

STIs Are Back. Innovative Testing Is Needed.



PODCAST 25

00:22

Dr. Jane Caldwell

The rise of sexually transmitted infections post-COVID.

Today *On Medical Grounds*, we will be speaking with Dr. Yukari Manabe. We'll discuss the alarming rise in sexually transmitted infections or STIs since the beginning of the COVID pandemic. Also, we'll discuss the rise of non-classical STIs such as Monkeypox, *Shigella*, and hepatitis.

Dr. Yukari Manabe is director of the Johns Hopkins Center for Innovative Diagnostics for Infectious Diseases, as well as the Associate Director of Global Health Research and Innovation at the Johns Hopkins Center for Global Health. She's an infectious disease clinician with areas of expertise that include HIV/AIDS, STIs, and tuberculosis. Hello, Dr. Manabe. Welcome to *On Medical Grounds*.

Dr. Yukari Manabe

Thanks, it's really lovely to be here.

01:20

Dr. Jane Caldwell

Here's a basic question. Why do we call them STIs instead of STDs?

Dr. Yukari Manabe

In the past, they were called sexually transmitted diseases, now they're called sexually transmitted infections. They are one and the same, it doesn't matter which you call them.

01:35

Dr. Jane Caldwell

Okay. All right. What do you feel are the major drivers for the recent increase in STIs?

Dr. Yukari Manabe

STIs have actually been increasing since 2016. So, if you're considering that recent, really the last five to 10 years, they have been increasing over that period.

I think overall, the early surveillance data from 2020, (usually they lag about two years), are also discouraging. I think this is all still going the wrong direction. Major drivers, I think are, because we don't detect enough infection, particularly asymptomatic infection. I think that we probably need to do a better job communicating the risk of STIs to the general public here in the United States.

02:23

Dr. Jane Caldwell

Isolation, masks, and social distancing during the COVID pandemic helped reduce outbreaks of influenza and RSV. Why not STIs?

Dr. Yukari Manabe

Though people were very good about wearing masks, particularly early on in the pandemic, I think that that the same was not true in terms of social distancing and sex. What's really interesting is if you look at the lockdown period around March of 2020, maybe through June of 2020, in fact there probably were fewer STIs, but we made up for lost time in the latter part of that year, and we continue to see more cases.

Part of it also though was that there was less detection as well, so I'm not sure the numbers were as accurate. People didn't have good access to getting STI testing. The data from 2020 are varied because you can see that there was much less testing during the lockdown period. For example, chlamydia looks like it might have gone down in 2020, but if you look at the actual testing rates, there was much less testing, particularly during the lockdown period. What's interesting about chlamydia, particularly in women, is it can be asymptomatic. So (for people with) symptomatic infections, people tend to look hard to try to get testing and treatment. Whereas when you're asymptotically infected, you have less of an opportunity then to detect that asymptomatic infection.

03:40

Dr. Jane Caldwell

I see. What are the classical STIs of concern right now?

Dr. Yukari Manabe

The reportable ones are obviously gonorrhea, chlamydia, and syphilis. HIV is also a sexually transmitted infection, although sometimes we categorize it separately. I think those are sort of the classical STIs of concern right now because they're reportable and they're tracked, and so we can see how they go year on year.

Other infections that are probably important but are not reportable are things like *Trichomonas vaginalis* can cause bacterial vaginosis in women, but also men can get infected of course, because it's transmitted between men and women. As I said, HIV is treated as a separate category, and overall I think that HIV trends are starting to go down.

But again, different money goes towards HIV control than sometimes STI control. And of course, that's part of the crux of the problem. We need to put more, we need to invest more, if we want to get STIs under control in the United States. And our public health system, as you know, has been very stressed over the last three years because of COVID.

Many of the people that actually work on STIs have been flipped over to COVID. Many of the machines that are used to diagnose STIs have been flipped over to COVID, and as a result, many of the infrastructure elements necessary for us to both diagnose and treat STIs have really been moved over to deal with the current pandemic.

We really need to develop deeper infrastructure in our public health system if we want it to address things that are basically a problem instead of always having to move to the next thing. Monkeypox also, similarly, took a lot of the focus of public health officials and practitioners away from STIs.

05:29

Dr. Jane Caldwell

How are STIs diagnosed?

Dr. Yukari Manabe

So most often you get a swab or a urine specimen for people who have genital STIs and you would do a molecular test. That's the most reliable way. Of course, in some resource-limited settings, and even here in the U.S., you might do what we call a Gram stain, someone has a drip, you would put that onto a slide you would stain it and you could see, for example, gonorrhea. Chlamydia is not easy to diagnose that way. Gonorrhea can also be cultured. Chlamydia is very difficult to culture, so molecular testing has really allowed us to diagnose many more STIs than we had in the past. Nonetheless, when someone comes in, those tests don't often come back quickly. It may take six to 12 hours, maybe up to 24 to 48 hours in places that are more rural, that are sending their testing to some central reference location. Therefore, if someone comes in with symptoms consistent with an STI, they will go ahead and get empirically treated for everything while waiting for the results.

So though we test and treat, sometimes we treat and then wait for the results of the test, and that's something that I think we should try to address.

06:39

Dr. Jane Caldwell

Are there any new technologies for more rapid test results?

Dr. Yukari Manabe

That's the thing that I think we've been most interested in trying to develop here at Johns Hopkins in our Center (for Innovative Diagnostics for Infectious Diseases).

So, point-of-care diagnostics mean tests that can be performed using the instructions for use by any paraprofessional. You don't need to be trained. You can just read the instructions and do the test. That kind of point-of-care testing is really necessary. There are three tests that are currently available. They take anywhere from 40 to 90 minutes and most people know, when you've been to a doctor's appointment or seen a clinician, rarely does your appointment last an hour or an hour and a half. You might not be in the office. So we'd really like to develop tests that can be done, say in 15 minutes, because most people are willing to wait 15 minutes. I think most people are not willing to wait an hour and a half. So if we want point-of-care tests, we're going to have to develop ones that are even faster than the ones we have now. They have to be affordable. And now that we should all be more concerned about our environment, we also want ones that have less of a plastic footprint. Many take a lot of plastic in the cartridge, and then that just goes into the garbage. And much of that goes to places where it's not sustainable. So I think that the parameters for a new point-of-care test out are there. I think COVID was a real shot in the arm for diagnostics for infectious diseases. From my point of view, point-of-care tests that are fast, easy to use, have a low plastic footprint, and can occur within a clinical encounter are really the characteristics we are looking for.

The U.S. government, and in particular senators Lamar Alexander and Roy Blunt, in April of 2020 decided to put a huge amount of money into diagnostics of COVID.

They said we need more tests. And so, a billion dollars flowed into research mechanisms to try to develop tests faster. And that influx of money has meant that there are many more platforms for point-of-care testing of infectious diseases than there have been previously. Many of these potentially could pivot and start detecting sexually transmitted infections.

So COVID has been a real shot in the arm for infectious disease diagnostics at the point of care.

09:03

Dr. Jane Caldwell

Are there any multiplex tests for STIs?

Dr. Yukari Manabe

Yes, most often gonorrhea and chlamydia are detected together and that's because those are the top two reportable infections. There are ones that also include trichomonas.

There is a point-of-care test that has all three for women with vaginal swabs, and you can use those multiplex tests to try to look for a bunch of things. Some of the problems though, are that the guidelines say test if these things are negative. So of course, with a point-of-care test, often you would want to just do them all at once.

So how does that reporting happen? If the first two are negative, then do I report the third test, even if I've multiplexed all three tests? So it's become complicated for clinicians. People who don't test and treat STIs often may also struggle with knowing if they get all of the results and they may think, oh, I should treat for everything that's positive, that may not necessarily be the case.

I think the ones that are multiplexed most often are gonorrhea and chlamydia, sometimes with trichomonas.

10:09

Dr. Jane Caldwell

How do you feel that point-of-care or at home testing with COVID will impact STI testing in the future?

Dr. Yukari Manabe

The interesting thing is that the public has become much more knowledgeable as a result of COVID.

I think that this is great. I think understanding what it is that you're getting when you go, being a knowledgeable consumer is important. So when you go to the doctor, I've never heard people tell me, talk to me, and ask me as much as they are now—"is it a molecular test, is it an antigen test?". I can honestly say that before COVID, I don't think anybody ever asked me that question. When they were getting a flu test, they weren't like, is this an antigen flu test or is this a molecular test? So I think that the public's knowledge about point-of-care tests has really gone up. Also, there have been very few self-tests, meaning over-the-counter or OTC tests for infectious diseases. The only one that we had in the past was for HIV and there was only one.

So now we have a whole bunch of over-the-counter tests, both molecular and antigen tests, that people can perform in the comfort of their own home. And I have been pleasantly surprised. I would say that the majority of the American public is very capable of doing an over-the-counter test for COVID. And I think that now that they have that self-reliance and understand how to do it, I think people are very interested in having diagnostic certainty. I think you would want to know, do I have flu? Do I have COVID? What is my respiratory infection? And is it treatable? You particularly want to know about the ones where you might have a treatment option.

Finding out that you have the common cold rhinovirus maybe is not so helpful because we can't do anything. But it is helpful and that it helps you know that you might not be then eligible for treatment.

12:01

Dr. Jane Caldwell

So could you summarize what is needed for near-patient testing for STIs to be a success?

Dr. Yukari Manabe

I think they have to be rapid within 15 minutes. They have to be easy to use, they have to have a low plastic footprint, and they have to have high accuracy. We can't have tests which are not sensitive or specific. Right? You wouldn't want to be like, I think you have gonorrhea. I think that's not good enough. I think you want to know that you definitively have gonorrhea, so they do have to have good accuracy. But I think we're on the verge of having ones that fulfill those criteria even for OTC.

12:25

Dr. Jane Caldwell

So we've talked a lot about testing. What are, what are some common treatments?

Dr. Yukari Manabe

There are antibiotics for bacterial STIs. Gonorrhea and chlamydia are treatable. Gonorrhea, though, you know, is poised to be the first superbug, right? There are very difficult to treat strains of gonorrhea now, and that are emerging. I think that we need to be good stewards of the tools that we have for treatment. We need to make sure that we're giving them specifically to the people who need them. We may want in the future to also have tests to tell us whether or not you have a resistant strain, rather than waiting to get treated and find out you don't feel better, and then to come back and say, oh, by the way, you have a resistant strain that won't be sensitive to the antibiotic with which we treated you.

Trichomonas is also treatable and so is syphilis. Syphilis is a huge problem. Syphilis is interesting in that our oldest drug, or one of our oldest drugs, penicillin, is still the drug of choice. There are only a few bacteria that are like that, that are still very sensitive to penicillin. Of course, it's a shot which people don't really enjoy, but I do think that it's really quite remarkable that syphilis has remained sensitive to penicillin.

13:36

Dr. Jane Caldwell

Let's discuss some prevention strategies.

Dr. Yukari Manabe

Well, they're sexually transmitted infections, so barrier strategies do work as long as you use them properly. Abstinence works, but I will say that that has been a behavioral strategy that has never worked particularly well in the past. And I do think that people are starting to talk about chemical prevention. You can take medication to try to prevent STIs. So if you are a high-risk person, you've had a lot of STIs in the past, there recently was a trial that showed that doxycycline taken on demand within 72 hours of a sex act that was unprotected does decrease the amount of gonorrhea, chlamydia, and syphilis that you get in both HIV-affected and people who are not living with HIV. There are different prevention strategies that are coming down the pipe, and I think are important. We have specific strategies for HIV prevention, many of which are also chemicals that we have. Things like, tenofovir or, its combination therapy.

And that does work when taken daily, but it only works if you take it. And so some of these long-acting injectables are very attractive because then you might not have to remember to take the medications every day. There's a new one, cabotegravir, that's come out (for HIV prevention) and that one has shown to be superior to a daily pill and it's quite easy.

And so I think there's a lot of hope on the horizon for people who can't change their behavior for whatever reason, that they could take medication and therefore prevent infections like HIV that might not be, they are treatable, but they are not curable.

15:42**Dr. Jane Caldwell**

Many STIs are asymptomatic. Are there certain populations who should be regularly screened for STIs?

Dr. Yukari Manabe

Yes, the new guidelines actually, point out particularly for women under the age of 25, that you should get annual screening for sexual health. So you should be screened for gonorrhea and chlamydia, as well as trichomonas yearly, and this is a recommendation from the Centers for Disease Control. I do think that coming up with ways for women to have easier access to STI testing would be important with this recommendation. Taking time out to go to a physician may not always be possible. Most women, though, do get annual pelvic exams for reproductive health and therefore could also get STI testing at the same time. I think that that is a good strategy, but there are women who often don't have access. So getting women access, I think will be very important to fulfill that recommendation.

16:35**Dr. Jane Caldwell**

And this might be where over the counter or at home testing could fill that gap?

Dr. Yukari Manabe

Absolutely. Or even if they could just be made available at public health places, people could go pick them up.

There are also mail-in self-collection services that are available in some states where you can sign up online and say that you would like to be tested. They will send you a kit. You self-collect and then you send it back, and then the results are posted and you get a message saying that you have your result is ready.

We at Johns Hopkins have a site called "I Want the Kit" for the state of Maryland and also some other states. And I think this is a really important way to try to increase access for people who really don't like to go to public health STI centers.

17:19

Dr. Jane Caldwell

What role does education play in prevention and treatment?

Dr. Yukari Manabe

Yeah, it's huge. I think that you would be surprised how little people know about sexually transmitted infections, despite the fact that they are old; they've been around for a very, very long time. So when people talk about STIs, there's a lot of stigma around it. I think that a lot of people don't want to talk about gonorrhea, chlamydia, and syphilis.

I think these are all taboo subjects in many circles, and I think we have to change that. I think it shouldn't be a stigma, especially if it's treated. You should be able to, or if it's treatable, you should be able to go get testing and then be treated and it should be just like anything else, if you have the flu, you want to be treated.

18:08

Dr. Jane Caldwell

Okay. Do you consider Monkeypox an STI?

Dr. Yukari Manabe

Yes. So we do know in the recent outbreak, that was global, but there have been other outbreaks in the past that Monkeypox is considered by the World Health Organization as sexually transmissible. It can obviously be transmitted through other contact, but it's really intimate contact that led to the recent global outbreak. I think then that people should be aware when it is sexually transmitted, it can have different manifestations than you might normally see. So people are used to Mpox being a skin rash, which you can still get, but you can also get deep-seated lesions, say in genital or rectal spaces, that can be quite painful. That wouldn't be obvious because the place of inoculation was there.

So it is sexually transmissible and important to realize that it may have an atypical presentation when it is sexually transmitted.

19:06

Dr. Jane Caldwell

What is your opinion of syndromic management and approach, which doesn't rely on the use of laboratory tests, but uses easily recognizable signs and symptoms to guide treatment?

Dr. Yukari Manabe

So syndromic management will likely never go away even if we get great point-of-care (tests). So though I think it contributes to antimicrobial resistance, I think that it's likely going to continue for quite some time until point-of-care tests become really easy to use and really inexpensive, particularly in low and middle income countries, or even in places in the United States that are quite resource limited.

As a result, syndromic management is a way to help a person who's having symptoms right now, and they're going to want to be treated right now, and they may not have a result during the time of their clinical encounter.

20:02

Dr. Jane Caldwell

What is your greatest concern with STIs in future global health?

Dr. Yukari Manabe

My greatest concern is that we don't have enough people who are championing both the testing and diagnosis of STIs. Until we understand the full extent of the epidemic, or the syndemic, since we have other epidemics going on, we really won't be able to control sexually transmitted infections. They are tenacious, they are old and wise, and if we want to get them under control, I think that we are going to have to be as innovative and crafty as the bugs themselves. So I do look forward to a time where everybody screens and we overscreen in order to try to decrease the trends that we've been seeing over the last eight to 10 years.

20:57

Dr. Jane Caldwell

If I were a genie and could grant you a public health wish, what would it be?

Dr. Yukari Manabe

As a person who works on infectious disease diagnostics, I would love to see diagnostic testing for all. I think that innovation without access is not innovation at all. And so I hope that the innovation that we are coming up with at the bench will soon be available globally and that diagnostic testing can be available everywhere.

The Lancet Commission recently put out a diagnostic brief and showed that half of the world doesn't have access to diagnostics. I think this is terrible, so if you were a genie, you would make it accessible to all.

21:39

Dr. Jane Caldwell

Dr. Manabe, we appreciate your work in global health and infectious diseases. Thank you so much for taking time from your busy schedule to speak with us.

Dr. Yukari Manabe

My pleasure.

Dr. Jane Caldwell

And thank you for listening to the *On Medical Grounds* podcast. We know your time is valuable. The resources that were referred to in this podcast can be found at OnMedicalGrounds.com. Be sure to click the subscribe button to be alerted when we post new content. If you enjoy this podcast, please rate and review it and share it with your friends and colleagues.

This podcast is protected by copyright and may be freely used without modification. For educational purposes, find more information or to inquire about commercial use, please visit our website OnMedicalGrounds.com.