

Congenital Cytomegalovirus (cCMV)

*A Report to Supplement the Washington CMV Project's
Petition for Targeted CMV Screening in Washington State*

Contributions by:

Mallory Baker, Au.D.
Amanda Devereaux RN, BSN
Khaliah Fleming, MPH, MCHES
Christina M. Long, D.O.
Ann J. Melvin, M.D., MPH
Henry C. Ou, M.D., M.A.
Jennifer Taylor, ARNP

...and families impacted by congenital CMV

Contents

[Introduction](#)

[Background](#)

[Criteria 1: Screening Tests Available](#)

[Criteria 2: Diagnostic Tests and Intervention Available](#)

[Criteria 3: Prevention Potential and Medical Rationale](#)

[Criteria 4: Public Health Rationale](#)

[Criteria 5: Cost Benefit/Cost Effectiveness](#)

[Family Stories](#)

[Appendix](#)

[References](#)

INTRODUCTION

Congenital cytomegalovirus (cCMV) is the **leading viral cause of birth defects in children.**

It will cause more disabilities in children than many other well-known syndromes and infections, such as Down Syndrome, Fetal Alcohol Syndrome, Toxoplasmosis, Spina Bifida, and HIV/AIDS.

cCMV has a higher occurrence rate than any of the other disorders and diseases on the Washington State Newborn Screening Panel.

cCMV **can cause life-long disabilities for the child,** including microcephaly, liver and spleen issues, seizures, hearing loss, vision loss, and developmental delays.

cCMV is the **leading cause of non-genetic hearing loss in children.**

Despite the **high prevalence** of congenital CMV, there is a **low awareness** among women of child-bearing age.

Education about CMV combined with simple and easy prevention strategies, such as hand-washing and avoiding contact with saliva, can make a positive impact on pregnant women. Education and prevention can help them avoid contracting the virus and passing it on to their unborn child.

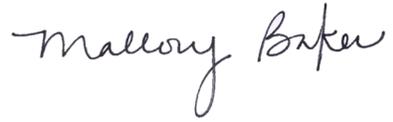
On February 7, 2021, the Washington CMV Project submitted a petition to the State Board of Health to mandate targeted CMV screening for infants who do not pass their newborn hearing screening. The petition was discussed on March 10, 2021 at the Board of Health board meeting. It was denied with the proviso of rediscussing the petition in October.

Since the March 2021 meeting, the Washington CMV Project combined relevant research information, expert contributions, and family testimonials into a comprehensive report on cCMV. It includes information on how cCMV can be included in the Newborn Screening Program. The report provides the Board of Health with more information to make a decision during the October 2021 meeting especially since **congenital cytomegalovirus (cCMV) matches the criteria set by the state for inclusion in the Newborn Screening Program.** Early screening for congenital CMV, during the newborn period, provides optimal opportunity for effective treatment and intervention. Some hospitals in Washington State have already adopted a targeted CMV screen and developed protocols to include it as standard of care. The following report is presented developed to explain the need for cCMV screening, discuss the feasibility of adding it to the screening program, and illuminate the personal stories connected with this disease.

This report includes the contributions of medical professionals and families. Questions were asked to best provide the Board of Health with answers to the most frequently requested information about cCMV, targeted CMV screening, and its suitability as a disorder to be included in the state's Newborn Screening Program.

For additional information, clarification, or assistance with contacting local and national experts, please contact the Washington CMV Project.

Thank you for your time, attention, and consideration.

A handwritten signature in cursive script that reads "Mallory Baker".

Mallory Baker, Au.D., CCC-A
Founder | Washington CMV Project
Pediatric Audiologist | Seattle Children's Hospital

BACKGROUND

Congenital cytomegalovirus (cCMV) is the leading viral cause of birth defects in infants each year.

cCMV has a higher occurrence rate than all other disorders and diseases on the Washington State Newborn Screening Panel.

WHAT IS CONGENITAL CYTOMEGALOVIRUS (cCMV)?

- Congenital cytomegalovirus is a virus that infects an unborn fetus. This prenatal infection can cause life-long disabilities for the child, including microcephaly, liver and spleen issues, seizures, hearing loss, vision loss, developmental delays, and sadly, death.
- cCMV is the leading cause of non-genetic hearing loss in children.
- Healthy individuals who acquire a CMV infection may not present any symptoms or their symptoms may be mild to severe. Common symptoms may include fever, swollen glands, fatigue, and a sore throat. (CDC). Due to the ease of transmission and possible asymptomatic carriers, pregnant women are at risk of contracting CMV and without knowing it.
- Those with a weakened immune system are at a greater risk for developing health complications from CMV. These groups include bone marrow transplant patients, those with HIV/AIDS infections, **and unborn babies** (congenital CMV).

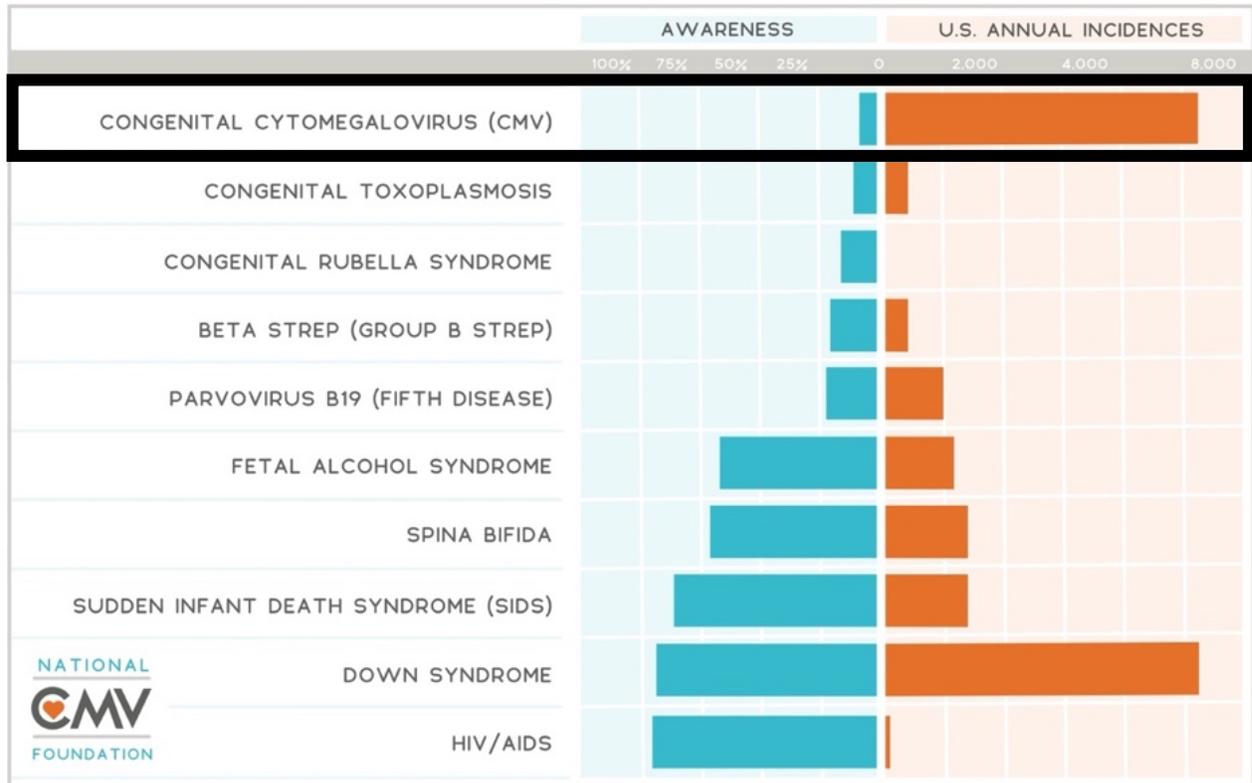
Prevalence of cCMV

- The CDC reports a prevalence of **1 in 200 babies are born positive for congenital cytomegalovirus** (CDC). This means approximately 30,000 babies in the United States will be born with cCMV each year. Using this occurrence and 2019 birth data, approximately 424 babies may have been born positive for congenital CMV in Washington State.
- **A 2011 study completed in Washington State, showed a prevalence of 1.4 in 100 babies are born positive for congenital CMV.** (Misono, 2011). Based on 2019 birth data and a 1.4% prevalence, approximately 1,207 babies may have been born positive for congenital CMV in Washington State. (DOH)
- Of the children born positive for congenital CMV, 10% will be symptomatic while 90% will be asymptomatic. However, **asymptomatic infants can still develop medical complications** from the cCMV infection later in life.

Awareness of CMV

- Studies show low awareness of CMV among women of child-bearing age - **91% of women were unaware of CMV and the impact of the infection on an unborn baby.**

(Doutre 2016) The below graph compares the awareness (women of child-bearing age) of the prevalent disorders in the United States. cCMV has the lowest awareness yet the highest prevalence.



WWW.NATIONALCMV.ORG

Doutre, S. M. Barrett, T. S. Greenlee, J. & White, K. R. (2016). Losing Ground: Awareness of Congenital Cytomegalovirus in the United States. Journal of Early Hearing Detection and Intervention, 1(2), 39-48.

Transmission

- CMV is transmitted through the exchange of and/or exposure to bodily fluids, including saliva, urine, blood, semen, tears, and breast milk. (CDC)

Seroprevalence

- According to a 2006 study, **the seroprevalence of CMV in children under the age of 11 years was approximately 40%**. This suggests that “large percentages of women in the United States enter their childbearing years susceptible to a primary CMV infection.” (Staras 2006). However, research also shows that a secondary infection or break through can also cause issues for the unborn baby.
- By the age of 40 years, approximately 50% of the population will be seropositive and infected with CMV at some point in their life. (Staras 2006) This population puts unborn babies at risk.

Prevention

- Prevention strategies revolve around appropriate hygiene habits and reducing exposure to saliva. The main five prevention tips include:
 1. Wash your hands
 2. Avoid kissing children on the lips
 3. Do not put a pacifier in your mouth
 4. Do not share a toothbrush
 5. Do not share utensils
- The National CMV Foundation uses the following infographic.



- The Washington CMV Project has created similar infographics with the same message reworded to focus on two main prevention strategies – 1) Wash your hands and 2) Avoid contact with saliva.



- **Studies report that prenatal CMV education and behavior modification will positively reduce CMV infection in women.** (Hughes 2017)

TESTING FOR CONGENITAL CMV

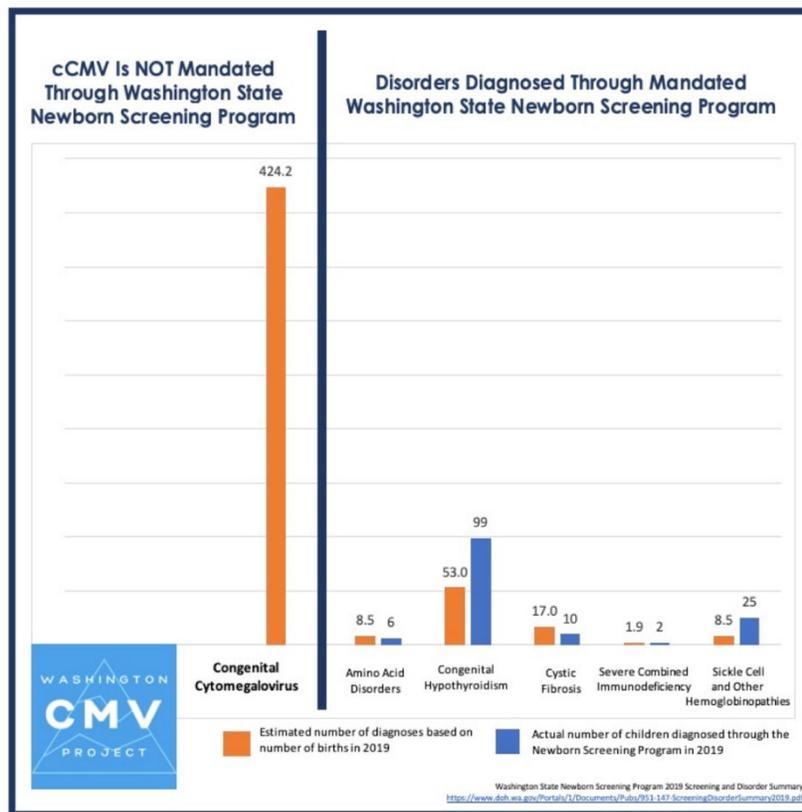
- Testing saliva via DNA detection of the virus through polymerase chain reaction testing (PCR) or rapid culture is shown to have a high sensitivity (>97%) and specificity (99%) for detecting congenital CMV infection. (Boppana 2010). Urine collection and testing can also be used to detect cCMV. However, saliva is an easier body fluid to collect in infants. One drawback of testing saliva is potential contamination from breastmilk. It is recommended that any saliva collection occur at least 60-90 minutes after breast feeding. (Haller 2020).
- Data of dried blood spot (DBS) PCR testing shows low sensitivity (between 28.3% - 34.4%) in detecting cCMV. (Boppana 2010) This limits its ability to be an effective tool for cCMV screening. A current CDC study “indicates a higher analytical sensitivity compared to the Boppana et al. (2010) study and suggests that as more sensitive PCR methodologies emerge, DB- based screening may become a viable, low-cost screening option.” (Haller 2020) A recently published study reported an 85.7% sensitivity to DBS PCR, a higher sensitivity than previously suggested in the literature. (Dollard 2021) However, this sensitivity is still low compared to saliva PCR tests.

WHAT IS TARGETED CMV SCREENING?

- **A targeted CMV screen, would mandate birthing facilities screen infant upon a referred second hearing screening.** Due to the higher cost of saliva and/or urine screening tests and the low sensitivity of DBS testing, a targeted screening protocol was adopted in six states with screening laws. When a newborn does not pass an initial newborn hearing screening, the Joint Committee on Infant Hearing (JCIH 2019) recommends a second screen. The JCIH 2019 position statement also endorses a saliva or urine CMV test after a referred hearing screening. **It is critical that cCMV testing be completed within the first 21 days of life.** Testing outside of this timeframe makes distinguishing between congenital or acquired infection much more difficult.
- In 2019, 730 infants, in Washington State, did not pass their follow up hearing screening (second hearing screen) (EHDDI) This is equivalent to 0.8% of Washington births. These are the infants who would have qualified for a targeted CMV screen.
- Not all children with congenital CMV will present with hearing loss at birth. However, in the absence of universal screening, targeted screening is the next best option to test and identify the children who could develop sequelae later in life.
- For more information about targeted CMV screening, see “[Criteria 1: Screening Tests Available](#)”

STATE OF cCMV EDUCATION, AWARENESS, AND SCREENING IN WASHINGTON

- Washington does not have a CMV screening or education mandate. Few hospitals in the state are performing targeted CMV screening.
- Congenital cytomegalovirus (cCMV) has a higher occurrence than any other disorder currently mandated through the Washington State Newborn Screening Program. There is a close relationship between the ESTIMATED occurrence of each disorder and the ACTUAL number of infants diagnosed with the disorder through the Washington State Newborn Screening Program. But, since cCMV is not mandated, there were approximately 424 babies that should have been diagnosed in 2019. These babies could have been treated. They could have received early intervention. However, they were not screened.



- Nationally, six states have passed laws requiring a CMV screen for infants who do not pass their newborn hearing screening evaluation at birth. Ten states enacted laws mandating prenatal education to women who are pregnant, thinking of becoming pregnant, or are of child-bearing age. Recently, Minnesota passed the first universal CMV screening law mandating that all infants are screened for CMV at birth.
- Prenatal care providers do not typically provide education about CMV to pregnant women.
 - A CDC report in 2007 surveyed OBGYNs asking about their practice habits in educating and counseling patients about CMV. Less than half of the OBGYNs

surveyed stated any type of prenatal CMV education. (CDC 2007) A more recent study from 2020, **reported 51% of OBGYNs surveyed never counseled women about CMV.** (Pesch 2020)

TREATMENT AND MANAGEMENT

Infants

- For symptomatic infants, antiviral treatment includes a regimen of ganciclovir and valganciclovir. Studies show this treatment may improve hearing loss and developmental outcomes (CDC). Anti-viral treatment for asymptomatic infants is currently being studied (Park, A. ValEAR Trial).
- While there is no cure for cCMV infections, **studies show that early intervention can lead to improved outcomes for children.** Early identification of hearing loss can make a significant difference in a child's speech and language development, cognitive abilities, and overall development. Hearing loss attributed to cCMV is known to be progressive and fluctuating. (Fowler 1997) This makes diagnosis difficult, particularly if a child passed their newborn hearing screening but develops hearing loss later in life due to cCMV.

Mothers

- There is currently no standard of treatment for a pregnant woman infected with CMV during her pregnancy.
- **Women have a 1 in 3 chance of passing the infection onto their unborn baby.**

CRITERIA 1: Screening Tests Available

Available screening technology: Sensitive, specific and timely tests are available that can be adapted to mass screening.

Testing saliva via DNA detection of the virus through polymerase chain reaction testing (PCR) or rapid culture is shown to have a high sensitivity (>97%) and specificity (99%) for detecting congenital CMV infection. (Boppana 2010). Urine collection and testing can also be used to detect cCMV. However, saliva is an easier body fluid to collect in infants.

(See the previous section “[What is targeted CMV screening?](#)”.)

In November 2020, Valley Medical Center (VMC) initiated a targeted CMV screening in their well-baby nursery and Neonatal Intensive Care Unit (NICU). Dr. Christina Long and Jennifer Taylor, ARNP were asked to explain the VMC screening protocol to provide context for the Board of Health.

Currently, Valley Medical Center will screen all babies who do not pass their second newborn hearing screening. They screen using a PCR saliva screen and collaborate with providers at Seattle Children’s Hospital. For further information about the Valley Medical Center protocol and process, see [Appendix A](#).

Contributions to this section were provided by Christina Long, M.D. and Jennifer Taylor, ARNP

How is the CMV saliva screen performed?

“The RN obtains a viral swab (a common swab in all medical labs and transported in universal transport media). The nurse places the swab in the cheek of the infant and saturates the swab in saliva, taking care to avoid scraping mucosal cells. The infant should not have received breastmilk within the previous hour prior to obtaining the swab.”

What types of tests are completed? When?

“The test is a neonatal CMV saliva screen. It is a qualitative PCR CMV test using saliva. It is run using an ESwab stored in Universal Transport Media. It is performed after the second hearing screen which should occur before a baby is discharged from the hospital.”

How does this test tie into hearing screenings?

“The test is only performed if an infant does not pass their second hearing screening. The first screening is typically done around 12-24 hours of life (though this does vary on occasion). If an infant refers their first hearing screening, they are rescreened 2-4 hours later if they are scheduled to be discharged that day or they are rescreened the following day if they are not being discharged that day.”

Is the process different if the baby is in the well-baby nursery vs the NICU?

“Yes, the process is different in the NICU. In the NICU we perform the same process if an infant refers the second hearing screen at less than 30 days of life. Many of our NICU infants are hospitalized for months prior to receiving their hearing screen. Premature infants and sick infants have other reasons they may refer a hearing screen. If done at months of age, prior to discharge, it is too late to diagnose congenital CMV, so we do not send a swab on these infants if they do not pass their hearing screens.”

What VMC personnel is required to complete this protocol? Do these people have other responsibilities or were they hired to fill a CMV screening role?

- “The protocol requires a hearing screener to notify the bedside nurse.
- The bedside nurse obtains the swab and sends it to the lab
- The lab personnel then sends the swab to the lab (either UW or SCH)
- The SCH Newborn Rounder follows up on the lab results and contacts SCH Infectious Disease and the PCP (and decide if the PCP or the newborn rounder is going to call the parents with the results)
- All of these personnel have other responsibilities and are not hired for a specific CMV screening role”

What are the challenges to your screening protocol?

- “Hearing screener fails to notify the RN of the referred second hearing screen.
- Lab fails to notify of a positive result that could result in a delay in notification and referrals. The SCH Newborn Rounder is supposed to follow up on these daily but if this was not done and the lab also didn’t call about a positive result, that could also delay notification and referrals.”

What benefits have you witnessed?

“We have not yet had a positive result at VMC since we started screening in November 2020. There have been two positive CMV patients after screening at Providence Medical Center. The benefits is that these children were referred to SCH Infectious Disease within a short period of time and treatment was started appropriately, potentially improving or conserving their hearing.”

What is the timeline from birth to diagnosis?

“This typically takes about 1 week from birth to initial positive screen. Diagnosis is not formally established until a confirmatory urine CMV test is also completed and the family meets with Seattle Children’s Infectious Disease. Ideally treatment starts within 1 month of life.”

What happens when a congenital CMV test returns as positive?

“The process at VMC does not confirm congenital CMV. If a child has a positive screen, they are referred to SCH Infectious Disease and they have confirmatory testing done within that department.

- *Who contacts the family?*

- The SCH Newborn Rounder contacts the PCP first and decides together if the PCP or the Newborn Rounder is going to contact the family
- *What resources are available?*
 - If a child is tested for CMV due to a referred hearing screen, they are provided with a take home parent education sheet about CMV.
 - SCH Infectious Disease provides more resources and education to the family once they are referred.”

What additional costs are incurred?

“According to the VMC Lab, the cost for each CMV screening test is \$287.82. We haven’t yet had a full year of CMV screening, so we don’t yet have the annual cost for CMV screening.”

CRITERIA 2: Diagnostic Tests and Intervention Available

Diagnostic testing and treatment available: Accurate diagnostic tests, medical expertise, and effective treatment are available for evaluation and care of all infants identified with the condition.

Contributions to this section were provided by Ann Melvin, M.D. and Henry Ou, M.D.

What tests are available to diagnose congenital CMV infection?

“There are several tests available to diagnose CMV infection including serology, polymerase chain reaction (PCR) nucleic acid testing and culture. To diagnose congenital CMV, the testing needs to be done within the first 3 weeks of life. A positive test after this time indicates CMV infection, but not necessarily congenitally-acquired infection. The most sensitive assays are urine and saliva PCR, which make them good screening tests, as infants with congenital CMV typically shed high levels of virus in their saliva and urine. Saliva is a much easier sample to obtain, which makes it ideal as it doesn’t delay hospital/clinic discharge waiting to collect a urine sample. There is a greater risk for a false positive result with the saliva sample, particularly if the infant is being breast fed. In the past, urine culture for CMV was considered the gold standard, however, this has largely been replaced by PCR which is more sensitive and more available.

Blood PCR is also an option, however, not all congenitally infants are viremic at the time of testing. Serology is not very helpful in diagnosing congenital CMV”

Once a child receives a positive CMV viral test result, what happens?

“The first step after obtaining a positive saliva or urine result for CMV is to confirm the test with a second sample (preferably a urine PCR if the first test was a saliva sample) so that there are two separate positive tests. What we have been doing at this point is letting the families and primary care providers (PCP) know about the referred hearing screen and the positive CMV test and asking the PCP to order a urine for CMV PCR as well as getting the infant scheduled with audiology for a formal hearing evaluation”

What labs are able to complete this type of saliva testing?

“The labs at the University of Washington and Seattle Children’s Hospital are able to do this testing as are most of the big national labs.”

Are there additional tests you order? Why or why not?

“If the baby confirms as CMV positive, there is the possibility that there are other abnormalities, so we request a cranial ultrasound and blood work to assess for thrombocytopenia and hepatitis. We also refer the infant to an ophthalmologist to assess for evidence of CMV retinitis. Even babies who appear asymptomatic can have subclinical lab abnormalities and abnormal head imaging. These have implications for prognosis.”

Who can fill this role in our area?

“Generally, the infants are seen by pediatric infectious disease, audiology, otolaryngology, and ophthalmology. Of these, pediatric infectious disease physicians are the most limited, but there are pediatric infectious disease physicians at Seattle Children’s Hospital, Mary Bridge Hospital, Swedish Hospital and Providence Infectious Disease Clinic, Spokane.

What type of confirmation process is required?

“Repeat CMV testing as above initially – generally with a different sample type”

Who is notified of the positive saliva test?

“The provider in the hospital who orders the test is initially notified of the results. In the hospitals where targeted CMV screening has been implemented, the family and the PCP are then notified of the positive result and recommended next steps.”

What diagnostic tests/evaluations, across disciplines, should the child receive?

“It is recommended that infants who have referred on their newborn hearing screen receive a subsequent Brainstem Auditory Evoked Response (BAER) test to as a measure of the brain’s response to sound. Once the child is a little older (10-12 months) they will undergo additional behavioral testing of their hearing. In addition, since CMV-related hearing loss has a tendency to get worse after initial diagnosis, we also recommend additional audiologic testing to monitor for progression. Ophthalmology would perform a dilated retinal exam.”

Antiviral Treatment:

• ***What are the criteria for obtaining anti-viral treatment?***

“The studies on treatment for congenital CMV have shown that infants with symptomatic congenital CMV who start ganciclovir/valganciclovir in the first month of life have improved neurodevelopmental and hearing outcomes. Standard practice is for infants with documented congenital CMV and CMV-related symptoms to be treated with oral valganciclovir for 6 months.”

• ***What current research supports this treatment and recommendation?***

- Kimberlin DW et al. Effect of ganciclovir therapy on hearing in symptomatic congenital cytomegalovirus disease involving the central nervous system: a randomized, controlled trial. *J Pediatr* 2003;143:16-25
- Oliver SE et al. Neurodevelopmental outcomes following ganciclovir therapy in symptomatic congenital cytomegalovirus infections involving the central nervous system. *J Clin Virol* 2009; 46S:S22-S26.
- Kimberlin DW et al. Valganciclovir for symptomatic congenital cytomegalovirus disease. *N Engl J Med* 2015;372:933-43.

“There is an on-going study (ValEAR) to see if treating infants with isolated hearing loss with valganciclovir after the first month of life is also effective. It will be several years before the results of this trial are available.”

• ***What is the benefit of antiviral treatment? What do you consider when making this recommendation?***

“As currently there is no systematic screening for CMV even if there are findings at birth such as a referred hearing screen, the usual scenario is that an infant with hearing loss is not tested for CMV until they are older than a month. As a positive CMV result at this point could have been acquired post-natally it is necessary to obtain the dried blood spot left over from the neonatal screen from the state and have this sent for CMV PCR. By the time all of this happens the infant is usually at least 3 months of age and we don’t have data supporting treatment at that point. As valganciclovir has potential side effects and needs to be monitored closely, the decision of whether or not to treat is not straightforward. Since CMV replication can be on-going in these infants, and there is the potential for reactivation, and we know that CMV-related hearing loss can be progressive, it is quite likely that treating even after the initial month of life may be beneficial. Therefore, treatment is usually offered, and many parents opt for treatment at this point. **However, it is likely that we have lost the window for optimum benefit by that time.** As a surprising number of infants also have brain abnormalities on imaging it is possible that even late treatment may impact development, although again, the data is only for early treatment.”

“There is a brief window of time early in a baby’s life during which treatment with antiviral medications will have a benefit. Saliva PCR screening after referring on a newborn hearing screen is a quick test that can be done while a baby is still at the hospital/birthing facility. After discharge from the facility, the chance of identifying congenital CMV early enough for treatment to be beneficial is significantly lower.”

- ***Where can antiviral treatments and interventions occur within Washington State?***

“Antiviral treatment decisions and management are best done with a pediatric infectious disease physician – there are pediatric infectious disease physicians at Seattle Children’s Hospital, Mary Bridge Hospital, Swedish Hospital and Providence Infectious Disease Clinic, Spokane. With the advent of increased use of telehealth, most of the consultation and management could be done without the families needing to travel to the Seattle or Spokane areas.”

CRITERIA 3: Prevention Potential and Medical Rationale

Prevention potential and medical rationale: The newborn identification of the condition allows early diagnosis and intervention; There is sufficient time between birth and onset of irreversible harm to allow for diagnosis and intervention; The benefits of detecting and treating early onset forms of the condition (within one year of life) balance the impact of detecting late onset forms of the condition; Newborn screening is not appropriate for conditions that only present in adulthood.

Contributions to this section were provided by Ann Melvin, M.D. and Henry Ou, M.D.

Is there sufficient time between birth and onset of irreversible harm to allow of diagnosis and intervention?

“As discussed above, antiviral treatment within the first month of life has demonstrated benefit for both developmental and hearing outcomes for congenitally infected infants. If the CMV testing is done at the time of the referred hearing screen, it is possible to get the repeat CMV testing and work-up completed within that first month so that the infants can benefit from treatment. There is sufficient time to potentially reduce harm only if early screening for CMV is performed. Once a child has left the hospital/birthing facility, the chance of diagnosing them with CMV-related hearing loss early enough for treatment to be beneficial is much lower.”

From your perspective, why is it important that families know if their child has congenital CMV if they are asymptomatic at birth?

“Sensorineural hearing loss (SNHL) develops in 10-15% of infants with congenital CMV even if they are otherwise asymptomatic. Therefore, identifying these infants early allows for earlier diagnosis and management of SNHL. Those infants with hearing loss at birth are more likely to have progressive hearing loss and other abnormalities and are the most likely to benefit from early treatment. These infants frequently appear to be asymptomatic, but in reality, are not and are at risk for developmental delays. These infants benefit from early intervention beyond the hearing considerations. Identifying CMV infection early allows for the chance that with antiviral treatment, the amount of hearing loss the child develops might be reduced. This could mean the difference between a child who has more moderate hearing loss that can be aided with conventional hearing aids versus a child who is profoundly deaf.”

What are the medical advantages of early diagnosis rather than later diagnosis?

“As detailed above, the benefits of antiviral therapy for congenital CMV are only documented when initiated within the first month of life. While we will consider treatment of children up to 6 months of age, the benefit is only well established if started in the first month of life. Early diagnosis and treatment may reduce how much hearing loss a child with congenital CMV will develop. Since this hearing loss is due to inner ear damage, once lost, it can never be recovered. As a result, prevention of hearing loss through antiviral treatment is critical and time sensitive.”

CRITERIA 4: Public Health Rationale

Public health rationale: Nature of the condition justifies population-based screening rather than risk-based screening or other approaches.

The National CMV Foundation contributed the following letter to support CMV education and targeted CMV screen in Washington State.



June 22, 2021

Dear Members of the Washington State Board of Health,

Congenital Cytomegalovirus (cCMV) is an important public health crisis. cCMV is a leading cause of childhood disability, causing thousands of infants to be born with or develop permanent disabilities and health conditions each year.¹ Early intervention, monitoring, and treatment (when appropriate) can help infants with cCMV to have the best possible outcomes.³ However, without universal screening, fewer than 5% of infants with cCMV will be identified, and even infants born with symptoms are rarely diagnosed.⁴ 1 in 5 infants with cCMV will end up with a disability or permanent health condition.² Screening for cCMV needs to be done within the first three weeks of life. After this point, it can be difficult, if not impossible, to make a cCMV diagnosis, and opportunities for early intervention are gone.² Children with cCMV are at risk for hearing loss, developmental delays, and other health conditions. If these children are identified with cCMV at birth, they could be monitored, receive early intervention services, and receive antiviral treatment if appropriate.

To expound upon the critical need for screening, an international congenital cytomegalovirus recommendations group recommended that, “consideration should be given to universal neonatal cytomegalovirus screening to enable early detection of congenital cytomegalovirus-infected infants, facilitating early detection and intervention for sensorineural hearing loss and developmental delay where appropriate.”³ Furthermore, Cannon and colleagues reported that cytomegalovirus screening of all neonates could significantly improve the outcome of those with cCMV who develop delayed hearing loss¹; and that, “several thousand children with congenital CMV could benefit each year from newborn CMV screening, early detection, and interventions.”¹

Due to the costs and logistics associated with implementing a CMV universal newborn screening program, several states have implemented a targeted screening approach, testing infants for CMV if they refer the newborn hearing screening.² While this approach does not allow for the diagnosis of every baby with cCMV, the approach has been touted as a step towards universal screening. This approach allows for protocols to be initiated, laboratory testing to be established, and education to be provided. This approach identifies approximately 57% of all infants with

cCMV.⁵ Although not the “gold standard” of universal screening, over 50% is a significant improvement from less than 5% of infants with cCMV being identified.

The National CMV Foundation supports all efforts to increase CMV awareness and CMV newborn screening. Although universal CMV screening for newborns is ideal, targeted screening programs are an essential step towards this goal.

Sincerely,

Khaliyah Fleming

Khaliyah Fleming, MPH, MCHES
Executive Director
National CMV Foundation

Amanda Devereaux

Amanda Devereaux RN, BSN
Program Director
National CMV Foundation

References

1. Cannon MJ, Griffiths PD, Aston V, Rawlinson WD. Universal newborn screening for congenital CMV infection: what is the evidence of potential benefit? *Rev Med Virol* 2014; 24: 291–307.
2. www.nationalcmv.org
3. Rawlinson, et al. Congenital cytomegalovirus infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy. *Lancet Infectious Disease. Lancet Infect Dis.* 2017 Jun; 17(6): e177–e188.
4. Sorichetti B, Goshen O, Pauwels J, et al. Symptomatic congenital cytomegalovirus infection Is underdiagnosed in British Columbia. *J Pediatr.* 2016;169:316–317.
5. Fowler KB, McCollister FP, Sabo DL, et al. A Targeted Approach for Congenital Cytomegalovirus Screening Within Newborn Hearing Screening. *Pediatrics.* 2017;139(2): e20162128

CRITERIA 5: Cost Benefit/Cost Effectiveness

Cost-benefit/Cost-effectiveness: The outcomes outweigh the costs of screening. All outcomes, both positive and negative, need to be considered in the analysis. Important considerations to be included in economic analyses include: The prevalence of the condition among newborns; The positive and negative predictive values of the screening and diagnostic tests; Variability of clinical presentation by those who have the condition; The impact of ambiguous results. For example, the emotional and economic impact on the family and medical system. Adverse effects or unintended consequences of screening.

Contributions to this section were provided by Mallory Baker, Au.D.

Cost-benefit/Cost-effectiveness

The following studies report the cost effectiveness of screening for congenital CMV. A summarized breakdown of these studies was reported in “Economic assessments of the burden of congenital cytomegalovirus infection and the cost-effectiveness of prevention strategies.” (Grosse, 2021)

The abstract conclusions are provided for quick reference for each study.

- *Cost-benefit analysis of targeted hearing directed early testing for congenital cytomegalovirus infection.* (Bergevin, 2015)
 - “Conclusions: The CMV education and treatment program costs are modest and show potential for significant cost savings.”
- *Integration of congenital cytomegalovirus screening within a newborn hearing screening programme.* (Beswick, 2019)
 - “Conclusion: Incorporating cCMV testing into Universal Newborn Hearing Screening within Queensland is realistic and achievable, both practically and financially.”
- *Cost-effectiveness of Universal and Targeted Newborn Screening for Congenital Cytomegalovirus Infection.* (Gantt, 2016)
 - “Conclusions and relevance: Newborn screening for cCMV infection appears to be cost-effective under a wide range of assumptions. Universal screening offers larger net savings and the greatest opportunity to provide directed care. Targeted screening also appears to be cost-effective and requires testing for fewer newborns. These findings suggest that implementation of newborn cCMV screening programs is warranted.”
- *First estimates of the potential cost and cost saving of protecting childhood hearing from damage caused by congenital CMV infection.* (Williams, 2015)
 - “Conclusions The costs of targeted screening for cCMV using salivary swabs integrated within NHSP resulted in an estimate of cost per case that compares favourably with other screening programmes. This could be used in future studies

to estimate the full economic value in terms of incremental costs and incremental health benefits.”

- Virginia 2019 Impact Statement – See [Appendix B](#)

Economic Analysis

- Lucas and colleagues attempted to report the lifetime economic burden of congenital CMV for patients. (Lucas 2019) This study and the subsequent framework was the first time an economic assessment for congenital CMV was presented in literature. It may act as a guide for any future discussions and decisions about the economic impact of CMV in Washington State.

The prevalence of the condition among newborns.

- Due to the lack of universal screening and data collection of children with congenital CMV, it is difficult to calculate an exact prevalence. The Center for Disease Control and Prevention (CDC) states a **prevalence of 1 in 200 (0.5%)**. **This is a higher prevalence than any other disorder currently on the Washington State Newborn Screening Panel.** (Washington State Department of Health. Disorders Detected by Newborn Blood Spot Screening. Apr 2015. DOH 951-145.)
- A 2011 study aimed to calculate the prevalence of congenital CMV infection in children with hearing loss in Washington State. (Misono 2011) This study showed a **1.4% prevalence of congenital CMV among the children of Washington State** (1.4 in every 100). Additionally, it concluded that a large portion of children with permanent hearing loss in Washington state were CMV positive at birth. This data is comparable to the data from a 1993 study suggesting a 1.3% prevalence of congenital CMV (Fowler 1993).

The positive and negative predictive values of the screening and diagnostic tests.

Based on the data of the 2011 study titled, “Saliva polymerase-chain-reaction assay for cytomegalovirus screening in newborns”, Boppana and colleagues reported the following information regarding PCR saliva predictive values.

- Liquid-saliva PCR assay
 - Sensitivity: 100% (95% CI, 95.8 to 100)
 - Specificity: 99.9% (95% CI, 99.9 to 100)
 - Positive predictive value: 91.4% (95% CI, 83.8 to 96.2)
 - Negative predictive value: 100% (95% CI, 99.9 to 100)
- Dried-saliva PCR assay
 - Sensitivity: 97.4% (95% CI, 90.8 to 99.7)
 - Specificity: 99.9% (95% CI, 99.9 to 100)
 - Positive predictive value: 90.2% (95% CI, 81.7 to 95.7)
 - Negative predictive value: 99.9% (95% CI, 99.9 to 100)

Variability of clinical presentation by those who have the condition.

There is significant variability in the presentation of congenital CMV among newborns. As mentioned previously, 10% of infants will be symptomatic at birth with 90% showing

no immediate symptom. It is the wide variability that makes proactive screening important.

In the 2017 consensus statement about congenital CMV, definitions were described and summarized to help identify and categorize the variability of the condition. (Rawlinson 2017)

“Moderately to severely symptomatic congenital cytomegalovirus disease

- Multiple manifestations attributable to congenital cytomegalovirus infection: thrombocytopenia, petechiae, hepatomegaly, splenomegaly, intrauterine growth restriction, hepatitis (raised transaminases or bilirubin), or
- Central nervous system involvement such as microcephaly, radiographic abnormalities consistent with cytomegalovirus central nervous system disease (ventriculomegaly, intracerebral calcifications, periventricular echogenicity, cortical or cerebellar malformations), abnormal cerebrospinal fluid indices for age, chorioretinitis, sensorineural hearing loss, or the detection of cytomegalovirus DNA in cerebrospinal fluid

Mildly symptomatic congenital cytomegalovirus disease

- Might occur with one or two isolated manifestations of congenital cytomegalovirus infection that are mild and transient (eg. Mild hepatomegaly or a single measurement or low platelet count or raised levels of alanine aminotransferase). These might overlap with more severe manifestations. However, the difference is that they occur in isolation.

Asymptomatic congenital cytomegalovirus infection with isolated sensorineural hearing loss

- No apparent abnormalities to suggest congenital cytomegalovirus disease, but sensorineural hearing loss (> 21 decibels).

Asymptomatic congenital cytomegalovirus infection

- No apparent abnormalities to suggest congenital cytomegalovirus disease, and normal hearing.”

The impact of ambiguous results. For example, the emotional and economic impact on the family and medical system. Adverse effects or unintended consequences of screening.

- In the study titled “Attitudes toward newborn screening for cytomegalovirus infection”, 85% of parents reported they would want their child tested for CMV even if testing was not routine, they had to pay \$20, or problems never appeared. The cost, stress, and possibly unnecessary doctor appointments did not deter them from preferring the screening (Din 2011).
- A more recent study (Tastad 2019) showed that, once women were informed about CMV and the risks it presented to a baby, nearly all women (96%) supported prenatal education and newborn screening.

FAMILY STORIES

Washington families impacted by congenital cytomegalovirus were contacted and asked to share their CMV journey with the Washington State Board of Health and Department of Health. The option to share was voluntary and proved to be a difficult and emotional journey for many.

“I cried while writing it and struggled to send it because I couldn’t get the words right.”

“... I’ve been working on her story to share. It is taking me longer than anticipated to write because it can be so traumatic reliving some of those memories.”

Each family was encouraged to write their story in whatever style was easiest them... a letter, narrative story, question and answer. The prompt provided to each family was, *“What would you like the Board of Health to know about congenital cytomegalovirus?”*

These are the stories and thoughts of families who are living with the impact of cCMV every day. This is what each family wanted you to read, to know, and to understand.

NOTE: The following families have provided their personal stories for the audience of Board of Health. Each family has consented to allow their names, images, and stories to be shared in this specific format. They are not to be used in any other medium or context. Contact information for families can be obtained through the Washington CMV Project.

Thank you for your respect and consideration.

A Mother's Journey *written by Lisa Aamot*

My name is Lisa Aamot, and 4 years ago I almost died from CMV. I was 33 weeks pregnant when I was diagnosed. That sounds clearcut and simple, but what I want people to know is that it should have been, but instead it was devastating and lonely. The weeks leading up to my diagnosis I was in immense pain, and knew something was wrong. My OB didn't have CMV even on his radar, and I had never even heard of it. Looking back I had symptoms that should have been met with a test for CMV, but because of the lack of education on it in WA it was missed until the damage was life threatening. My condition declined to the point I was ambulated to UW L&D with my Liver, right Lung, and right Kidney in the early stages of failure. Something was attacking them, and it also sent me into pre-term labor. After almost a week in the hospital fighting to keep my baby inside and myself alive, I was diagnosed.

We were sent home to wait until our daughter came. We were sent home without any further education, not even a pamphlet, or answers as to what to expect. We assumed CMV was rare, and you can imagine our shock when we learned it is in fact very common. Not rare at all. There's just no education or awareness in our state. I had to do my own research and try my best to learn what to expect and how to advocate for my baby. When she was born, she tested positive. She looked perfect and healthy, but knowing CMV could continue to cause damage to her hearing and development throughout her childhood was a low point. I feel fortunate that I have a college background in Childhood Development, and know how to research, and advocate for our daughter. It shouldn't be put 100% on the parent though. Not something that impacts so many families each year. Kinley, our daughter, is now 4. She has braved so many tests; from hearing to MRI's for her seizures. It's hard to put into words how much CMV has impacted our lives. I wish I could speak more eloquently on the topic, but the truth is I'm sad and angry and exhausted from trying to be a voice where there is such a void in WA. Our state is behind. Maybe knowing about CMV wouldn't have changed the course of events, but I can tell you this: being educated by my OB or doctor before it hit us would absolutely have made a world of difference. If nothing else, to let me know I wasn't crazy. I wasn't alone. It wasn't some rare awful thing that was completely out of my control. Our story is just one, but one that no mother should have to walk through alone like I did. Education and awareness on CMV will without a doubt help women and babies in WA state.

Thank you for your time,
Lisa Aamot

Evelyn's Story
written by her mother, Melissa

Dear Washington Board of Health,

I sat down to write our CMV story many times, but no words quite captured our initial experience with the virus like the ones I wrote below in an email update to friends on our daughter's journey into this world in the Fall of 2016. I hope you take the time to read through all of the facts and family submissions and testimonials so that together, we can take action against a virus that has impacted so many in such a wide spectrum of severity.

----- **message** -----

From: Melissa

Date: Wed, Oct 5, 2016 at 2:59 PM

Subject: Evelyn Update...

Hi Ladies,

I'm finally coming out of a fog from the past 12 days and wanted to first say THANK YOU for being such an amazing group of friends. The never-ending prayers, positive thoughts, meals, check-ins, love, etc have all been overwhelming. I have an update on Evie below and I can honestly say I was not strong enough to go through this alone so I deeply appreciate all of the love and support you guys have provided.

Over the past 12 days we have been getting different updates on Evelyn's stats and progress day in and day out so please forgive me for not sending regular progress reports. I'll start from the beginning, read if you want, or don't, either way I think that typing this out might be therapeutic for me...or it will cause PTSD, we'll see which one rules out.

The short story is that Evelyn had/has congenital Cytomegalovirus (CMV) which is a virus I gave to her and can be caught just like the common cold, only unlike a cold, this virus can be deadly for newborns. I've attached some visual stats on the virus as I think it helps paint a better picture. She has been improving over the last 12 days and they are talking about sending us home tomorrow if she can pass the 90 minute car seat test today (showing she's able to keep her oxygen level up while in the seat).

The long version is as follows...

I went into labor at about 1am on Friday the 23rd, (one day before her 24th due date). I labored at home for a few hours, came in and was dilated to 7cm and had Evelyn at 7:49am. My doula didn't even make it in but Justin was a rock-star and we thought all was great for the first 10 minutes or so of her life.

Pretty soon after she entered the world it was apparent that she wasn't able to maintain her temperature, it was low-not high like you would think with an infection. She was also showing signs of pinpoint Petechiae all over her skin/body which are little round red/purple dots that act like a bruise and could come out with trauma (going through the birth canal) or, as we later learned, correlate with a low Platelet count and in turn congenital Cytomegalovirus (CMV).

Evelyn was brought to the NICU within the hour of entering this crazy world and we started to rule out possibilities. Was this a bacterial infection? A virus? If so, what virus? We were able to rule out the bacterial infection within 48 hours and once the CMV results came back positive we immediately started treatment which is an anti-viral called gancyclovir. While all of this was going on Evelyn was fighting low bilirubin counts, fluid in her lungs, an enlarged spleen, a broken collar bone, 4 cysts in her brain and I'm sure others that I'm forgetting now. The bilirubin counts/liver function and enlarged spleen were clear indicators of CMV, the broken collar bone was from birth, and the fluid in her lungs was probably a combination of her taking a big gulp of fluid during her fast delivery and the CMV.

We've been poking and prodding her, checking blood counts, eyes, ears, spinal fluid etc and she has been a trooper through it all. Evelyn started with a 37k CMV count in her blood early last week and we just found out today that it is down to 12k, so clearly the antiviral is working. We also got a 1,600 CMV number in her spinal fluid but there was blood in there from the tap so we aren't positive whether or not this number is a 'false positive' but that is what we are holding out hope for as having CMV in her spinal fluid could be detrimental to her brain development. I wish I could tell you what these numbers mean on a scale, all I know is that "0" is a negative CMV result and that every case is different in regards to the how the body fights this infection. We are going to be talking to a few different ID (infectious disease) specialists to better understand our specific case moving forward. Dr. Zerr at Seattle Children's has had our case from the start and we feel we are in great hands as she is the Division Chief of the Infectious Disease research center, specializing in CMV.

They call CMV the silent virus as usually there would be no signs or indicators that a newborn or infant is infected until you start to notice that milestones aren't being hit. For example, "my 4 month old isn't babbling like she should"... We feel fortunate that there were indicators for us, that Ev is labeled a "text book" CMV case, and that we got on the antiviral as soon as we could. Looking at the facts it's crazy to think that CMV is found in 70%+ of kids at daycare yet the awareness among pregnant women is so low.

We have a long road ahead of us as we will never truly know how CMV affected Evelyn during this early phase of life. We will be watching for milestones to be hit and will be following up with specialists weekly/monthly/yearly. We will most likely be doing an MRI sooner rather than later as CMV is the leading non-genetic cause of childhood hearing loss and can cause vision loss as well. Evie passed her hearing test on her right side right away but not her left, we are hoping to get that re-tested today and her eyes were checked for a second time yesterday, showing no signs of retinitis which is great though who knows how development will change over time.

We are staying positive that she is tracking and trending well and that we will continue to get good news in the future. She has a full head of hair and looks just like Margot did as a baby though petite as she's ~2-3 lbs lighter. She is one tough cookie to go through all of this and has clearly proven she's a fighter. I don't wish this upon anyone and will certainly be advocating for CMV awareness and I hope that all of you do the same as we all know someone with kids in daycare, who are pregnant, etc.

I'm going to take a deep breath, dry my eyes, and feed my new little one with the hope that we will be home tomorrow. Thank you for humoring me and reading until the end ;-)

Forever Grateful,
Melissa (Justin, Margot, and Evie too!)



Thank You For Being A Hero
written by a mother whose daughter who has cCMV

How would it feel to be able to make a difference? How good would it feel to walk into a room and have someone thank you for absolutely changing their life, for changing the life of their child, and for preventing something potentially life threatening from happening to their child? There's a word for that, and it's called being a hero.

When we think of heroes, we think of the firefighters on 9/11, or good samaritan's helping a stranger, or our brave soldiers who fought for our freedom.

Today, you have an opportunity to be a hero, and to save lives.

If I had a hero like you, my daughter's life would be forever changed. You could have prevented her from becoming deaf. You could have given her words to speak. In fact, my beautiful blue eyed curly haired Shirley Temple looking daughter could have spoken the words 'Thank you' to you. She would hug you. You would be a hero. You could have prevented the brain calcification that she has which has impacted her development, and that of which prevents her from very very basic learning. You could have given her friends. You could have given her the ability to walk and dance without aggressive therapies. You could have seen her smile to her favorite nursery rhyme, and see her thrive in preschool, because right now she cannot. This was taken away from her. You can make this situation right. You can make a difference.

You would have looked at me as a mother and told me you prevented so many worries in the middle of the night, and hung up the phone from so many calls to doctors and insurance companies. You would have held my hand and told me if she was having seizures or not. You would have wiped away my tears and told me that my family would be ok. You would have told me not to worry about losing my job or my health insurance after taking so much time off to care for my child. You would have taken away stress between my spouse and family.

You cannot do that for me, but you CAN do that for hundreds of future mothers and fathers. You can be a hero.

....and when you take action, perhaps our paths will cross, and I will thank you not for my daughter, because she will never see the benefits, but so that her struggles will not be in vain. For all the other mothers, fathers, and caretakers out there, for your future generations, future children and grandchildren.

Thank you for being a hero.

Tom, The Fighter ***written by his mother, Katie***



This is Tom The Fighter!

He battles with us each morning about wearing his cochlear implant and hearing aid.

Before this he battled a bone infection, spending 11 days in the hospital last year, getting a PICC line and an NG tube.

Before that he fought to learn to stand and walk, due to his damaged balance systems.

Before that he fought to be understood as a developing baby that couldn't tell us he couldn't hear.

Before that he battled his CMV infection as a newborn, silently, when no one knew he was fighting.

And before that, no one tested him for CMV.

Congenital CMV causes more cases of congenital disease than the combination of 19 currently screened conditions in most American states.

1 in 200 babies is born with congenital CMV.

1/5 of those babies have life long consequences.

A blood or urine test is all that would have been needed for us to know that Tom had congenital CMV. We would have had the upper hand. We could have done the fighting to preserve his hearing, and minimize the damage done by the infection.

Tom is healthy today. He is proud of being deaf, and loves signing with those around him. We love him exactly the way he is. But the fact is, that he caught the virus before being born. If screening for CMV was part of the uniform newborn screening, we could have known.

What would you like the Board of Health to know about congenital CMV?

We were so scared and so worried. I work as a developmental physical therapist, I knew what my child was supposed to be doing and he wasn't doing it. Tom was so little and he was falling behind so quickly. Family, friends, and physicians tried to reassure us that things were going to be fine but we knew in our heart there was something going on with our baby. We asked for help and tried to get answers. We made calls to the clinics to try to schedule ourselves instead of waiting for them to call us. We called again and again, and again, and offered to take any cancellations. We drove all over the state trying to get the soonest appointments we could for audiology, ENT, ophthalmology, cardiology, GI, anyone who could help solve the puzzle of our little 11 month old baby boy. We had to create our own urgency because without a diagnosis, no one could prioritize us over any other new patient. Meanwhile, our child was losing more hearing everyday. From when we started having concerns about his hearing, to ultimately being diagnosed with profound hearing loss, we waited 7 months. We waited another 4 to get our

diagnosis of congenital CMV. He was 20 months old when we finally knew that he had been fighting this devastating virus since before he was born. Had we not pushed every referral coordinator along the way it would have taken much longer. Had we had newborn testing done after he failed his first hearing screen, we would have known within the first days of his life. The shock would have still evoked grief of what we were losing, but at least we would not have been losing time. We would have known the battle we were up against and could have equipped ourselves with knowledge and a team of providers rather than feeling so alone, scared, and worried.

Appendix A.

Continuation of [Criteria 1](#) by Christina Long, M.D. and Jennifer Taylor, ARNP

The current CMV screening protocol at Valley Medical Center

“The current process CMV screening protocol at Valley Medical Center is as follows:

1. All infants undergo hearing screening prior to discharge. If an infant does not pass their second hearing screen, the hearing screener notifies the bedside RN of a second referred hearing screen
2. The RN releases a standing saliva CMV order for a second referred hearing screen (ordered as a miscellaneous send out) and contacts the Seattle Children’s Hospital (SCH) Newborn Rounder (ARNP or PA-C) that an infant has referred their second hearing screen and will have the saliva CMV test performed.
3. The SCH Newborn Rounder keeps a paper log of all pending CMV testing.
4. The RN obtains a viral swab from the hospital lab. The RN then collects a specimen via a swab in the cheek of the infant. Once collected, the lab then sends the sample to the UW virology lab where it is tested for CMV. This usually takes between 4-6 days and then UW sends a report back to VMC with the results.
5. The SCH Newborn Rounder follows up on pending CMV labs daily. The lab will call the SCH Newborn Rounder with all positive results.
6. If CMV testing is positive the patient should be referred urgently to Seattle Children’s Infectious Disease. The SCH Newborn Rounder will place the referral and alert the infant’s PCP. The SCH Newborn Rounder will also email Ann Melvin, MD, of Children’s Infectious Disease at ann.melvin@seattlechildrens.org to notify her of any positive results.

The process at Providence Medical Center is similar to VMC except that the Providence SCH Hospitalists are the ones who are notified and also who follow up on the labs. The swabs are sent to the Seattle Children’s Microbiology lab and the SCH lab calls the Hospitalists to notify if a positive result.”

Appendix B.
Commonwealth of Virginia

**Department of Planning and Budget
2019 Fiscal Impact Statement**

1. Bill Number: HB2026

House of Origin Introduced Substitute Engrossed
Second House In Committee Substitute Enrolled

2. Patron: Stolle

3. Committee: Passed both Houses.

4. Title: Newborn screening; congenital cytomegalovirus.

5. Summary: Directs the Board of Health to amend regulations governing newborn screening to include screening for congenital cytomegalovirus in newborns who fail the newborn hearing screen.

6. Budget Amendment Necessary: See item #8.

7. Fiscal Impact Estimates: See item #8.

7a. Expenditure Impact:

<i>Fiscal Year</i>	<i>Dollars</i>	<i>Positions</i>	<i>Fund</i>
2019			
2020	\$60,000	0	Nongeneral
2020	\$198,589	0.5	General
2021	\$138,638	1	Nongeneral
2021	\$35,500	0.5	General
2022	\$138,638	1	Nongeneral
2022	\$35,500	0.5	General
2023	\$138,638	1	Nongeneral
2023	\$35,500	0.5	General
2024	\$138,638	1	Nongeneral
2024	\$35,500	0.5	General
2025	\$138,638	1	Nongeneral
2025	\$35,500	0.5	General

7b. Revenue Impact:

<i>Fiscal Year</i>	<i>Dollars</i>	<i>Fund</i>
2019	0	
2020	0	Nongeneral
2021	\$138,638	Nongeneral
2022	\$138,638	Nongeneral
2023	\$138,638	Nongeneral
2024	\$138,638	Nongeneral
2025	\$138,638	Nongeneral

8. Fiscal Implications: This bill would have a fiscal impact on the commonwealth.

Virginia Department of Health: The Office of Information Management has estimated that enhancements to the Virginia Infant Screening and Tracking System (VISITS) to capture congenital cytomegalovirus (CMV) data would be \$164,589 with annual maintenance costs of \$1,500. According to § 32.1-68 of the Code, the screening program shall include provisions for education, post-screening counseling, and laboratory testing. The department estimates that a wage position at a rate of \$29,000 per year would be required to implement the program, educate and train stakeholders about CMV, assist in VISITS enhancements requirements, monitor and document CMV infants and their outcomes and report findings. Furthermore, an education campaign to include CMV information on print materials, website updates, and when traveling to relevant national conferences would cost an estimated \$5,000 per year.

Department of General Services: The Division of Consolidated Laboratory Services will need to implement a new fee for the required testing of CMV. DCLS does not currently offer CMV testing and would require appropriation to both implement and sustain the testing in support of the VDH/Early Hearing Detection and Intervention (EHDI) Program. Based on DCLS' preliminary analysis, this testing is estimated to cost \$37 per test for reagents and consumables. DCLS would require a minimum of 12 months to stand up, validate and implement this testing and as a result it is assumed that no revenue from testing services will be realized until 2021. There is a first year implementation cost of \$60,000 for Lab Information Management System (LIMS) development and hardware. There is currently only one FDA-approved newborn CMV testing kit available for purchase. The price quote for the testing kit was based on an annual sample volume of 1625 samples/year; and the instrumentation needed for this testing is provided by the vendor through the purchase of reagent kits. Annual costs assume an estimate of 1625 samples per year with a 10 percent in-lab repeat rate and running the testing Monday – Friday. In order to address the increase in workload, two wage positions will be needed at a rate of \$36,250 per position.

Department of Medical Assistance Services: If commercial laboratories were utilized for CMV screening, there would be a fiscal impact on the Department of Medical Assistance Services (DMAS) and managed care organizations (MCOs). Comments from this agency are pending.

9. Specific Agency or Political Subdivisions Affected: The Virginia Department of Health and the Department of General Services.

10. Technical Amendment Necessary: No.

11. Other Comments: None.

Commonwealth of Virginia. Department of Planning and Budget. 2019 Fiscal Impact Statement.

CONTRIBUTORS

Thank you to the following contributors.

Professional Contributors

Mallory Baker, Au.D.

*Pediatric Audiologist, Seattle Children's Hospital
Founder, Washington CMV Project*

Amanda Devereaux RN, BSN

Program Director, National CMV Foundation

Khaliah Fleming, MPH, MCHES

Executive Director, National CMV Foundation

Christina M. Long, D.O.

*Clinical Associate Professor of Pediatrics
Medical Director, NICU, Valley Medical Center
Chair, Department of Pediatrics, Valley Medical Center*

Ann J. Melvin, M.D., MPH

*Professor, Department of Pediatrics, University of Washington School of Medicine,
Clinical Director, Division of Infectious Diseases, Seattle Children's Hospital*

Henry C. Ou, M.D., M.A.

*Otolaryngologist, Childhood Communication Center, Seattle Children's Hospital
Associate Professor, Department of Otolaryngology – Head and Neck Surgery, University of Washington*

Jennifer Taylor, ARNP

Nurse Practitioner, Newborn Services, Seattle Children's Hospital and Valley Medical Center

Family Story Contributors

Lisa, *mother*

Melissa, *mother*

Anonymous, *mother*

Katie, *mother*

REFERENCES

- (2019). Year 2019 Position Statement: Principles and Guidelines for Early Hearing Detection and Intervention Programs. *Journal of Early Hearing Detection and Intervention*, 4(2), 1-44. DOI: 10.15142/fptk-b748
- (Washington State Department of Health. Disorders Detected by Newborn Blood Spot Screening. Apr 2015. DOH 951-145. <https://www.doh.wa.gov/Portals/1/Documents/Pubs/951-145-NBSDisordersDetectedbyBloodSpotScreening.pdf>)
- Bergevin A, Zick CD, McVicar SB, Park AH. Cost-benefit analysis of targeted hearing directed early testing for congenital cytomegalovirus infection. *Int J Pediatr Otorhinolaryngol*. 2015 Dec;79(12):2090-3. doi: 10.1016/j.ijporl.2015.09.019. Epub 2015 Sep 25. PMID: 26432541.
- Beswick, R., David, M., Higashi, H., Thomas, D., Nourse, C., Koh, G., Koorts, P., Jardine, L.A. and Clark, J.E. (2019), Integration of congenital cytomegalovirus screening within a newborn hearing screening programme. *J Paediatr Child Health*, 55: 1381-1388. <https://doi.org/10.1111/jpc.14428>
- Boppana, S. B., Ross, S. A., Novak, Z., Shimamura, M., Tolan, R. W., Palmer, A. L., ... & Britt, W. J. (2010). Dried blood spot real-time polymerase chain reaction assays to screen newborns for congenital cytomegalovirus infection. *Jama*, 303(14), 1375-1382.
- Boppana SB, Ross SA, Shimamura M, Palmer AL, Ahmed A, Michaels MG, Sánchez PJ, Bernstein DI, Tolan RW Jr, Novak Z, Chowdhury N, Britt WJ, Fowler KB; National Institute on Deafness and Other Communication Disorders CHIMES Study. Saliva polymerase-chain-reaction assay for cytomegalovirus screening in newborns. *N Engl J Med*. 2011 Jun 2;364(22):2111-8. doi: 10.1056/NEJMoa1006561.
- Cannon, M. J., Griffiths, P. D., Aston, V., & Rawlinson, W. D. (2014). Universal newborn screening for congenital CMV infection: What is the evidence of potential benefit? *Reviews in Medical Virology*, 24(5), 291–307. <https://doi.org/10.1002/rmv.1790>
- Centers for Disease Control and Prevention (CDC). Knowledge and practices of obstetricians and gynecologists regarding cytomegalovirus infection during pregnancy--United States, 2007. *MMWR Morb Mortal Wkly Rep*. 2008 Jan 25;57(3):65-8. PMID: 18219267.
- Centers for Disease Control and Prevention. 2020. About Cytomegalovirus (CMV). <https://www.cdc.gov/cmV/overview.html>
- Centers for Disease Control and Prevention. 2020. Cytomegalovirus (CMV) and Congenital CMV Infection. <https://www.cdc.gov/cmV/index.html>
- Centers for Disease Control and Prevention. Cytomegalovirus (CMV) and Congenital CMV Infection. <https://www.cdc.gov/cmV/clinical/congenital-cmv.html>
- Commonwealth of Virginia. Department of Planning and Budget. 2019 Fiscal Impact Statement. HB2026. Virginia Legislative Information System. <https://lis.virginia.gov/cgi-bin/legp604.exe?191+oth+HB2026FER122+PDF>
- Din, E. S., Brown, C. J., Grosse, S. D., Wang, C., Bialek, S. R., Ross, D. S., & Cannon, M. J. (2011). Attitudes toward newborn screening for cytomegalovirus infection. *Pediatrics*, 128(6), e1434-e1442.
- Dollard SC, Dreon M, Hernandez-Alvarado N, et al. Sensitivity of Dried Blood Spot Testing for Detection of Congenital Cytomegalovirus Infection. *JAMA Pediatr*. 2021;175(3):e205441. doi:10.1001/jamapediatrics.2020.5441
- Doutre S, Barrett T, Greenlee J, White K. Losing Ground: Awareness of Congenital Cytomegalovirus in the United States. *J Early Hear Detect Interv*. 2016;1: 39–48. 10.15142/T32G62
- EHDDI 2019 Statistics <https://www.doh.wa.gov/Portals/1/Documents/Pubs/344-042-EHDDI-FlowChart.pdf>
- Fowler, K. B., McCollister, F. P., Dahle, A. J., Boppana, S., Britt, W. J., & Pass, R. F. (1997). Progressive and fluctuating sensorineural hearing loss in children with asymptomatic congenital cytomegalovirus infection. *The Journal of pediatrics*, 130(4), 624-630.
- Gantt S, Dionne F, Kozak FK, et al. Cost-effectiveness of Universal and Targeted Newborn Screening for Congenital Cytomegalovirus Infection. *JAMA Pediatr*. 2016;170(12):1173–1180. doi:10.1001/jamapediatrics.2016.2016
- Gievers, L. L., Holmes, A. V., Loyal, J., Larson, I. A., Oliveira, C. R., Waldman, E. H., & Khaki, S. (2020). Ethical and Public Health Implications of Targeted Screening for Congenital Cytomegalovirus. *Pediatrics*, 146(1), e20200617. <https://doi.org/10.1542/peds.2020-0617>
- Grosse SD, Dollard SC, Ortega-Sanchez IR. Economic assessments of the burden of congenital cytomegalovirus infection and the cost-effectiveness of prevention strategies. *Semin Perinatol*. 2021 Apr;45(3):151393. doi: 10.1016/j.semperi.2021.151393. Epub 2021 Jan 23. PMID: 33551180.
- Haller, T., Shoup, A., & Park, A. (2020). Should hearing targeted screening for congenital cytomegalovirus infection Be implemented?. *International Journal of Pediatric Otorhinolaryngology*, 110055.
- Hicks, T., Fowler, K., Richardson, M., Dahle, A., Adams, L., & Pass, R. (1993). Congenital cytomegalovirus infection and neonatal auditory screening. *The Journal of pediatrics*, 123(5), 779-782.
- Hughes BL, Gans KM, Raker C, Hipolito ER, Rouse DJ. A Brief Prenatal Intervention of Behavioral Change to Reduce the Risk of Maternal Cytomegalovirus: A Randomized Controlled Trial. *Obstet Gynecol*. 2017 Oct;130(4):726-734. doi: 10.1097/AOG.0000000000002216. PMID: 28885428.
- Kimberlin DW, Jester PM, Sánchez PJ, et al. Valganciclovir for symptomatic congenital cytomegalovirus disease. *N Engl J Med*. 2015;372(10):933-943. doi:10.1056/NEJMoa1404599

- Lucas, A., Sinha, A., Fowler, K.B. *et al.* A framework for assessing the lifetime economic burden of congenital cytomegalovirus in the United States. *Cost Eff Resour Alloc* **17**, 21 (2019). <https://doi.org/10.1186/s12962-019-0189-0>
- Marsico, C., & Kimberlin, D. W. (2017). Congenital Cytomegalovirus infection: advances and challenges in diagnosis, prevention and treatment. *Italian journal of pediatrics*, 43(1), 38. <https://doi.org/10.1186/s13052-017-0358-8>
- Misono, S., Sie, K. C., Weiss, N. S., Huang, M. L., Boeckh, M., Norton, S. J., & Yueh, B. (2011). Congenital cytomegalovirus infection in pediatric hearing loss. *Archives of Otolaryngology–Head & Neck Surgery*, 137(1), 47-53.
- Park, A. Randomized Controlled Trial of Valganciclovir for Cytomegalovirus Infected Hearing Impaired Infants: ValEAR Trial. <https://clinicaltrials.gov/ct2/show/NCT03107871>
- Pesch MH, Anderson C, Mowers E. Improving Obstetric Provider Congenital Cytomegalovirus Knowledge and Practices. *Infect Dis Obstet Gynecol*. 2020 Nov 8;2020:8875494. doi: 10.1155/2020/8875494. PMID: 33223803; PMCID: PMC7669343.
- Rawlinson, W. D., Boppana, S. B., Fowler, K. B., Kimberlin, D. W., Lazzarotto, T., Alain, S., ... & Greenlee, J. (2017). Congenital cytomegalovirus infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy. *The Lancet Infectious Diseases*, 17(6), e177-e188.
- Ronchi, A., Shimamura, M., Malhotra, P. S., & Sánchez, P. J. (2017). Encouraging postnatal cytomegalovirus (CMV) screening: the time is NOW for universal screening!. *Expert review of anti-infective therapy*, 15(5), 417–419. <https://doi.org/10.1080/14787210.2017.1303377>
- Stephanie A. S. Staras, Sheila C. Dollard, Kay W. Radford, W. Dana Flanders, Robert F. Pass, Michael J. Cannon, Seroprevalence of Cytomegalovirus Infection in the United States, 1988–1994, *Clinical Infectious Diseases*, Volume 43, Issue 9, 1 November 2006, Pages 1143–1151, <https://doi.org/10.1086/508173>
- Tastad KJ, Schleiss MR, Lammert SM, Basta NE. Awareness of congenital cytomegalovirus and acceptance of maternal and newborn screening. *PLoS One*. 2019;14(8):e0221725. Published 2019 Aug 26. doi:10.1371/journal.pone.0221725
- Torpy JM, Burke AE, Glass RM. Cytomegalovirus. *JAMA*. 2010;303(14):1440. doi:10.1001/jama.303.14.1440
- Washington State Department of Health – Birth Data Dashboard. <https://www.doh.wa.gov/DataandStatisticalReports/HealthDataVisualization/BirthDashboards>
- Williams EJ, Gray J, Luck S, et al First estimates of the potential cost and cost saving of protecting childhood hearing from damage caused by congenital CMV infection *Archives of Disease in Childhood - Fetal and Neonatal Edition* 2015;100:F501-F506.