

REMOTE CART  
NCHAM-Webinar Series:CMV 101 -(Adobe 4.1)  
11:30 a.m. - 1:30 p.m.  
August 31, 2020  
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11:49 AM (ET)

CAPTIONER: Standing by. .

»: For everybody that is joined the webinar we will be starting the CMV 101 webinar in about seven minutes. Stay tuned.

ALLYSON WARD: This is Alyson Ward. We will be starting the CMV 101 webinar in about five minutes.

ALYSON WARD: If you have joined us today for the CMV 101 webinar, we will be getting that going in a minute. We are working out a couple of things to make sure that that our webinar is accessible to those that are deaf and hard of hearing by getting the captioning of and going and it looks like we are just about there. Hang tight. We will start just about two minutes.

Okay. Welcome to CMV 101. You should be hearing audio at this point. If you are not receiving a strong audio signal, you might need to adjust the settings on your computer or headset and if you still do not have a video, audio, might need to sign off and come back in. Please check the quality of your audio transmission at this point and we will see how good we are. Hopefully, we can move forward here.

It looks like most people have good to excellent audio, which we will take for sure. And also as we get started I would really like to have a better idea of who our audience is today. If you will take just a minute and fill out this poll and let us know who we have on the line today.

Very good. It looks like we have a pretty great mix of individuals. Welcome. We are happy to have you join us today. And the webinar, we will go ahead and get started right now. This webinar will be recorded and I will go ahead and start the recording right now.

»: Audio recording for this meeting has begun.

ALYSON WARD: So as mentioned, the webinar is going to be recorded and will be processed and posted on the website within the end of this week. Please do not select full screen mode on your computer as that will really change the way that your computer displays AdobeConnect and we want to make sure that you experience the full gamut of the functions that we have.

And just to give you a heads up on the form up today, I will do a quick welcome and then introduce our parents tori who is going to be Rob Tetrault from CMV, Canada, and we will turn it over to him in just a minute and then we will be hearing from Dr. Gail Demmler-Harrison and she will be doing the presentation of CMV 101. Before we get started I do want to remind everybody that we are still going to have a CMV meeting hopefully on August 22 through 24, 2021 and we were so sad that we cannot go to Ottawa right now and just the pandemic certainly has changed a lot of things in the world. We hope to be able to see you in Ottawa next August.

So toward the end of the webinar I will be opening up a question and answer box for any questions that you may have with Dr. Gail Demmler-Harrison and that will appear as her presentation comes to an end.

So first off, as I mentioned we are going to hear from Rob Tetrault from CMV, Canada,.

A little bit about Rob: He is the father of four and he is president and the founder of the Canadian CMV foundation and an award-winning portfolio manager. Since their son a's diagnosis in 2008, Rob and his wife Michelle have dedicated their life to fighting CMV. A passionate advocate for the cause, is optimism with the respect for the eradication of CMV is positively contagious and I completely with that though agree with that. Rob is a very passionate person in general and very passionate about eradicating CMV and Rob, I will turn this time over to you.

ROB TETRAULT: Thank you. Thank you. Whoever wrote that that is a fantastic bio. Thank you for joining. I am in the of the conference, the public health the policy conference, which we are supposed to be an Ottawa for today. You guys will love Ottawa next year. Put it on your calendar. Do not miss it. It is so culturally diverse and beautiful and so much to do. It is our capitol and just a great, great city. Don't miss it next year. It will be a believable and thank you for the great introduction and thank you for being here. And I am the president and founder of the CMV, Canada, foundation. The reason we want everyone here, the co-chairs and Alyson, we think I am obviously biased because I'm a parent, but parents are a very, very important part of the story and obviously, we would not be where we are today with that you guys that are doing the hard work, the researchers, the audiologist, the entire group of people that have dedicated their entire lives.

But we are representing the parents side today and I will do a short intro today. You will hear some of stories from some other parents and my story is a little bit different. My son was born in 2008. He does not have profound hearing loss. But he was a catalyst to create a movement piece that my wife and I would decide to make a difference in that difference we told ourselves would be that we need to change the status quo in this country. We did not like how our experience was and we did not like how my son was treated and how the diagnosis went. We decided to make a difference and that difference is the result in the current today is the CMV, Canada, and we are solely dedicated to raising research and awareness and advocating for change for CMV. My son is

now 12 and will be stepping into junior high next week, crazy how quickly that happened. I am getting so old.

Regardless he is doing fantastic. His name is Alexander and he is a beacon of joy and just a wonderful human being and incredibly humble and passionate guy in his own way. But for us when we said we would make a difference, we knew there was no universal screening and we know that he would have been missed if it wasn't for completely random event. You got treated as one of the first children in our province to be treated for CMV, the old school type of valiant career, what was it, six weeks, I think it was but anyway regardless we decided we would start by raising money and raising money and advocating and we wanted to change the rules and Manitoba respectively with respect to screening and so we got to work my wife and I.

Since then we raised about \$700,000 and that money has gone toward advocating and supporting and changing policy and changing procedures in Canada.

We have had a little bit of success and we've had target screening passed by the first province in Canada. The province is like a state for you guys. The first province in Canada got it past and that was about four years ago and then we got the universal screening passed. And by the way, do not miss the Friday talk. The focus will be on the universal screening in Manitoba and Ontario and the neighboring province.

We continue to raise money and we recently hired staff and CMV Canada is now growing and the Facebook page and YouTube page, we recently put up the video page for the case of universal CMV screening. We are not stopping. Us as Canadians and me as chair and president of the CMV, Canada, page I am not going to stop. I am not going to stop at do we get universal screening passed everywhere in this wonderful country and then further, we are going to eradicate CMV and we will do that together. Parents advocating for change and you wonderful people, everyone who is working toward finding a solution,, either treatment or vaccine or whatever it may be. We will work together and make this

happen. We need parents to advocate and we are not going to stop advocating. One thing I want to make sure is that you know we will always be here to support you. You guys have a wonderful organization in the US. They are going to be speaking tomorrow or later this week. We will have a webinar series. So after this week, a weekly series which is noon Eastern every day this week starting in about three weeks from now or two-and-a-half weeks on the 16th, we will have a webinar series and that is going to be a focus on bringing some of the presenters that would have presented today and tomorrow and Ottawa. They will have 20, 25 minutes, to give us a little bit of a tease of what they are working on and what to expect next year. I recognize my time is short today and I want to remind you all and the first of all thank you for coming here today. The chair and co-Chair of the public policy conference, thank you for being here today. Please do not miss Ottawa 2021. Do not miss the rest of the week. We have someone wonderful parent speakers. They are awesome and they will tell wonderful stories about their kids. Again, thank you for taking the time, go to our website, more importantly go to our Facebook page, <https://www.facebook.com/cmvcanda>, we have testimonials and stuff and do not miss Ottawa 2021. It is the best city and will be so, so good. I am so proud of the line and work we have done to make this happen. Alyson, I will stop here. I will bring the phone back to you.

ALYSON WARD: Thank you, Rob. And as all the attendees can hear the enthusiasm in Rob's voice, we completely agree that that parent passion has really fueled a lot of change in the US and Canada and really across the world in raising awareness of CMV. I got shot a text right after we started that Alyson, you forgot to introduce yourself, but that really is a function of me getting nervous and having too many moving parts. So my name is Alyson Ward and I work at the National Center for Hearing Assessment & Management. We are located in Utah. And we provide technical assistance to all of the states and territory Newborn Hearing Screening Program's.

And the link between hearing status and CMV is really how NCHAM which is our acronym has really gotten involved in CMV and started the cap public health and policy conference. I think that was in 2014. So the '20 conference in

Ottawa it was going to be our fourth meeting. And every year, every year we have had the conference every other year and it has gotten more and more successful and more and more attendees from different countries and really has been a catalyst for a lot of legislation and also just awareness campaigns even without legislation across the US and elsewhere.

So just a little bit about us. And I am going to now move to introduce Dr. Gail Demmler-Harrison. I know her patients called her Dr. Gail. She is a professor of pediatrics at Baylor College of Medicine and an attending physician at Texas Children's Hospital at Houston, Texas. She is an expert with over 30 years of experience in diagnosing and treating babies born with congenital CMV. And she also does research on the biology, epidemiology, diagnosis, and treatment of congenital CMV and has a special interest in the long effects of CMV on the growth, development, vision, and hearing on the children as they grow into adults and she is an advocate for CMV awareness and holds this in the medical and public community and I will attest to just the amazing person that Dr. Gail is and what love and caring that she shows each of her patients individually and Gail, I will turn this time over to you.

GAIL DEMMLER-HARRISON: Thank you, Alyson for that wonderful introduction. And I am going to advance my slide. I am not seeing my slides on the screen. Okay. Here we go everyone. Welcome. I have a blank screen now. Sorry. I apologize. My screen is blank.

ALYSON WARD: I can advance your slide. I was just showing the header slide. I am not sure why your screen is blank. It looks like maybe you got kicked out of AdobeConnect again. But do you want -- okay. We will take a minute.

GAIL DEMMLER-HARRISON: It looks like I am back in. Okay.

ALYSON WARD: I am looking for your name back here to move you back up. Here we are. And we are off and going again.

GAIL DEMMLER-HARRISON: Okay. Brilliant! Welcome to congenital CMV 101 the basics. This is going to be a whirlwind tour of just some hot points and high points of congenital CMV but for some disclosures. I will talk about the off label uses of different things with finding supported by the clinical trials, expert opinion and consensus panels from the guidance of AAP. I received research from different sources and I may research the data from this support. We will go over the biology and epidemiology and clinical manifestations and diagnosis and treatment and prevention in a pretty world when tour.

So first who is CMV, CMV stands for cytomegalovirus, a.k.a. cyto, cell, megalo equals big and virus equals poison. It is ubiquitous of virus with protein manifestations. One of the first virologist studied congenital CMV and it is known as an opportunistic virus. It tends to prey on those less robust immunologically. It is a stealth virus and under the radar and most infections are silent. I call it the most common virus that people have never heard of and especially I call it the elephant in our living room. And those of you involved in this, get this, you are right there in the living room and no one even acknowledges you are there, but we need to change that.

Let's look at this with facial recognition CMV. It is a large double-stranded DNA virus and has about 240 KB genome and 162 capsomeres arranged in what is called the icosahedral symmetry. It is very unique and sometimes annoying bio characteristics. First the latency persistence and reactivation. What is that? It is a resting dormant state, but it is also very expressive at the cellular level. It is expressing numerous viral proteins and mRNAs which mediate immune evasion. And that happens in a variety of our human cells. It can then also reactivate and produces an active infection. We can detect them and it happens in a variety of human cells in our body.

It also can cause some dramatic and symptomatic infections. In the asymptomatic infection it is silent. But it produces no obvious symptoms and the person and these are most infections.

Now symptomatic infections are those active viral infections that produce symptoms and signs that we can see or feel. Many different signs and symptoms can occur in these are actually a minority of the CMV infection's.

And then finally, CMV can cause primary or first infections with CMV. And recurrent infections are, either reactivation's where your own endogenous CMV reactivates in your body and most recurrent infections are probably reactivation's.

But we can occasionally experience a reinfection with a new sort of CMV that might impact your body.

Let's now dive into the epidemiology of CMV as it relates to congenital CMV. CMV infections are common and just about everybody will acquire CMV at some time in their life. In utero or congenital infections, what we are going to discuss, postnatal infections can occur in infants from maternal breast milk or contact with other people. Toddlers are hot zones for CMV and they transmit between each other and adults very commonly. Adolescence is another time of increased CMV acquisition as they get to know each other in many different ways and the in adulthood, as well as you raise your own children or get to know other adults in ways that are intimate to where the virus can be transmitted.

It is not only person to person but can be transmitted by blood transfusions and by organ transplants as well. So let's look at congenital CMV. And these are just broad numbers and generalizations. These numbers can vary depending on the study, the demographics of the population study and the method use. But this is sort of an easy way to look at congenital CMV. At least in the US, there is about 4 million births annually. And if you are in Canada, just put in your annual birth and we can say 1% of babies are congenitally infected with CMV. And this ranges from .2 to .4%. Of the baby infected year after year 10 to 50% of them will have symptoms in utero that includes us in that the baby may have congenital CMV and most of the babies will have some form of neurologic problems and five to 8% of them will experience fetal or neonatal deaf tragically.



The vast majority of babies with congenital CMV are asymptomatic or very, very mildly symptomatic where you cannot pick them out of the newborn nursery at birth, but they are shedding large quantities of the virus. Up to about 25% will have hearing loss if you follow them long enough up to age 18 years of age. In the early years, from about age five to eight, 10 to 50% have hearing loss and a minority will experience some mild vision loss, not as significant as those in the symptomatic category.

Now it all begins with the mother, but let's look at pregnant women in United States. And I am sure it is very similar to pregnant women in Canada and other parts of the world. Most women when they enter the child bearing years are seropositive. It is 55 to 85% and depends on the demographics of the population studied. Less than 1% will experience a current infection during pregnancy and transmit it to their baby, but the good news is that these babies almost always are born without symptoms or minimal symptoms and rarely will have problems at birth. There is a great amount of research going on the role of the current maternal CMV infections and hearing loss. So this particular side of the graph may involve as we gain more knowledge.

Some of these will enter seronegative and they never had a primary infection and are now to the virus. About 4% of the range, generally one to 7%, but it can go up to 15% if you are a daycare worker and 50% if you're living with a toddler actively shedding CMV will experience a primary CMV infection. If you experience a primary CMV infection while you are pregnant about 40% of the time and there is a range of 30 to 55% but about 40% of you will transmit the virus to your baby. And then like we discussed some will have symptoms at birth and suffer the sequela. Most will be asymptomatic. But what does CMV do to our babies? Some babies are symptomatically at birth and I look at symptomatic CMV in three categories. Symptomatic CMV have some sort of symptoms at birth that we will go over in a minute. Symptomatic with central nervous system or brain involvement, that is we know their brain or their sensory organs are affected. And then a new emerging neuro phenotype that we are trying to raise awareness here and describe more detail is a primary neuro phenotype

symptomatic CCMV. They don't have the usual symptomatic manifestations that we associate with congenital CMV. Here are two babies. One is term in one is preterm and they are both born with congenital CMV. So what are the symptoms? The babies of symptomatic CMV are the tip of the iceberg. They have the classic signs and symptoms and they can have one or more of these or combination thereof. They can be small for gestational age. Jaundice usually with direct hyperbilirubinemia. They could have a skin rash on enlarged liver and spleen, low platelets, or abnormal liver enzymes. They can also if they have central nervous system involvement and probably at least two thirds of them will, microcephaly, which is small head size and other neurological signs like bitterness or sword not moving well or seizures or infantile spasms, and him be sis, which means one side of the body doesn't work well. If your baby shows that it prefers one side or the other as an infant before the age of three years that is not normal. Or they might have abnormal tones, hypertonic and stiff or hypotonic and kind of a sloppy.

And then some babies with symptomatic CMV will be able to find brain imaging abnormalities and this is a list of some of the findings. Large ventricles, calcification of the brain, periventricular which means it is thin and water filled and the whole brain may not develop well and might have very severe brain disruption sequence and more controversial mild forms are the lenticulostriate (Indiscernible). And then one again, the primary neural phenotype CMV shows they can present only with microcephaly or neurologic findings on exam and can have a variety of abnormalities often in these babies the diagnosis is delayed and suspected if your baby is showing microcephaly like these babies did. But otherwise, they are totally normal.

Here is an example of a little fellow that was born with congenital CMV very seriously involved. Has severe microcephaly and severe findings on his cranial CT. He was very young. And Dr. Gail Demmler-Harrison is holding this little guy. The classic sign on imaging, this is a classic sign and this is the answer on the board question. It causes the linear periventricular calcification. But this class presentation is not the most common presentation.

Some babies have very mild or moderate variations in this with enlarged ventricles and the fluid filled sacs of the brain, or the brain is just a little bit thinned and watery compared to a normal brain.

And sometimes there can be cortical mal development. This is generally called polymicrogyria -- this particular baby had good variation in how the brain was formed. These are all visible forms. But on the other side the brain was very smooth and not very functional.

Babies with congenital CMV and neurologic involvement and sensory involvement can have vision problems. This is the back of their eye that could have inflammation and it could be on the outside and not cite threatening. But it also could be very site threatening. It could be in active retinoids. Sometimes the optic nerve is involved and it has atrophied.

Babies that have severe CMV involvement may have cortical blindness with CVI and then some babies may have eyes that turn in or out. And one of the most common things that you see is hearing loss. Sensorineural hearing loss is almost always progressive and can be one side or both side, unilateral or bilateral and it can be present at birth or congenital or present later and be later onset.

I also want to emphasize that we have found that babies with congenital CMV are more often than babies without congenital CMV to have hearing loss due to persistent middle ear effusion, which can compound their ability to hear. If you have a baby with this make sure you look at the middle ear fluid. Some babies need the PE tubes or other interventions to help with that particular condition.

Now those are the babies with the symptomatic CMV, the tip of the iceberg. What about the vast majority, the silent majority, the babies with asymptomatic CMV? That is about 90%, 85 to 90% whether there are no symptoms at birth and have normal hearing at birth. That is totally asymptomatic but there is another category of the asymptomatic baby with CMV and those are asymptomatic with isolated hearing loss and that is an emerging kind of

awareness. There is no apparent symptoms at birth, but they fail or refer on the newborn hearing. It can be congenital and be one side or both sides and still be associated with congenital CMV.

And what I would like to emphasize is that many of these babies actually will have brain imaging findings of subtle CNS involvement. If they fail the newborn hearing or confirm a hearing loss, make sure you have this imaging performed. Here are some examples of children born with AcCMV on the CT scan. We see some calcification, slightly enlarged fluid-filled sacs of the brain. And on the neonatal head ultrasound, which is very common, they could have ventriculomegaly, and many other things like cysts and calcifications.

But what about the long-term outcomes? Are these findings that we find in these babies, are they significant? Does it impact their long-term outcome? Probably not significantly like with the babies with the symptomatic CMV but in one of the studies we looked at asymptomatic CMV and identified through newborn screening and those with normal hearing by age two did not have significant IQ differences at data points of five years and 18 years. However, if they had hearing loss presenting by age two years, on or before, the full scale IQ lower and the receptive vocabulary scores were lower even when there hearing loss was identified and they had speech language therapy. There are many evolving areas of knowledge with early detection and intervention, can be minimize this impact further? So biology, epidemiology, clinical manifestation, let's go to diagnosis. Everybody, take a deep breath. I know I'm going fast. But how about diagnosis of congenital CMV? There are three key parts, timing, specimen, method.

There is a critical window of opportunity for diagnosis of CMV and that is the first 21 days of life. Most people agree on that but some experts extend that to the first 28 days of life. But after that, the baby can acquire CMV and be expressing it from breastmilk or other modes of infection. Really important that the testing be done early in the baby's life. We can use a variety of specimens like saliva, urine, blood, plasma, dried blood spot, or tissue. The most commonly

used specimens are saliva swabs or urine specimen. They are very generally easy to obtain with saliva being the easiest and urine the second easiest. Sometimes they will have CMV in their blood. That is not always that is why we encourage the year or saliva. We do request your into confirm saliva. Occasionally, the saliva can be both negative or false positive from a recent breastmilk. There is a variety of methods. Culture or shell vial is normal, but most laboratories are moving to PCR with either a quantitative way to actually find out how much CMV is in the body fluid. What do we need? What is a big knowledge gap? A point of care easy to perform bedside test. That is where the R&D can go so every birthing center can have a test and every baby can be tested for CMV before he or she leaves the nursery.

I have just lost my slides.

ALYSON WARD: Gail, it looks like you were pushed out again. It looks like you will need to log back in or I can just advance your slide for you.

GAIL DEMMLER-HARRISON: I need to log to know.

ALYSON WARD: All right. Hang tight.

GAIL DEMMLER-HARRISON: It is probably from my end, the firewall. Let me log back in. Connecting. Let me take a drink of water and stand up and stretch. There we go. All right.

ALYSON WARD: I see. I am moving you back up.

GAIL DEMMLER-HARRISON: To is just the seventh inning stretch.

ALYSON WARD: You should be ready to now rock 'n' roll.

GAIL DEMMLER-HARRISON: Okay. Are we ready? Newborn screening. So we went over method and now we will go over timing. So diagnostic testing, that is now. Newborns was signs or symptoms of CCMV tested. With their many that are not tested, especially the primary neural phenotype. We do not capture all babies. Some babies and I know many of you and the audience can attest to this, now targeted newborn screening is evolving. That is where normal newborns or fail to refer newborn screens are NBHS

tested. At my hospital I was very, very happy to hear that Canada is moving toward that and many states had that now. In this country as well this is evolving. This is sort of a first step forward.

The universal newborn screening, we are waiting. That is where all newborns are screened and tested for this automatically before they leave the birthing center.

And where are we on this? Now with targeted newborn screening in the US, there are a variety of states that do perform targeted testing. Many birthing places like I said do that. If you are expecting a baby soon, ask your pediatrician if your birthing center performs that. You can go to the website and they have a list of hospitals known to be performing targeted newborn screening for babies who were on the newborn hearing. Where are we on this? So the recommended universal screening panel application or RUSP application was submitted by March 27, 2019, by the national CMV RUSP multidisciplinary nomination team. I helped in that effort and it is wonderful and it is currently under review. If you want to support this effort sign the petition at the link here or go to the national CMV website and let your voice be heard. In my opinion babies need to be screened if we are going to first know the prevalence and see the elephant in the living room and help these babies with the proper guidance. Can you go I can time? Yes, you can. They don't really think about this until three to six months of age. But that clinical window of opportunity has been lost. You can have this tested for CMV DNA by PCR methods. It can vary by state and by country as far as how you can retrieve it. There is a reference lab and a growing number of reference labs can test it. And if it is positive it does confirm it. If it is negative, it does not exclude it because false negatives occur because not all babies with congenital CMV have a significant level of virus in their blood. And there are time limitations for storage. In the state of Texas where I am, they are discarded after one-year.

So let's move into treatment now. This is right here. The babies with the symptomatic CMV, they have been the target for antiviral treatments. And

antiviral treatments for this has been under investigation since the early 1990s. There was a phase 3 randomized trial of the IV ganciclovir for six weeks for congenital CMV with CNS involvement. It showed it was helpful. In improve their head size growth and improve their development of milestone and it also reduces their risk of hearing loss later and hearing loss progressive. Those babies were followed six months to a year so the effects were immediate. We don't know if the effects are long-lasting.

Then there was a second phase 3 randomized clinical trial when the oral version of valganciclovir came and that was sort of a breakthrough. It allowed the baby to be treated at home who had congenital CMV and this child looked at six weeks for the standard then and six months in this particular study enrolled babies that had congenital CMV with or without CNS involvement. And treatment for six months was shown to be more beneficial than treatment for six weeks. The results of that trial has led the American Academy of Pediatrics committee of infectious diseases and international consensus committee to recommend that babies with symptomatic CMV receive antiviral therapy. It should be started in the first month of life and carefully monitored. I would say putting a baby on this is very serious and I was see them every two to four weeks and monitor the safety and adjust the doses as they gain weight. It does make outpatient management feasible and affordable. But let is not forget that antiviral therapy is only one part of the interventions that are very helpful for babies. Functional therapies of all sorts are critical to helping them be the best person that they can be.

What are some antiviral treatment questions that need to be answered? Follow up in the clinical trials have only been for six months to two to three years. Will be apparent benefits of antiviral therapy last in their lifetime? Will it help the good ear or the bad ear? And do we need to treat these babies longer than six months since it is a lifelong disorder? These are unanswered questions.

Let's go here to the asymptomatic babies. Should they be treated? Any questions. Should be treat the babies with asymptomatic CMV to prevent

hearing loss progression or later hearing loss? It is currently not recommended by most experts for them to routinely receive antiviral treatment. Because the safety and the efficacy has not been determined in clinical trials for normal newborns.

But we do have two antiviral trials ongoing that I would like you to know about. One is looking at the valganciclovir for CMV and hearing impaired infants. There are clinical trials that are spearheaded by Dr. Albert Park, which is the center PI. There is a randomized placebo-controlled clinical trial multicenter to look to see if valganciclovir can reduce hearing loss progression in babies asymptomatic that would otherwise have normal congenital hearing loss and you can learn about this [clinical trials.gov](https://clinicaltrials.gov).

Now another clinical trial that is up and running is totally asymptomatic babies normal at birth. It is funded by the NIH, NIAID-CASG - Dr. David Kimberlin PI. And one again, [clinical trials.gov](https://clinicaltrials.gov) you can learn more about this. If your baby is born with asymptomatic CMV, what can you do? There should be good anticipatory guidance to know your baby is at significant risk for later onset a progressive hearing loss. Get regular hearing evaluations every six months for three years or annually, or as needed if clinical change or suspicion of hearing loss progression happens. We would check their hearing every three months or so and then hearing aids or Cochlear Implants as indicated and speech language therapy and all sorts of communication aids and educational accommodations are available. There is a lot to hear what is happening here at the mom level? Prenatally testing?

Why don't we test women for congenital CMV infections? It is not routine for obstetricians to do so. The test are available. If you are negative going into your pregnancy, try to stay that way. If your antibody positive at the beginning of your pregnancy, then have the IgM test done. Your infection could have been at least six months ago if negative. But if positive, you could have the avidity index done. If it is low, it probably occurred four months or less of. If it is high, it



occurred four to six months ago. This is a lot of work and a lot of ambiguity and obstetricians do not routinely do this.

What they do is a second trimester usually 20 week fetal ultrasound and they are finding things that suggest your baby has congenital CMV. There is echogenic bowel, or IUGR (Indiscernible) and here is one case I would like to share with you. There is a 25-year-old mom with her second baby and had an ultrasound at 20 and 24 weeks, which showed Abner MALDI. Her infection was shown. She had amniocentesis, which detected large quantities of the virus in the amniotic fluid. And if we look at the placenta here, we can see that it is swollen over three to four times normal, which happens. The baby had fluid in the abdomen and the baby had calcifications around the ventricles.

So what can we do for those babies? There is no standard treatment. There is a lot of controversy and there is a lot of ongoing research. I cannot tell you there is treatment, but there is ongoing research. And so CMV hyperimmune globulin treatment remains controversial. There were four prospective observational studies that were promising and showed reduction in maternal fetal transmission and severity of disease in the baby. One RCT did not mistreat a significant benefit and another in the US has not been analyzed yet. It remains investigational and research only and not standard treatment at this time. If you think it might be good for you, consult with your obstetrician.

Another not formally approved treatment, but gaining some traction is the valacyclovir which is the oral form of acyclovir. There have been studies done in France and now there is a double-blind placebo-controlled study coming out looking at this versus a placebo. It showed a reduced rate of fetal infection in women who experienced a primary early infection. It appeared safe and many OBs are looking at this as a way to reduce the transmission rate. If you have a primary CMV infection you might want to know, you might want to ask your primary OB about this.

What about here? What if we could prevent the CMV infections? Wouldn't we be happy? That is a lot of work managing the babies infected in

utero or after birth. What can we do for prevention? Well, everybody is looking for the CMV vaccine to prevent the infection in mom or baby. The CMV vaccine research has been ongoing since the 1970s. There is no successful vaccine. It was a priority for the national Institute of Medicine.

Many vaccine candidates are under evaluation with active pipelines, too many to list, but there is no vaccine yet. What can we do? We can prevent it in other ways. We know it is transmitted through close contact and toddlers are hot zones. We know there are certain workers and moms that are at increased risk. We can reduce the risk by reducing the contact with the CMV secretions. This is what I call about the information vaccination.

Now there are three simple BoardDocs -- -- three simple precautions. Do not kiss young children near or on the mouth and do not share food or drink or pacifiers or toothbrushes and wash hands after all diaper changes and after wiping runny noses and drooling. It is recommended now by the CMV experts and the international consensus guidelines and supported by clinical trials.

I think it is important and I respectfully disagree with ACOG and perhaps we should focus some of our efforts on our obstetrical colleagues for CMV awareness. And this is sort of the women that should know. Basically, every women, but also high risk women involved with children on a daily basis. And if we do the CMV inspection like do women know about CMV? This is the graphic I lifted from their website. It is common. But only 8% of women know about it. They know about a lot of other things that can affect their baby. And we did a study of medical students at the Baylor College of Medicine and these are men and women with degrees and advanced degrees and you can see that two thirds of them had never heard of CMV going into medical school, amazing.

So a variety of states in this country and it looks like candidate too and many other European countries are looking at legislation to help increase CMV awareness. You can go to the national CMV website and look at the details of each state and where your state is.

And there are varieties of awareness sites on the Internet if fueled by parents and professionals, but you would have to know that CMV exist to search for them. Like I said what else? There's a huge elephant in the living room. It is time for us to meet the congenital CMV challenge and take the next step forward like many of you amazing parents are doing an amazing professionals. If we stumble it will not be because we lack for technology, vision, motivation. I see many of you trying to do this now. It is the only way we are going to say goodbye to the elephant in our living room. With that I would like to say thank you and I call this the end.

(Laughter)

ALYSON WARD: Very nice, Gail, thank you so much. I know you were imparting and lot of information in a short amount of time. We do have one question rolling in. I did open up the question and answer box on the left side of your screen. Please go ahead and enter your questions in there. The first question for you, Gail, is I wonder if more awareness of how viruses can spread due to COVID can impact CMV rating. Is more parents are taking these more basic precautions now in general, so curious to what your thought is between the relation between COVID and CMV.

GAIL DEMMLER-HARRISON: That is a very good question. Because many of the COVID precautions are in public with people that we do not know and we are trying to protect from sort of a respiratory spread. I think the transmission of CMV is a little bit different in that CMV is more intimate contact, more family contact, and less casual contact endless respiratory contact. So it would be interesting to speculate all the COVID precautions and all of our self-isolating, does it reduce congenital CMV or increase it? I can tell you and my congenital CMV clinics, I am getting plenty of new referrals.

ALYSON WARD: Interesting. Thank you for sharing that. The next question is has CMV been identified in middle ear?

GAIL DEMMLER-HARRISON: Yes. Absolutely. One of my colleagues did traditional viral culture in middle ear fluid. So yes, it has been found in the

middle ear fluid to great. The next question is what types of brain imaging do you recommend, CT versus MRI versus HUS?

GAIL DEMMLER-HARRISON: Good question. It depends on the patient. There is no one answer that fits all. For all babies with congenital CMV that I see, I recommend after a good clinical evaluation is a head ultrasound. It is easy. The risk is known and it might provide some information. It reassures the baby's exam is normal and their head circumference is normal and there is no hearing loss and their head is growing normally, stop at that.

If the baby has hearing loss or neurologic symptoms, we go to an MRI. We can do the neonatal sequence MRI where they may not need stations and the baby can sleep through it. At they have her hearing loss significantly we often have to look at the internal auditory canal preparing them for possible Cochlear Implant and also to look at a structure to see if they have shredded Cochlear nerves. CT scan I rarely do now unless I need a quick picture for some reason or sometimes my ENT colleague needs a CT of the temporal bone. So there is not one answer for everybody. But I think every baby even if they are asymptomatic should get a head ultrasound.

ALYSON WARD: Great. Thank you Gail. The next question is I did not understand the reason the vaccine is not been developed since efforts have been done since the 1970s. What is happening with the development of the vaccine?

GAIL DEMMLER-HARRISON: Good question. It is a smart virus. If you gave it an IQ test, it would be off the chart. We do not understand everything about the immunity. And without that we cannot produce a reliable vaccine. The virus is a master immune invader. So traditionally the ways to look at the vaccine development have not worked. And activated and pieces of the virus that we make the most antibody to and pieces of the virus that we make the most neutralizing antibodies to don't seem to work. There are new strategies where they look at bigger pieces and more pieces of the virus to see if that works, but it is a good question. It is not going to be an easy road. It is not been an easy

road. But thank goodness our pharmacology colleagues continue to press on and keep trying new and innovative ways to try to make a vaccine.

ALYSON WARD: Great. Thank you, Gail. The next question is is there any data that has been collected on relationship cultural disparities with CMV?

GAIL DEMMLER-HARRISON: Absolutely. That is a good question. CMV is an equal opportunity virus and everybody will get infected. There are certain demographics that might be more affected by congenital CMV but maybe not more affected by symptomatic CMV. We know with teenage pregnancies there is a greater risk for congenital CMV disease. Certain races and ethnicities, African-American and Hispanic ethnicity, there seems to be in some studies a greater increase, but not in others.

In the study that we did, women who were primarily of Caucasian middle-class had a .4% chance of having a baby with congenital CMV and most of them or primary. It depends on the demographics of the population. But there are some disparities with congenital CMV yes.

ALYSON WARD: Interesting. Thank you. This is a semi-related question. If you tested positive for having CMV prior to pregnancy, do you not have to worry during pregnancy?

GAIL DEMMLER-HARRISON: Good question. I never tell anybody that is pregnant or a mom not to worry about anything because that is what we do. But if you are CMV sero positive prior to pregnancy and it did not occur right before pregnancy but happened years ago then your risk of a recurrent infection through reactivation or reinfection is very, very low. It is less than 1% and probably less than one in a thousand.

It is a difficult thing to study, but that is based on traditional studies. So I think you should be cautious and avoid a reinfection with CMV because we don't totally understand immunity to CMV and immunity to even natural immunity with CMV is important. I think you should be aware that there is CMV and practice precautions against reoccurrence.

ALYSON WARD: Excellent. And a question that popped up as you were answering that is how do I know if I had CMV before?

GAIL DEMMLER-HARRISON: Very easily. You can get the CMV IGV test. Assuming your immune system is normal and you can make the IGV antibody.

ALYSON WARD: One of the questions is like I know that you shared the diagnosis is best done during the first 21 to 28 days. But can it be diagnosed later in some children? If a child is two to three years old and the family is trying to figure out the ideology in the hearing loss, is it too late to get the CMV diagnosis?

GAIL DEMMLER-HARRISON: That is an excellent question. And many families are on the sort of diagnostic odyssey and I see many families like this in my clinic. You can try to go back in time with the newborn dried blood spot. Occasionally, you get lucky and you can find it and it is worth a try, but sometimes they have not gotten to your child's blood spot after two years so try that.

The other thing is you can get the CMV IGV status on the child. If it is negative, the baby has never had it than you can exclude it. But if the baby IGV is positive that it means CMV is possible. So that we look at other things to see if we can make a case for possible congenital CMV and those that have antibodies. Often we have to move forward with this. This is your phenotype baby. Your baby has hearing loss, but we are monitoring your baby up for the progression of hearing loss and look for some other simple causes to evaluate such as a malformed Cochlear nerve or something like that.

But we move forward with assuming it might be congenital. But that is a hard one. That is why all babies in my opinion should be offered congenital CMV universal screening. Then you would not be stuck in that diagnosis.

ALYSON WARD: The term diagnostic odyssey is so detailed. I think so many families just never know. And the dried blood spot really varies by state or

province. It is really challenging. And so another question, what are the concerns of medication given to the babies oral versus IV.

GAIL DEMMLER-HARRISON: The IV form again the valacyclovir has more risk. And so you need an IV or central line for six weeks. That has risks. And in two thirds of babies, they will have problems with their blood count with the IV form and if few minor problems with their liver enzymes. And so it is a little bit more rough, if you will,, more intense therapy.

And again, valacyclovir, the oral form gets into the bloodstream about the same level as the IV form, but only about 20% of the babies have a problem with neutropenia or low blood count and rarely any problem with the liver enzymes. They might have a little tiny bump in their liver enzymes after a few months of therapy, but most seem to handle it well. Some of my family so the babies don't like it and some say the babies love it. It does not seem to interfere with their digestion or sleeping although some families have sort of reported that, but I have not seen that as a consistent thing.

In general, the oral form is easier and more convenient and less toxic than the IV form, but some babies need the IV form that cannot take the oral form or are very, very sick.

ALYSON WARD: Okay. So we have time for just a few more questions. Is testing before pregnancy, is it possible to know how long ago a mother may have had CMV? Can you tell if they had a recent infection versus an infection from a few years ago?

GAIL DEMMLER-HARRISON: From a few years ago, no. If you have the IGG or IGM positive it was probably a while ago. That last six months or more. If it is -- if it is limited, they can time it within four months.

But we don't have the diagnostic repertoire to tell you that you caught your cap is two years ago or 10 years ago. We do not understand the evolution of the CMV immunity to be able to be able to provide you with that information unfortunately.

ALYSON WARD: Okay, great. Thank you so much. I think you departed again, a lot of information. I do want to remind everybody that the slides and the presentation is recorded today and we will have them posted at the website. They will be up by the end of the week or the first part of next week. There was a comment that came in as a point of clarification for the recommended universal screening panel that CMV is currently under review, but there waiting for nominations to resubmit the package. So I think some of that is a little bit delayed right now.

Please keep the CMB 2020 Ottawa meeting on your radar. It will be August 22 through 24 in Ottawa. There are some things we have to shift around timewise but look for e-mails coming out from the CMB public health and policy conference coming out in the next couple of months. And if you would please give us your feedback like really we want to hear from you. We want to know about the information if you learned it today was useful and how the content really relates to your every day.

As well as it plugs you and get you set up for a significant of attendance. Call the link and click the purple text on the screen right now and that will take you to both the evaluation and your certificate of attendance. Thank you so much for attending today.

Tomorrow presentation will be at 10:00 Mountain Time and 12:00 Eastern and we will be hearing about the experience in Oklahoma doing CMV awareness. Thank you so much and have a good afternoon.

1:02 PM (ET)