# Hearing Loss in cCMV, in partnership with Midwestern University and Phoenix Children's Hospital

Presenter: Nathan Page, MD; Aditi Bhuskute, MD

- All right, welcome everyone to today's course in our hearing loss congenital CMV series, "What Healthcare Providers Need to Know Now" in partnership with Midwestern University and Phoenix Children's Hospital. So glad to have everyone here with us for the next hour. I want to welcome Dr. Nathan Page and Dr. Aditi Bhuskute as our speakers today. If you would like to learn more about our presenters, additional information and their bios are on the course registration page. And at this time I'm gonna hand over the mic to you, Dr. Page.

- Thank you. We're glad to be here today. This is a topic that we think is really important. We're glad to have this series being presented with some of our colleagues. It's something that we have been working on for a few years and we wanna share some of our work with you and hopefully we find some really relevant information for everyone's practices. In the corner, you'll see this, we'll talk about it some more later, but the Stop CMV Arizona is our little branch of advocacy for patients with congenital CMV and for advancing understanding and education. There may be a similar organization in the state where you are, so if you are interested in finding out more, these are branches that come from the National CMV Foundation but are run locally.

So to start off, here's the official work. Here are disclosures. There's nothing crucial to pick up there. These are our learning outcomes for today's lecture. So, recognizing clinical features of hearing loss unique to infants and children with congenital CMV. We want you to be able to explain the rationale for consideration of cochlear implantation in children with congenital CMV and outline current evidence for screening protocols and treatment of children with congenital CMV. And as you heard before, we try to make it easy with little cues up in the corner when there's something that will be on the examination afterwards. I'm gonna start with some basic information about congenital CMV. These slides are courtesy of Dr. Muldoon. Some of you may have heard her lecture yesterday.

I think she has one more lecture in this series. She is a dedicated scientist and a parent of a child with CMV and has great information and presentation gifts. So if you are not signed up for her lecture, I would recommend doing so. I'm gonna share a couple of things that I think are really important from her work that I think everyone should be aware of. So the big picture, what is CMV? This is a common virus. Most of us have probably contracted it. It typically presents with cold-like symptoms, nothing major, not even something we may even really think about. It's thought that most adults have been infected by the time they're age 40. And they're very common in young children, especially in daycare populations where viral infections get passed around rapidly and frequently.

It is in the herpes virus family. And that means that like other herpes viruses, it tends to stay in your body forever. It can be in a latent state and never reappear, or it can show up later on and reactivate and create problems. And so both of those can be issues for congenital CMV. So, and a key part, something we learned about when COVID came through and we had a pandemic to deal with, is that you can have a hidden infection with no symptoms and that it can impact others. In this case, the most important person it can impact is the unborn child of the patient. So congenital CMV is definitely preventable. And part of what we wanna share in this portion is what you can do about it.

So because CMV is a virus that is in bodily fluids, primarily saliva and urine, contact with saliva and urine can create the opportunity for spread. So CMV can survive on objects where those are contacted. So many of those things you read, teething rings and objects related to food and beverages are all places where the virus can stay and it could be transmitted to another person. So what can we do? All of these actions could help potentially prevent transmission. And in particular, the time to prevent that is during pregnancy. As we mentioned before, congenital CMV for most people typically

causes minimal symptomatology. But for a pregnant woman contracting CMV or reactivating CMV can transmit to the fetus who then suffers the consequences.

So all of these actions, good hand washing, avoiding contact with saliva and not sharing utensils to avoid that can make a big difference in preventing transmission. This is why we think it's important to share that message here in a talk about hearing loss, is that the awareness CMV is remarkably low compared to other conditions. So if you look at this chart, the blue bars that you can see here are the number of, sorry, are the percentage of women who have heard of the condition. CMV here at the top, very low overall in this large survey of women in terms of awareness of the disease. As we get to more and more well-known diseases, as you see down here at the bottom Down syndrome and congenital HIV or AIDS, that almost everyone was aware of.

The orange or yellow circles you see here are an indication of the number of children that are disabled by this condition. So here at the top you see CMV, which it affects nearly as many or about as many children as have Down syndrome every year, compared to HIV, rubella, group B strep at a much lower level. And so what you, what is important here, we think, is the gap between those. So, the amount of disability caused by CMV significantly outstrips the awareness of CMV, and that's something that we're trying to fix. And so I hope helping you be aware of more of these things now and continuing to sort of spread the word through our other efforts is a way that we'll be able to successfully close that gap.

Here's one small success is that this proclamation came out on June 1st from the governor of Arizona declaring June Arizona CMV Awareness month. And if you read that proclamation, it talks about some of these simple behavioral interventions, again, in the hopes that we can make this people more aware of it. And the more I've learned about, you know, I remember thinking when I was much younger about, you know, National Donut Day or whatever it is that comes up and you think, "Oh, these just are

just silly things that people do." But it turns out that awareness days like this of important topics and important topics in healthcare do make a significant difference in what? In awareness.

So in, we hope that in Arizona having this month declared will result in a number of different outlets talking about CMV and that way helping people to feel, become more aware and do more research into finding out what this is all about. So, now we're gonna turn the time over to Dr. Bhuskute to talk a little bit about screening and testing.

- Yeah. Hi everyone. Nice to be here. So, as Dr. Page mentioned, CMV is a very, congenital CMV is very prevalent, yet widely unknown and not universally screened. And as ENT and audiologists, we really think about CMV in the context of hearing loss. But children with congenital CMV can have significant other medical issues, comorbidities, things like that, that all providers would want to be aware of. So universal CMV screening is not standard of care in the United States. We do several universal screenings in the United States, including through newborn blood spot, testing for metabolic diseases and universal hearing screening, which has been a campaign for the past several decades by the AAP and audiology guidelines and early hearing and detection.

2013, Utah kind of led the way in target, doing hearing targeted screening for congenital CMV. So those children who failed their newborn hearing screenings were then subsequently tested for congenital CMV in the neonatal period. In 2023, Minnesota became the first state to implement universal congenital CMV screening. And there are several states around the country, as you can see in this demographic that's below, that have started either the process of screening or at least engaging some stakeholders to discuss it given its prevalence. There are also individual children's hospitals throughout the country that do either targeted or universal CMV

screening. So it is, people are becoming more aware, they're definitely shifting towards that, but we have a lot of work to do.

So there's several different ways that we can screen, and I mentioned some of them on the previous slide, but our, you know, an ultimate goal would be universal hearing CMV screening, just like metabolic screening and hearing screening so that we can ID every case and monitor them closely like we need to. This obviously is a very expensive endeavor, so not necessarily the most practical to start with, which is why some people started with hearing targeted screening for those who failed their newborn hearing screening results. This obviously decreases the scope and the cost and may improve diagnostics for children with hearing loss in terms of understanding etiology, counseling and projected hearing loss and how long we need to monitor them.

Downside is, is that there's a significant number of children born with congenital CMV that don't have hearing loss at birth, and we're missing those, that population. And then there's the also an expanded targeted approach where you screen not only those who have failed a hearing screening, but those that show clinical signs and symptoms such as abnormal imaging, thrombocytopenia, small for gestational age or IUGR for intrauterine growth restriction versa or other physical exam findings such as microcephaly, hepatosplenomegaly, or petechiae. So there's several screening methods, but all of them, in order to get a true diagnosis, should be done before three weeks of age. Given the prevalence of CMV in our population, after the age of three weeks, we do wonder whether or not this is a congenitally acquired infection or one acquired by, say, a family member or anyone that has visited the baby after that point.

CMV screening methods include saliva, urine, or dried blood spot, and you can test for CMV in the dried blood spot for many, many years after the fact. It just is a matter of whether or not that dried blood spot has been saved by the state. I am now in California where they save the dried blood spot for 10 years. Previously when we were,

when I was practicing in Phoenix, they actually only saved their dried blood spots for about nine months, I believe. So there's a limited diagnostic ability if we're, if the state is not saving those dried blood spots. So what, is there a utility in testing after three weeks? And it's an interesting question because in the world of hearing loss, we do have a significant population of children that we don't have an etiology for hearing loss.

And you know, we kind of think about whether or not they're genetically acquired or environmentally acquired etiologies for hearing loss. And there was an interesting article published in actually this year in the "International Journal of Pediatric Otolaryngology" regarding patients who had failed their hearing screening and whether or not CMV testing was feasible after three weeks. And what you see is that there's a group, they divided the children in four groups, those that were, that had CMV-associated hearing loss, those that had sensorineural hearing loss from other etiologies. Group three didn't fit either one or two. And group four was just age-matched normal hearing controls. And what they found is there was a significant portion of the testing that was done either by CMV PCR titer or culture that had very similar kind of patterns as those children with known congenital CMV and sensorineural hearing loss that were tested afterwards.

And the question does arise that if the pattern was similar to those with known congenital CMV, is that a potential etiology for all of these children that we don't have a potential reason for their hearing loss? And whether or not testing for CMV after three weeks of age was still have some utility? So an interesting food for thought, definitely something that needs to be pursued and looked into further. The other question that arises is, can we detect congenital CMV in pregnancy with more accuracy? And it's hard because CMV infection is very much like the common cold. There's no way to really know whether or not that particular infection was a reactivation, a new infection, and both of those things do significantly affect perinatal outcome.

So the traditional testing strategy for congenital CMV is to test IgM and IgG. Both of these markers are related to active first time infection, versus which would be IgM, which is kind of a more immature antibody that your body produces. And then IgG is, if we already have immunity to that particular infection, IgG levels increase because we are reactivating something that we have already been exposed to. So really IgM is very important in saying, "Hey, is this a new infection in a pregnant mother that could potentially affect the, affect her fetus?" And traditional testing shows that if you test for both IgM and IgG, you can get about an 84% kind of accuracy in whether or not this is a primary infection or a secondary reactivation.

But there, but a lot of these women needed follow-up testing. And so recently they've discovered particular proteins on the IgM that they can test for that are much more accurate, particularly p52 and anti-gB. I won't go into what these proteins are, but if we're testing for those particularly, you do see that we get a little bit more conclusive results. So somewhat promising in just figuring out whether or not this is a reactivation, a new infection and correlating that clinically as to whether or not the, there would be any potential side effects for the unborn child. So I kind of briefly mentioned this before and when I was talking about screening, but there are a significant amount of children who have congenital CMV that do not have any sort of symptoms at birth.

And so if you, I kind of, we kind of broke it down into a schematic here that you can see, congenital CMV is about 1 in 100 to 200 live births, but only 10% of those children have symptomatic congenital CMV. And what I mean by that is other findings such as issues with their liver or microcephaly or thrombocytopenia. So issues basically symptomatic congenital CMV and of those with symptomatic congenital CMV, 30 to 50% will have abnormal hearing. And however, even those children with normal hearing screening at birth can develop hearing loss. And that's about 50/50. Now there's 90% of children with congenital CMV can have no symptoms at all. Of those 15, 10 to 15% can have abnormal hearing. And so it's the kids who have normal

hearing with congenital CMV that we're potentially missing with targeted hearing screenings or those with symptomatic congenital CMV that we're missing as well.

And that's where the advocacy for universal hearing screen, universal congenital CMV screening is so important. So the question that comes up a lot is if we can identify these children with congenital CMV, is there utility in treating with some sort of antiviral treatment? Currently, consensus guidelines suggests that therapy should not be routinely recommended for children with congenital CMV and isolated sensorineural hearing loss. But we do routinely treat children with symptomatic congenital CMV with antiviral therapy. And so I wanted to go over a little bit of the literature behind this so we have some understanding as to why, what's being studied and potential side effects. So can early treatment change hearing outcomes? That's the big question, right?

If we treat with valganciclovir, can we prevent hearing loss? Is there some sort of hearing protective mechanism from treating congenital CMV early? So in symptomatic patients the answer is potentially, but it's short-term. So I kind, I broke it down to two different studies that I found regarding short-term and long-term outcomes. So those who were treated, meaning those children with symptomatic congenital CMV, who were treated with a course of valganciclovir for six whole months did show modest improvement in hearing and neurocognitive outcomes. However, when you see the results of this, there is some hearing deterioration over time within one year. And so, but their hearing tend tends to be a little bit more stable.

And so there is some value in doing that. If you look at the exact data I, it can show, I have it written here, but basically over the course of six months, those who did not receive treatment had hearing deterioration, 41% versus none. And at one year, the untreated group, 68% of infants had hearing deterioration versus the treatment group had 21%. If, there's very little study, very little literature out there looking at long-term

outcomes. But there is something that people are looking at and what you can see is over the course of two years, those with congenital CMV did have worsening of their hearing but at a slower rate. So definitely something that needs to be studied more.

In asymptomatic patients, there's definitely a positive literature as well. I have two studies here that showed that in retrospective review of children with sensorineural hearing loss who had antiviral therapy, there was improvement in hearing loss over the course of a year. And if we observed these kids over a longer period of time, there was some improvement in hearing loss over that year as well. So 69% of ears improved or returned to normal and 76% of children with bilateral hearing loss had improvement as well. Over the course of 4 to 10 years, which is even harder to study, they did show that the children who were treated with, for isolated asymptomatic congenital CMV and hearing loss, there was at one year, 23 outta 23 children had normal hearing and those who had long-term hearing loss over the course of 4 to 10 years were those that were untreated.

So there is some argument to say that we should be treating these children with isolated sensorineural hearing loss and congenital CMV. The argument for not treating is the potential side effects of this treatment. Traditionally, this is done through IV valganciclovir therapy that can cause severe neutropenia in children and would require obviously IV access and more invasive techniques and very close monitoring of platelet levels, white blood cell counts. So it's not without its own potential side effects. The mechanism of hearing loss in congenital CMV is widely unknown, but there are some theories. Whether or not it's the loss of spiral ganglion nucleans, immune-mediated injury in response to the virus or direct injury from the virus itself.

So the argument for antiviral therapy would be more related to prevention of direct cell injury from the virus itself and potentially reducing immune-related response and injury to the cells as well. So the reason I bring up treatment is there are some clinical trials

that are going on regarding the safety and utilization of valganciclovir in the treatment of asymptomatic congenital CMV and hearing loss. This first one here is an older study that's still ongoing where they're trying to figure out, those who have congenital CMV, will they develop sensorineural hearing loss after if we give four months of antiviral therapy compared to those who were untreated. And this is mostly a safety and efficacy study regarding valganciclovir, particularly what they're looking for is giving it in an oral form and they wanna estimate the proportion of subjects with asymptom, the asymptomatic congenital CMV, who then develop sensorineural hearing loss by 18 months of life with four months of therapy instead of six.

So kind of trying to reduce the side effect profile of the valganciclovir therapy. There's another clinical trial that is ongoing right now called the ValEAR trial. This is spearheaded by Albert Park from University of Utah, talking about the clinical benefit and safety of oral antiviral therapy for hearing-impaired infants. And so they're actually conducting a multi-centered, double-blinded, placebo-controlled trial to determine whether or not hearing impaired infants with asymptomatic congenital CMV have better hearing and language outcomes if they receive oral valganciclovir treatment. They also wanna determine the safety of that oral treatment, given the potential side effects for IV therapy. And they're also looking at some primary and secondary objectives, particularly related to hearing in hearing-impaired infants with isolated hearing loss with antiviral drug.

Can they reduce the mean slope of total hearing thresholds over the course of 20 months? And secondarily, can they not only determine if valganciclovir improves the following outcomes, including the slope of the better ear and word percentile of score for words by 20 months as well. So really interesting research. I think it's definitely some, I commend them for spearheading this because oral therapy is something that can be, that is a little bit more practical and if we can show that it improves specific

hearing outcomes, we can make an argument that it's worth the potential risk. And I believe I'm gonna hand it over to Dr. Page.

- You are, but before you do-

- Yeah.

- There's a question in the box

- Oh, okay.

- That I wanna bring up.

- Yeah.

- From Laura who mentioned exam question one, which talks about oral versus IV treatment and she wants some clarification. We talked about both options. How does that really look for these infants? Should we be considering one or the other from a practical standpoint?

- Good question. So right now, standard of care is those who have symptomatic congenital CMV are treated with IV valganciclovir therapy for six months, is the standard. The goal of the two clinical trials that I'm showing is can we reduce how long that therapy is done? That was the first trial that I showed. So, four months instead of six. And does it potentially improve hearing outcomes in asymptomatic patients, which is a new concept. And then the second one would be was the oral therapy and can we show specific hearing outcome improvements? So right now the standard of care is IV therapy for only symptomatic congenital CMV. Right now there's not outside of a research setting, people giving oral valganciclovir for hearing loss alone.

- Thank you for answering that. I just looked over that question to remember what we wrote there and there's another key part of that, which is that, that question is for a child who failed their newborn hearing screen. And the question is, should you offer them treatment? And the focus on there is really a question for audiology more than for the medical personnel who would be offering the treatment because that patient has not been formally diagnosed with hearing loss at that point. So all we have is a failed hearing test and nobody should be offered symptomatic treatment at that point without further diagnostic testing.

- Correct.

- We appreciate the question. If there are other questions that come up, please feel free to to send them and if they're relevant, we'll answer them as we go. And if not then we will, we'll pick 'em up at the end. So I want to take a little different direction. So I'm gonna talk about what we know about the natural history of hearing loss for congenital CMV and then focus the rest of the time on treatment. So there are a number of issues regarding congenital CMV that make it a little bit unique compared to other etiologies of hearing loss. And so here's a little outline and then I'm gonna go through some of these in more detail.

So as was brought up before, it's most commonly, hearing loss is most commonly present at birth in these children, but late onset still has a significant, is still a significant factor. So we have both of those situations to deal with. They frequently have unilateral loss and they frequently have progressive loss. All of these things weigh in when we look at considerations for follow up and treatment. In one study of hearing trajectory in children with congenital CMV, they looked at the difference between the symptomatic and asymptomatic patients. And in the symptomatic patients, 51% of ears, so this is

looking, you know, each baby counts twice 'cause they're counting each ear individually. 51% of ears had some congenital hearing loss.

17% of ears develop hearing loss over the follow up period. In the asymptomatic group, only 5% had hearing loss, 5% of ears again, had hearing loss present at birth and 11% developed delayed onset hearing loss. So this is one attempt to give some numbers to this group to try to figure out how we're gonna manage those. In addition, those babies who had MRIs that showed white matter lesions, something commonly seen in congenital CMV, were four times more likely to have developed delayed onset hearing loss. So that may be another factor that helps us understand who might be at the highest risk. So here you see in these red circles, little areas of light spots, those are the white matter lesions that can develop in patients with congenital CMV that can at this point are not considered predictive in general in how we estimate what the children's outcomes are gonna be, but certainly can be used to help raise the question of congenital CMV in some of those patients that, for example, didn't have serology testing when they were infants, but have patterns of hearing loss that are consistent.

Unilateral hearing loss is very common in this population. So these are two studies that again looked to help us determine a little bit more about what to expect from these children in, over the course of time. So in one study, looking at children who were born with unilateral hearing loss or with asymmetric hearing loss in the better hearing ear, 12.5% had decline. That was over a long follow-up period of four and a half years. But 70% had a decline in their impaired ear. So there was a significant drop in the worse ear, but still with 70% of the worse hearing ears losing hearing over time. But yet one out of eight of the normal or better hearing ears also dropped over the time period.

In the second study, they demonstrated that 75% of the children born with congenital unilateral hearing loss develop hearing loss in the normal ear over long-term follow up. And I've got a graph to show that on a subsequent slide. So this is, I think this is a

Kaplan Meyer curve. This is a great way to measure these kind of issues. So on the Y axis here we have the proportion of children with delayed onset hearing loss, and on the X axis we have age. The blue line here is the patients who had normal hearing in both ears at birth with congenital CMV and these patients were followed over time. And each tick up you see here is from a patient who has developed sensorineural hearing loss.

So you see this gradual climb over time up here to age 18, but the total here is around say 18%. So by age 18 in somewhere in the teen percentages of kids develop hearing loss if they were born with normal ears at birth. The second group here, the red or brown line here is are patients who were born with unilateral, congenital sensorineural hearing loss. And same process, but you see how quickly that ramps up until we're around 75%. So as, when I was in training, we learned that children with congenital CMV could have progression but only for the first few years of life. So we used to say follow them closely up to about 3 years of age and at that point you're pretty safe to leave them alone.

And then as numbers suggested higher, people said 5 years of age and then 12. And now really it's pretty clear that there can be decline up to age 18. Less commonly in those children who were born with normal hearing in both ears, but very common in children who have at least some hearing loss at birth or very early onset. So that's a key finding in consideration of how we manage these kids. So we'll talk about them more in the treatment section. As well as how we follow these kids and how we consider surveillance. Here's one more slide that I think is very helpful to see. So these are children with congenital CMV who developed hearing loss over time. And this is the same group of kids but looking at severity.

So the white is normal hearing, all the way down to red is a profound hearing loss. And so you can see this is A, are the worst hearing ears and B, were the normal hearing

ears or better hearing ears. And so when we start the study, there are only 6 patients of this group of 20 that had some hearing loss in one ear and they had normal hearing in their other ear. As we follow over time, you see that both the severity increases and the number of children increase. So by the time we get to 18 years of age, we now have 20 children who've developed hearing loss and the proportion of children with severe to profound hearing loss has changed dramatically.

In the normal hearing ear, we start with these kids who are all normal and you see that there's still a significant proportion of normal hearing ears by the end of the study, but there's development of hearing loss even in the better hearing ears over time. So again, I think this emphasizes that the worst hearing ear is certainly at the greatest risk of progression over time, but that even the normal hearing ears and even the children with bilateral normal hearing at birth are still at risk for progressive hearing loss over time. This is one study that I think is very helpful as well in understanding the role of congenital CMV and creating inner ear damage. So this study looked at children with inner ear impairment from congenital CMV, sorry, children with congenital CMV and then examined those with inner ear impairment looking at vestibular and cochlear impairment.

And what they found is that the first trimester was the most concerning area where there was the most significant damage. Those children typically had vestibular and cochlear damage causing hearing loss and vestibular impairment. And that makes sense given the, what we understand about the development of the inner ear. So the odds ratio you see there is 4.5. So if, that's in comparison with children who contracted congenital CMV in the second or third trimester. So if the, or I should say the mothers who contracted CMV during the first semester, first trimester had a 4.5 times likelihood of having hearing loss compared to the other two. In the second trimester, those children typically only developed a vestibular impairment and those infections that occurred in the third trimester resulted in no cochlear or vestibular impairment.

Again, as we saw in the previous study, when they looked at brain imaging, in this case, prenatal brain imaging, so these are our fetal MRIs or ultrasounds that demonstrate a brain lesion, they had a much higher risk of developing inner ear impairment. So that was an odds ratio of eight. So eight times the likelihood of developing inner ear impairment if you had lesions versus those fetuses who did not have lesions seen on preoperative imaging. Again, I think this takes us back as we looked at the sort of the public health component of this that we're looking at children, we're looking at particularly the timeframe of that first trimester where some pregnant women may not even know they're pregnant and may contract CMV from exposure to their other children or providing childcare for other's children.

All right, I wanna talk about management. This is a key area certainly for Dr. Bhuskute and I, and I'm certain for most of you as well. This is one of my congenital CMV patients who presented very late. So they were, she was diagnosed in infancy and had hearing loss at birth. She was fitted with a hearing aid, maybe had benefit early on and then over time really wasn't benefiting much and was eventually fitted with a Baja. And she wore a soft-band Baja for a number of years with some benefit. But as she got older, the family became interested in a surgically implanted device and actually came to see me to talk about surgical implantation of a Baja and we elected to place a cochlear implant instead.

And I'm gonna talk you through some of the rationale for that over the next few slides. For all of these kids, as we've talked about, audiometric surveillance is key. So we know that we need to follow them over time. We need to make sure that their hearing impaired ear doesn't worsen and we need to make sure that their normal hearing ear doesn't develop hearing loss. For the children with hearing loss, wearing a hearing aid or a bone conduction device can be valuable and may be all they need for many of them. But cochlear implants are certainly an option for a lot of these kids who have

severe to profound hearing loss even unilaterally. And I wanna talk especially about that today.

So this is, this patient I can't take credit for, this is Dr. Bhuskute's cute patient. But as we look at the data we saw from before, the candidacy for cochlear implantation, which is present very young, significantly increases as we head toward the teen years. So this looks like in the final stages at 18, about 13% of kids with congenital CMV were candidates for cochlear implantation. And so this is an option that we should be looking at for these kids who qualify because of the benefits, given their risk of progressive loss over time. Indications as we know, bilateral severe to profound sensorineural hearing loss. Just in the last few years, unilateral profound sensorineural hearing loss has become an FDA-approved indication for cochlear implantation.

Prior to that FDA approval, certainly it was still being done, but on a much more limited scale. Congenital CMV was one of the diagnoses that we frequently use to justify a request for cochlear implantation from an insurance company because of those progressive risks. And large vestibular aqueduct might be another where we know there's a significant likelihood of progression over time and we lose some of the capabilities that a bone conduction device might offer. So when we look at the rationale for cochlear implantation in these patients, it is certainly common that they have congenital unilateral hearing loss. The risk of contralateral loss is key because you lose the ability to that bone conduction device, which is being used in a cross setting, right?

So cross hearing aid would be another option for some of those kids that you're using it, you're piggybacking from the other ear to provide sound and eliminating their head shadow effect. But if they have progressive loss or if they develop loss in their normal hearing ear, that no longer becomes an option for them. And if that happens in years from the time of onset as we saw in many of these kids, age 8, age 10, age 15, the

possibility of implanting the ear that was deaf at birth can be lost. At least the potential for good outcomes in that ear can be lost. So a cochlear implant is the only option we have for utilization of the deaf ear to provide hearing.

So that rationale is something that we use in our cochlear implant team as we have these discussions and as we look at, as we talk to families about what they're considering and the value of preparing the ear, the previously deaf ear in the case of progressive loss in the contralateral ear in the future. This is a slide that I think is really fascinating. This comes from Toronto, which has an outstanding cochlear implant program both clinically and from a research standpoint. And the idea of their study was to look at brain organizations, so cortical organization in patients with unilateral hearing loss. Now this was not in only CMV kids. The info on this slide is for a group of children with unilateral hearing loss or single-sided deafness, not necessarily from CMV.

A study has shown, large study shown that sound localization was almost always improved in these kids. That 80% showed meaningful improvement in speech perception, both in noise and in quiet. And that patients with shorter duration of deafness had improved outcomes. These are all questions that we had as we think about expanding cochlear implantation in more and more kids with unilateral hearing loss or single-sided deafness. I think a lot of people in the community, both audiologists and surgeons, speech therapists with interest in this area, were concerned that trying to implant the deaf ear in a child who already had good hearing on the other side was unlikely to provide significant benefit, but that has not been the case.

So speech outcomes certainly show benefit in most of those kids and the changes in the brain are impressive. So what they looked at in that study was children with normal binaural hearing, children with unilateral hearing loss who used various cross devices or bone conduction devices, and then children who underwent cochlear implantation for single-sided deafness. And what they found was that within six months of cochlear

implantation in their deaf ear, those children had developed patterns of cortical activation that were very similar to children who were born with and maintained binaural hearing. So the idea here is not just that we can potentially provide a better hearing outcome immediately, but we actually change how the brain is organized to provide more typical cortical organization for those kids.

All right, so for a summary of hearing loss and congenital CMV, these are the the key things that we'd want everyone to recognize. Hearing loss in congenital CMV requires long-term follow up. We know to age 18 based on what we're seeing in the data already and possibly even longer. It, there may be that these children or now these adults will continue to have progressive hearing loss over time, although that data does not yet exist. Progressive hearing loss is very common in this population. As we talked about with my patient earlier, she developed some progressive loss. She had some loss at birth, had significant progression to where hearing aids were no longer of benefit and ultimately relied on a Baja, I didn't come back to her story, but she elected for a cochlear implant and has done tremendously well with even though she was implanted late, I wanna say 11 or 12 years old, she'd been using her devices for a long time.

She had progression, we think around age three. So she had a fairly long duration of deafness and has developed excellent speech reception and understanding in the previously deaf ear. So that's only one case, obviously, but that is the kind of story that I think spurs us on to considering that kind of intervention for those other kids in the future. We know that antiviral therapy has short-term benefits with hearing loss. Long-term benefits are still being studied and the risk benefit ratio, as Dr. Bhuskute discussed, is still questionable. There are some places that will treat children with only isolated hearing loss with antivirals, but current consensus guidelines would recommend treating only children who are symptomatic. That may change in the future as we gather more information.

Early identification treatment is imperative not only for congenital CMV kids but for children with hearing loss because of the potential benefit to them of early intervention for them with speech and amplification, et cetera, in all children with hearing loss. Because of the risk of contralateral hearing loss in patients with single-sided deafness with CMV, cochlear implantation should be considered. That's something that we feel strongly about, that we've seen great benefit from, and I think that will become more widespread in the future as the data continue to accrue. Screening strategies do vary, as you saw from state to state, but all of the strategies lead to earlier diagnosis and earlier intervention and we hope, we think improved outcomes for children with congenital CMV.

That's another topic for study, something we're working on here. In Arizona, we've done a pilot study looking at the feasibility of universal screening and were able to successfully screen 250 children for CMV. The challenges were many in terms of setting that up, including coordinating with different hospitals, arranging for the mechanism for things to go to the lab when that hasn't been arranged, follow up for the kids who had positive screening and of course, cost. So screening every child is a significant cost and so states will weigh that into consideration when they look at potentially mandating screening for all children. So while we are proponents of a universal screening mechanism, we think that'll identify the most kids, all of the screenings that have been done have been successful in identifying children with hearing loss with congenital CMV earlier, potentially leading to better outcomes.

And so we applaud those advocates in other states who've been able to successfully bring screening to their state. That is our material for today, guys. I'll make one more plug for our Stop CMV Arizona organization. We are proud of what we've accomplished so far and members of that organization are in large part those who are presenting in this series of lectures on congenital CMV. We feel we've made a little bit

of progress and we're hopeful to see much more progress as people become more aware of what's going on and develop interest in joining the fray.

- With that, we have a couple questions. One very closely related to what you were just talking about, Dr. Page. So I'll start with that one. And then we have a two-part question from someone else as well. So the first one is from Alexandra. "For places that don't currently regularly screen for congenital CMV, are infants who are diagnosed with sensorineural hearing loss currently typically tested for CMV as part of a workup for hearing loss? And how do we know a child's hearing loss is likely secondary to congenital CMV and therefore recommend appropriate monitoring or following if it's not being regularly screened?"

- Those are excellent questions. So I'll answer the second one first, which is that realistically we don't. That is a huge knowledge gap. So I would say that in our clinic, we very frequently see children who present with hearing loss, say for example, congenital profound unilateral hearing loss, that could very well be consistent with congenital CMV diagnosis. But if they present to us at one or two years of age, we have no way of confirming that diagnosis. Sometimes an MRI will demonstrate those white matter lesions, which can suggest CMV as a diagnosis and maybe push us that direction, but we can't confirm. And so screening is really mandatory for us to be able to gather enough information to be able to know how to appropriately follow those kids.

And so I think it leaves us with a huge knowledge gap. The first question is harder to answer because the variability is so widespread. From the, you know, Dr. Bhuskute talked about the timing of testing. Right now most experts agree that if you test, if you want to diagnose congenital CMV, the tests need to be performed before three weeks of life. And because it is such a prevalent virus, if you test after three weeks of life, you can't confirm whether that was a congenital or an acquired infection. And if it's an

acquired infection, the risks are really very low. It's essentially harmless to anyone who's already been born. And so it is trying to screen early by a universal screening mechanism or utilizing something like a blood spot analysis are the only ways to do that.

So, you know, in Arizona we don't keep the blood spots very long, so a late identification doesn't allow that possibility. In a state like California it sounds like going back could be an option to test them. But testing a five-year-old child for CMV is not helpful because we, it's much more likely at that age that they've developed an acquired CMV infection, not a congenital one.

- After about four years of work, my partner, my new partner here has developed a way for us to ask for the newborn blood spot to be tested. It has significant restrictions. We can only ask on Thursdays, but there has been some progress in doing so, and I have tested one newborn's blood spots since I've been here for that. So it really depends on how long they're keeping the blood spots to, for that to be a feasible option. But I agree with Dr. Page that really the answer is screening and until that point, us as hearing professionals are gonna be monitoring all our patients with hearing loss closely and trying to rule out other etiologies until we have that testing mechanism.

- Yeah, even with some of those ongoing, the blood spots screening is not as sensitive as saliva screening and urine screening.

- Correct.

- And so we know that even in those cases we're gonna miss some kids who definitely had congenital CMV as the etiology of their hearing loss. So we'll still push for the others. The expanded targeted screening looks like a great method to collect more of the kids who are at risk. The listing that I gave there is from Utah, who has been, was

the first state to put in some hearing targeted screening and now is expanding that to include these other areas. And we are trying to put in some clinical criteria, not statewide, but at our hospital to start with, to be able to do that type of screening and be able to pick up those kids early because we think there's enough clinical justification for that without, although we may not yet have the data to take it to our state legislature.

- For the sake of time, we have a couple other questions. So the next is a two-part question from Carol. So we have, "Is it known how long congenital CMV can be shed? Given that it can present asymptomatically or symptomatically, is there any way to know when things are quote unquote safe? Related to that, what would be your recommendation for any professional such as DHH teachers, SLPs and those working exclusively with hearing-impaired children if they become pregnant, how to best protect themselves aside from things mentioned earlier in this lecture?"

- These are great questions and you're getting a little outside of my expertise to go into some of the detail there. I was just pulling up another talk that I gave several months ago because we had a little bit more of that data in there. I don't know the data about shedding, but there's one concern I'm afraid that I have to share, which is that we know that babies with congenital CMV can shed for months.

- Mm-hm.

- So you remember the arguments about COVID when people said, "Well, if it's X number of days afterwards, it's probably gone." And there definitely have been demonstration that those babies shed for months. And so presumably patients who are asymptomatic carriers of congenital CMV also could potentially be shedding virus for months. And so there's not an easy way to say that you could just wait a certain amount of time and be done. The other challenge is if kids are acquiring this, say at

daycare, and they have just a routine snotty nose like every other viral infection, how do you know when they even contract the congenital CMV? And so I think it will be taking much wider precautions overall.

Now in the clinic when you're talking about, you know, doing audiology for example, your risks are lower. You're looking to avoid contact with bodily fluids, particularly saliva. Hopefully you don't have too much urine contact during your sessions. But that's something for childcare professionals that we look at for sure. So those who are changing diapers, especially are gonna be exposed to urine. But you know, with babies, infants, toddlers, I mean there's a fair amount of saliva in my clinic, there's no question. And so all of the precautions that would lead you to be able to avoid contact with saliva are really the keys. And so some of that is, you know, wearing gloves when appropriate and washing hands frequently to avoid, you know, it's not absorbed through your skin, it's usually from your contact with other, you know, mucus membranes or things like that.

And so washing your hands well, if you have contact with saliva, things like that are really the ways to go. There. I wish there was a way to say after X number of weeks of them being sick or whatever, it's no longer an issue. As far as I know that data doesn't exist and the long-term shedding in the urine is enough to raise concern that there could be long-term spread in saliva as well.

- Next question is from Lori. "For new for parents, the need for a knowledge that their child's hearing loss will likely deteriorate as they age is important and can cause much stress at the same time. How do you recommend counseling successfully?"

- Oh, that's a great question.

- Yeah.

- Do you want to take it? You want me to?

- Yeah.

- We both probably have our own ideas about this.

- So I feel like when you're counseling parents with hearing loss, there is a certain amount of stress that goes along with that diagnosis in general. It, my go-to is to give numbers and statistics. I feel like that's helpful, especially for some parents. If we're talking about risk to the contralateral ear, like Dr. Page mentioned, we can say about 10 to 12% of normal hearing ears can deteriorate. So we wanna monitor your child's hearing closely and you know, ensure them that as a hearing loss team, that we are here for them and if they have any concerns, we will address them and monitor their hearing closely and provide resources as well. But it is hard because the diagnosis of congenital CMV or hearing loss when you're the one telling them for the first time that that's happening, it's not an easy conversation to be had and sometimes needs multiple conversations to really understand the implications.

- Yeah, I think there's definitely, we've all seen it if we take care of children with hearing loss that parents go through this grieving process. You know, sometimes parents grieve heavily even when their child just has a very mild, easily manageable hearing loss. And so I agree with what Dr. Bhuskute said. I think that sharing with them what we do know in terms of numbers and risk, it can be helpful for some people and providing hope. One of the things for everybody when I talk to 'em about hearing loss or another difficult diagnosis is to offer them the best I can, what hope there is. And I think with hearing loss, there's always hope. We've got great interventions, we've got hearing aids that become progressively better.

We've got, you know, bone conduction implants and cochlear implants. For those kids who none of those are an option, we have ASL. Which for some parents I know is still a feel, they feel a loss at that. But I want them to see, you know, this is something your child can work through, this is something you can work through. This is something that we can provide benefit for and that we have a team of people, you know, Dr. Bhuskute said, telling them about resources. I think we want to say, look at all these things we have for you. Sometimes the resources are overwhelming between the state and advocacy groups, parent groups like Hands and Voices, plus your medical team, your speech therapist, your early interventionists, can be a lot of people there. But helping people know that we have people that are there for you. You're not alone in trying to deal with this.

- And last but not least is a question from Wendy. "Do you find that pediatricians know about congenital CMV? Are they educating parents? and do parents know this is a potential cause for their child's hearing loss?"

- No.

- Yeah. Short and sweet. Yeah, I mean this is the whole reason we're doing these lecture series is that there is a humongous knowledge gap in the prevalence of congenital CMV and knowledge about congenital CMV. So very, very important.

- Yeah, we have some data. Dr. Bhuskute worked on a survey when she was here with us in Phoenix and some of that data will come out still that was used to survey pediatric residents and attending physicians and I, who else? Audiologists.

- Audiologists, speech pathologists.

- And overall it was there were disappointingly low numbers in terms of knowledge about CMV. For something that is so widespread and can cause so much harm, it's something that we are just not really aware of. And so, no, I would say pediatricians are not counseling and obstetricians are not counseling about it. And, we've talked to some OBs as well who say, "You know, I got all these things to deal with, this is just not even on my radar." And so that's something that we'll have to change over time as well.

- And I think that's all the questions.

- Thank you everybody. Thanks for the good questions. We appreciate all the interest and engagement.

- [Farzana] All right, well thank you Dr. Page and Dr. Bhuskute, it was a pleasure to have you join us today and share your expertise with us.

- Thank you.

- [Farzana] And thank you so much for taking the audience questions. We always appreciate an interactive session. For our members, this is our second course in our seven part live series running throughout the month of June at various times and dates. So we hope to see you in the upcoming courses in the series. We are at the top of the hour. So a couple of thoughts before we sign off today. Today's live recording will be available in our library in the next few days. So take your time and review the research and resources at your own pace. And remember, you need to pass the multiple choice exam with a score of 80% or higher given two attempts and within the next seven days. Thanks to our members who participated in today's course, we look forward to your feedback on the course evaluations. Have a great rest of your day and take care everyone.

- Thank you.