fellow presenters, Dr. Ogun Brown and Dr. Mitchell. What I'm going to do is briefly cover the epidemiology both nationally and in New York state of gonorrhea. Then we're going to go into surveillance of drug resistant or reduce susceptibility Gonorrhea. And last we're going to talk about patterns of presentation of resistance. And then I'm going to switch it over to Dr. Ogden brown. So first, this is the most recent year of data that we have available nationally. We are in the midst of a public health sexual health crisis with regards to STIs. The infections continue to forge ahead, compromising the nation's health. In 2021, more than 2.5 million cases of chlamydia, gonorrhea and syphilis were reported. As you can see, from

these numbers, with regards to gonorrhea, there was a 28% increase in the number of diagnoses since 2017. In New York State, including New York City, there were approximately 9000, early syphilis diagnoses 43,000 gonorrhea diagnoses, over 101,000, Chlamydia diagnoses, and sadly, an additional 41 cases of congenital syphilis and newborn infants. So this is the historical slide for the nation. This basically shows the rate of reported gonorrhea cases since 1941. Gonorrhea became a nationally notifiable disease in 1944. And you can see the rises and the drops in the number of in the rate of gonorrhea over the years. What I We'd like to focus on are the two orange arrows right here, which indicate that these were the rates that we see in 2021. The last time similar rates were seen were in the early 1940s. And then just before the 1970s, and they both coincided with increases, very high increases, in fact, in gonorrhea diagnoses in the country, and we are on a similar take in gonorrhea diagnoses, and at this point, we do not see a decline, and it's going to continue to go up. This slide here represents the number of diagnoses in New York state including New York City, the orange portion of the slide represents counties outside of New York City, the lilac portion here represents the diagnosis in New York City. This is since 1960, all the way to 1920 to 2021. Similar picture nationally, we mirror the country as a whole. While most of the cases tend to be in in New York City. The rest of state tends to follow a similar kind of like a path but with lower number of diagnoses. What's really interesting here to see is that New York state as a whole hit its peak in the mid 1980s. And then with tremendous investment in public health, focus on disease investigation, Partner Services, appropriate use of antibiotics, and all of that, we were able to really bring down the numbers. And the lowest state saw in terms of numbers was in 2009. That was the lowest number of diagnoses. And then since since that period, there's been a rapid uptake, an escalation in the number of new diagnoses of gonorrhea. And as you can see, 153% increase since 2009, which is tremendously concerning. So in this slide, this is the, again back to the national picture in terms of sex of persons diagnosed with STI and race and ethnicity. So in 2021, the rate of reported gonorrhea was higher among men, that's 249 per 100,000, compared to women, which is which was about 177 per 100,000. Now, among men, those aged 20 to 24 years had the highest reported cases of gonorrhea, 844 per 100,000, followed by men in the age group of 20, to 25, and then 30 to 34. Now among women, the the only time you'll see this, women having a higher rate is in those that are aged 20 to 24, where they were 873 per 100,000 compared to males. And then again, the rates in those between 15 and 19, and 20 to 2525 to 29 are quite high, and then it starts to decline. But so what it's giving you a picture of is is that those in the in the 20 to 3029 to 30 age group are bearing the brunt, or the highest number of diagnoses in the country. Again, when you look at it, by sex at birth, and race and ethnicity, again, the distribution among males is quite high compared to females. And when you use the white non Hispanic population as a reference group, you can see that in both males and females in the white population, the numbers are quite low, compared to their counterparts in the Black or African American population, where you see the numbers you know, quite high, and they're they're bearing the the highest burden followed by those in the American Indian and Alaska Native groups. So that's the national picture of, of STI, by race and ethnicity and by sex at birth. Now in New York state, by age, so you can see this breakdown, the blue bars represent males, the yellow bars represent females and again, a similar picture in nationally, between in the 15 to 19 years age group, you're seeing that the yellow bars the females have quite almost a doubling of numbers of rate compared to their males, counterparts of the same age group. But then the switch occurs where after that the male population far highly dominates the number of

diagnoses in 2021. After the age of 24, the decline in the number of females is, is quite steep, but it It is still higher overall for the state. And here's the interesting picture of this, up until a certain point of time, in the early 2000s, the males and the female population in New York State, they were running quite close in terms of their numbers. But in somewhere in the summer after that the Populate the numbers started switching and the gap grew quite large with the male population far exceeding the female diagnoses. We attribute portions of this to be because of men who have sex with men a greater focus and increase in screening. They also happen to be the highest group that are at risk for HIV and other STIs. So more of that population tended to have be diagnosed with gonorrhea. In 2020, once the pandemic started the COVID 19 pandemic started, the numbers switched a little bit to wherein the female population in New York State kind of overtook the male diagnoses. And that population started plateauing out in and in 2021. Even though the male numbers caught up back to where they were pre pandemic, the female population numbers have not declined as much. So meaning that there is a hidden reservoir of of cases out in the general community as a whole. So again, back to the national picture, in terms of where most of these diagnoses are occurring. During 2012 to 2021, the number of gonorrhea cases reported from STD clinics, which are these purple and red lines here for males and females. They decreased about 10.3% among males, and decreased about 25.2%. among females, while the number here that you're seeing non STD clinics, which are urgent cares, emergency rooms, hospital, non traditional STD clinics, they've skyrocketed. So you're seeing about a 202% increase among males, and about 82% increase in females being diagnosed at these non STD clinics. So why is this important? Right? This is important because these these clinics, and these providers, they see a lot more variety of cases and not as specialized in diagnosing and treating as these STD clinics are. And so knowing the appropriate or the right approaches in terms of testing, and especially treatment and dosage, and all of that is critical, especially given that we're seeing a lot more of sexually transmitted infections. One,

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we're seeing newer sexually transmitted infections like M pox, or formerly known as monkey pox, and all of that. And we're seeing new diseases that are developing overseeing diseases that are developing resistance, like for example, the most recent being Shigella. So it is very important that providers who are not familiar or not so used to seeing STI cases, be more up to date in terms of the treatments that are offered and the testing processes and procedures that occur. So just to highlight, this is in January of 2023 of this year, CDC broadcasted a health alert to all the local health departments in the state. Basically, what they were telling us what they're recently to Massachusetts identified two gonococcal infections with concerning lab results. The first case had a cultured isolate, which showed a decrease susceptibility to sift cracks on suffixing and azithromycin. And with also resistance to ciprofloxacin, tetracycline and penicillin. Both the cases luckily, were treated and were successfully clinically and microbes are biologically cured following treatment with software absent so even though they had reduced susceptibility, they were able to be treated with subtraction, which is the current recommended treatment for gonorrhea in the US. So where do we get most of our information with regards to gonorrhea and the susceptibility and resistance pattern? So, what you're seeing here is the map of the United States along with laboratories and testing centers that are specialized specifically for to collect information on reduced susceptibility or drug resistance. These are called jiske or gonococcal. Isolate surveillance project sites. CDC established this in 1986 To monitor trends

with for Neisseria gonorrhea strains in United States in order to establish evidence based rationale for selection of gonococcal therapies, right. So these are considered sub Sentinel surveillance based sites and they collaborate with STD clinics in the state and local public health regional labs and with CDC. So what happens at these sites at these sites isolates are collected a monthly from the first 25 men with symptomatic gonococcal urethritis seeking care at the STD clinics. Additionally, other information that is collected from these persons in addition to samples are clinical and demographic data, which are from their medical record. These isolates are then shipped to participating clinics from the participating clinics to the regional labs, and then to the top of that are participating in the antibiotic resistance laboratory network. So, in 2020, isolates were tested to determine the mix or what it's called the minimum inhibitory concentrations for penicillin, tetracycline, sepco, acciones, suffixing, ciprofloxacin, azithromycin, and gentamicin. So in 2017, just was expanded in a subset of clinics, clinical sites to conduct surveillance on non urethral isolates. So those isolates coming from pharyngeal rectal and endo cervical isolates. And further CDC also established the enhanced gonococcal isolated surveillance program or II just to help to understand if orange pharyngeal or rectal anatomical sites, they foster resistance or end to evaluate susceptibility patterns between males and females. So now, these sites not just collect 25 isolates from men, but they also collect it from females as well to understand the changing patterns. So, as you can see from this infographic, this is data from all the way from 1988 to 2021. It basically shows the, from these clinics from these job sites, the medications or the antibiotics that are used to treat gonorrhea over that time span. So in 2021 6%, of just participants were treated with software X, and 250 milligrams, and 88.5% were treated with SEF crops and 500 milligrams, which is, which is now the new treatment approach advocated by CDC, with their treatment guideline changing in 2020. What has happened is that during the 1990s and 2000s, the flora quinolone resistance started emerging in the United States and became prevalent first in Hawaii and and California. And we're seeing mainly men who had sex with men, and eventually that spread to mostly United States. So what CDC did in 2007, based on studying the different patterns of resistance, is that the stopped recommending fluoroquinolones for treatment of gonorrhea and now cephalosporins are the only remaining recommended antimicrobial class. Additionally, as some of you might be aware, when you treat for gonorrhea, they also simultaneously treat for chlamydia because there is a high likelihood of CO infection or comorbidity occurring. So to ensure treatment of CO occurring pathogens like chlamydia, and reflecting concern about emerging gonococcal resistance, CDC in the 2000s in the 20 in 2010, recommended a combination therapy for gonorrhea with with self correction 250 milligram intramuscular or suffixing, 400 milligram orally, and they also added in azithromycin, orally or doxycycline, orally for for for chlamydia, even if the if the nucleic acid amplification was negative at that time. So the follow that approach to treating a both chlamydia and gonorrhea

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so now,

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what we're seeing here is the different patterns of elevated MCs, minimum inhibitory concentrations for azithromycin suffixing and Steph Curry axon from these jobs site. So between 2012 and 2021, the percentage of gonorrhea isolates collected from these clinics In

that exhibited SEF Triax zone, minimum inhibitory concentrations, which is defined as greater than or equal to point 125 micrograms, the fluctuated between point one to point three, and percent. So, as you're seeing here, over time, the number of isolates that were showing elevated, minimum inhibitory or mix, two receptor Meissen started going up. And so this informed CDC that they needed to change their protocols to prevent, you know, resistance to azithromycin, not just for gonorrhea, but for all other microbes that as it from mice, and maybe used to be two as a treatment of choice. And, and this, as you see from 2000 to 2019, is all the different antibiotics at CDC and these just sites test for and as you're seeing here, over time, the number of the resistance of these specific gonococcal isolates to ciprofloxacin, tetracycline and penicillin have have increased almost where these are now considered the organisms that are considered to be resistant to most of to these three, with increasing resistance or reduced susceptibility to edit or Meissen. The good news is that suffixing and Saqqara axon still are these micro these gonococcal isolates are these gone, Neisseria are demonstrating not yet demonstrating any kind of susceptor resistance or reduced susceptibility. So these remain right now the treatment of choice and Dr. Ogden Brown will talk more about this in his presentation. Additionally, as you can see from this, the percentage of urethral isolates collected from men who have sex with men who attend these clinics has also been going up. Now, one thing I want to state that, for the longest time, even in New York State, what we were seeing was more of the specimens that are collected from persons who present with with gonorrhea tend to come from urethral sites, that means either a urine specimen or a swab of the of the urethra. But what we highly recommend is that, that the clinicians and collect specimens from not just the neutral sites, but also from the fairings and rec from the rectum, because these are most likely to sometimes be missed. And even if the urethra sites test negative, there's likely to be a positive indication of infection in the fairings or in the rectum. And only collecting from one site is likely to lead to continued transmission, especially in individuals who engage in oral or anal intercourse. So as you can see, with the rise in the number of urethral, isolates collected from men who have sex and men, that were better able to determine what which of these specimens are going to be resistant or compliant, or actually be able to better treat it by anti Mike bill, drugs that are currently recommended. And so from this, we're able to see that the over time, men who have sex with men and men who have sex with women only that the azithromycin resistance has been increasing over time in both these groups. The prevalence of of resistance has been increasing over time, and that has become a concern and and so now, CDC has switched their recommendations and so you're seeing that for the same population, there SEF Triax, prevalence of resistance is not as high and with proper use and and a proper follow up of individuals. Over time. We hope that we will not be seeing any new resistance developing. Now having said that, it is very important that for those individuals who are diagnosed with pharyngeal gonorrhea, that these individuals be invited back after they are treated and tested again to do what is called test of cure, because pharyngeal gonorrhea is notoriously difficult to cure. And so to follow up with these persons that have been diagnosed to ensure that that that the treatment is no has been effective, and the nd microorganism is no longer showing signs or infection in the fairing. So, keeping these keeping these patterns of resistance and these these treatment modalities in mind, we again are recommending that sound clinical judgment be used. That means doing a test of multiple sites Ah urethral sites, pharyngeal sites as well as rectal sites, and then based on that approach, applying the right treatment modality to the organism to

ensure that there is proper cure. So what I'm going to do now is I'm going to turn it over to Dr. Ogun brown to talk more about the clinical aspects of gonorrhea.

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Thank you, Dr. Miranda very much. I want to thank the conference organizers for inviting me to participate and thank my co panelist, Dr. Miranda and Michel for putting up with me and having a little bit of overlap, I suspect. In all of our talks, I've been asked to address the issue of clinical management. And I hope what I have to say in the next 25 minutes or so is useful to people from a practical standpoint. And I'm not going to reproduce for this audience. Presuming that most of the people listening in have some familiarity with STI treatment and references for STI management. I'm not going to reproduce the current recommended guidelines per se right now. Because I assume everybody has familiarity with it. But I just want to post here, what some of the latest updates are. And Dr. Miranda alluded to some of this already. But as was discussed for some years, it had been recommended that combination therapy be used for gonorrhea treatment including ssef Triax, and Ernie zithromax. And, and that is no longer recommended where gonorrhea is the disease of concern. And azithromycin was eliminated as a recommendation in part because of rising rates of resistance and also concerns about excess utilization of Asia throw mice and in the community for reasons that are not necessarily wanting to. I'm not sure we're having that much of an impact on community wide use of Asia through Meissen just because we're restricting its use and gonorrhea treatment. But that's for another discussion. The Ceph Triax on dose has been increased as you well know from recent 250 milligrams to 500 milligrams I am once and that's also modified to suggest use of a full gram for people weighing over 150 kilos, which is over 300 pounds, pharyngeal infections of any sort and receiving any sort of treatment now require test to cure at seven days. And I'll get back to this issue. But you have to be a little bit circumspect about test of cures using nucleic acid amplification testing modalities. As I think anybody here can appreciate these are highly sensitive tests. Dr. Mitchell, I'm sure we'll talk about some of this and you run the risk of non specificity. When you do a nats test too soon after treatment, you may actually find that the test is positive but the person doesn't really have representative organism at the site of infection. So you have to be a little bit careful about interpreting the results of nats tests early on. I wish I could tell you how many days it takes to eliminate exactly the remnants of gonorrhea after successful therapy, but I'm not sure anybody really knows seven days is probably an adequate period of time. But patients don't read the textbooks as you well know. And so some people are going to be falsely positive that seven days too so just keep that in mind. For comparison, I also put up other recommendations the I use the recommendations from 2020 Does the International Union of STI treatment, a global organization they recommend safe tracks on a gram with or without a azithromycin and the British STD and HIV treatment guidelines recommend SEF Triax on one gram. So our colleagues in other parts of the world recommend somewhat more safe tracks and when we do hear as alternatives the CDC recommends that gentamicin can be used to under 40 milligrams I am once plus a zero Meissen two grams orally once or suffixing 800 milligrams orally once but you need a test of cure to be done with suffixing therapy and I think Dr. Miranda alluded to worsening susceptibility for suffixing certainly when compared to SEF Triax on I think suffixing utilization has been of concern for some time. And right now the recommendations are for for pharyngeal infection itself trioxide will be the only drug use and as the fixing not be used in that circumstance. And again test a cure should be done for all treated

pharyngeal infections. And those are sort of the updates in the CDC recommendation. Now, how we got here shouldn't be that surprising. The story of gonorrhea, acquiring resistance is older than I suspect anybody in the audience right now. In fact, from the very onset of the availability of antibacterial agents in the 1930s, I'll say GC has declared itself somewhat unique in its capacity as a community acquired organism to develop step by step by step by step resistance to almost every antibiotic we throw at it. This is very unusual. I mean, we usually talk about multi drug resistant organisms, TB not withstanding, we're most of us used to talking about hospital acquired pathogens. But here's a community acquired pathogen, that it's just regularly thumbed its nose, let's say, at every antibiotic that we've used against it. And this timeline has been reproduced many times in the 1930s. It was the introduction of sulphonamide, anti microbials. They were very effective initially, but within a short period of time, they lost efficacy. And thankfully, shortly thereafter, we had the introduction of penicillin antibiotics in the 1940s, the new miracle drug, and within a couple of years to several decades, penicillins became useless, and so on and so forth. tetracycline, were used for many years in the 80s. They were no longer considered useful. When I first started in practice fluoroquinolones, were going to be the new miracle kid on the block, and we use fluoroquinolones quite frequently for the treatment of gonorrhea, but they too, have become useless in the face of marching resistance. And then as was discussed, we have this issue around suffixing. And then SEF Triax underneath zero Meissen. So there's no reason I hate to say this pessimist somewhat pessimistically, I suppose to think that whatever we decide to do GC is going to stay one step ahead of us. And we have to stay nimble and continue to develop effective therapies for this organism. But it is troubling and it's been going on for a long time. And if you'll if you'll permit me for a few minutes, just to show you some things that I've collected over time that relate to previous treatments for GC that no longer are considered effective, or reasonable. Here's a monograph from latterly, which was a drug company that first brought out sulfa Daya zine in the 1930s in the 1940s. And these were abstracts pertaining to sulfa dicing views for various treatment of various infectious diseases. And I would have to say that they were probably more abstracts in this monograph pertaining to sulfa Dyson's use for John gonorrhea than anything else. There were six or seven of these things, and they all touted the miraculous efficacy of sulfa. Daya zine. Here's a study in Pennsylvania in Philadelphia treatment of gonococcal urethritis 200 cases 96% were apparently cured. Here's a another study from London that suggested that all cases were rapidly cleared up and the drug was well tolerated. Just taking a step back a little bit further from the introduction of the sulfonamides. Here's a pamphlet that I don't know where the heck I came up with this thing. But this was put out by Abbott Laboratories in the 1920s for something called meta Fenton in the treatment of gonorrhea, and medicine is I've come to discovers a mercurial compound that has to be used topically if you're as old as I am, you probably remember being painted with mercuric Rome for almost any infection, topical infection. Well, here's a circumstance where they were actually instilling mercurial compounds into the urethra, in an effort to eliminate gonorrhea. Just try to imagine that urethra is irrigated with warm one to 8000 potassium permanganate solution. There's instructions on how to do this. And then if you take a step back even further, into barbarity, let's say, when there were no pharmacologic agents that were felt to be successful for treatment. What often ended up happening was people develop urethral strictures from chronic inflammation, and they had to undergo treatment with one of these medieval looking devices which are ureteral dilators to To

break the strictures, so I guess we should consider ourselves somewhat lucky to have SEF Triax on still available to us.

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Now, when you think about resistance to GC, you know, in the old days, we would probably know pretty quickly if there was resistance to GC, because we used to assess GC infections using these techniques. On the left hand side is the classic candle jar that we use to send specimens to the labs with in the middle is something called a Gen backplate, which was a commercially prepared chocolate agar plate with additives and a little co2 dispenser that created the proper environment for growing GC. And then the lab could actually as on the right, do a variety of tests to try to determine susceptibility. So we knew when we were testing people for GCC, who had potential resistance and who had who didn't have potential resistance. Now, of course, that's not true. Because these are the tests that we generally use. And I'm sure Dr. Mitchell will talk some more about this. But you know, the miracle of nucleic acid amplification tests in terms of their sensitivity, certainly for chlamydia infection, shouldn't be downplayed. But by the same token, we don't really come up with rapid turnaround results for resistance. And we have to depend oftentimes on surveillance systems to tell us if there's resistance in the community. And one of the problems that comes up and this has always been I think, a big problem in STI care, is if you think you're dealing with resistance, how do you know it's resistance or failure of therapy versus reinfection? It's always been a problem, I think, well, you know, you should suspect treatment failure if symptoms don't resolve within three to five days after treatment, and those without sexual exposure, post therapy. Of course, you know, it's always questionable whether we're getting accurate histories and can say that people haven't been exposed within a couple of days after treatment. But sometimes you can rely on that history. most effective therapy for gonorrhea should result in significant substantial resolution of symptoms, perhaps not complete resolution, but substantial resolution within three to five days and if somebody's not responding properly, and resistance has to be considered. Second bullet suspect treatment failure if nats test remain positive, again, more than seven days post treatment without sexual exposure, post treatment, and it gets back to this issue that I mentioned before, which is nats tests ought to become negative, as you move out a week to two weeks from successful therapy, if they remain positive is a concern that you haven't eliminated infection. And of course, you should suspect treatment, failure of susceptibility testing suggest this if you have that available. So what does the CDC say in terms of treatment failure? If you think treatment failure is suspected? Well, first of all, this is a big problem, as I think everybody will allude to, during this session of talks, we need to be on top of this issue of our treatment failure. So the first thing is you need to obtain specimens for culture and Nat and testing by E test this diffusion or Agra dilution. So in your clinical setting, you have to have some mechanism for obtaining cultures, even if you're regularly doing nucleic acid amplification testing, you have to be prepared, that if you have somebody who fails therapy, and you think it's because of failure therapy, not reinfection, you have some mechanism for doing culture, because that's not going to tell you whether you have resistance or not. The second thing you wouldn't be doing is contacting a public health agency in your jurisdiction, that would be probably for many people be the city, New York City's Department of Health with the New York State Department of Health, you should be prepared to do that because again, this is something of a public health urgency. What do you do for the patient in front of you? Well, most recommendations say right now treat

again with routine regimen such as F Triax. On 500 milligrams I am once and we'll talk a little bit more about that. And you should switch off if they're getting suffixing because it concerns about suffixing truth suffixing decreased susceptibility gives f Triax on if they got suffixing. You can consider as mentioned before, the alternative to save triaxial which is gentamicin to under 40 milligrams I am once plus oral azithromycin two grams orally once. Now I don't know the members of the audience here if they have access to im medication in their clinical setting. Some people probably have to send patients to emergency rooms or urgent care centers. Some people may be put off by the idea of having to give im injections agenda Meissen and aminoglycoside. Concerns about nephrotoxicity and ototoxicity. I will say that you know, single doses of aminoglycosides like gentamicin are probably not concerning so far as nephrotoxicity. Odo toxicity are concerned, it's prolonged administration and elevated levels, they're of a concern. And you could stock this medication if you were so disposed to give im injections in your clinic. And of course, you need to evaluate any sex partner during the preceding 60 days. A presentation. Now, if you're not really comfortable, and you're not sure, and you really want some guidance, you have lots of opportunities, lots of people you can turn to first of all, I certainly would urge you to consider turning your infectious diseases colleagues in again in your clinical facility are in your area. You can contact the National Network of STD clinic clinical prevention training center via their consultation lines available online that through the CDC, the CEI line, Dr. Irvin assures me that the I guess he used to refer to it as a warm line. I don't know if it's become a hotline now. But that number certainly can be used. It's in the slide set and in your materials that you've been giving, you can make use of that. If you're seeking guidance in terms of treat treatment, and another CDC number, the 800 number can be used. So there's lots of resources that you can turn to if you need guidance, or just a sounding board to discuss whether you think you're dealing with resistance and how best to approach a patient like that.

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Know what other options exist we talked about retreating with Ceph Triax and we talked about giving gentamicin Well, the development of novel alternative GC therapies has been a national priority for over 10 years, but progress has been slow. As most of you are probably aware of the development of new antibody bacterial anti antibiotic agents has slowed. The drug companies have mostly turned their attention to other drugs and are not developing antibacterials and antibiotics quite like they were 30 years ago. But several agents have entered advanced clinical trials, there's reason to be somewhat optimistic about this. I'll mention some of them. So lythrum ISON was a drug that generated some interest a number of years ago, it's a fourth generation macrolide keto light related to AIDS allies like exito mice and unfortunately, the solitaire you trial data published in The Lancet infectious diseases within the last couple of years, which was of an open label non inferiority trial outcome being microbiological eradication after seven plus or minus two days, for uncomplicated general GC showed eradication of only 80% and those receiving so lythrum Meissen versus SEF Triax, RNA zithromax. And where eradication was 84% and hence the drug was felt to be not non inferior. I hate double negatives, but there you go, not non inferior adverse events were also more common with dilithium ice now you may notice of course, that the response rate the even those getting set Triax on a zero Meissen was rather low as well. But I think this was in an intention to treat analysis and so people who didn't show up were regarded as failures as well. I think for those people who they had microbiologic data 100% of people getting subtracts on a central Meissen cleared infection but they were

clear failures with so lythrum Meissen. So as far as I'm aware, there are no further ongoing studies looking at so lythrum ISON um, it's a little more hopeful in this areas of lift validation and gentler Tennyson are both novel DNA Topo isomerized two inhibitors. Now these are drugs with mechanisms similar to the fluoroquinolones but with different indistinct binding sites. So although resistance rates to fluoroquinolones have reached as high as about 30% in the community, these agents are believed to retain activity against GC. And a couple of publications suggest that this is true. Taylor published a study in the New England Journal a few years ago of a phase two trial, uncomplicated Euro Gen GC, there were 179 participants, there were two doses of drugs study drug being examined versus standard safe Triax zone, and the microbiological rates were excellent 96% 96% and 100%. From commented rectal infection, but not pharyngeal infection was also eradicated. And I think Dr. Miranda alluded to this before, and I'm not going to dwell on it. But pharyngeal infections are really a problem with GCC and need to be monitored closely. And we need to again sort of get our game up in terms of doing three side testing, and pharyngeal testing because it is problematic and needs to be monitored carefully. Adverse effects were a bit higher and steady arms for success Triax Oh, it was mostly GI and it wasn't terrible. And there are, as I understand it, now, phase three studies underway looking at Zola days and versus SEF Triax on and hopefully we'll get some results, and maybe this will be a promising drug for us. And the same could be said for jepto, Tennyson. Some of the same authors published data on this particular drug in the Clinical Infectious Diseases journal again, in sort of the same period, again, a phase two trial, many fewer participants, there were two doses studied, the overall eradication rate, again, was excellent 96%, no significant adverse events. And here two, phase three studies are ongoing. And so hopefully, we will have some information in the not too distant future about whether these drugs will be useful. And I would like to just say that, you know, a cautionary tale These findings are promising. But if the past is prologue, then there's no reason to suggest that these drugs are going to even if they turn out to be efficacious, they're going to retain efficacy forever. And so we have to think about other strategies and continue efforts to develop new agents. One of the things that's drawn attention is the idea of repurposing older antibiotic agents for the use of against the treatment of GC. And there was a published trial in the Netherlands, called the new BOGO trial. I don't know what that stands for something in Dutch, I suspect, looking at ertapenem, which is a carbon Panem that we use sometimes because of ease of efficacy, a single day dose treatment for patients that can be discharged getting a carbon phantom doesn't have Pseudomonas activity, but it's otherwise a very broad based active agent. It has activity against GC. In this study, they looked at it versus Sef, triaxial, djent and fosfomycin, which you may have some familiarity with fosfomycin. It's a phosphonic acid derivative that's being used now for resistant urinary tract pathogens. They include anal rectal Yura Gen GC patients, and checked eradication by gnats after seven days. And ertapenem work great. It was 100% safe trachsel is 99%. The fosfomycin You'll notice was terrible 12%. And so our dependent was felt to be non inferior compared to safe Triax on and I think that that holds some promise for us. I don't know where the guidelines folks are going to come out on this. I'll mention two other drugs that just out of curiosity sakes love fabuland is a fluro mutal in drug which is quite different from most other classes of drugs, that's released for use for community acquired pneumonia. It appears to have a quite broad activity against a whole range of STD pathogens, but it's a complicated drug. It's got a lot of drug drug interactions can't be used in pregnancy. And I don't know if there are any studies ongoing right now looking at it. Somebody asked me about AIDS as tree Anam, which is a drug

it's been around for a long time. This drug actually does mono back tam related to beta lactams carbapenems it has GC activity and could conceivably be purposed for this. But as far as I know, there are no clinical trials ongoing right now. Dr. Miranda alluded to the some of the epidemiology around this. I mean, thankfully, although we talk a lot about this, it hasn't been a process that's taken off with alacrity in the United States. And he mentioned this report from the Massachusetts states lab, just in January of this year that reported on two cases, one with Frank urethritis. The other one was on screening that had SEF Triax on mi C's of one mic per ml with a susceptible range is considered less than point two five mites per ml. And these were basically isolates resistant to most everything else. And when they were studied closely, they were found to have complex mosaic pen a 60 allele mutations, which affect penicillin binding proteins, and it's not a single mutate point mutation. But these are usually complex mutations, and I'll get back to that in a second. And the strain typing that was done suggested that this was a strain type that had been seen in Asia and Pacific in the Pacific for many years actually now, and keeps cropping up as a strain associated with GC resistance to SEF Triax on. But remarkably, both cases were treated successfully with standard therapy and 500 milligrams by himself Triax on. The first such case, though, in the United States was reported a couple of years back in Las Vegas, this was a case of your thright is also treated with what was at that time standards have Triax on therapy, and they responded to therapy. So it's something that needs to be

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considered.

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I put this here because this is recently reported data as well. This is from the UK 10 cases had been reported of GC resistance SF Triax zone, I cautiously say resistance. And I'll get back to that in a second. This is from December 2021, to June of 2022. It pays to note that, in a period of six years, between 2015 and 2021, there were nine cases, so 10 cases in a six month period, suggest a remarkable increase the numbers of cases, eight out of 10 of these individuals had traveled outside of the UK or had contact with travelers, again, this nexus with people from Asia in the Pacific, perhaps transmitting infections. And there were a mix of symptomatic and asymptomatic infections, eight of them were treated with a gram Assef Triax zone to receive a zero all had negative gnats and cultures by two to three weeks. And again, here's the strain type 8123. That came up. And I put this up as just sort of a brief survey of a variety of other reports that have appeared over the last several years in the literature, of failure of therapy and rising NICs in SEF Triax zone to SEF Triax zone amongst GC isolates from all over the world, from Asia, England, continental Europe, Australia, so on and so forth. And this stored items are specimens that only came to light from surveillance, the others are a lot of one off cases with people with clinical disease. And just to make the point is that in most of these cases, people were clinically cured with increased doses of SEF Triax zone, not a lot of need to resort to other therapies. So why does that Triax on seem otherwise successful when we keep talking about resistance? Well, I think it's important to understand that CLSI that determines what designates resistance and susceptibility, and again, I suspect Dr. Mitchell, we'll get into this a little bit more, has not established breakpoints for the resistance in GC isolates. We know that there's reduced susceptibility, but what constitutes resistance where we can't use a drug effectively anymore

has not been well established. So we know that drug bugs with MI sees below a certain point, they're susceptible, above a certain point maybe less susceptible, but not necessarily resistance resistant. And you can understand that you could probably push the dose of the drug up high enough that you might actually be able to eliminate infection. And I think that's what we're seeing with many of these cases, beta lactams rely on concentration dependent killing, you need to maintain levels above the mid of the organism for a set period of time, in this case, maybe about 24 hours, and then you can get killing. And so higher doses may achieve the goal for now. But that doesn't mean it's going to continue forever. So I think, again, besides developing other drugs, I think one of the other things is we need to think about out of the box, we need to think about other approaches to GC and GC control from a clinical standpoint, in order to get a handle on this problem. It's also interesting to note that, in many of the instances, as I've alluded to some of the strain typing suggests that there's clonal expansion here of single clones that are causing disease in these communities that are seeing these infections. So that with proper public health interventions, you could conceivably control this because it's coming from one place spreading to a variety of susceptible individuals. I mentioned just a couple of things here to say that I think that these things have some bearing on this. I think screening measures are critically important. We need to up our game in health care to include routine screening, where it's been indicated in the CDC recommends in women Euro genital testing under 25 years and old Over at risk, extra genital testing based on risk at the moment in males. Neither the CDC or the USPS TF recommend testing those at standard risk. But that may change for MSM are those on HIV PrEP, Euro general and extra general testing should be conducted on three to six month intervals. And we need to be doing this I dare say that we're not as assiduous about this as we could be. Other things I think that are important that come to mind are the availability of point of care testing. And I'll say a little bit more about this. But there are GC point of care test systems that look pretty good. And again, I think Dr. Mitchell may allude to some of this. They include products from binax, Visby, and BD is in trials right now that don't have something at market and these are currently FDA approved and CLIA waived, and I think they would have a role here in helping us control this. Rapid resistance testing is another strategy that might enable us to control infection in the community better, expedited partner therapy, vaccines, and post exposure prophylaxis, other strategies to name just a few. Point of Care tests I alluded to those I just mentioned, this is an article, the lead author's name was Stracke, or appeared in sexually transmitted diseases earlier this year in the Baltimore City STI clinic. Nobody should be that surprised about this 26% of men and 64% of women with GC, Chlamydia diagnoses receive same day treatment, which means a whole lot of people are not getting same day treatment, which means these people can go out and spread infection or may not actually ever get treatment. So again, point of care testing seems to have a role here. If we can give people immediate diagnoses, and treat them right away. I think that that would be useful. It's almost like the HIV cascade and linkage to care. You know, we've demonstrated that we have more success if we move people rapidly to therapy and I suspect the same can be said for STI treatment. resistance testing by molecular means. You know, I in passing, I sort of alluded to the fact that beta lactam resistance like SEF Triax, on resistance is genetically complex, but fluoroquinolone resistance is not it's really a single point mutation. And if we can test isolates for the single point mutation, we may be able to determine that isolates in the community are is are susceptible or resistant to fluoroquinolones that we might actually have another arrow in our quiver, as they say, for treating GC and it would be nice to be able to use

fluoroquinolones where they can be used and to avoid using things like SEF Triax zone. And there's a study Jeff Klausner and colleagues published in Cid in 2021, that showed that if they did this, they got 100% response rate in patients who had isolates that were susceptible to fluoroquinolones. And there are commercial tests available in Australia and Europe to my knowledge right now, but not in the US that allow for gnats testing for GC and at the same time, determining fluoroquinolones susceptibility or resistance, so maybe there'll be more to come on this.

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Vaccination

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is an interesting area of vaccine with 50%. Efficacy could decrease prevalence by 90%. Over 20 years if given the old preteens Good luck with that anybody involved in HPV vaccine knows knows that the troubling issues there, but creation of an effective vaccine for GC has been elusive. There's new interest in these men meningococcus gruppi, outer membrane vesicles as a target, and there have been several epidemiologic studies that suggest that people who have gotten the men B vaccine for prevention of men and meningococcal infection, demonstrate epidemiologic protection against GC and there's enhanced interest in this. And I think we'll see more literature about this. And lastly, this is a reproduced table from a very recent article in the New England Journal looking at post exposure prophylaxis with doxycycline for STIs. I'm sure the audience is probably familiar with this article. It was showed demonstrate mostly efficacy for the prevention of chlamydia and syphilis. But prevention of GC was nothing to sneeze at either. And I think at here's the data in the PrEP cohort, any GC and any GC and the persons living with HIV cohort, and although the numbers are not as dramatic with as they were with chlamydia and syphilis Was there still was about a 50% reduction in the incidence of GC and those individuals who got post exposure prophylaxis with doxycycline. So there may be a role here as well. And I don't know if people are ready to start to pile into the use of Doxy as post exposure prophylaxis, but I suspect we'll hear more about this as time goes on. And so the future doesn't look too bleak. But I think we have to keep our game up here because GC is a wily adversary. And with that, I guess I'll stop and hand it over to Dr. Mitchell.

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About the laboratory site. So in in 2013, the US in general and CDC really started to put a lot of emphasis on antimicrobial resistance. And they came out with an antimicrobial resistance Threat Report that had a bunch of different organisms, organisms in it. And one of those was Neisseria Gonorrhea. And so they had a list of 18 organisms that they classified as urgent, serious or concerning threats. And because of various characteristics that I think had been mentioned here today. They put Neisseria gonorrhea as an urgent threat. And they did this because it has shown over the course of time that it can rapidly develop resistance to various antibiotics. And so it seems like, as we've shown here today, as you start to treat it with one, one antibiotic, it develops resistance. And as you continually change, it continually becomes resistant to those antibiotics. And so it is unique in that perspective, that it is changing rapidly. And it's also a community associated resistance as opposed to healthcare associated. So everything else on their list was pretty much a healthcare associated infection. So Neisseria

gonorrhea is really unique in that. And so they've updated this report, this one that I've shown here today is from the 2019 report, but they updated it again in 2022. And it still has remained on that list of it's an urgent threat, it's a public health crisis, we need to take care of it before it becomes a real problem. And so they look at not just the risk of it, nationally, but they also look at the risk of it globally. And so as you've heard here today, there really hasn't been much resistance of any scene in the US. However, we've seen it in a lot of other countries. And so because of travel and not restrictions, it is of concern to the

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US.

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So CDC has put a bunch of money into all of its antimicrobial resistance threats. But in particular, what I'm showing here is Neisseria gonorrhea and how much they've invested in New York. So if you go onto the CDC website, there's a nice map, you can click on each state and see how much they've invested in resistance to all the various pathogens that are on their list as well as overall and so they've invested $165,000 In Neisseria gonorrhea, and they do a lot of different things with the state, public health partners, hiring and training, increasing epidemiological investigations, improving culture techniques, they work with STD clinics, they go about all these things. And so this is really an investment, the number of dollars that New York gets every year is steadily going up. And so they keep trying to expand their ability to do surveillance and testing in order to improve upon this. And so Dr. Miranda talked a little bit about this, but these are just some of the programs that are available in New York State that are being funded by CDC in order to address the resistance in Neisseria gonorrhea and gonorrhea surveillance in general. So there's the just site which again, just monitors antimicrobial resistance trends, and gonorrhea. And so there's two sites in New York state. One is in Erie County, which is like the Buffalo region, and one is in New York City. And so they have protocols to talk about which number of specimens are going to be screened. So they screen the first 25 of men are from urethral sites, they have a whole algorithm so they pick to high risk areas, and then they do screening programs. They've partnered with STD clinics all over this state and all over the country in order to do this. There's also the surge program, which began more recently it was in 2016. And so that's a program funded to enhance domestic gonorrhea surveillance and infrastructure build capacity for rapid detection and response and then rapid field investigation to stop the spread of resistant infections. And so that's a little bit newer program to New York State, but that's another one that we participate in. And then there's the STD surveillance network or the SSU in network, which is a collaborative network of the state, county, and city health departments. And it's funded by CDC to increase surveillance activities in order to detect, monitor and respond to trends and STDs to the enhanced collection and reporting. And then the final one. That's just very briefly shown on here is the AR lab network, which are the ones in blue, so they don't have New York, listed because when this map was created in 2021, we weren't funded. However, Wadsworth center is now funded to do resistance testing for Neisseria gonorrhea under the AR lab network. And so we'll talk about that in a few slides. So as you can see, here, there's multiple mechanisms of resistance for Neisseria gonorrhea. So it's an ever evolving organism. And it has lots of ways that it changes and adapts in order to develop resistance to all the various drugs. And one of the reasons is that

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Coxide

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are easily easily able to acquire genetic material from different lineages. So they can uptake mutations from through both transformation. So uptake it through the environment as well as conjugation. So they're able to take up genetic material from other species as well as through plasmids. And so that, in and of itself creates lots of these different mutations that are very difficult to overcome. And so, because of this over time, has developed a lot of resistance to various drugs including decreased susceptibility as a through myosin. So again, that from mutations that acquired from other Neisseria species, as well as plasmid borne resistance to both penicillin and toucher cycling's. In addition to that, as Dr. Ivan bomb mentioned, a lot of them are point mutations. And so it makes it a little bit more difficult, difficult to detect these because they're not just presence or absence. So it's not like methicillin resistant staph aureus, where you're just looking for the presence or absence of a dream, you're looking for point mutations. And so that makes the technology needed to detect those a little bit more tricky. So this is just a map, again, reiterating what we've heard through today. So you can see over time, there is a little bit of increased resistance. And it's, it varies based on where you are within the world. So this came from a 2017 and 2018 study that the who did, looking at reports of resistance to the four different drugs that I've shown here, in 73 countries. And so you can see, overall, there's, you know, not a lot of testing and not a lot of resistance to sophistic fixing and subtract zone. However, you can see large levels of resistance to azithromycin and Ciprofloxacin. Because these have changed even from the report that they did before this, and they've done another one reached recently, with the who, there's great concern that these trends for self try axon are going to change and go in the direction of azithromycin and ciprofloxacin, and they sort of have started to go that way, in various parts of the world, but again, not in

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the United States.

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So this case has been talked about already. So I won't go into a lot of details. But the US had its first case of resistant gonorrhea into patients in Massachusetts this year in January of 2023. And so because of that, and it's close proximity to New York State, the New York State Department of Health put out an advisory to all of the laboratories as well as physicians in the state to be on the lookout for resistant cases for treatment. And so went through, you know what to be out on the lookout for how to submit specimens, just to sort of raise awareness and try and improve testing in New York state. So we, we took the approach of let's jump on it while we can and get people's attention. Okay, so now let's just talk a little bit more about the testing in particular. So it used to be that all gonorrhea testing was done predominantly by culture. However, that has changed over the last few years. And now it's done much more by nucleic acid amplification testing, which is really great. We get fast results. You can get faster treatment that way. However, it's also led to a few detriments so the commercially available nucleic acid

tests they don't provide for a sample that can then be cultured from so Dr. Ivan brown showed the two different was common tests, which those ones lyse the cells right on collection. And so, by the time that arrives at a lab, there's no way that they can do culture on those specimens. So you need to collect a separate specimen if you're gonna get culture and so most, most facilities, and physicians aren't doing that, and therefore, there's no culture to be tested. And so that has made it very difficult for any laboratories to effectively do antimicrobial susceptibility testing. And so unless a physician is requesting that, and there's a concern that it might be, it's not going to routinely happen in a facility lab. And edition, it was mentioned earlier that the NAT testing is really great. But it's also very difficult to use for a test of cure, because it's so sensitive, a patient may have dead organism for for weeks, and you might still get a positive results. So sometimes they haven't fully cleared all of the dead cells. So you'll get a positive and it's not really indicative of a test of care. So if you ever think that there's not a complete clearing, again, that's where you would need a culture to confirm whether or not it's actively growing. And so with the decrease of culture specimens, we really can't do an microbial susceptibility testing. And so, as a as a state and as a, as a country, it really is unknown the real burden of antimicrobial resistance, because we aren't, we aren't getting enough of a sampling to really make a huge gathering rather than just sites, which is a good indication, but it's not a full a full picture. And so CDC has been really wanting to expand the the testing capabilities across the country to improve these. In addition, that the antimicrobial susceptibility testing is needed to correlate the genotypic and phenotypic result. And so there's a lot of work being done to create nucleic acid amplification tests for detecting resistance, however, we need the culture to go alongside of it so that we can be sure that when a certain mutation or a certain gene is present, that we actually are correlating those results and making sure that it is indeed resistant. Sometimes we can see mutations and without having that phenotypic result, we don't know whether or not it's a mutation of no consequence or a mutation that leads to resistance. And then lastly, the one downside of only having to play nucleic acid testing is that GC is very hard to culture. And so by not having a culture and a lot of the hospital labs across the state, as well as the public health labs across the state. We're losing the skills and our microbiology staff. And so both at the hospital level and at the public health level, this is concerning, because it's one of the more difficult organisms to culture. And so you saw the, the glass jars and the gym bag plates, a lot of those things have been gotten rid of. And so it's really hard to bring those things back on after you've made strides to get rid of them. So this is just a quick summary of everything that is approved. So in 2014, is really when all the nucleic acid testing came on board, and got FDA approval for both GC and CT. And those are commonly tested together, as many of you know, because they often are co infections, they go hand in hand. And so almost every test out there has both of those available. When they were initially approved, they were only approved for genital specimens, and they had very limited other specimens. And so people quickly realized that this wasn't really an effective way to do screening, and that you needed to have the ability to do other specimen types. And so, as we've heard already today, it's very important to have those extra general sites, the rectal and the oral pharyngeal sites, because the the urine and the urethral sites aren't, aren't going to capture everything. And so since then, the nets have been expanded for approval to include the extra general specimens. And that's been really important, they still are a little more limited. However, they're much better than they were originally. And then, as Dr. Agon Brian mentioned, it's really important to have the ability to do point of care tests and so on 2021 The first net was approved for point of care. It really hasn't. So it's the

beings health IO system, it really hasn't taken huge hold in most places because it's it's relatively expensive. And it's been predominantly used in research settings. However, the ability to do a point of care test is very important. And so I think CDC as well as the who has really been pushing to get more point of care tests available. The One limitation of the net testing currently is that there is no FDA approved assays for resistance testing, whether it's point of care or in the laboratory, there's nothing currently available to look at antimicrobial resistance.

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So there is only one on the market that's pending approval, and it's the speedy X. And it detects resistance to Ciprofloxacin. And so I actually met with one of their reps at a meeting recently. And they are still proceeding with this assay. However, they got delayed with the COVID pandemic. And so it's not ready to go just yet. But the the target that they're using is the gyro a gene mutation. And it's an it's an S 91, F and some not one location. And that mutation in that gene leads to resistance to Ciprofloxacin and so that that product, I think, is expected to come on the market within the next year or two, they're hoping. In addition, there's some other genes that are well characterized, that people have been looking at. And it's the goal of the speedy X to incorporate these as well, eventually, in the 23 s gene, there's a mutation in the C two 611 teeth, at least goes through myosin resistance as well as a 23 S, mutation and a plenty 59 G that also leads to high level resistance. So the whole medicine and so those are important assays to get on the market again, because they're not a presence or absence of a gene. And they're a single point mutation, they're difficult to make a nucleic acid test for you have to really look at like melting curves and things like that. It's not a quick presence or absence, which is what most nucleic acid tests work based on. These are important, because as Dr. Ogden Brown mentioned, they could allow for more treatment options, so well, they're not looking at resistance to subtraction, which is the main treatment, they are looking at a potential for treatment with one of the other antibiotics that used to be used, but isn't used as often. And so that it is it is a valuable test, even though it's maybe not quite as ideal as something would be for like the detection of resistance to subtract zone. And currently, there's nothing in development or the approval process for stuff Triax zone or suffixing. So at the Wiser center, we have been, we've been doing GC testing for a long time, but we have been doing it in a very limited capacity. So we have a real time PCR, which confirms identification. Most most facilities are not getting this from us, they're getting it from their commercial laboratory partners or their state, or their local public health laboratory partners. We get very few every day screenings at last rites, and we and we want that we want all the main testing to go to your normal laboratories, we don't want to do just the basic positive negative, we don't work in a step fashion. And so that's really, that's really not where we play a role where we do play a role as the ability to offer antimicrobial susceptibility testing. So we've been on the the hunt first for samples that physicians or labs may think are resistant to have those samples come to us. And so when we get a isolette, or a primary sample that we can culture from, we run an E test to look for resistance to subtract zones to fix the intercepts or myosin. I have that written down twice sorry, that should say, ciprofloxacin, and then others have 100 class. So occasionally, we'll get requests for some of the other drugs that used to be used or for things like penicillins. If we see resistance, we also are doing whole genome sequencing. And we're doing whole genome sequencing on these isolates. So that we can look for those various point mutations and make some correlative data. And addition, if we get several samples that a physician or

health department think are related. We're also doing whole genome sequencing to assess relatedness. So we can do that to various pipelines that we have here. So this is just an example of a resistant plate that you can see on the right and we follow the CSI and the just criteria for MI C's. So as was mentioned before, there's breakpoints for all of the various drugs however, the breakpoints for SEF Triax. On and 16 are limited. They don't have they have a breakpoint that says it's susceptible, but they don't have a break point for resistant and so in the laboratory, we call them susceptible and not susceptible. And that's because I think the drug is new enough. They're still trying to figure out where you would see resistance and not. And so we don't actually report out resistant for those drugs we report out not susceptible. And again, we do we do the top four drugs at the Lazarus center, and then we would do the other ones upon request. So you can see on the right side of the screen, there is a sample that's resistant to the drug on the, the right side of the strip, but you can see a clearing in the zone for the drug that is susceptible to so the it's just a really simple test. Again, the key is to be able to get a culture here, which is very difficult. up sorry, went the wrong way. So in New York State, there's, I'm sure you're all aware, there's a laboratory reporting of communicable diseases. And so Neisseria gonorrhea is is listed as part of that. And so we've been asking for since 2020, for samples that appear to be resistant or have decreased susceptibility to the cephalosporins, or is it through myosin to be sent to the state. Because most laboratories aren't testing for this, we really don't get very many from this. However, we're really hoping by educating and reaching out to partners and public health departments that we're going to start getting more of these, because we do really think it's, it's a valuable way to do surveillance and keep an eye on what's going on in New York State. And in addition, we're going to be updating these very soon, during the approval process now, but we're asking for iceless to be submitted from extra general sites, as well as those that are suspected to have resistance or decreased septic

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susceptibility. So we,

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at the Wiser center, we take a lot of different types of specimens, we've tried to increase what we're willing to take so that we can make it the easiest for every one of our partners, to get isolettes to us or samples to us so that we can figure out more about antimicrobial resistance. So we take isolettes those are like the icing on the cake. For us. We like those the best, but we realized that that's that's really very difficult, and most facilities no longer have the ability to do culture. So we also take what we call a GC screen. And so for that we're looking for a swab once it's collected to be plated right on to the gym bed plate, which is shown here or on modified there, Martin, gym, bed plates are a little bit hard to get right now. And so we've had success reaching out to our partners and getting modified there, Martin plates with a co2 disc placed in a bag. And so I'm happy to chat with anybody if they want more information. We've also had success of getting a swab collected and put in an Amish style. So when it arrives here, it's nice and happy. The key is just not to have them put in a refrigerator, they need to come like as soon as possible from collection, and they can't be refrigerated juicy is really not hearty. And so it it dies really quickly. Unfortunately, we also take primary samples, we've had the best luck with the collection of an E swab. The key is it just can't come on in the nucleic acid to so the typical Hologic Aptima those tubes, it likes it right on collection. And so we can't ever get a culture out

of that all we can say is positive negative. specimens of interest, we are looking obviously for those that may have resistance or treatment failure specimens from extra gentle sites so blood conjunctival, pharyngeal rectal, we had a CSF recently, anything extra gentle as much more likely to have some sort of resistance. And then we're also interested in getting specimens and isolates from women, especially in those age groups or it's not as common. We have a FedEx account through the CDC that will help pay for shipping of isolates to the Wadsworth center. So we're trying to make it very easy for our partners to get us the samples if they want to. And if they suspect resistance, there's also shipping materials available from the New York State ordered us so not the plates, but you can get all the boxes and the specimen shipping. And we report everything out via e Claire. So we will report all of our drug susceptibility results out both to the submitting lab as well as the county so that everyone can see the results. And we do a turnaround time of around seven days. We've also been doing a lot of outreach and trainings to various public health labs across the state. So we've been talking to our local health departments, trying to teach them how to get the specimens to us so several of them I have been collecting swabs to send to us as well as to send to their normal testing site for the nucleic acid testing. And so this is just an example of one that we did with a county where we did it via zoom. So we didn't have to travel to the county. So we just showed them how to once they had the swab how to go about cleaning it, since somebody in that facility was familiar with it, we sent a little packet of information. So if that's of interest to anybody, you can reach out to me anytime. So what's next for us? We're hoping, you know, to continue to educate, train and partner with public health labs and facilities across the state, this is a new program that we really feel is important to build. And so we've been working closely to build partnerships with our epidemia ology partners as well, we have funding through CDC to do this work. And so we've been partnering with them, we're working on developing new assays to detect resistance, because we don't always have a culture, we're trying to do this from the primary sample. So we have some work in progress, doing a real time PCR assay, as well as a sequence based approach. So our sequencing based approach is amplicon based. So we're looking at, we can look closely at the genes.

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And look at those point mutations.

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And with that, I left some resources here that I think because of the materials you guys got,

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I think we can take questions. Great. Thank you all very much. We're right at time at 130. But there were a couple of questions that came in and one is reporting that someone went to a recent lecture in Boston that recommended that sexual contacts to a patient with known got a cocktail infection should not be treated, unless they were to test positive themselves or have symptoms, rather than the traditional empiric partner therapy. And this was advised as as a method to preserve subtract some for those who need it. So is this a current recommendation that you're aware of? I'm not

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familiar with that. I don't think this I don't think the CDC is promoting that.

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I, I would agree. I have not heard that from CDC.

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Yeah, I mean, you know, the epidemiologic treatment where the risk is high. And this is a circumstance where it would be regarded as high is a tried and trued method for controlling disease in the community. And I think that there's no reason to withhold treatment. I mean, this would basically put the kibosh on EP T expedited partner therapy entirely, you know, if that was the case, and I don't know anybody promoting that. Sounds good. Sounds like a reasonable thought. But I don't know anything about it.

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I did hear at one meeting that that approach being used among those who were taking doxycycline as prevention, to await testing in that group that is also not recommended by CDC. But I did hear discussion a while. And then there were some other questions about access to resistance testing through Wodsworth labs. But I think you really addressed that in your presentation. We are a little bit late. And I just want to say ask if all of you when we planned this session, it was shortly after the Massachusetts cases were reported. And I really expected to have heard that there were more cases by now, since they were, you know, really discovered by luck, not by symptoms. So are you all surprised? Were you expecting more cases?

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I mean, I can chime in from the Wadsworth side we've, we've started testing more, but we really haven't.

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I'm not sure if it

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was outside. I would just say we would catch it right at this moment. Because we aren't getting enough of a sampling at Wadsworth. But I am a little surprised

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I've been waiting for this for years. I mean, we've been talking about this for several years now. So I guess the Massachusetts case has made it more urgent, but I've been kind of surprised that we haven't seen more of this over several years. So

1:29:29
yeah, great. Okay, so thank you all for joining tomorrow.

[End Transcript]