IDAHO
CMV Advocacy Project

To Whom it May Concern,

Thank you for your support of the Idaho CMV Advocacy Project and bill #S1060. We are passionate about getting CMV legislation passed in Idaho! In this folder you will find:

Who We Are
- Statement of Purpose
- CMV Parent Letters
- Biographies of the CMV Advocacy Team
- Letters of Support

CMV Education and Awareness Flyers
- Facts About CMV Packet
- Facts About CMV Flyer
- "What You Need to Know" Brochure
- CMV Prevention Flyer
- Protect Yourself Flyer
- Educate Yourself Flyer (2 Versions)

Legislation
- "What Would CMV Legislation Mean for Idaho?" flyer
- Senate Bill S1060, Health care/Cytomegalovirus
- Utah State CMV Code

Important Literature
- Scholarly Articles
- Bibliography

We appreciate your interest in our endeavors and in CMV awareness and advocacy. We look forward to working with you in the future.

Sincerely,

The CMV Advocacy Project
Rebekah Hall, Erica Jensen, Jessica Rachels & Claire Szewczyk

Statement of Purpose for Cytomegalovirus (CMV) Bill

The purpose of the CMV bill is twofold. First, it will ensure that the women of Idaho and their doctors have access to the most accurate and up-to-date information available regarding cytomegalovirus prevention, infection, and treatment. Appropriate dissemination of this information will foresee-ably prevent the infection of numerous babies in utero, thereby saving the state of Idaho millions of dollars in the care and treatment of various disabilities that are associated with congenital cytomegalovirus infection. Secondly, because cytomegalovirus is the leading non-genetic cause of hearing loss, the CMV bill will provide for mandated CMV testing for any infant who fails his/her newborn hearing screen. This would allow for early detection of hearing loss and, therefore, improved treatment and long-term outcomes for individuals with CMV-related hearing loss. This first year we will focus only on the education and awareness piece, next session we will address the hearing screening.

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CMV Advocacy Project

Rebekah Ponsford-Hall, PsyD
1906 South Elder Street
Nampa, Idaho 83686
(626) 372-2517

To Whom It May Concern:

I'd like to tell you about my daughter, Keira. She is a four-year-old girl with an effervescent laugh and eyes that sparkle and light up a room. She is also the biggest challenge I've faced in my life. The condition she has is preventable and I am passionate about the fact that every pregnant woman in Idaho should be aware of it. My daughter was born with **cytomegalovirus*** (CMV). Harmless to most, CMV is a common virus that infects 80% of us by the time we reach adulthood. However, it can have devastating effects when transmitted to a fetus by a pregnant mother.

When I was pregnant with Keira in 2012, my OB/GYN repeatedly told me that my pregnancy was "boringly healthy." Yet my baby was born with tremendous challenges. Born at 37 weeks, she was technically full term, but she weighed only 4 lbs., 13 oz. She also had microcephaly, an enlarged liver and spleen, petichiae on her skin, and cysts on her brain; all symptoms, I would soon learn from specialists, which were characteristic of CMV.

At my 6 week, postnatal follow up appointment, my OB/GYN attested that CMV had hardly been covered in medical school and after over a decade of practicing obstetrics, he believed Keira to be the first time he had encountered CMV. Unfortunately, my OB/GYN was not alone in believing that CMV was rare. I have since learned that only 13% of women have ever heard of CMV and fewer than half of all OB/GYNs are educating their patients about CMV.

Keira has cerebral palsy, vision impairment, and failure to thrive. She will never walk or talk. She receives her nutrition entirely by G-tube. At age 4, she cannot hold up her own head. She is at high risk for hearing loss and seizures. It is very unlikely that she will outlive her parents or her brothers.

Since her birth, Keira has undergone 14 surgical procedures and spent 100 days in the hospital. She is followed by 16 medical specialists and 7 types of therapists. She takes 7 medications on an ongoing basis. She averages 6 appointments per week, not including school. **To date, Medicaid has paid out $278,303.47 on Keira's behalf.**

Here is what I wish I had been told and the information that I believe all women of childbearing age should have access to:

-1 in 150 children is born with CMV

-CMV is more common that HIV, Spina Bifeda, and Downs Syndrome

-1 in 5 babies born with CMV will be permanently disabled by it

-CMV can be prevented using basic hygienic precautions

-Testing for CMV before and/or during pregnancy can aid in prevention and treatment

-Vancyclovir and Immune Globulin Injections may help treat CMV during pregnancy

I had never heard of CMV until it was too late for my daughter. If my OB/GYN and I had been aware, we may have been able to prevent it and/or mediate its devastating effect on my daughter.

It's unconscionable to continue to keep this information from pregnant women. In the U.S., typical prenatal care routinely screens for a numerous conditions (including HIV, cystic fibrosis, and toxoplasmosis) that are far less common, less devastating, and/or less burdensome on society than CMV. CMV needs to be added to the list of conditions that are screened and followed by physicians.

It has been estimated that educating the public in our state would cost $40,000 the first year and $26,000 annually after that. Several states (including Utah, Texas, and Tennessee) have already begun to implement CMV legislation. I pray that Idaho will soon follow*.

Thank you for taking the time to read our story. Do not hesitate to contact me if you have additional questions.

Sincerely,

Rebekah Ponsford-Hall, PsyD
CMV Mom

** For more information about CMV, visit nationalcmv.org or the Center for Disease Control website*
** To review the CMV bill passed in 2013 by the state of Utah, visit le.utah.gov//~2013/bills/static/hb0081*

Jessica and Patrick Rachels
PO Box 402
Ponderay, ID 83852

To Whom it May Concern:

Hi, my name is Jessica Rachels, and I live in North Idaho. I would like to share with you a little about my daughter Natalie who is a beautiful, social, ten year old girl who caught a nasty virus that I had never heard of while she was still in the womb. My hope is that in educating you about this virus, you can share what you have learned, and we can lessen the chances of your loved ones ever being stricken with this virus. But first, allow me to tell you about Natalie.

Natalie Rachels was born with congenital Cytomegalovirus, (CMV). CMV is a nasty virus that is a member of the Herpesviridae (Herpes) family. It is common and affects people of all ages. By the age of forty, between 50% and 80% of people in the US have contracted CMV. Usually it presents itself as a common cold, although, if the person has a weakened immune system or is an unborn child, it can drastically affect the body. In Natalie's case we were unaware that anything was wrong for several weeks after birth. The first red flag was that her due date was off by a month because an ultrasound revealed that her head size was smaller than average. The obstetrician did not believe that this information was important. So nothing was done, no further tests were recommended and/or administered. After she was born, Natalie repeatedly failed her newborn hearing screenings. At first the nurses and doctors were not alarmed, since babies can be born with a thick coat of vernix which can coat the inside of the ear. She kept failing the screenings; therefore, we were sent to Kootenai Medical Center in Coeur d'Alene for more intensive testing, which showed that Natalie had profound and severe hearing loss. The doctor then ordered a CT Scan which showed that the ear structures were perfectly normal, but that her brain had been damaged. Blood work from Natalie and me showed that we both contracted the CMV virus. Natalie was about two and a half months old, and still seemed like a typical baby minus being deaf and having some reflux issues.

Today Natalie is ten years old. Her father and I were told years ago that she wouldn't make it to see her double digits. We celebrated her tenth birthday, and took her to a roller skating rink, where she seemed to enjoy being pushed around the floor in her wheel chair. Natalie has been in and out of the hospital over the years. She has had ten major surgeries and will have more in the future.

Her care—which includes medical care, therapy, surgeries, personal care items, medical equipment, and the aid of caregivers—over the past ten years has cost over $1,000,000.

The virus caused many different issues including Cerebral Palsy, hearing loss, feeding issues—she currently is fed with the aid of a gastrointestinal tube; scoliosis, hip displacement, muscle tone issues which creates stiffness in some areas of her body, and floppiness in other areas; seizures—thankfully no grand mal seizures, which are kept to a minimum with the help of the implantation of a Vagus Nerve Stimulator; minor visual issues, and pulmonary complications which includes asthma.

Even with all of her difficulties, she is such a happy little girl. Natalie is very social, and loves being around people. She loves toys that light up, and her favorite game is playing peek-a-boo with loved ones who go in and out of the front door. For some reason the door opening and closing makes her giggle and laugh. Thanks to modern medicine, she has bilateral cochlear implants and has the gift of hearing. She enjoys bike rides with her family on her special bike, which has a wheelchair in the front and the driver sits behind pedaling. She enjoys playing on her iPad with touch applications as well as cause and effect applications. She has such a sweet and tender soul that has touched many people. Her smile and laugh can light up a room. Yes, her time is limited, but what an impact and difference this little girl is making on the world!

Due to not being properly educated about the virus while pregnant with my daughter, I worked in a daycare center. My doctor did not think it was important to educate me about CMV; in doing so he

took away my right and choice to protect my child. He could have given me a brochure about CMV, which would have explained how to prevent contracting the virus by practicing universal hand washing procedures, not kissing toddlers on the lips, and not sharing food or drinks. While I worked at a day care center, I had an increased exposure to CMV because of the high rate of coming into contact with bodily fluids, through which CMV is passed. It is not airborne.

Her father and I are advocates for the prevention of the CMV virus. We have given presentations, and have attended two CMV International Conferences. Our dream is to educate others about CMV so that more children can be spared this horrific virus. CMV is the most common congenital infection, and is one of the leading causes of Cerebral Palsy in children. With a law that mandates education and targeted screening, Idaho can see a reduction in the incidences of CMV related illness. Additionally, infants that have contracted the virus in utero will have a faster diagnosis and treatment as a result of the newborn screening. According to the CDC website, "About 1 in 150 children are born with congenital CMV infection. This means that in the United States, about 30,000 children are born with congenital CMV each year. About 1 in every 5 children born with congenital CMV will develop permanent problems, such as hearing loss or developmental disabilities, due to the infection. In the United States, more than 5,000 children each year have permanent problems caused by congenital CMV."

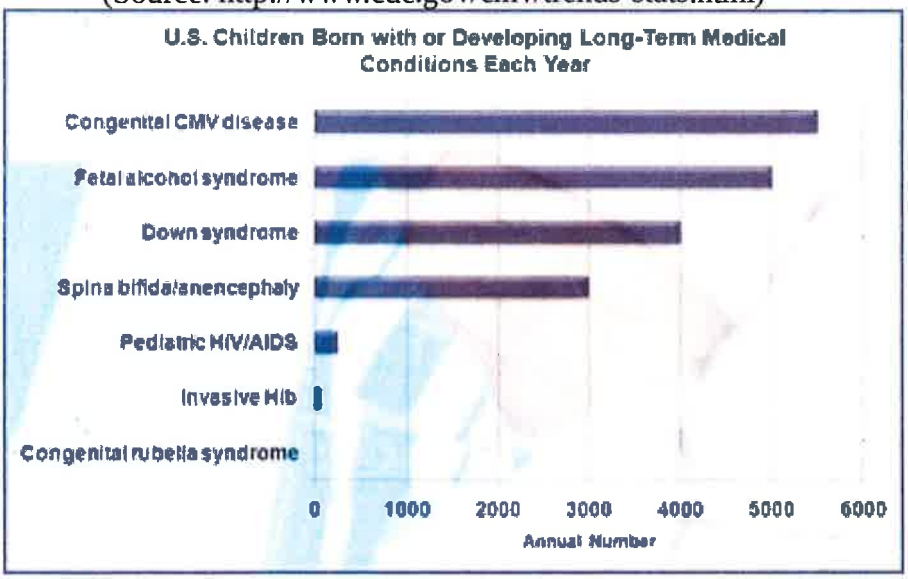
If you are interested in learning more about the virus, please visit the CDC website www.cdc.gov, and you will be amazed at what you never knew about this virus. The National CMV Foundation website address is www.nationalcmv.org. This is an excellent resource for additional information. How is it possible that a common virus such as CMV, which causes a child to be born disabled every hour is still unknown by many?

Sincerely,

Jessica Rachels & Patrick Rachels

Jessica and Patrick Rachels

(Source: http://www.cdc.gov/cmv/trends-stats.html)



Erica Jensen, RN-BSN
12354 S. Abbott Downing Way
Nampa, Idaho 83686
(208) 546-2650

To Whom It May Concern:

I would like to share a bit of my experience with cytomegalovirus (CMV) with you, and why I think it is so imperative that more women be made aware of this virus. CMV is very common, with the vast majority of people being infected with it at some point in their life by adulthood. Normally it is not a big deal - the infected person may notice cold symptoms for a couple days, or they may not be symptomatic at all. However, if the infected person is pregnant, the virus can pass through the placenta. The virus that was pretty harmless to the mom, may now wreak havoc with the baby as he or she is growing and developing. This virus can cause the baby to be born with cerebral palsy, deafness, microcephaly, liver and spleen problems, or even cause death.

At the end of 2010, my husband and I found out that we were expecting triplets. While we were certainly thrilled at the prospect of expanding our family (by quite a bit!), we understood that there are inherent risks with carrying multiples. Because of this, our wonderful family physician referred me to not only an OB/GYN, but also to Dr. Renee Bobrowski, a maternal fetal specialist who specializes in high risk pregnancies. Toward the end of my first trimester I had my first appointment with Dr. Bobrowski, where we found out that we had lost one of the babies. We were heartbroken at this loss. A few days after our appointment with her, I had my first appointment with my OB/GYN and I mentioned to him that I had been feeling sick with cold symptoms for quite awhile and had tested positive for mono about a week earlier. I was concerned that this could affect the babies, and hoping for some reassurance that that hadn't caused the miscarriage. He was quick to reassure me that mono wasn't something to be worried about in pregnancy, and that it'd just take awhile to feel better. I kept pressing the issue and he decided that since I had already seen Dr. Bobrowski once, he'd run it by her. I want to really reiterate at this point that if I had not already seen Dr. Bobrowski because of the triplet pregnancy, this information would not ever have made it to her and I'd have likely gone undiagnosed. I was no longer going to continue seeing her because a twin pregnancy was not as high risk, so the fact that I happened to see her before the OB/GYN could find out that I lost the baby is something my husband and I will forever be so thankful for. I can't even adequately articulate those feelings.

After running my situation past Dr. Bobrowski, she recommended that I be tested for CMV. She said that CMV can give a false positive for mono and with my symptoms it would be worth pursuing. Well, come to find out I did have CMV. He told me this was a very, very big deal and that I may end up losing both babies, or that they could be born with significant disabilities. He was crying as he was telling me this diagnosis, so the severity was not lost on me.

Although obviously overwhelmed and scared, I was also really irritated. So irritated that I didn't know about this! I am a registered nurse, and did my preceptorship in labor and delivery and

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CMV Advocacy Project

About Us

The Idaho CMV Advocacy Project is dedicated to promoting awareness and education to Idaho women who are pregnant, planning to become pregnant or just want more information regarding Cytomegalovirus (CMV) and the dangers it can cause to unborn children. It was founded by two parents of children with CMV, Jessica Rachels and Rebekah Hall, and Idaho State University Doctor of Audiology student Claire Szewczyk.

Jessica Rachels

While pregnant with her second child, she was running a small in home childcare and working one day per week at a childcare center. Her OB doctor was aware of her occupation but did not see the importance of educating her on CMV. Regrettably, Jessica continued working in a high risk environment and her choice to protect her unborn baby was taken away. Natalie her daughter was born at 39 weeks and seemed to be a typical, healthy baby minus continuing to fail her newborn hearing screening, a small head size (which was mentioned later), and reflux issues. At two and a half months of age, blood work confirmed CMV and intensive hearing tests showed that she had profound and severe hearing loss. Today Natalie is a happy, social, smiley, giggly eleven year old girl despite being severely affected by CMV. She's undergone ten surgeries, has implanted devices, uses a wheelchair, and is developmentally at a four to six month old age. After attending two CMV conferences Jessica and her husband, Patrick feel blessed to be apart of the Idaho CMV movement. They are excited to see how God can use them and others to educate people around the state on CMV and prevent other babies from being afflicted by this horrific virus.

Rebekah Hall

With a doctorate in clinical psychology from Fuller Theological Seminary's School of Psychology in Pasadena, California, Rebekah works professionally as a diagnostician and treatment provider for children with developmental and intellectual disabilities. She and her husband, Jeff, also a psychologist, had worked in the field for nearly a decade before the birth of their daughter, Keira. After what was thought to be a normal, healthy pregnancy, Keira was born very sick and was diagnosed with CMV at 3-days-old. Keira suffers from microcephaly, cerebral palsy, failure to thrive, and vision impairment. Rebekah is happy to be part of the team that is working toward passing CMV legislation in Idaho to help educate physicians and parents-to-be about the prevention and treatment of CMV.

Erica Jensen

Erica is a Bachelors prepared registered nurse who lives in Nampa with her husband and three daughters. While her first pregnancy was free of any complications, her second pregnancy quickly became high-risk. Originally pregnant with triplets, she and her husband found out that they had lost one baby during the first trimester. But because she was pregnant with multiples, she was already established with a high-risk maternal fetal specialist who was aware of CMV. She was tested for and diagnosed with CMV after persistent cold symptoms and a fever during her first trimester. Even though Erica had worked in healthcare for years, CMV was not something she was familiar with. After much research, she and her doctor settled on a treatment of immunoglobulin infusions, and an amniocentesis later confirmed that the treatments had worked and both of the babies were born free from CMV.

Erica is thrilled to be a part of the team working to raise awareness of CMV, and hopeful that it will make a real difference in the lives of Idahoans

Claire Szewczyk

A first year Doctor of Audiology student at Idaho State University, Claire first became interested in Cytomegalovirus (CMV) when she volunteered for the Cytomegalovirus Public Health and Policy Conference in 2014. As an undergraduate preparing for studies in hearing sciences, she was fascinated that CMV was the number one non-genetic cause of sensorineural hearing loss in children. In 2015, she worked as a member of the Early Hearing Detection and Intervention program in Salt Lake City and a part of the Utah Cytomegalovirus Public Health initiative. It was there she became engaged in advocacy for CMV and helped with a variety of public awareness campaigns. Now as an Idaho citizen, she is proud to be working with a project campaigning for the passage of CMV legislation, as well as dedication towards providing awareness and education of the virus to women across the state.

Renee A. Bobrowski, MD, FACOG

Stella Puppy, LLC
5220 N. Lakemont Lane Boise Idaho 83714

February 11. 2017

Health and Welfare Committee
Idaho State Legislature
Boise Idaho 83702

RE: Senate Bill No. 1060

Dear Committee Members:

I am writing in support of Senate Bill No. 1060 with the goal to not only increase awareness of Cytomegalovirus (CMV) but provide education for prevention.

I am a Maternal Fetal Medicine (MFM) physician, specializing in the care of high risk pregnant women. But long before I became an MFM, I was an intern in Obstetrics and Gynecology and delivered my first baby affected by congenital CMV. That was 28 years ago, and unfortunately it would not be my last. I have seen firsthand the devastating effects of in utero infection, which include hearing and/or vision loss, microcephaly/brain abnormalities, profound mental delay, failure to thrive, seizures and death.

Intrauterine CMV infection is the most common of all recognized intrauterine infections, with the Centers for Disease control estimating that it occurs in up to 2.3% of all live births. Outcomes range from asymptomatic to profoundly symptomatic requiring life long, intensive medical care. Current evidence indicates that most but not all symptomatic congenital CMV infections result from primary infection of the mother.

A CMV vaccine is not currently available, nor anticipated in the near future. There is no cure for CMV. Treatment during pregnancy and/or in the newborn does not guarantee a child will not suffer the sequelae of CMV. It is frequently a life altering disease, affecting not only a child but the entire network of family and friends. We are therefore, at the present time, left with trying to prevent transmission.

The economic and emotional costs of caring for a single child with congenital CMV are enormous. The most recent estimate of nationwide cost of caring for children with congenital CMV was $1-2 billion in the 1990s. Thus the cost of funding this and similar programs in all 50 states is far less than treatment and care for one child affected by

congenital CMV, making it a most worthy investment. Sadly the greatest loss for an affected child is the unrealized potential to lead a happy and productive life.

It has been suggested that up to 85% of women, i.e. future mothers, are NOT aware of CMV infection, transmission or its effects. And one cannot prevent something one is not aware of. Manicklal et al stated in Clinical Microbiology Reviews (2013 Jan:26(1):86-102) that 'successful implementation of strategies to prevent or reduce the burden of congenital CMV infection will require heightened global awareness among clinicians and the general population." There are currently only 5 states with legislation enacted to provide for public education about CMV infection. Idaho has the opportunity to lead the country in developing their public health initiative against CMV.

It is difficult to argue against funding for education in order to prevent even one child being affected by CMV. It is, after all, education that makes prevention a reality.

I kindly ask your support for Senate Bill No. 1060 so that we can build a strong CMV education program for the families of Idaho.

Respectfully,

RBobrowski

Renee A. Bobrowski, MD, FACOG

February 17, 2017

Hannah Josephson
8969 Bennett Road
Nampa, Idaho 83686

To The Idaho State Legislation,

My name is Hannah Josephson, I am a Registered Nurse in the Neonatal Intensive Care Unit at Saint Alphonsus Regional Medical Center. I am writing in support of bill number S1060, seeking funding to educate the public about CMV or cytomegalovirus. This bill is important to me both professionally and personally.

As a nurse I have taken care of patients diagnosed with CMV. Oftentimes in the NICU we test infants for CMV and it is the first time parents have ever heard of the disease. They are left feeling scared and uncertain. An infant diagnosed with congenital CMV who is symptomatic can spend anywhere from two to six weeks in the NICU for treatment. A long stay in the NICU is a huge burden on a family, both financially and emotionally.

I am also a close family friend of one of the bill presenters, Rebekah Hall. Rebekah and I have known each other for almost 20 years. We have become close friends as adults as a result of having children attending the same school and being classmates and friends. I have had the pleasure of watching Jeff and Rebekah raising their sweet little girl, Kiera. Kiera was diagnosed with congenital CMV as an infant, and has suffered many of the comorbidities associated with this diagnosis. I have watched them as they navigate taking care of two active boys and a child with special needs. They have an amazing support system; but the multiple hospitalizations, surgeries, therapies, and daily challenges associated with having a special needs child have provided hardships on this family.

I feel it is very important that you support bill S1060. I believe that providing education to women and families about the effects of CMV and ways to prevent being infected during pregnancy will prove to beneficial to the state of Idaho. Preventing just one infant from from contracting congenital CMV will more than outweigh the costs to the state for providing this education.

Sincerely,

Hannah Josephson
Charge Nurse
Saint Alphonsus Regional Medical Center, Neonatal Intensive Care Unit

I explained to the nurse that CMV parents, scientists and doctors have been trying for years to raise awareness, but the real risk of CMV to pregnancies remains little discussed—a real tragedy for daycare workers in light of recommendations made by the American Academy of Pediatrics (AAP): "In view of the risk of CMV infection in child care staff and the potential consequences of gestational CMV infection, child care staff members should be counseled about risks. This counseling may include testing for serum antibody to CMV to determine the child care provider's protection against primary CMV infection..."[v] (pg 145, AAP Red Book, 2012; pgs 144-145, AAP Red Book, 2015).

According to the study, "Child Care Provider Awareness and Prevention of Cytomegalovirus and Other Infectious Diseases" by Rosemary Thackeray and Brianna M. Magnusson, "Women who are exposed to CMV prior to conception or within the first trimester of pregnancy and seroconvert have increased risk of their infant being infected with CMV (Hyde et al. 2010)." Despite a daycare worker's high risk of contracting CMV, only 18.5% of licensed "in-home" daycare providers have heard of it according to Thackeray and Magnusson who also state: "Providers do not know how to appropriately sanitize surfaces to reduce spread of disease." For example, using baby wipes may clean a surface, but they do not sanitize it. The authors conclude: "Awareness of CMV and how to prevent transmission of infectious disease is low. Intervening with child care providers and parents through child care facilities are key opportunities to reduce prevalence of CMV infection and other diseases" (Thackeray and Magnusson, 2016).

Between "7.9–10% of daycare workers contract CMV infections each year." ("Losing Ground: Awareness of Congenital Cytomegalovirus in the United States, Doutre et al, 2016) [vi]

Sincerely,

Lisa Saunders
CMV Awareness and Policy Advocate, Parent Rep., Congenital Cytomegalovirus Foundation
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PO Box 389, Mystic, CT 06355

[i] (Joseph, MSc, Serene A, et al, 2006)
[ii] (Centers for Disease Control and Prevention (CDC), n.d.)
[iii] (Elizabeth Ann Saunders, 2006)
[iv] (Doutre, S. M. Barrett, T. S. Greenlee, J. & White, K. R. , 2016)
[v] (Infectious Diseases American Academy of Pediatrics, 2012, 2015)
[vi] (Doutre, S. M. Barrett, T. S. Greenlee, J. & White, K. R. , 2016)

To whom it may concern:

I am in support of Idaho's Educational CMV bill.

I was unaware that cytomegalovirus (CMV) was an occupational risk for daycare educators[i] when I became a licensed home daycare provider in Maryland in 1987. I didn't know that CMV was the leading viral cause of birth defects and could devastate my own pregnancy with Elizabeth, who was born severely disabled by congenital (present at birth) CMV in 1989. Today, most U.S. daycare providers are still not aware of their increased risk for contracting CMV. According to the *New York Times*, CMV Is a Greater Threat to Infants Than Zika, but Far Less Often Discussed (2016).

At the time of Elizabeth's birth, I was operating my licensed home daycare center and volunteering in our church nursery, additionally putting my pregnancy at risk. Elizabeth was born with an abnormally small head, known as microcephaly, was profoundly mentally impaired, legally blind, and had cerebral palsy. After her birth, I was given information from the Centers and Disease Control Prevention (CDC) informing me that "People who care for or work closely with young children may be at greater risk of CMV infection than other people because CMV infection is common among young children..."[ii] This information came too late to spare my daughter the years of suffering that lay ahead of her. Nowhere in my daycare licensing literature or training was CMV mentioned. CMV prevention measures were not discussed in my prenatal doctor visits.

Though Elizabeth grew into a very cheerful girl who won the "Best Smiling Award" at school, she couldn't hold up her head and lived as a three-month-old for 16 years, requiring several surgeries such as spinal fusion. She developed epilepsy and was gradually losing her hearing by the time she died at 16 during a seizure[iii] in 2006 while we were living in New York. I had a bad dream shortly after Elizabeth's death about new parents wondering why I hadn't done more to warn them about the precautions to take against CMV. Although I wrote about Elizabeth's adventurous life with her tomboy sister and a series of dysfunctional pets, including a homeless older dog that joined her on the couch in my memoir, "Anything But a Dog: the perfect pet for a girl with congenital CMV" (Unlimited Publishing, 2008, Thousand Books Project Team of Tokyo, Japan, 2017), congenital CMV still remains largely unknown. Recent HealthStyles™ surveys in the U.S. concluded that only 5% of men and 9% of women have heard of CMV (2015 and 2016).[iv]

In 2010, my husband and I moved to Connecticut. In 2012, I received an email from a distressed grandmother about her grandson born with congenital CMV in a Connecticut hospital (I am the parent representative of the Congenital Cytomegalovirus Foundation). The mother of her grandson was a high school student interning in a Connecticut daycare center. The young mother, just like me over 20 years earlier, was unaware she was putting her pregnancy at greater risk by working in daycare with young children. When I visited the family in the hospital, the attending nurse asked me, "Knowing what you do about CMV, why haven't you launched an awareness campaign?"

February 17, 2017

To Whom It May Concern:

My name is Jessica Stich-Hennen, AuD. For the past 10 years, I have been working as a pediatric audiologist in Boise, ID. During my career, I have worked with several children and families who lives were impacted by congenital Cytomegalovirus (CMV).

In adults, CMV is typically harmless. Unfortunately, CMV is most harmful to a fetus during pregnancy. The virus can cross the placental barrier and cause irreversible birth defects (microcephaly, brain damage, hearing loss, vision problems, cerebral palsy). The CDC reports 1 in 150 babies are born with CMV and 1/5 will have long term medical complications.

The purposed Senate Bill #1060 will provide education and awareness regarding CMV in Idaho. Women of our state will be able to understand how to prevent CMV infection and why it is important. When considering the financial burden of medical procedures/treatments in caring for one child with congenital CMV, the $60,000 requested by Senate Bill #1060 is nominal. Respectfully, consider passing Senate Bill #1060.

Thank you for your time.

Sincerely,

Dr. Jessica Stich-Hennen, AuD, PASC
Doctor of Audiology
Specialty Certification in Pediatric Audiology

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The Honorable Marv Hagedorn
P.O. Box 83720
Boise, ID 83720-0081

RE: Senate Bill 1060

Dear Senator Hagedorn,

I am writing to request your support of Senate Bill 1060, which provides for much-needed public health funding to provide information on cytomegalovirus (CMV), it's symptoms, prevention and potential birth defects caused by infection during pregnancy.

As a School Counselor in our Idaho public schools and now, as a contract Service Coordinator at A&R Case Management, I have seen the devastating effect of cytomegalovirus (CMV) on children and families. CMV is a common childhood infection, with most children testing positive for the virus by age 5. However, if women have not been exposed to CMV as a child, an infection during pregnancy can cross the placenta and infect the baby. Depending on the stage of pregnancy this can cause a variety of delays or conditions in the child, from severe neurological damage (cognitive delay, cerebral palsy, microcephaly, seizures) to sensory impairments like hearing loss and blindness.

I have worked with a number of families living with CMV and they spend thousands of dollars a year in therapy and medication and countless hours with doctors, therapists and hospitals. A few common concerns are:

- Applying for and receiving Social Security, Medicaid and Developmental Disability programs to help provide funds and medical care.
- Transportation to and from 4-5 therapy appointments per week for treatment of cerebral palsy, speech delay, feeding, occupational therapy and physical therapy
- On-going medical fragility and frequent hospitalizations for the child throughout their lifetime
- Development and monitoring of IEP plans in school

This Senate Bill provides funding for information on CMV: How it is transmitted, how it is prevented and what to do if you are pregnant to prevent infection. Idaho OB/GYNs are not currently discussing cytomegalovirus with women before or during pregnancy. We have the information ready to share and we can prevent thousands of CMV infections each year! The savings to the State Medicaid budget would be tangible as CMV related delays cost Idaho millions in Medicaid spending each year.

Please support Senate Bill 1060. Thank you for your time and consideration of this matter.

Respectfully submitted,

Susan

Susan Spelliscy, B.S. M.Coun.
Children's Service Coordinator

- **1 out of every 4 children born with congenital CMV will develop permanent disabilities** including but not limited to:
    - Hearing loss
    - Vision loss
    - Developmental concerns
    - Intellectual disabilities
    - Small head size
    - Cerebral palsy
    - Lack of coordination
    - Abnormal muscle tone
    - Feeding difficulties
    - Seizures
    - Death

Are there signs or symptoms?

- Most children and adults do not show symptoms when infected. **If symptoms are present, it is usually mild cold-like symptoms such as fever, fatigue, runny nose or congestion, sore throat, etc.**
- When children are born symptomatic, **symptoms might include**:
    - Hearing loss/Failed hearing test
    - Vision loss
    - Jaundice (yellowing of the skin)
    - Pneumonia
    - Rash
    - Enlarged liver/spleen
    - Small heads (microcephaly)
    - Seizures
- Congenital CMV can be diagnosed if the virus is detected in an infant's urine, saliva, or blood **within 3 weeks after birth.**
- Most infants, children, and adults **are not tested for CMV infection**.

IDAHO
CMV Advocacy Project

THE FACTS ON CMV

The dangerous virus that most women have never heard of..

What is CMV?

- Cytomegalovirus (CMV) is a common virus of the herpes family that infects people of all ages.
- 90% of the population will have contracted the disease by 80 years old.
- **CMV is one of the few viruses that can pass through the placenta**. Once the fetus is infected, the virus can cause damage to the brain, eyes and/or inner ears.
- **Congenital CMV is the number one cause of non-genetic sensorineural hearing loss in children.**
- Congenital CMV **causes more long-term health concerns than Down syndrome and fetal alcohol syndrome.**
- Most CMV infections are **asymptomatic or "silent"**, meaning **they do not show any signs or symptoms.**
- **Congenital CMV** is when the CMV infection occurs during a women's pregnancy and her baby becomes infected. CMV is the most common congenital infection in the United States.
- Roughly **30,000 children are born with congenital CMV each year.**

What prevention strategies are there to protect against CMV?

The best way to protect your baby is to protect yourself!

CMV is spread through the direct contact of bodily fluid including saliva and mucus.

- **Do not share food, drinks, toothbrushes, etc. with a child.**
- **Avoid kissing a child on the mouth and always wash your hands** when in contact with saliva.
- **Do not put children's toys and pacifiers into or around your mouth.**
- **Wash your hands, especially after**:
  - Handling children's toys
  - Feeding a young child
  - Wiping a young child's nose or mouth
  - Changing diapers

More Information

If you have concerns about CMV infection or are pregnant or planning to become pregnant, talk to your healthcare provider.

- National CMV Foundation http://nationalcmv.org
- Idaho Advocacy Project http://idahocmv.com
- Utah Cytomegalovirus Public Health Initiative http://health.utah.gov
- CDC – Cytomegalovirus http://cdc.gove/cmv

McVicar, S. B. (2016). Cytomegalovirus (CMV) Public Health Initiative. Retrieved from http://www.health.utah.gov/cshcn/programs/cmv.html

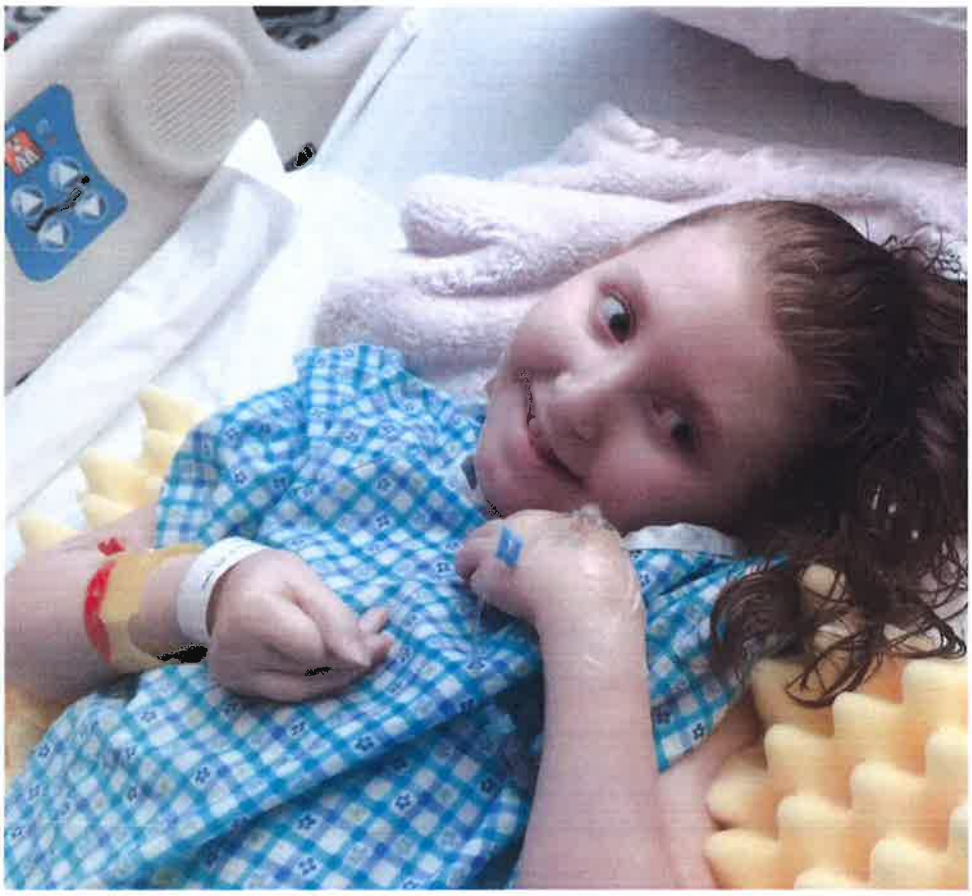
Congenital CMV. (n.d.). Retrieved December 18, 2016, from https://www.nationalcmv.org/congenital-cmv.aspx

What is the treatment for CMV?

- **No drugs or vaccines are presently available** to treat congenital CMV infection. There are some CMV vaccines being tested in humans.
- There is some data from ongoing studies on the use of antiviral medications in infants with symptomatic congenital CMV infection.
- Pediatricians are important in making sure children with CMV infections are treated as needed.
- **Asymptomatic babies appear healthy at birth but still can develop hearing loss and/or vision loss over time.**

Facts about pregnant women and CMV

- Almost half of women have **already contracted CMV** by the time they first become pregnant.
- 4% of women who have never had CMV will **contract it while pregnant**.
- Women who acquire the disease during pregnancy are **more likely to pass the disease to their fetus** verses a woman who becomes re-infected with the disease.
- 50-75% of CMV infections occur in **infants born by mothers where the virus had reactivated/re-infected**.
- **50-80% of the world's population (6 out of 7 people)** carry the dormant virus.
- **90% of healthy adults** will be infected by the time they are 80 years old.



CYTOMEGALOVIRUS (CMV)

can be **transmitted to an unborn baby during pregnancy** leading to **birth defects and long-term disabilities.**

Typically a harmless cold virus, CMV can be devastating to individuals who are immunocompromised or to an unborn child.

Some of the **permanent disabilities** CMV can cause include: **hearing loss, vision loss, developmental concerns, intellectual disabilities, small head size, cerebral palsy, abnormal muscle tone, feeding difficulties, seizures, and even death.**

If you are pregnant, planning to become pregnant, or need more information, please contact your physician and visit:

IDAHO
CMV Advocacy Project
idahocmv.com

CMV is spread through the direct contact of bodily fluids including saliva and mucus

Hearing loss is the most recognized symptom of CMV at birth

1 in 150 children are born with CMV

Nearly 1 in every 5 children born with congenital CMV will develop permanent disabilities

Most CMV infections are "silent" meaning women infected have no signs or symptoms

Newborn Signs and Symptoms

- Hearing/Vision Loss
- Jaundice
- Pneumonia
- Rash
- Enlarged Liver/Spleen
- Small Head
- Seizures
- Failed Hearing Test

The best way to protect your baby is to protect yourself!

DO NOT share food, drinks, toothbrushes, etc. with your child.

AVOID kissing a child on the mouth and always wash your hands when in contact with saliva.

DO NOT put child's toys and pacifiers into or around your mouth.

Wash your hands, especially after:

- Handling children's toys
- Feeding a young child
- Wiping a young child's nose or mouth
- Changing Diapers

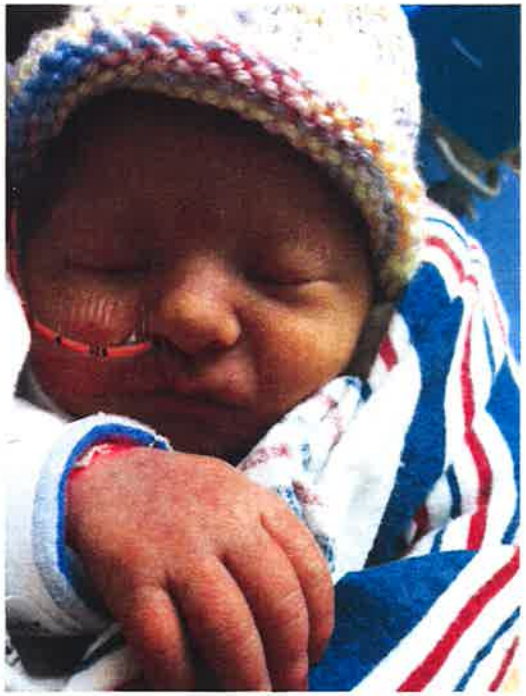
If you are pregnant, planning to become pregnant, or need more information, please contact your physician and visit:

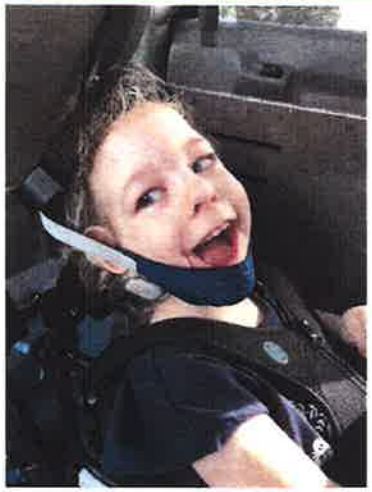
IDAHO
CMV Advocacy Project

idahocmv.com

Cytomegalovirus (CMV)

What you NEED TO KNOW





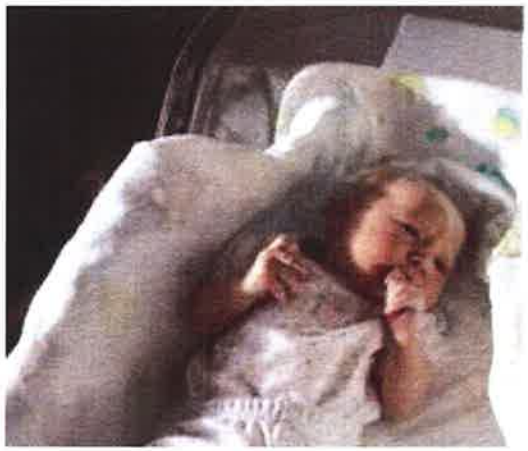
About CMV

Cytomegalovirus (CMV) is a common virus of the herpes family that infects people of all ages.

CMV is one of the few viruses that can pass through the placenta. Once the fetus is infected, the virus can cause damage to the brain, eyes and/or inner ears.

Permanent Disabilities

- Hearing loss
- Vision loss
- Developmental concerns
- Intellectual disabilities
- Small head size
- Cerebral palsy
- Lack of coordination
- Abnormal muscle tone
- Feeding Difficulties
- Seizures
- Death



Did you know?

- **Only 9% of women know about CMV**
- 1 in 150 children are born with congenital CMV
- CMV is spread through the direct contact of bodily fluid including saliva and mucus
- Most CMV infections are "silent", meaning women infected have no signs or symptoms
- **Hearing loss is the primary symptom of CMV at birth**
- 40% of women who become infected with CMV for the first time during pregnancy will pass the infection to their unborn child
- **Nearly 1 in every 5 children born with congenital CMV infection will develop permanent disabilities!**

THE BEST WAY TO PROTECT YOUR BABY IS TO PROTECT YOURSELF!

Cytomegalovirus (CMV) is a common virus of the herpes family that infects people of all ages.

CMV is one of the few viruses that can pass through the placenta. Once infected, the virus can cause damage to the brain, eyes and/or inner ears of the fetus.

If you are pregnant, planning to become pregnant, or need more information, please contact your physician and visit:

IDAHO
CMV Advocacy Project
idahocmv.com

HELPFUL PREVENTION TIPS

CMV IS TRANSMITTED MOST EASILY FROM WET SALIVA TO WET SALIVA

DO NOT SHARE FOOD, DRINKS, TOOTHBRUSHES, ETC. WITH YOUR CHILD

AVOID KISSING A CHILD ON THE MOUTH

DO NOT PUT A CHILD'S TOYS OR PACIFIERS INTO OR AROUND YOUR MOUTH

WASH YOUR HANDS:

- After handling children's toys
- After feeding a child
- After wiping a child's nose or mouth
- After changing diapers

The best way to protect your baby is to protect yourself!

Cytomegalovirus (CMV) is a common virus that can pass through the placenta. Once infected, the virus can cause damage to the brain, eyes and/or inner ears of the fetus.

1 in 150 children are born with congenital CMV.

Nearly 1 in every 5 children born with congenital CMV infection will develop permanent disabilities.

If you are pregnant, planning to become pregnant or would like more information, please contact your physician and visit:

Idaho CMV Advocacy Project

idahocmv.com

CMV is a dangerous virus that most women have never heard of.. Educate yourself!

Cytomegalovirus (CMV) is a common virus that can pass through the placenta. Once infected, the virus can cause damage to the brain, eyes and/or inner ears of the fetus.

CMV is more prevalent than the Zika virus!

1 in 150 children are born with congenital CMV

Nearly 1 in every 5 children born with congenital CMV infection will develop permanent disabilities

If you are pregnant, planning to become pregnant or would like more information, please contact your physician and visit:

IDAHO
CMV Advocacy Project

idahocmv.com

CMV is a dangerous virus that most women have never heard of.. Educate yourself!

Cytomegalovirus (CMV) is a common virus that can pass through the placenta. Once infected, the virus can cause damage to the brain, eyes and/or inner ears of the fetus.

Babies born infected with CMV are frequently born to mothers who worked **as teachers or daycare providers** during pregnancy, and/or **parenting a toddler**.

If you are pregnant, planning to become pregnant or would like more information, please contact your physician and visit:

IDAHO
CMV Advocacy Project

idahocmv.com

What would CMV legislation mean for Idaho?

Every year, an estimated **150 babies** are born with CMV in Idaho.

Of those, an estimated **30 babies** will have permanent disabilities.

The healthcare costs for just one of these children can cost taxpayers as much as **$1,800,000.** This is for the care of just **ONE CHILD** through the age of 18.

A CMV bill in the state of Idaho would provide for:

1. Increased **education** of healthcare providers
2. Increased **public awareness**
3. **Mandated CMV testing** for infants who fail their newborn hearing screens

It is estimated that to put this legislation into practice would cost the state of Idaho **$60,000** in the first year and **$30,000** each year after.

In other words, if CMV legislation led to the prevention of just one baby from having severe CMV related complications in the first year, it could potentially save the state **$482,000.**

Similar legislation has been passed in **Utah, Tennessee, Hawaii, Connecticut, Illinois and Texas.**

For more information please visit:

The National CMV Foundation	nationalcmv.org
Idaho CMV Advocacy Project	idahocmv.com

IDAHO
CMV Advocacy Project

For more information please visit
idahocmv.com

Or email us at
idahocmv@gmail.com

LEGISLATURE OF THE STATE OF IDAHO

Sixty-fourth Legislature First Regular Session - 2017

IN THE SENATE

SENATE BILL NO. 1060

BY HEALTH AND WELFARE COMMITTEE

AN ACT

RELATING TO HEALTH CARE; AMENDING CHAPTER 10, TITLE 56, IDAHO CODE, BY THE ADDITION OF A NEW SECTION 56-1055, IDAHO CODE, TO PROVIDE THAT THE STATE DEPARTMENT OF HEALTH AND WELFARE SHALL MAKE AVAILABLE CERTAIN INFORMATION REGARDING CYTOMEGALOVIRUS.

Be It Enacted by the Legislature of the State of Idaho:

SECTION 1. That Chapter 10, Title 56, Idaho Code, be, and the same is hereby amended by the addition thereto of a NEW SECTION, to be known and designated as Section 56-1055, Idaho Code, and to read as follows:

56-1055. CYTOMEGALOVIRUS INFORMATION. (1) The department shall make available the following information to the public, particularly pregnant women and women who may become pregnant:

(a) Incidence of cytomegalovirus (CMV);

(b) Transmission of CMV;

(c) Birth defects caused by congenital CMV;

(d) Available preventive measures; and

(e) Other information relating to CMV deemed pertinent by the department.

(2) The department shall make available the information described in subsection (1) of this section to:

(a) Health care providers licensed under title 54, Idaho Code, offering care to pregnant women and infants;

(b) Daycare and child care programs and facilities licensed under title 39, Idaho Code, and persons employed by such programs or facilities;

(c) School districts and persons offering health care or health education in a school district;

(d) Religious, ecclesiastical or denominational organizations offering children's programs as part of their services, and persons employed or volunteering for such programs; and

(e) Other persons and entities that would benefit from such information, as determined by the department.

STATEMENT OF PURPOSE

RS25093C1

The purpose of the bill is to ensure the women of Idaho and their doctors have access to the most accurate and up-to-date information available regarding cytomegalovirus (CMV) prevention, infection, and treatment. Appropriate dissemination of this information will foreseeably prevent the infection of numerous babies in utero, thereby saving the State of Idaho millions of dollars in the care and treatment of various disabilities that are associated with congenital CMV infection.

FISCAL NOTE

$60,000 in the first year for educational materials and $30,000 per year ongoing to the Department of Health & Welfare.

Contact:

Senator Lee Heider
(208) 332-1000
Representative Paulette Jordan
(208) 332-1175

26-10-10 Cytomegalovirus (CMV) public education and testing.

(1) As used in this section "CMV" means cytomegalovirus.

(2) The department shall establish and conduct a public education program to inform pregnant women and women who may become pregnant regarding:
  (a) the incidence of CMV;
  (b) the transmission of CMV to pregnant women and women who may become pregnant;
  (c) birth defects caused by congenital CMV;
  (d) methods of diagnosing congenital CMV; and
  (e) available preventative measures.

(3) The department shall provide the information described in Subsection (2) to:
  (a) child care programs licensed under Title 26, Chapter 39, Utah Child Care Licensing Act, and their employees;
  (b) a person described in Subsection 26-39-403(1)(c), (f), (g), (h), (j), or (k);
  (c) a person serving as a school nurse under Section 53A-11-204;
  (d) a person offering health education in a school district;
  (e) health care providers offering care to pregnant women and infants; and
  (f) religious, ecclesiastical, or denominational organizations offering children's programs as a part of worship services.

(4) If a newborn infant fails the newborn hearing screening test(s) under Subsection 26-10-6(1), a medical practitioner shall:
  (a) test the newborn infant for CMV before the newborn is 21 days of age, unless a parent of the newborn infant objects; and
  (b) provide to the parents of the newborn infant information regarding:
    (i) birth defects caused by congenital CMV; and
    (ii) available methods of treatment.

(5) The department shall provide to the family and the medical practitioner, if known, information regarding the testing requirements under Subsection (4) when providing results indicating that an infant has failed the newborn hearing screening test(s) under Subsection 26-10-6(1).

(6) The department may make rules in accordance with Title 63G, Chapter 3, Utah Administrative Rulemaking Act, as necessary to administer the provisions of this section.

Enacted by Chapter 45, 2013 General Session

FISCAL NOTE

H.B. 81 1st Sub. (Buff)

SHORT TITLE: **Cytomegalovirus Public Health Initiative**

SPONSOR: **Menlove, R. (Menlove, R. Sub.)**

2013 GENERAL SESSION

STATE GOVERNMENT (UCA 36-12-13(2)(b))

This bill costs the Department of Health $30,800 ongoing General Fund beginning in FY 2014 and $4,000 one-time General Fund in FY 2013 for a 0.5 FTE educator and educational materials.

STATE BUDGET DETAIL TABLE	FY 2013	FY 2014	FY 2015
Revenue	$0	$0	$0
Expenditure:			
General Fund	$0	$30,800	$30,800
General Fund, One-Time	$4,000	$0	$0
Total Expenditure	$4,000	$30,800	$30,800
Net Impact, All Funds (Rev.-Exp.)	($4,000)	($30,800)	($30,800)
Net Impact, General/Education Funds	($4,000)	($30,800)	($30,800)

LOCAL GOVERNMENTS (UCA 36-12-13(2)(c))

Enactment of this bill likely will not result in direct, measurable costs for local governments.

DIRECT EXPENDITURES BY UTAH RESIDENTS AND BUSINESSES (UCA 36-12-13(2)(d))

Enactment of this bill likely will not result in direct, measurable expenditures by Utah residents or businesses.

PERFORMANCE NOTE (JR 4-2-404): Not Required

2/8/2013, 08:19 AM, Lead Analyst: Frandsen, R./Attorney: AKJ

State of Utah, Office of the Legislative Fiscal Analyst

The Laryngoscope

A Diagnostic Paradigm Including Cytomegalovirus Testing for Idiopathic Pediatric Sensorineural Hearing Loss

Albert H. Park, MD; Melanie Duval, MDCM; Stephanie McVicar, AuD, CCC-A; James F. Bale, Jr., MD; Nancy Hohler, AuD; John C. Carey, MD

Objectives/Hypothesis: To determine the feasibility and cost effectiveness of incorporating cytomegalovirus (CMV) testing to determine the etiology of pediatric hearing loss.

Study Design: Retrospective study of children presenting with sensorineural hearing loss (SNHL) at one institution from 2008 to 2013.

Methods: Children aged 3 years or younger who presented to the senior author (A.P.) between May 2008 and September 2013 with confirmed SNHL were evaluated. These children underwent a sequential diagnostic paradigm that incorporated CMV testing if no obvious etiology could be determined from the history or physical examination.

Results: One hundred eleven children with SNHL were evaluated between 2008 and 2013. Eighty-three children underwent CMV testing, imaging, and a genetic evaluation. Those with confirmed or probable CMV-induced SNHL made up 30% of all children tested (n = 25), the largest group identified. CMV screening had the lowest cost compared to genetic testing or imaging for all types of hearing loss, except for those with auditory neuropathy spectrum disorder.

Conclusion: We present the first sequential diagnostic paradigm utilizing CMV testing for children presenting with SNHL. The relatively high incidence of CMV-induced SNHL, the low cost for this assay, and the indirect benefits from early diagnosis support the role of early CMV testing for these patients.

Key Words: Cytomegalovirus, sensorineural hearing loss.

Level of Evidence: 4.

***Laryngoscope*, 124:2624–2629, 2014**

INTRODUCTION

Cytomegalovirus (CMV), a member of the β-herpesvirus family, is the most common infectious cause of congenital sensorineural hearing loss (SNHL).[1] Between 1% and 4% of seronegative pregnant women will seroconvert during pregnancy. With a prevalence of approximately 1% in the United States, it is estimated that 40,000 congenitally infected neonates are born annually.[2] Almost 400 children die each year from this disease, and approximately 7,000 develop permanent disabilities.[3] The most common permanent disability from CMV infection is hearing loss. It is estimated to account for 20% or more of SNHL in young children.[4] More children may be affected by CMV than by other, better known childhood conditions, such as Down syndrome, fetal alcohol syndrome, and spina bifida.[5] This hearing loss has detrimental effects on speech and language development and incurs the major cost associated with congenital CMV infection, estimated to be $4 billion a year.[6,7]

Despite the known significance of this infection, there has been a paucity of studies evaluating the yield of CMV testing for the hearing-impaired child. A recent Triological Society Best Practice article— "What Is the Optimal Workup for a Child with Bilateral Sensorineural Hearing Loss?"—failed to mention any role of CMV testing for these children.[8] Rutherford et al. surveyed members of the American Society of Pediatric Otolaryngology to determine the trends in the evaluation of pediatric SNHL.[9] The authors noted that few respondents ordered CMV testing and mentioned that testing for infectious causes for SNHL is low-yield. The goal of this study is to evaluate the feasibility and cost effectiveness of incorporating CMV testing into a sequential diagnostic paradigm for idiopathic pediatric SNHL.

MATERIALS AND METHODS

We conducted a chart and database review of children aged 3 years or younger who presented to the senior author (A.P.) between May 2008 and September 2013 with confirmed SNHL. Since 2008, these children underwent a sequential diagnostic paradigm that incorporated CMV testing if no obvious etiology could be determined from the history or physical examination (Fig. 1).

SNHL was defined as a bone conduction threshold of 30 dB HL or worse in one or both ears at one or more frequencies

From the Division of Otolaryngology–Head and Neck Surgery (A.H.P., M.D.); the Division of Medical Genetics, Department of Pediatrics (J.C.C.); University of Utah; the Utah Department of Health (S.M.C.V.); the Division of Pediatric Neurology, Department of Pediatrics and Neurology (J.F.B.), University of Utah School of Medicine; and the Audiology, Primary Children's Medical Center (N.H.), Salt Lake City, Utah, U.S.A.

Editor's Note: This Manuscript was accepted for publication May 5, 2014.

Presented at the American Society of Pediatric Otolaryngology Meeting, Arlington, Virginia, U.S.A., April 26, 2013.

The authors have no funding, financial relationships, or conflicts of interest to disclose.

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DOI: 10.1002/lary.24752

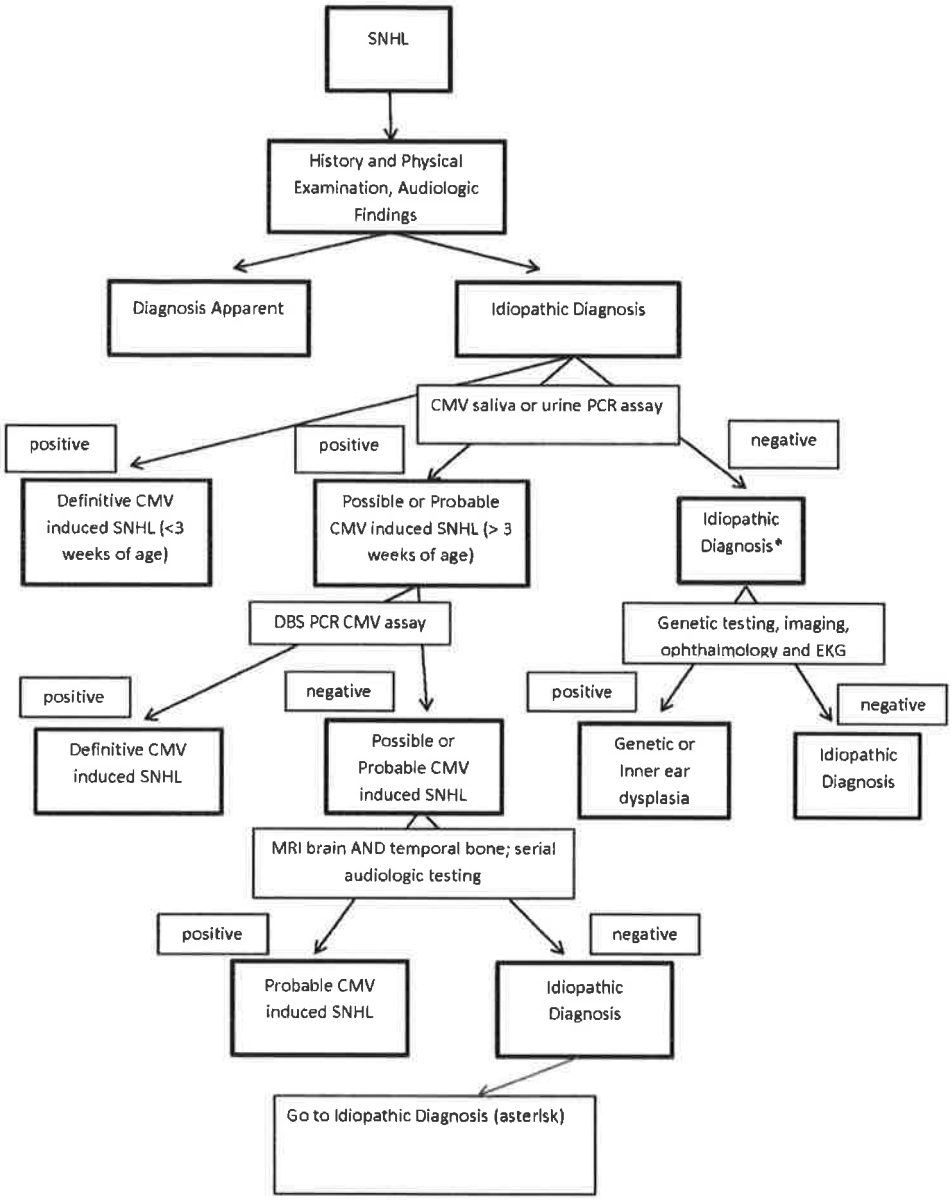

Fig. 1. Flowchart illustrating a sequential diagnostic paradigm that incorporated cytomegalovirus testing if no obvious etiology could be determined from the history or physical examination.

from 500 Hz to 4000 Hz based on results obtained via auditory brainstem response testing (using correction factors and reported as estimated hearing level or eHL) or behavioral thresholds obtained utilizing visually reinforced audiometry or conditioned play audiometry. Hearing loss was classified as follows: mild (30 – 40 dB), moderate to severe (41 – 70 dB), and severe to profound (71 – < 90 dB HL).

Once SNHL was confirmed, all children were evaluated with a complete history: physical examination including evaluation for dysmorphic features and family history and pedigree. If this evaluation did not suggest an underlying etiology of SNHL, CMV testing was recommended.

CMV testing was performed by saliva or urine CMV polymerase chain reaction (PCR) assay, followed by neonatal, dry blood spot (DBS) CMV PCR if urine or saliva assay was positive and the child was older than 3 weeks of age at the time of testing. Because the Utah Department of Health maintains a child's DBS sample for 3 years, testing these specimens for congenital CMV was only possible if the child was younger than 3 years old at the time of evaluation. A confirmed diagnosis for congenital CMV or CMV PCR assay can only be established if the child is tested younger than 3 weeks of age[10]; after that age, a positive CMV PCR assay could represent a postnatally acquired infection.

In children with positive CMV testing, a confirmed diagnosis of CMV-induced SNHL was defined as a positive CMV PCR saliva or urine assay in an infant less than 3 weeks of age—or a positive DBS neonatal CMV PCR result in a child older than 3 weeks of age. For children with a positive urine or saliva CMV assay who are older than 3 weeks of age, CT or MRI brain imaging suggestive of CMV and/or documentation of progressive SNHL were categorized as having probable CMV-induced SNHL. Imaging findings suggestive of CMV included periventricular cysts, polymicrogyria, white matter abnormalities, microcephaly, and intracranial calcifications.[11] In those children with a positive urine or saliva CMV assay who were older than 3 weeks of age, a negative DBS CMV PCR result and normal brain imaging were categorized as not having CMV-induced

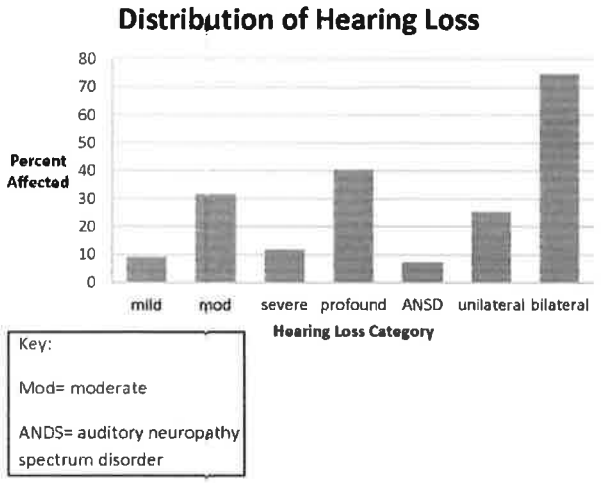

Fig. 2. Hearing loss for the 111 children evaluated between 2008 and 2013.

SNHL and went on to undergo further testing to elucidate the etiology of their hearing loss. Those patients with negative CMV testing underwent temporal bone imaging, ECG, or evaluation by a geneticist.

A large, multihospital standardized-cost accounting database that collects financial and clinical datasets was used to compare the costs for diagnostic testing. This database collects actual patient costs incurred per encounter. Both individual and simultaneous costs of the diagnostic testing were compared. MRI imaging costs included the sum of the professional, sedation, and facility costs. The average costs were as follows: MRI scan of the temporal bone $1591; Gap junction protein beta 2 (GJB2) screen $611; and CMV PCR saliva or urine assay $66. The cost of sequential testing began with the cost of a specific test for 100 patients, followed by a calculation of subsequent testing based on the diagnostic yield for the original and subsequent tests. For example, if the cost for initial screening of a GJB2 mutation yielded a 15% positive result for children with bilateral mild SNHL, the calculated cost of this approach would be $66,710 (100 children × $611 + 85 children × $1591 × 0 (0% yield) + 85 children × $66).

Institutional review board approval from the University of Utah and Primary Children's Hospital was obtained for this study.

RESULTS

Distribution of Hearing Loss and Etiology Based on Examination and History

One hundred eleven children with SNHL less than 3 years of age were evaluated between 2008 and 2013. The distribution of their hearing thresholds is shown in Figure 2. Profound SNHL made up the largest group with 45 (40.5%) affected children. Eighty-two children (75%) had bilateral SNHL. Eight children (7%) had auditory neuropathy spectrum disorder. An etiology for the SNHL could be determined from the history, physical examination, or audiologic findings in 26 children (Fig. 3). A genetic etiology was the most common cause, usually from an undefined familial predisposition to hearing loss (31%) or Down syndrome (12%). Other genetic conditions identified included branchiootorenal, Pendred,

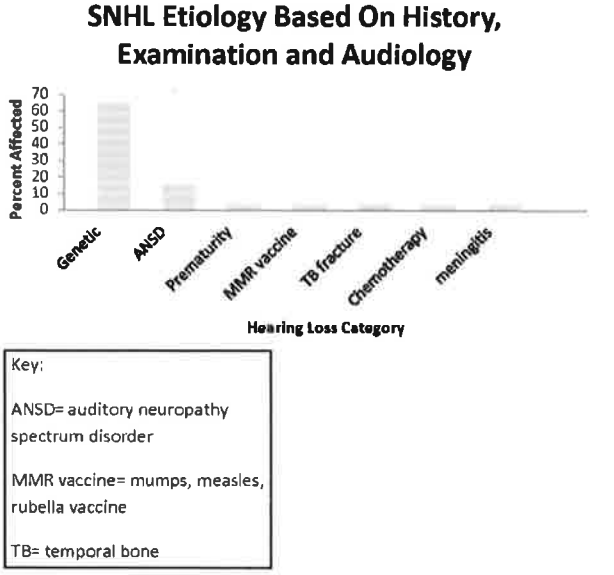

Fig. 3. Etiology determined for 23 children determined by history and physical examination.

Alport, Waardenburg, and CHARGE (coloboma, heart defects, atresia of the nasal choanae, retarded growth and development, genital hypoplasia, ear anomalies, and/or deafness) syndromes. Auditory dyssynchrony was identified in four children. Acquired SNHL causes included a complication from MMR vaccination, a temporal bone fracture, meningitis, and complications from chemotherapy and from prematurity.

Distribution of Hearing Loss Etiology Based on CMV Testing, Imaging, and Genetic Evaluation

Eighty-three children underwent CMV testing, imaging, and an evaluation by a geneticist. The distribution of etiologies following this approach is shown in Figure 4. Those with confirmed or probable CMV-induced SNHL made up 30% of all children tested (n = 25), the largest group with a known etiology of hearing loss

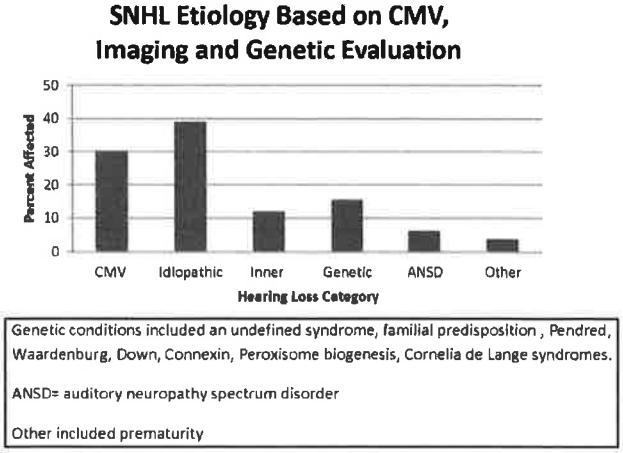

Fig. 4. Etiology determined following cytomegalovirus testing, imaging, and genetic evaluation.

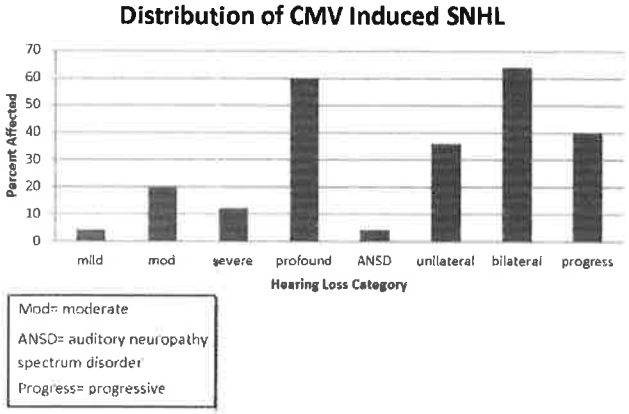

Fig. 5. Distribution of hearing loss attributed to congenital cytomegalovirus infection.

identified. Sixteen children were diagnosed with confirmed CMV, and nine children were diagnosed with probable CMV. Six of the 16 children with confirmed CMV were diagnosed via detection of viral DNA from archived neonatal DBS testing. DBS testing was available for six children out of the nine children with probable CMV-induced SNHL. Those without a known etiology were the largest group at 39% (n = 33). Ten of these children had a positive urine or saliva CMV PCR result after 3 weeks of age. They did not have imaging suggestive of CMV or a history of progressive SNHL. A genetic etiology made up the third-largest group (15%). The distribution of those with a genetic etiology included an undefined syndrome, a familial predisposition to hearing loss, and a number of different syndromes (Figure 4). An inner ear dysplasia made up almost 12% of the affected children. An enlarged vestibular aqueduct (5%) was the most common abnormality identified—followed by cochlear nerve deficiency (4%) and cochleovestibular dysplasia (4%).

Characteristics of CMV-Induced SNHL Patients

Twenty-five children with probable or confirmed CMV-induced SNHL were evaluated with an average follow-up of 305 days. The average initial age at evaluation was 352 days (range 24–1387 days). Only five infants were evaluated at 1 month of age or younger. The average age of CMV testing was 256 days (range 0–1,387 days), slightly earlier than the initial evaluation. Nine children who underwent CMV testing were younger than 1 month of age.

The distribution of CMV-induced SNHL is shown in Figure 5. Profound SNHL made up the largest group with 16 (60%) affected children. One child had bilateral normal otoacoustic emissions but demonstrated a mild SNHL at 2k Hz, bilaterally, and at 500 Hz in the right ear. Sixteen children (64%) had bilateral SNHL. One child (4%) had auditory neuropathy spectrum disorder. Progressive SNHL was identified in 10 (40%) of the children.

Cost Estimates of SNHL Evaluation by Test

The anticipated diagnostic yield by test is shown for GJB2 screening, imaging, and CMV PCR testing in Table I. Because most insurance providers do not cover GJB2 screening in Utah, very few of our patients underwent this test. For that reason, the anticipated diagnostic yield by hearing loss was based on a prior study from our group and from Preciado et al.'s study from 2004.[12,13] The yield for imaging and CMV testing was determined from the 83 children in this study who underwent CMV, genetic evaluation, and imaging. The estimated cost of all three tests, if performed for 100 children with SNHL, is shown under simultaneous testing. This calculation is based on the sum for institutional cost for GJB2 screening ($611), imaging ($1591), and CMV PCR testing ($66). This calculation is based on the assumption that a child underwent CMV testing before 3 weeks of age and did not require DBS CMV PCR testing. The addition of DBS testing would increase the cost by another $66 because both tests cost the same. The following rows indicate the anticipated cost if GJB2, imaging, or CMV testing was performed first. The cost assumes that a positive result would obviate the need for additional testing. CMV screening had the lowest cost for all types of hearing loss. The lowest cost for each hearing loss type was indicated in bold.

DISCUSSION

This study is the first report of a sequential diagnostic paradigm incorporating CMV testing for

TABLE I.
Cost Estimates of Alternative SNHL Evaluation Approaches Based on Diagnostic Yield.

Testing	Bilateral Mild	Bilateral Moderate-Severe SNHL	Bilateral Severe-Profound SNHL	Unilateral	ANSD	Overall
GJB2 screen*	15%	5%	37.7%	0%	0%	19%
Imaging	0%	8%	0%	18%	50%	11%
CMV PCR	20%	23%	36%	36%	17%	30%
Simultaneous	$226,800	$226,800	$226,800	$226,800	$226,800	$226,800
GJB2 screen	$66,710	$218,515	$65,192	N/A	N/A	$195,317
Imaging	N/A	$221,384	N/A	$164,512	**$162,400**	$219,353
CMV PCR	**$55,480**	**$176,154**	**$45,704**	**$108,424**	$138,653	**$160,740**

*Diagnostic yield based on Preciado et al.[12] and Dent et al.[13] study
ANSD = auditory neuropathy spectrum disorder; CMV PCR = cytomegalovirus polymerase chain reaction; GJB2 = gap junction protein beta 2; SNHL = sensorineural hearing loss.

pediatric SNHL in children. We were able to demonstrate that a significant number of children tested positive for CMV infection. In fact, CMV testing had the highest diagnostic yield of all tests performed in this patient cohort.

One may question whether this relatively high yield for CMV testing is due to a higher prevalence of this infection in Utah. A number of studies have demonstrated variability of prevalence by region between 0.4% and 0.7%.[7,14,15] Between March 8, 2004, and December 23, 2004, infants born at one of four Utah hospitals in the Salt Lake Valley were screened for congenital CMV infection.[16] These hospitals serve the Salt Lake Valley, a metropolitan region with approximately one million inhabitants. In 2004, there were approximately 55,000 live births in Utah. The population sampled during this study corresponded to 35% (3,074/8,686) of the infants born at the hospitals. Nine of 3,074 infants (0.29%) were congenitally infected with CMV, indicating a low prevalence of intrauterine CMV infection in Utah (95% CI: 0.15%–0.57%). Thus, even in a low-prevalence state like Utah, early CMV testing can detect a significant number of children with SNHL.

The challenge in diagnosing these patients is the need for early virologic testing. Confirmed CMV diagnosis requires laboratory testing of neonatal samples within the first 3 weeks of life because postnatal exposure to CMV is not typically associated with SNHL.[10] Use of archived neonatal DBS for CMV PCR testing was instrumental in diagnosing six of the 15 (40%) children with confirmed CMV. Unfortunately, Boppana et al. have demonstrated poor sensitivity with this assay.[7] In July 2013, Utah became the first state to implement early CMV testing of all infants under 3 weeks of age who fail their newborn hearing screen twice. We anticipate that a much larger proportion of children will be diagnosed before 3 weeks of age, which will reduce the need for DBS testing and avoid the inherent limitations of this assay.

The overall cost to the patient by performing the CMV testing first was found to be less than if GJB2 screening or imaging was performed first. This result was seen for all types of hearing loss. The diagnostic yield from imaging was less than that reported in a prior study from our group.[17] It is unclear why we found a lower incidence of inner ear abnormalities in this series. Using the 21% value from our earlier study for imaging, however, would have still demonstrated a higher overall cost compared to that of CMV or GJB2 screening with this modality.

Additional indirect benefits not shown in this calculation may also be obtained from a positive CMV diagnosis. A positive diagnosis also identifies those children at risk to develop progressive worsening of their hearing. These children can be targeted for frequent audiologic testing to detect any change in their thresholds. These children may shed the virus in their urine and saliva for years. Careful hygiene through frequent hand washing, avoidance of kissing on the lips, and not sharing utensils and toys can reduce potential transmission. These preventative measures have been demonstrated to reduce transmission to pregnant mothers, the group at highest risk for congenital CMV transmission.[18–20]

Early identification of CMV-induced SNHL provides an opportunity to use antiviral therapy to prevent progressive SNHL. The National Institute of Allergy and Infectious Disease Collaborative Antiviral Study Group (CASG) recently presented a phase III trial of 6 weeks versus 6 months of oral valganciclovir for children less than 30 days of age with congenital CMV disease.[21] They demonstrated that 6 months of oral valganciclovir treatment of infants with congenital CMV disease improves audiologic and neurodevelopmental outcomes to at least 2 years of age. They also found less neutropenia in this trial compared to an earlier CASG study using intravenous gancliclovir and no excess neutropenia with continuation of antiviral therapy from 6 weeks to 6 months.

One strength of this article was the ability to follow the clinical course of a large number of children with SNHL seen by a single investigator utilizing a standard diagnostic approach. An outstanding collaborative environment with the Primary Children's audiology, genetics, neurology, and otolaryngology services made this study possible. The existence of only one children's hospital in the state also improved our ability to minimize any lost patient data.

The major limitation of this study is its retrospective design. Because the electronic medical records are centralized and integrated, we were able to obtain audiologic, clinical notes, imaging, and laboratory results for all patients studied. The relatively low diagnostic yield for imaging and high yield for CMV testing will require confirmation from future prospective studies.

CONCLUSION

In conclusion, we present the first sequential diagnostic paradigm utilizing CMV testing for children presenting with idiopathic SNHL. The relatively high incidence of CMV-induced SNHL, the low cost for this assay, and the indirect benefits from early diagnosis support the role of early CMV testing of these patients.

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Cytomegalovirus Infection in Pregnancy: Should All Women Be Screened?

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Cytomegalovirus (CMV) is the most common cause of congenital infection and complicates approximately 1% of all live births. Primary maternal CMV infection carries a 30% to 40% risk of vertical transmission to the fetus. In cases where maternal CMV infection is suspected, it is important to evaluate the risk to the fetus to provide appropriate counseling and guidance to parents. This article reviews the published literature and summarizes current diagnostic and management recommendations to help answer the question, should all women be screened for CMV infection in pregnancy?
[Rev Obstet Gynecol. *2010;3(4):172-179 doi: 10.3909/riog0131*]

Key words: Cytomegalovirus infection • Pregnancy • Antiviral agents • Hyperimmune globulin • Congenital infection

Cytomegalovirus (CMV) is the most common cause of congenital infection.[1] Moreover, congenital CMV is the most frequently identified viral cause of mental retardation and is the leading nongenetic cause of neurosensory hearing loss.[2,3] In developed countries, congenital CMV infection occurs in 0.3% to 2.4% of all live births.[4] Infection in the newborn can be acquired through close contact (via contaminated blood, urine, and secretions), vertically through transplacental transmission, and postnatally through breast milk.[1] Most symptomatic neonatal CMV infections occur when a woman is newly infected just prior to or during pregnancy.[5,6] Primary maternal CMV infection in

pregnancy carries a 30% to 40% risk of vertical transmission.[1] Of all pregnancies with confirmed vertical transmission, only 10% to 20% of the fetuses will have evidence of clinical infection at birth.[1] As compared with women who are infected in the latter half of pregnancy, women who develop primary CMV infection in the first trimester are more likely to deliver fetuses with sensorineural hearing loss (24% vs 2.5%) or other CNS sequelae, such as mental retardation, cerebral palsy, seizures, or chorioretinitis (32% vs 15%).[7] Mothers who are CMV seropositive prior to pregnancy can also develop a secondary CMV infection either due to reactivation of virus residing at specific sites in the body (primarily the salivary glands) or reinfection with a different viral strain.[6] Such infections tend to be less severe and are usually asymptomatic for both mother and newborn. Infants born to such mothers can also have sequelae of congenital CMV, but this is far less likely (estimated at 0.2% to 2%).[8] In cases where maternal CMV infection is suspected, it is important to evaluate the risk to the fetus of being infected and/or symptomatically affected by CMV to provide appropriate counseling and guidance to parents. We present a case of fetal CMV infection to illustrate and highlight some of the diagnostic and therapeutic issues raised by CMV infection.

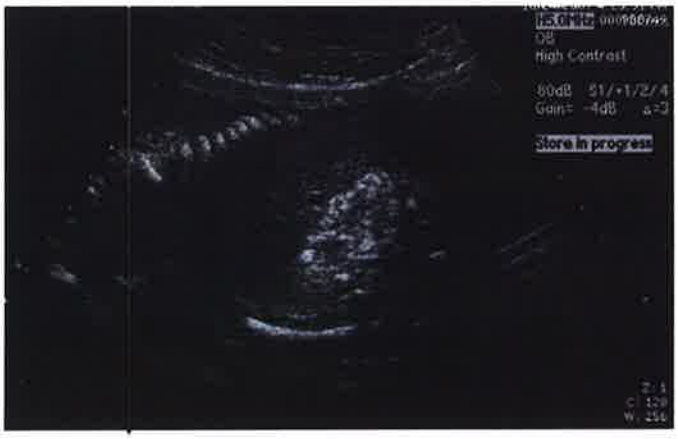
Case Report

A healthy 29-year-old woman (G2, P1) with a well-dated spontaneous conception was seen for routine ultrasound examination at 18-0/7 weeks of gestation. The fetus was noted to have echogenic bowel (Figure 1) and intrauterine growth restriction (IUGR) with an estimated fetal weight in the 9th percentile. Her past obstetric history was remarkable for severe preeclampsia resulting in an induction of labor and vaginal delivery at 34 weeks of gestation 2 years earlier. Maternal serologic tests performed in light of the ultrasound findings revealed elevated CMV IgM and IgG titers. Amniotic fluid was strongly positive for CMV DNA by quantitative real-time polymerase chain reaction (RT-qPCR). After extensive counseling as to the diagnosis of fetal CMV and their options, including pregnancy termination, the couple chose to continue the pregnancy. After consultation with an infectious disease specialist, CMV immune globulin (200 U/kg, for a total dose of 10 g intravenous [IV]) was recommended starting at 25 weeks of gestation with subsequent doses of 5 g IV planned at monthly intervals. Fetal magnetic resonance imaging (MRI) at 25 weeks of gestation showed no evidence of intracranial calcifications or abnormalities.

At 30 weeks of gestation, following 2 doses of CMV immune globulin, the fetal heart-rate tracing was noted to have absent variability and repetitive late decelerations (category III). A biophysical profile was 2/10 (2 points for amniotic fluid volume only) and umbilical artery Doppler velocimetry showed reversed end-diastolic flow. A viable female infant was delivered by emergent cesarean weighing 920 g with Apgar scores of 2, 7, and 10 at 1, 5, and 10 minutes, respectively. Cord blood analysis showed an arterial pH of 7.16 and base excess of −12.5 and venous of pH 7.29 and base excess of −8.9. The neonate was intubated and admitted to neonatal intensive care. Chest radiography showed ground glass opacities consistent with congenital CMV pneumonia. Hematologic abnormalities included thrombocytopenia, coagulopathy, elevated transaminase levels, and hyperbilirubinemia. CMV antigenemia was present in the infant's blood, and CMV DNA was identified in urine and cerebrospinal fluid. Placental pathology showed diffuse fibrin deposition and villous edema. Specific immunostaining of the placenta was positive for CMV (Figure 2).

The infant was treated with IV ganciclovir (6 mg/kg twice daily) with subsequent resolution of laboratory and imaging abnormalities over a 10-day period. Ultrasound examination

Figure 1. *Representative perinatal ultrasound image showing fetal echogenic bowel. Fetal echogenic bowel refers to increased echogenicity or brightness of the fetal bowel noted on second trimester ultrasound examination. The diagnosis of echogenic bowel should be reserved for fetuses in which the echogenicity of the bowel is equal to or greater than that of adjacent bone. The differential diagnosis of fetal echogenic bowel includes cystic fibrosis, infection with cytomegalovirus or toxoplasmosis, meconium ileus, and chromosomal abnormalities (including Turner syndrome and trisomy 21, 13, or 18).*



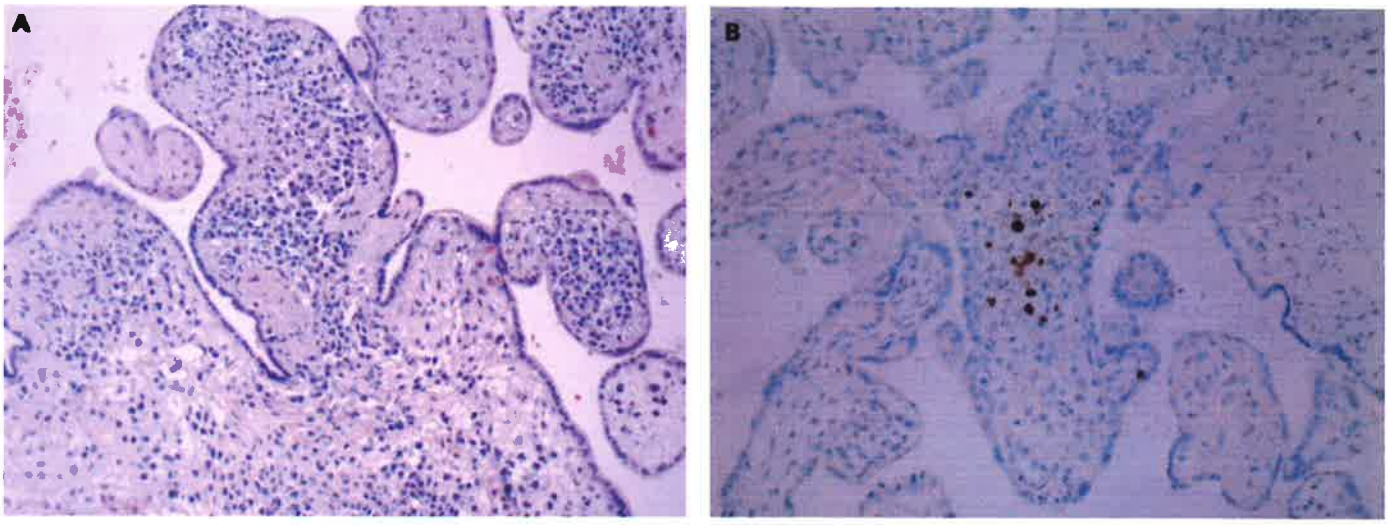


Figure 2. *Representative histologic images of a placenta with cytomegalovirus (CMV) infection.* (A) *Placental histology shows moderate villous edema, intervillous fibrin deposition, amnion hyperplasia, and grade I inflammation.* (B) *Specific immunostaining confirms the presence of CMV infection.*

of the head and abdomen showed no evidence of calcifications, ventriculomegaly, or hepatosplenomegaly prior to treatment. Ophthalmologic examination showed no evidence of retinitis. However, the infant failed multiple newborn hearing screens and appeared to have profound bilateral deafness. Antiviral therapy was continued for 6 weeks. The infant was discharged home in stable condition on day of life 55.

Discussion

CMV infection is very common in the United States, with 50% to 80% of reproductive-age women showing serological evidence of previous infection.[9] Reproductive-age women of middle and higher socioeconomic status are at higher risk for primary CMV, as approximately half are seronegative for CMV antibodies and are therefore susceptible to infection during pregnancy. In day care centers, approximately 80% of young children will develop CMV within 2 years.[10] Although these children are typically asymptomatic, they will continue to shed virus for years after initial acquisition. Many women with exposure to young children will acquire a CMV infection within 1 year.[1,11] Women with impaired cellular response (eg, patients with HIV/acquired immunodeficiency syndrome [AIDS] or those receiving immunosuppressive therapy) are at higher risk of acquiring CMV infection and, because they are less likely to produce neutralizing antibodies, they are also at higher risk of transmitting the virus to their fetuses.[5]

In day care centers, approximately 80% of young children will develop CMV within 2 years. Although these children are typically asymptomatic, they will continue to shed virus for years after initial acquisition.

How Should the Diagnosis Be Confirmed in the Mother?

Maternal CMV tends to be asymptomatic and patients will rarely be diagnosed by clinical symptoms alone. For most infections, evidence of maternal seroconversion (defined as a conversion from a negative to a positive IgM or a 4-fold increase in IgG antibody titer over a 4- to 6-week period) is sufficient to confirm the diagnosis of a primary infection. However, the accuracy of maternal anti-CMV IgM to predict primary maternal infection is complicated by the fact that IgM antibodies can persist for months or even years after primary infection, and also can be found in the setting of reactivation or reinfection with a different strain of CMV.[12]

Another method of determining the timing of maternal CMV infection is to measure antibody avidity, which refers to the strength of antibody binding to a target antigen. As the immune response to a particular antigen matures over time, avidity increases. Thus, detection of low-avidity anti-CMV IgG early in pregnancy suggests a recent acute infection, and can be used to identify pregnant women at increased risk of having an infected fetus.[4,13] In contrast, the presence of high-avidity antibodies at 12 to 16 weeks of gestation indicates a past infection, likely prior to conception. Improvement in CMV IgM testing has been reported by performing gel electrophoresis Western blotting of CMV viral polypeptides and

may provide the most accurate way to diagnose a primary maternal CMV infection.[12] Although available in Europe, this test is not available in the United States.

How Should the Diagnosis Be Confirmed in the Fetus?

In cases of confirmed maternal CMV infection, it is important to evaluate the risk of fetal infection to provide appropriate counseling and guidance to parents. Perinatal ultrasound can aid in identifying structural or growth abnormalities that may suggest symptomatic fetal infection. These abnormalities include echogenic bowel, IUGR, ventriculomegaly, placental thickening, brain calcifications, evidence of hydrops fetalis, and/or abnormal amniotic fluid volume[14,15] (Table 1). These ultrasound findings are not specific for congenital CMV infection, and there may be other causes for these findings[16] (Table 2). Moreover, only 15% of CMV-infected fetuses will display ultrasound abnormalities.[14] However, the presence of ultrasound abnormalities in a pregnant woman with confirmed primary maternal CMV infection is strongly suggestive of fetal infection.[14]

Table 1
Ultrasound Features of Congenital Cytomegalovirus Infection

- Cerebral ventriculomegaly
- Microcephaly
- Hyperechogenic fetal bowel
- Hepatosplenomegaly
- Cerebral periventricular echogenicity/ intracranial calcifications
- Intrauterine growth restriction
- Abnormal amniotic fluid volume
- Placental enlargement
- Ascites and fetal hydrops

Table 2
Differential Diagnosis of Congenital Cytomegalovirus Infection

- Rubella
- Toxoplasmosis
- Syphilis
- Herpes simplex virus
- Enterovirus

In cases of confirmed maternal CMV infection, it is important to evaluate the risk of fetal infection to provide appropriate counseling and guidance to parents.

Amniocentesis may be performed to confirm fetal infection, and is recommended in situations where maternal primary or undefined CMV infection is detected in the first half of pregnancy or in cases where sonographic fetal abnormalities are suggestive of infection. Amniotic fluid should be sent for viral culture and for polymerase chain reaction (PCR) testing for the CMV genome. False-negative results may occur if amniocentesis is performed prior to 21 weeks of gestation because the virus is slow growing and may not be excreted by the fetal kidneys in sufficient quantities for detection in early pregnancy.[4] If viral culture and PCR for CMV are both negative, congenital CMV can be effectively excluded at that time; if positive, this suggests the presence of fetal infection, although the impact on the fetus cannot be determined. Further evaluation by serial ultrasound examinations for signs of fetal brain involvement (intracranial calcifications, ventriculomegaly, microcephaly) or DNA quantification by RT-qPCR may provide additional prognostic information.[17] Fetal thrombocytopenia detected by fetal blood sampling has also been reported to be an independent predictor of poor fetal outcome,[18] but is not generally recommended.

Following birth, CMV infection in the newborn should be confirmed by isolating the virus in the urine and/or saliva in the first 2 to 3 weeks of life. Thereafter, PCR can detect the viral genome in the newborn's blood with equal sensitivity and specificity. CMV IgM antibodies are present in only 70% of infected infants and do not effectively rule out congenital infection.[4] Infants with congenital CMV infection should undergo further testing (including a detailed physical examination and additional radiologic and hematologic tests) to determine whether the infection should be classified as symptomatic.

What Is the Prognosis for the Fetus?

A diagnosis of fetal CMV infection does not equate to an affected fetus, as 80% to 90% of fetuses with congenital CMV infection are asymptomatic at birth. For the 10% to 20% of fetuses who are symptomatic at birth, however, outcomes are generally poor.[1,5,19] Signs and symptoms may include neurologic deficits (eg, seizures, chorioretinitis, hypotonia, hearing loss, microcephaly, and intracranial calcifications) as well as hematologic abnormalities (eg, petechiae, thrombocytopenia, and evidence of liver disease as manifested by jaundice, transaminitis, hyperbilirubinemia, and hepatosplenomegaly). Infants may also show evidence of growth restriction and failure to thrive.

Of CMV-infected children who are asymptomatic at birth, 8% to 15% will develop hearing loss and psychomotor delay later in life.[20]

In vitro and animal studies suggest that CMV hyperimmune globulin (HIG) may be effective in minimizing the damage caused by CMV infection.

Of CMV-infected children who are asymptomatic at birth, 8% to 15% will develop hearing loss and psychomotor delay later in life.

Should CMV Hyperimmune Globulin or Antiviral Agents Be Recommended in Pregnancy?

Because of the poor prognosis associated with primary maternal CMV diagnosed early in pregnancy, elective termination should be discussed as an option. Women who wish to continue the pregnancy may be offered one of several medical therapies; however, these should all still be regarded as investigational.

Ganciclovir has been used extensively in newborns with symptomatic CMV infections. In such newborns, a 6-week course of IV ganciclovir has been shown to significantly reduce the incidence of hearing loss, although some newborns will experience neutropenia.[21] Information on the safety and efficacy of ganciclovir in pregnancy, however, is extremely limited. Animal data have shown an increased risk of fetal malformations when ganciclovir was used in higher than normal doses in pregnancy, although case reports in humans suggest no increased risk of malformations.[5]

In a small pilot study, oral valacyclovir was administered to 21 pregnant women with confirmed CMV-symptomatic fetuses. The medication was well tolerated and a decrease in CMV viral load was noted in the cord blood of the treated fetuses; however, given the small sample size, no clear improvement in perinatal outcome could be demonstrated.[22] Further studies are necessary to determine the safety and efficacy of antiviral agents in the treatment of CMV during pregnancy.

For example, when pregnant guinea pigs were exposed to CMV followed by administration of a neutralizing antisera, fetal survival increased significantly as compared with those animals who did not receive passive immunization, and a similar reduction was noted in fetal infection, placental inflammation, and IUGR.[23,24] CMV HIG consists of enriched CMV-specific immunoglobulins and has been studied extensively in post-transplant patients for CMV prophylaxis.[25,26] It is marketed in the United States as Cytogam® (CSL Behring, King of Prussia, PA).

Nigro and colleagues[27] conducted a multicenter, prospective study of 181 pregnant women with primary CMV infection. Of these women, 79 underwent amniocentesis and 55 were found to have CMV-positive amniotic fluid. Of these, 31 women elected to receive 200 U/kg CMV HIG administered monthly, 14 women elected not to receive HIG, and 10 women elected to terminate the pregnancy. Only 3% (1/31) of fetuses who received HIG were symptomatic at birth as compared with 50% (7/14) of the infants whose mothers declined HIG. In this nonrandomized study, administration of HIG to the mother and the presence of fetal ultrasound abnormalities prior to treatment were important predictors of fetal outcome. In a second study by the same investigators, 3 women with CMV-associated fetal cerebral abnormalities received HIG infusions during pregnancy. In all 3 cases, the fetal ventriculomegaly regressed, other associated abnormalities resolved, and the 3 infants were reportedly developing normally by age 5.[28]

Additional case reports from other investigators have suggested that antenatal administration of CMV HIG may be associated with more favorable outcomes in fetuses suspected of having congenital CMV infection.[29-32] CMV HIG has been given by maternal IV injection, intra-amniotic injection, intraperitoneal injection into the fetus, and by direct IV injection into the umbilical vein. The optimum dosage, route of administration, and indications for its use, along with confirmation of its efficacy in randomized, prospective clinical studies, still need to be identified. However, the use of CMV HIG and/or antiviral agents such as valacyclovir in fetuses with confirmed CMV infection may be an option for women who plan to continue the pregnancy.

Is There a Vaccine Available Against CMV?

In 1999, the Institute of Medicine report entitled, *Vaccines for the 21st Century: A Tool for Decision Making,* stated that development of a CMV vaccine was the highest priority for new vaccines.[33] Recently, a vaccine targeted toward CMV envelope glycoprotein B, an antigen that typically induces a serum antibody response, entered phase 2 clinical trial.[34] This vaccine

Recently, a vaccine targeted toward CMV envelope glycoprotein B, an antigen that typically induces a serum antibody response, entered phase 2 clinical trial. This vaccine has already been shown to be immunogenic with an acceptable risk profile.

has already been shown to be immunogenic with an acceptable risk profile. In this trial, CMV infection occurred in 18 of 225 subjects in the vaccine group (8%) and in 31 of 216 subjects in the placebo group (14%). Four congenital CMV infections occurred as a result of maternal infection during pregnancy. There were 3 congenitally infected infants in the placebo group (1 of which went on to develop severe neurologic sequelae) and 1 congenitally infected infant in the vaccine group (who was asymptomatic).[34] Although these numbers are too small to support any definitive conclusions, they are consistent with our knowledge of decreased CMV transmission in women who carry protective antibodies. Future studies are necessary to demonstrate the safety and efficacy of this vaccine before it can be used for primary prevention of congenital CMV.

Prevention of CMV in Pregnant Women

Given the limited success of vaccine prevention of CMV, attention has been directed at patient education as a means of preventing the acquisition of infection (Table 3). Because 15% to 70% of children in day care acquire CMV infection, attempts at prevention have focused primarily on mothers of small children. It has been shown that CMV-seronegative women have a 5- to 25-fold increased risk of developing CMV if exposed to children in day care.[11] In a study of 166 seronegative women with a young child in day care, women given information concerning handwashing, gloves for diaper changes, and avoiding certain types of intimate contact (sharing utensils, kissing on the lips) were compared with those not given this information.[35] Both groups showed an overall seroconversion rate of 7.8%. However, CMV-seronegative mothers who knew their infant's serostatus and were pregnant had a lower risk of seroconversion (5.8%) as compared with those who were not pregnant (41.6%), suggesting that knowledge of their infant's status and the motivation during pregnancy to avoid becoming infected led to a decrease in acquiring CMV. This also suggests that personal knowledge of a woman's own susceptibility to CMV through screening may be useful when designing and implementing prevention strategies.

Currently, the American College of Obstetricians and Gynecologists (ACOG) recommends that all women be educated about the ways that CMV infection may be acquired in pregnancy.[36] They recommend careful handling of potentially infected articles, such as diapers, and thorough handwashing when around young children or immunocompromised individuals. The Centers for Disease Control and Prevention (CDC) confirms the ACOG recommendations, but also adds that pregnant women with children under the age of 6 should avoid sharing utensils and kissing their children on the lips or cheek.[37] Despite these recommendations, a recent survey study by ACOG of 305 obstetrician-gynecologists reported that only 44% routinely counsel their patients about CMV prevention.[38]

Table 3
Strategies to Prevent CMV Infection in Women Who Are or Will Become Pregnant

- Educate women with young children or who work with young children that they are at increased risk and that attention to hygiene will help prevent cytomegalovirus (CMV) transmission
- Careful handing of potentially infected articles, such as diapers
- Thorough hand washing when around young children or immunocompromised individuals
- Avoiding sharing utensils
- Avoid kissing children < 6 years on the mouth or cheek

Adapted from American College of Obstetricians and Gynecologists[36] and Centers for Disease Control and Prevention.[37,38]

Should All Patients Be Screened for CMV?

Although ACOG recommends that pregnant women be educated about CMV prevention, they have not endorsed routine screening in pregnancy.[36] The CDC also acknowledges that screening for CMV in pregnant women is not currently recommended. However, they add that, for women planning to become pregnant, routine CMV screening can help them to understand how careful they must be to prevent infection.[37] The reasons given for not recommending routine screening have included the difficulties in accurate diagnosis given the high false-positive rate of commercial IgM testing, the lack of effective treatment of infection during pregnancy, and the possibility of reinfection or virus reactivation in a seropositive woman. In a recent decision-analytic model evaluating options for maternal CMV screening, Cahill and colleagues[39] noted that universal screening was cost effective as long as CMV HIG achieved at least a 47% reduction in neonatal disease. In countries such as Italy where CMV

screening is more widespread, the high incidence of false-positive CMV IgM has been studied. In a series of 1857 pregnant women with a reported positive CMV IgM test, only 26% were thought to represent a true primary CMV infection as confirmed by additional testing with IgG avidity and CMV immunoblot technology, whereas 54% of cases were believed to represent previous infection without active disease, and 20% were thought to be reactivation/secondary infection.[40] Such studies underscore the need for appropriate confirmatory testing to determine the true fetal risk as well as appropriate specialists to provide counseling for the heightened patient anxiety that could result from more widespread screening. However, with improvements in serologic testing (eg, IgG avidity or IgM immunoblot technology) coupled with effective treatments (CMV HIG, antiviral agents, or vaccination), it is hoped that the introduction of more widespread screening of women for CMV serostatus prior to or at the onset of pregnancy will lead to significant improvements in clinical outcome.

Conclusions

CMV is an important cause of congenital infection and can result in significant perinatal morbidity and health care expense. Although existing data suggest a benefit to HIG prophylaxis, additional clinical trials are needed to confirm these observations. Until then, the use of HIG and other antiviral agents for treatment remains experimental. In the absence of proven therapies for congenital CMV infection, prevention is critical. Most importantly, patients, especially those exposed to young children, should be counseled about the importance of careful hand hygiene practices, an intervention that has been proven to decrease the risk of primary CMV infection and subsequent fetal transmission. ■

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Main Points

- Maternal cytomegalovirus (CMV) tends to be asymptomatic and patients will rarely be diagnosed by clinical symptoms alone. For most infections, evidence of maternal seroconversion is sufficient to confirm the diagnosis of a primary infection.
- Perinatal ultrasound can aid in identifying structural or growth abnormalities that may suggest symptomatic fetal infection. Amniocentesis may be performed to confirm fetal infection, and is recommended in situations where maternal primary or undefined CMV infection is detected in the first half of pregnancy or in cases where sonographic fetal abnormalities are suggestive of infection. Following birth, CMV infection in the newborn should be confirmed by isolating the virus in the urine and/or saliva in the first 2 to 3 weeks of life.
- A diagnosis of fetal CMV infection does not equate to an affected fetus, as 80% to 90% of fetuses with congenital CMV infection are asymptomatic at birth. For the 10% to 20% of fetuses who are symptomatic at birth, however, outcomes are generally poor.
- Because of the poor prognosis associated with primary maternal CMV diagnosed early in pregnancy, elective termination should be discussed as an option. Women who wish to continue the pregnancy may be offered one of several medical therapies; however, these should all still be regarded as investigational.
- Given the limited success of vaccine prevention of CMV, attention has been directed at patient education as a means of preventing the acquisition of infection. Currently, the American College of Obstetricians and Gynecologists recommends careful handling of potentially infected articles, such as diapers, and thorough handwashing when around young children or immunocompromised individuals. The Centers for Disease Control and Prevention adds that pregnant women with children under the age of 6 should avoid sharing utensils and kissing their children on the lips or cheek.
- For women planning to become pregnant, routine CMV screening can help them to understand how careful they must be to prevent infection.

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Cytomegalovirus Vaccine Development

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Abstract

Although infection with human cytomegalovirus (HCMV) is ubiquitous and usually asymptomatic, there are individuals at high risk for serious HCMV disease. These include solid organ and hematopoietic stem cell (HSC) transplant patients, individuals with HIV infection, and the fetus. Since immunity to HCMV ameliorates the severity of disease, there have been efforts made for over thirty years to develop vaccines for use in these high-risk settings. However, in spite of these efforts, no HCMV vaccine appears to be approaching imminent licensure. The reasons for the failure to achieve the goal of a licensed HCMV vaccine are complex, but several key problems stand out. First, host immunology correlation to protective immunity consist is not yet clear. Secondly, the viral proteins that should be included in a HCMV vaccine are uncertain. Third, clinical trials have largely focused on immune compromised patients, a population that may not be relevant to the problem of protection of the fetus against congenital infection. Fourth, the ultimate target population for HCMV vaccination remains unclear. Finally, and most importantly, there has been insufficient education about the problem of HCMV infection, particularly among women of child-bearing age and in the lay public. This review considers the strategies that have been explored to date in development of HCMV vaccines, and summarizes both active clinical trials as well as novel technologies that merit future consideration toward the goal of prevention of this significant public health problem.

Published in final edited form as:
Curr Top Microbiol Immunol. 2008 ; 325: 361–382.

EBioMedicine 2 (2015) 1027–1028

Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.ebiomedicine.com

Commentary

Prevention of Maternal–Fetal Transmission of Cytomegalovirus

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ARTICLE INFO

Article history:
Received 3 August 2015
Accepted 3 August 2015
Available online 5 August 2015

Annually in the United States approximately 40,000 pregnant women are infected with CMV (seroconvert) during pregnancy and probably an equal number in Europe. Of those seroconverting during pregnancy approximately 20% of their infants develop neurologic damage and/or hearing deficit. A hopefully final and definitive report by Revello et al. in this journal confirms that the majority of these infections are easily prevented by simple hygienic precautions (Revello et al., 2015).

Between 20% and 60% of women are susceptible (seronegative) to CMV at conception. Maternal immunity from a pre-conception CMV infection protects against a second CMV infection and protects the fetuses from severe postnatal neurosensory deafness and neurologic damage. Thus a primary maternal infection with CMV in early pregnancy causes the majority of congenital disease. After a primary infection during pregnancy, the fetal infection rate varies from 33% to 75% as gestation progresses and disease rates may be as high as 50% if infection occurs during early gestation (Bodéus et al., 2010; Nigro et al., 2005).

The majority of seronegative pregnant women acquire CMV from a child less than three years of age in the home or for pregnant women employed in infant day care centers, from children in their care (Adler et al., 2004; Adler, 1989). CMV seronegative health care providers caring for hospitalized young children and infants, are not at an increased risk (Adler, 2010). Infants acquire CMV in utero, via breast milk, or via contact with other children. These CMV infected infants, unlike older children and adults, have CMV in urine and saliva for an average of 18 months (Adler, 1991). In the US, 60% of the mothers of children in daycare are CMV seronegative, and at least 25% of all young children attending large group child care centers are shedding CMV. The annual infection rate for seronegative women without exposure to children is 2%, but 5 to 25 times higher for exposed women (Adler et al., 2004; Adler, 1989).

The U.S. Centers for Disease Control suggests that pregnant women reduce their risk of CMV acquisition during pregnancy using simple hygienic precautions but this suggestion is not often followed. Studies demonstrating the efficacy of hygienic precautions are compelling (Revello et al., 2015; Adler et al., 1996, 2004; Finney et al., 1993; Vauloup-Fellous et al., 2009). Our U.S. studies of CMV seronegative pregnant women with an infected young child found that the precautions were highly effective ($p < 0.008$) (Adler et al., 1996, 2005, 2015). Women were told about CMV, provided written guidelines detailing hygienic precautions, and provided a demonstration video. None declined testing and none complained the precautions were difficult or provoked anxiety. Overall of 37 pregnant women with a child shedding CMV, only one (3%) who received hygienic precautions seroconverted to CMV during pregnancy. This contrasts with an infection rate of 42% for 154 non-pregnant women and women trying to conceive who also had infected children.

A French study offered 5312 pregnant women CMV serologic screening at 12 week gestation and 97.4% agreed (Vauloup-Fellous et al., 2009). Seronegative women and their spouses received oral and written hygienic precautions. For 2595 seronegative women, the rate of maternal seroconversion during the first 12 weeks of gestation was compared to the rate between weeks 12 and 36. Prior to the receipt of hygienic precautions at 12 weeks the maternal seroconversion rate when adjusted for the number of woman–weeks observed was 0.035% per woman–week compared to a rate of 0.008% per woman–week after intervention ($P = 0.0005$). Maternal primary infections and seroconversions were distributed evenly throughout gestation.

Revello et al. in Italy prospectively observed that of 331 CMV seronegative pregnant women who receive oral and written hygienic precautions for preventing CMV acquisition from a young child only four (1.2%) women seroconverted to CMV during pregnancy (Revello et al., 2015). In contrast of 315 women in a comparison group, CMV infection occurred in 24 (7.6%) women during pregnancy.

In each report, the efficacy of hygienic precautions has been >75%. Given the ease and effectiveness of this intervention it is appropriate that CMV education and hygienic precautions be implemented clinically. All pregnant women with frequent contact with a child <3 years of age should be identified as early in gestation as possible and offered serologic testing (IgG antibodies to CMV only). If seronegative, women should be given the precautions. Subsequent testing during pregnancy would be optional based on the level of concern of the woman and

DOI of original article: http://dx.doi.org/10.1016/j.ebiom.2015.08.003.
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http://dx.doi.org/10.1016/j.ebiom.2015.08.004

the results of ultrasound findings. Screening for fetal disease by ultrasound is nearly universal in developed countries. If ultrasound findings are normal, the risk of CMV fetal or neonatal disease is low and hence repeat testing should be unnecessary (Nigro et al., 2005).

In each published study women knew they were seronegative and hence at risk. Is serologic testing necessary for motivation and for the precautions to be effective? We do not know. Also we do not know how often seropositive women become reinfected during pregnancy and if maternal reinfection leads to fetal disease. These questions can be answered in subsequent studies but are not reasons to delay implementation of the precautions for seronegative women.

Serologic screening of high risk pregnant women for CMV is as feasible as is current screening for syphilis, hepatitis, rubella, and HIV. The assays for IgG to CMV have an accuracy equal or great than the accuracy for the other infections. Serologic screening for CMV IgM or IgG avidity should not be done.

Although seronegative health care workers are not at risk, pregnant childcare employees are. Pregnant childcare employees should be informed about CMV, assess their risk by serologic testing or avoid if possible caring for children less than 2 years age for the duration of pregnancy. The efficacy of hygienic precautions for childcare employees is unknown.

For seronegative pregnant women who are at high risk because of exposure to a young child in the home or in large group childcare, hygienic precautions are simple, inexpensive, and highly effective.

Conflict of Interests

None.

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