



Jill: I'm here today with Dr. Connie Mao, director of Harborview Women's Dysplasia Clinic here in Seattle, Washington, where she focuses on HPV-related disease including cervical, vulvar, and vaginal dysplasia and genital warts. She's an associate professor of obstetrics and gynecology at the University of Washington, and she has spent the last 19 years doing research related to HPV infections and prevention of cervical cancer. And beyond that, she's a huge proponent of women and girls' health. So, thank you, Dr. Connie, for joining us today.

Dr. Connie: Thanks for having me.

Jill: Why don't you explain, in your words, what you do every day.

Dr. Connie: Well, I have a job that's very varied: I see patients, teach residents and some medical students, do research, make presentations, and talk to folks like yourself. So, lots of different things to keep me busy.

Jill: In terms of the patients that you see, are they of all ages, or do you have kind of a "sweet spot" of women that come to you?

Dr. Connie: I see women of all ages, and spend a lot of time seeing patients with HPV-related disease.

Jill: Can you explain, what is HPV and what does it stand for?

Dr. Connie: HPV is human papilloma virus. It is one of the few viruses that infects just skin cells and it lives all over us. And there are many different forms, but there are some specific types that can cause cancers mostly in the cervix but also can cause cancers of the vulva, the anus, the mouth, so it can live in other places, just less commonly.

Jill: How is it transmitted?

Dr. Connie: It's very common and there are many types that don't cause disease. So if we were to swab your skin and look for HPV virus, we would find it there. But most of them don't cause any disease. There are just a few that do, and they like to infect certain parts of your body, the ones that I mentioned previously. So, I think of them as ubiquitous, as everywhere. These viruses live everywhere and certain of them are just bad actors, so if you happen to come into contact with a bad actor, then it's less fortunate because you may have a problem from it.

Jill: As a woman, you can go and get a Pap exam, and the doctor says it's an abnormal Pap exam, or you've got an HPV infection. Can it come and go or to your point around, it can live on many parts of the body and infect certain parts, is it...once it's infected, it's always there?

Dr. Connie: No, we believe the body does mount an immune system to HPV, so if it's detected on the cervix, we expect that most people will actually clear that virus on their own without any long-term problem. So it's not like the old herpes virus that people would have their whole life and continue to have problems with. For the majority of people, we think it actually just goes away over a period of time.

Jill: And again, reiterate what it causes or what it can lead to in extreme cases.

Dr. Connie: In women's health care, our biggest concern is cervical cancer. And we know that it causes cancer of the cervix, it is really pretty much the sole cause for cancers of the cervix. Fortunately in this country, we have had a good screening program that has managed to really dramatically decrease the



risk of cancer, but if you lived in Africa where there are no programs, lots of young women can develop this disease and die. It's typically a disease that happens late-30s, so very young women with young children dying of this every day.

Jill: What drew you to study HPV and its impacts on the human body, both men and women.

Dr. Connie: Well, like with many things in life, it was sort of an opportunity that came up where there was a large study, one of the first ones of its kind—looking at abnormal Paps and how we manage them—kind of around the country. There was a need at the University to have somebody who was interested in working on this as a gynecologist, so I kind of jumped at that chance. And have been working on this award-winning HPV research group for 19 years now. It been just a wonderful ride for me.

Jill: Wow. And so, walk us through that: at the beginning you said that there was a hunger for knowing more about what happens in abnormal Paps, and over those 19 years, where have you come? What have been the milestones in progressing this?

Dr. Connie: Yeah, very big deal! When I started my training in the late 80s, we really didn't know what caused cervical cancer. We thought it might have been related to some sexually transmitted disease and people debated about what virus it was, and it wasn't until the advent of PCR testing for viruses that we could really determine that HPV was always there, we found it in all the cancers, and so within that period of time, not only did we identify the cause of cervical cancer, but we were able to develop a vaccine for it. So we've come a huge distance in 20 years.

Jill: In that discovery, how do you decide when a vaccine is in order?

Dr. Connie: Well, one of the problems with HPV is we know that it's very very common and it's not something that you can prevent easily, and so many many people have it, so this is the type of situation where many people have it, we don't have a specific treatment against the virus, so vaccination is the best ticket because it's kind of a random attack rate. You don't know if you're going to get it or not, and the vaccine will help protect you for sure.

Jill: Vaccines of all kinds have proponents and nay-sayers. Are there concerns people should have around the vaccine?

Dr. Connie: Well, there's probably two reasons that people have problems with the HPV vaccine. At first it has to do with the idea that maybe we're giving kids permission to be more sexually promiscuous earlier if we give them a vaccine. That really hasn't shown to be true; most people know that you can get a lot worse things than HPV from having sex. So one thing is that sort of conservative press saying "don't get the vaccine." And the second, of course, is any concerns about vaccines in general. This is a particularly safe vaccine because it's an empty protein capsid of the virus. And the different types that are in it, there is no active virus in it, no infection that you could get from it, so really the problems that we see primarily are sore arms and potential rare allergies to the vaccine. But it is a vaccine that is considered quite safe for everybody.

Jill: And sore arms simply because the needle goes in the arm? Yeah, that's the nature of any.... Is there a prime age at which the vaccine is useful for, or... You know, I never had it, and I'm a middle-aged woman—does it make sense for me to be thinking about it now or



Dr. Connie: Good question. The prime target for this vaccine is ages 9-12. All boys and girls should be getting the vaccine, and the idea is that they should get the vaccine before they become sexually active. We also have a catch-up group, people who are 12-26 who are interested in getting the vaccine. It's still a useful tool. After age 26 it can also potentially be useful, there's nothing magical that happens at age 26 except that insurance companies stop paying for it. And there is less benefit because people have likely been exposed already. And so we don't see as much benefit from the vaccine. So it's really our young people that are going to benefit the most from the vaccine at this point.

Jill: Obviously you're a proponent, since you're one of the minds behind it; are you also in the practice of evangelizing it to clinics or parent groups or what does that look like in terms of making it more of a social norm?

Dr. Connie: Yeah, I've done it; I've done a variety of things—going down to King County Library and giving a talk, and next week I'm giving a grand rounds at Children's Hospital to the pediatricians to convince them because there's some reluctance even amongst the pediatricians to really encourage families to do this. One of the problems is that it's a later vaccine, meaning it happens in the middle years when the kids are 9 to 12. They're not super happy to come to the doctor, they don't have a lot of reasons to come to the doctor, so bringing them in for three vaccines is often challenging in its own right. But yeah, just speaking to the pediatricians, hoping that they will increase the number of vaccines given out because without that we will never reach the point where we can get the herd immunity and really help protect the whole population.

Jill: I heard you say "boys and girls" ages 9 to 12. You tend to think of HPV related to cervical cancer and it being a girl problem. How do boys fit in that?

Dr. Connie: So, for boys, they don't get cervical cancer, obviously, but they do get anal cancers and oral cancers, and they are also the reason why the virus spreads from women to men, so for both of those reasons, it's important to vaccinate the boys.

Jill: I've never had an HPV screening, I've never been screened for HPV, I've only gone for a Pap exam. And I think that's probably what a lot of women do. Can you explain what an HPV screening entails and how is it different than a Pap exam?

Dr. Connie: So, Pap smears have been incredibly successful in our country, and one of the reasons they've been very successful is we do them often. We've done them yearly in the past, then every other year, every third year now, but we know that they're not very good tests. And what I mean by that is it really only picks up about 50% of the people who have disease when we do a single Pap smear. So there are a lot of problems with the test. But the reason it works so well is because we keep doing it over and over and over again, so eventually we find the problem.

What we've discovered about the HPV test is that by checking for the DNA, we can identify the people who are most at risk, and then do additional testing for those people. So it's a better test; in fact, having a negative HPV test is better than having 3 Pap smears in a row that were negative. That's how good the test is. So right now, we're offering it to women 30 and over, kind of a standard basis in this country. Sometimes we use it to follow up women who already are at high risk and have had problems already. So, if you're a young woman, we don't do the test routinely, we do it as follow up to abnormal tests and/or at the age of 30 we start to do it routinely with our Pap smears to increase the pick up that we're



going to have a problem. And that also allows us to space out the screening so that if you get a Pap smear and an HPV test and they're both fine, we can go as long as five years now without doing another screening. So it's really helpful in a sense that it's a much more accurate test.

Jill: And what's involved in the screening? Because I just said, "I haven't had one," and maybe I did and I don't even know!

Dr. Connie: Right now it's collected in the same manner as you have your Pap. It can actually be run on the same sample, so there's nothing additional to do. In the future we will likely see the availability of home swabs that you can do yourself. We have some really good evidence that doing a swab from the vagina is pretty darn good, and I suspect that companies will have those on the shelves in no time where a woman could do a test, mail it in, and then know if she needs to go in for her Pap smear based on that test. So there are, in the future, I think, other options coming besides just going for a Pap smear.

Jill: Are there any preventative things to HPV that a person can do to limit themselves to exposure beyond sexual activity?

Dr. Connie: Because it's so ubiquitous it pretty much....you can come in contact with any intimate contact with any partner, women and men. We used to have a lot of problems with women in the lesbian community thinking that they couldn't get it because they didn't have sex with men, but actually women can spread it to women as well, so, any intimate contact. The best way to decrease risk is to have fewer partners because that would expose you to fewer viral types. And the second is that condoms can be helpful but not completely protective, and that's because it lives on the skin, so it can be found on the skin of men and women, on the vulva, or on the testes area or on the scrotum, or hands, mouths. So, it can be passed in a variety of ways that the condom doesn't protect you from, so although it can decrease the rate of transmission, it does not protect fully.

Jill: Back to the screening, and paired with the Pap exam, it's done in much the same way as a Pap smear, would you even go so far as to advocate that a Pap smear...I guess, what is the purpose of a Pap exam separate from an HPV?

Dr. Connie: That's a really good question. You know, just about a year and a half ago, the FDA approved the HPV test as a replacement, as a potential replacement for the Pap, and that it can be done every 3 years by itself. All by itself, if you have a negative HPV, you don't worry about it, and after that, if you had a positive HPV you'd have some subsequent testing. In countries like Australia, New Zealand, the UK, the Netherlands, have all gone to primary HPV screening. So they're not going to do Paps first, at all. So it is coming, and in this country it is an option for us, and it's something to talk to doctors about. It's a relatively new thing for us, and also, in a country that's been very dependent on a whole industrial complex with Pap smears, it's very hard for us to switch gears very quickly, but I don't doubt that that will happen. Because especially in view of the fact that we're going to have lots of young people who are vaccinated, we need a more accurate test, a more sensitive test. Because going forward, the Pap smears will become less and less useful just because fewer and fewer people are going to have disease. And so, we will undoubtedly switch to HPV testing only at some point. At this point it's relatively new, so that people going to see their providers, providers may not even be, kind of on that page yet, but I suspect it is coming.



Jill: What if one of the women listening to this podcast today goes to the doctor and says, “You know, I’d really like the HPV test, and I’ll forego the Pap exam,” and the doctor says, “Hmm, I don’t recommend that.” How do you even ...It is a hard transformation, and I’m putting you in a very tough position by asking you this question, but what would you recommend for women?

Dr. Connie: Well, I think it is looking for a provider...if that’s of interest to somebody, looking for a provider who is aware of that... we’re lucky that certainly in Seattle, to have a lot of people associated with the university, people who are really progressive in their thinking about how medicine changes. I think you’ll find that more difficult as you get into smaller communities and folks who aren’t connected so much to sort of current events and things that are happening. But certainly if there’s a problem with a particular provider, you know, seeking out somebody with more expertise, especially a gynecologist, or even someone in a university setting, can really be helpful if someone wants sort of the latest, most current information available.

Jill: The vaccine, it’s been around now for a while, are you starting to see the rate of HPV come down? Are those kids, the children that have been vaccinated, now getting to an age where we’re starting to see a downward trend?

Dr. Connie: Right, so, we’re still in this country somewhere around 60% of our kids have gotten at least one vaccine. So we’re a bit behind countries like Australia, but we definitely have good evidence from Australia, where the line up the kids in middle school and give them all vaccines, that they have already seen almost an elimination of genital warts in kids under the age of 21. And they’ve also seen significant decreases in dysplasia, which is a pre-cancerous change, and it’s actually quite... it’s been measured. We haven’t really done that in this country because we don’t have the penetration for the vaccine yet. But we’re definitely seeing it in real time in countries in which it’s easier to get more people vaccinated.

Jill: And did they have to go through the big social evolution that we’re facing now to get it into schools?

Dr. Connie: They must have! But I think that they’re just more open to, this is a public health initiative. You know, I think in our country we give everyone a lot of freedom, but our price is that we give them a freedom to choose. And I think there’s less of that in many other places. And so, places in which they have higher vaccination rates, we’re definitely seeing great benefits, so I expect we’ll get there, it’ll just take us a little longer.

Jill: Relative to the HPV vaccine, are you hearing of more patients asking you about it, younger patients? Are women coming to proactively talk to you about it for their children or even relative to themselves? Are you seeing even young women, quite young women, patients, who are bringing it up as something they want to know more about or they’re interested in?

Dr. Connie: Well, I’m hoping that people – their primary providers are offering to them. I tend to see a lot of people, unfortunately, with disease, so they have an infection or they have pre-cancerous cells, and they’re asking me for the vaccine. And so, there can be some benefit to folks like that who have already had abnormal Pap smears, but really the greatest benefits are going to be before any exposure has occurred. Because it really is a vaccine designed to prevent problems before infection has occurred. Because once it has occurred, we don’t have a lot of evidence right now that it would reverse that process or prevent disease once it’s happened.



Jill: Are there any downsides to getting the vaccine beyond a possible allergic reaction, and are the rates of that very high?

Dr. Connie: Rates are very low for reactions, allergic reactions. There's not too much downside right now. You don't get a free pass on your screening, on your Pap smears or HPV tests later. Eventually that will be true when enough of our population is vaccinated, that that screening becomes irrelevant or more morbid just to do that. And so eventually, down the road, we'll be able to give that up. So getting vaccinated doesn't mean that you get to skip your Pap smears. But it's very well-tolerated, and not a lot of downside, really.

Jill: How far out do you think we are as a country in getting to the place that Australia is or Amsterdam, you mentioned a few different countries around the world, is that 3 years out, is it 5 years out?

Dr. Connie: Well, the uptake has been particularly slow here in the States, and I'm sure there are many reasons why that is true. We are hopeful that that will increase quickly over the next, I would say, decade. There also is a hope that we can start giving the vaccine at a younger age. So if we find over time that the longevity of the vaccine is such that we can offer it to children when they're little babies or toddlers, I think we'll have a better chance of getting them vaccinated at that point.

Jill: Because it's just part of all their other vaccinations.

Dr. Connie: And we initially started vaccinating the middle-age group, the 9-12 year olds, just because we didn't know how long it was going to last, so we wanted to be sure that the immunity was present when they were most likely to get the infection. And the most likely time to contact HPV is, the highest risk time, is age 20 – 24, as you might imagine, when kids go to college.

Jill: Yes, and explore a whole new part of life! You said in a 2012 interview with The Financial Times that the next generation of HPV vaccines will be even better and can protect against 80-85% of cervical cancers. That was in 2012; have we progressed since then?

Dr. Connie: We have! It's very exciting. So, the initial vaccine called Gardasil contained four types of HPV: two that protected against genital warts, and two that protected against two of the worst HPV types, 16 and 18. And those two types caused about 70% of the cancers in the world. So we had, we were about 70% covered with our first vaccine. Gardasil 9 just came out last year, and it covers five additional types of HPV, so now we're about up to 85% of all cancers, if the vaccine worked perfectly—which we know, it doesn't work perfectly, but it's quite good—that it would prevent about 85% of cancers related to these types of HPVs. So we've come...further. It's not likely we'll have a 3rd generation of HPV vaccines, because if we add more types, they contribute smaller and smaller percentages of cancers, and so, it's hard, physically, to make a vaccine with that many HPV types in it. But we can get rid of about 85% of cancers with this new vaccine that's currently on the market.

Jill: And do you see the HPV types, are they evolving and becoming harder to fight?

Dr. Connie: We're very fortunate that this is a very stable virus and doesn't mutate like some of the ones like HIV is notorious for. So, so far we have not seen mutations, nor have we seen upticks in infections of other types, although that's certainly a possibility. We have not seen that at this point.

Jill: And just to make it super clear, HPV leads to cancers or genital warts or both? Are those kind of the physical instantiations of the virus?



Dr. Connie: Right, so it's type-dependent. So typically certain types will cause warts and other types will cause cancers.

Jill: And if there is a woman at home and she thinks she might have an HPV infection, what are some signs or things she might see or feel that would tell her to go in and get screened?

Dr. Connie: Right, so the HPV that causes cervical cancer is completely asymptomatic. We really don't see anything until we have cancer. So that's a real tricky thing, and the only way to know is to get screened, with a Pap smear. The genital warts are usually fairly obvious. They're usually growths that people feel. They're not usually painful although sometimes they can cause a little irritation or itching. But they're usually fairly obvious when they occur on the vulva or for the men, anywhere in the genital area.

Jill: How often should, in your opinion, should women be going in to get screened?

Dr. Connie: That's a really good question. Our newest guidelines are, at minimum, every 3 years, and as I mentioned, if people get both tests and they're both negative, they can go as long as 5 years. So that's our current recommendation. There's not really a benefit to going in more often. I know that people get nervous, and they want to get screened as often as possible, but there's actually some downsides to being screened too often, and that is false positives that then cause diagnostic procedures which can be painful and stressful. And that's part of why we decrease the frequency of screening, because we were causing a lot of people to have false positives. And the same holds true with mammograms. As you know people have decreased the recommendations for mammograms over time for the same reason, that we find too much screening is actually....can be quite harmful.

Jill: Why can doing the screening and/or Pap exam create false positives? Is it simply because the virus sometimes comes and the body needs time to clean it out?

Dr. Connie: Right! Very astute, yes! So it's better for the virus to come and go on its own. And the typical life of the virus in the body is 7-10 months, so if it's gone by the next test, that's a great thing. So that's a nice reason not to do it too frequently, to try to pick up fewer infections. Because we want the ones that are persistent. The other thing that people should know about pre-cancerous cells of the cervix, is that it takes about 10 or 15 years, even if you have a pre-cancer, to develop cancer. And so we don't worry if we don't find it from one year to the next because we have many years to find it. And so people don't need to worry that they're going to develop something in a few months, that's not typically how this process happens. It's quite slow, and that's part of the reason we've been very successful in treating it and preventing it: we have lots of chances to find it before it becomes cancer.

Jill: You're involved, obviously, this is a component of women's health overall. And you've been studying in this for years, obviously. What excites you most about either this part of your study or women's health in general. What excites you most about where innovation is going or where new thinking is coming, or how even social norms are changing?

Dr. Connie: I think it's an exciting time for women's health overall. I mean, the HPV vaccine has certainly been an incredible breakthrough. But we have many new treatments and therapies that are preventing a lot of surgical interventions for women. It's a great time socially where the Affordable Care Act is now covering services for women that are really important and haven't always been paid for in the past. So, I think...I'm very hopeful that it'll just continue to get better for all of us.



Jill: Now, you're at Harborview, and so you see a lot of patients coming in that have already been diagnosed, do you also see just a hunger for education and new patients coming as a result, or is it mostly all referrals coming in?

Dr. Connie: I see a little bit of both, definitely people coming for expertise that we have, certainly lots of questions. One of the things that all providers have discovered about HPV testing as it's come out is that there's lots of questions that people have. And unfortunately, we don't have a lot of answers, especially in regards to how to prevent oral cancers and anal cancers and things like that. We're still learning lots, but it's definitely a discussion to have with providers and sometimes requires a lot of research to get the answers that folks need.

Jill: So one thing we always close our podcasts with is a piece of advice for our listeners that you want to share as kind of a closing note. What would you like to share with the genneve community?

Dr. Connie: I would say that it's important for everyone to know that HPV is a ubiquitous virus. You don't control who gets an infection, it's not anybody's fault if you get an HPV infection, and that we have very good methods of preventing disease from HPV, so getting regularly screened is super important. And then if there are any young people listening or if our listeners know any young people who should get vaccinated, please tell them to get vaccinated because the world will be a much better place if we don't have to have these problems.

Jill: Yeah, especially when there's a preventative measure that's now in place.

Dr. Connie: And quite effective.

Jill: That's great. Well, thank you, Doctor Connie, for joining us today. This has been great, a huge education for me, for sure, on HPV and something that has a stigma but doesn't need to.

Dr. Connie: Exactly.

Jill: Thanks again.

Dr. Connie: Thank you.