

American Academy of Audiology Position Statement on Early Identification of Cytomegalovirus in Newborns

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Abstract

The American Academy of Audiology recommends early identification of congenital cytomegalovirus (cCMV) through screening to allow for appropriate early diagnosis, intervention, and monitoring for congenital, progressive, and delayed-onset hearing loss in infants with cCMV.

Keywords

- ▶ CMV
- ▶ cCMV
- ▶ congenital
- ▶ cytomegalovirus
- ▶ hearing loss
- ▶ hearing screening
- ▶ newborn
- ▶ newborn screening

Early identification of cCMV is a valuable component in the diagnostic evaluation of infants with sensorineural hearing loss. The Academy recognizes the important role audiologists serve as clinical care providers and educators and advocates for early identification and audiological management of infants with cCMV.

Introduction and Rationale

Congenital cytomegalovirus (cCMV) is the leading cause of nongenetic childhood sensorineural hearing loss (SNHL). Universal newborn hearing screening (UNHS) is the standard of care in hospitals nationwide, and some infants with

hearing thresholds outside the typical range identified through UNHS will also have cCMV. Due to the time-sensitive nature of cCMV testing (must be completed by 21 days of age) and high loss to follow-up rates for hearing screening, cCMV screening should be completed at the birth hospital before discharge, although screening can be conducted post discharge. Models for early identification of cCMV include universal cCMV screening, hearing-targeted cCMV (HT-cCMV) screening, and expanded targeted cCMV screening. Universal cCMV screening is defined as cytomegalovirus (CMV) polymerase chain reaction or culture testing by blood, saliva, or urine screening of all babies for the CMV infection at birth. HT-cCMV screening programs test infants who do not pass two or more hearing screenings. Expanded targeted cCMV screening is testing that targets a range of symptoms

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Abbreviations

CMV	cytomegalovirus
cCMV	congenital cytomegalovirus
HT	hearing targeted
SNHL	sensorineural hearing loss
UNHS	universal newborn hearing screening

common to the infection, including, but not limited to, head size, birth weight, maternal HIV status, and jaundice. Screening for cCMV yields important information about the etiology of hearing loss and potential for delayed-onset or progressive hearing loss, as well as implications for vestibular function. A significant proportion of infants with cCMV at risk for delayed-onset SNHL will not be identified via HT-cCMV testing. Because of the number of infants who have no symptoms of cCMV at birth but may have delayed-onset developmentally significant manifestations, including SNHL, universal cCMV screening is recommended by many infectious disease experts. Early cCMV screening is critical for the accurate identification of hearing loss etiology and early treatment, including amplification, early intervention, monitoring of hearing, and referral to infectious disease physicians.

CMV Overview

CMV is a common herpes virus. Approximately 50–80% of adults in the United States will contract CMV before the age of 40 years.¹ Notably, CMV is generally considered harmless to healthy adults, and infected individuals may be asymptomatic. Symptoms, if present, are similar to the common cold.¹ cCMV is acquired during pregnancy and transmitted to the fetus in utero. According to the Centers for Disease Control and Prevention, cCMV is the “most common infectious cause of birth defects in the United States,” with ~1 out of every 200 infants born with the virus annually.¹ Unlike an adult infection, cCMV can cause serious health conditions for newborns, such as hearing and vision loss, seizures, developmental delays, and death. cCMV is most often associated with SNHL and causes up to 25% of congenital hearing losses by 4 years of age.^{1,2} Although the majority of cCMV cases are considered asymptomatic, symptoms of cCMV may appear later in life or be progressive.^{1–3} In many cases, hearing thresholds in the mild, moderate, severe, and profound range are the only symptom of cCMV infection at birth.

Despite the high prevalence of cCMV and its negative effect on infants, awareness of the virus is alarmingly low. The National CMV Foundation estimates that only 9% of women are aware of what cCMV is, how the virus is transmitted, or what simple prevention strategies are.⁴ Other studies show awareness of cCMV ranging anywhere from 7% to 22%, whereas awareness of less common conditions affecting newborns and infants is much higher.⁵ Mothers who are non-White, are Medicaid insured, and have a high school education or less are unlikely to know about cCMV. Because non-Hispanic Blacks and Mexican Americans, and low- or middle-income households, are more likely to have new cCMV infection compared with non-Hispanic Whites, and high-income households, targeted educational efforts may be necessary to benefit these vulnerable groups.^{6–8}

Misinformation about CMV is also common among medical providers. Families of children with cCMV report a medical bias, including health-care workers refusing to see their children, even years later. Per the American Academy of

Pediatrics 2021–2024 *Red Book* recommendations for CMV,⁹ health-care workers, including audiologists, even when pregnant, do not need to exclude children with CMV because many children who are presumed CMV negative may be asymptomatic and also shedding the virus. Standard precautions are recommended for health-care workers with all patients, regardless of known CMV status, to decrease risk of contracting CMV.⁴

Transmission of CMV

CMV can be transmitted in urine, saliva, tears, feces, blood, semen, and breast milk. Populations who are most at risk for contracting CMV while pregnant include the following:

- Mothers of toddlers and young children
- Day-care workers
- Teachers
- Health-care professionals who may come into contact with body fluids

The risk of CMV transmission is lower with standard hygiene procedures, including hand washing after encountering body fluids, not sharing cups or utensils, or kissing a child on the forehead or cheek instead of on the lips. Until an effective vaccine is widely available, prevention of cCMV is key to reducing transmission.^{4,10}

An initial CMV infection acquired during pregnancy is known as a primary infection and may result in infant cCMV. Secondary infections, which occur when the virus is reactivated during pregnancy or when the mother is exposed to a different strain of CMV during pregnancy, are associated with cCMV as well. Although women with primary CMV infection are at greatest risk of having a baby with severe disease from a cCMV infection, it is important to note that secondary reactivation and reinfection may impact fetal development. It is important for all women to be educated about CMV infection and transmission prior to conception, and following standard precautions is recommended regardless of maternal CMV status.^{4,11}

Effect of cCMV on Newborns

It is estimated that 85–90% of infants with cCMV are asymptomatic at birth or initially present with hearing loss only.⁵ The remaining 10–15% of infants with cCMV are born with symptomatic disease, including jaundice, rash, microcephaly, intrauterine growth restriction, hepatosplenomegaly, seizures, and retinitis. Infants born with symptomatic disease are at a higher risk for neonatal death and long-term neurodevelopmental effects.^{4,5} SNHL may occur in infants with or without symptoms. Infants with cCMV are more likely to fail their newborn hearing screening than infants who are cCMV negative.¹²

Outcomes for children with cCMV vary, ranging from no obvious impact to multiple health issues and other disabilities. Permanent sequelae are seen in ~40–60% of infants with symptomatic cCMV and in 10–15% of infants with asymptomatic cCMV.⁴

cCMV is the leading cause of nongenetic childhood-onset SNHL.^{13,14} Approximately 50% of infants who are symptomatic will experience SNHL, and 10–15% of infants who are asymptomatic will develop SNHL.¹³ SNHL may be congenital or may develop over the first years of life. Approximately 33–50% of cCMV-related SNHL is late onset, which typically occurs during the first several years of life.^{12,13} Thirty-three months is the median age of late-onset hearing loss in children who are symptomatic and 44 months of age in children who are asymptomatic.¹² This necessitates the need for continued audiology monitoring until the child is 5 years old.¹³ Children who are symptomatic generally have more significant SNHL and an earlier progression of SNHL. If a child does exhibit SNHL, it may continue to progress into the teen years.¹³ Approximately 30% of children with symptomatic cCMV and 50% of children with asymptomatic cCMV will have fluctuating SNHL. The fluctuations vary and can occur in only one ear, or only at a few frequencies, or in both ears.^{12,13}

The presentation of cCMV is varied. In addition to SNHL, common sequelae include the following.^{4,15}

Vision Problems: Children with symptomatic cCMV are more likely to have moderate or severe visual issues compared with children with cCMV who are asymptomatic at birth. Symptomatic cCMV, SNHL, and microcephaly are predictors of serious visual deterioration. Some children (1–2%) with asymptomatic cCMV that is either present at birth or develops during childhood may have minor vision issues due to scarring, eye muscle abnormalities, and abnormal pigment on the retina. Cortical visual impairment may occur. Annual comprehensive eye exams are recommended for children and teens with cCMV.⁴

Neurodevelopmental Issues: It is common for individuals with symptomatic cCMV, microcephaly, and moderate-to-severe brain calcifications caused by the infection to exhibit cognitive issues. Children will learn on their own timeline, so it is important to actively partner with educational providers. Children born with typical head size and minimal brain abnormalities on imaging generally have normal or near-normal learning abilities.⁴

Children with asymptomatic cCMV commonly have neurodevelopmental outcomes in the range of typically developing children. Some longitudinal research indicates that children who were asymptomatic and had SNHL displayed lower verbal skills compared with children without cCMV and typical hearing. Intellectual disabilities are more common among children with symptomatic cCMV. Some preliminary studies indicate a possible relationship between infants with symptomatic cCMV and autism spectrum disorder.¹⁶

Vestibular Disorders: A recent study found that children who are cCMV asymptomatic, regardless of hearing status, have a high degree of vestibular (45%), gaze (46%), and balance (30%) disorders.⁷ Congenital or delayed vestibular dysfunction can occur in infants with or without SNHL.¹⁷

Cerebral Palsy/Motor Delay: Infants with cerebral palsy and symptomatic cCMV are more likely to have severe functional deficits, dysphagia, and cognitive deficits. Hypertonia or hypotonia may be present, especially in children who are more severely impacted. cCMV is thought to be

present in some children with cerebral palsy, but a specific phenotype of cerebral palsy associated with cCMV has not been identified.¹⁸

Liver/Spleen Issues: Babies born with cCMV may have dysfunction of the liver and spleen; however, these issues typically resolve over the first few months of life. Babies with liver and spleen issues resulting from cCMV are considered symptomatic and should follow audiological monitoring protocols.¹

Treatment Options for cCMV

Early screening is imperative for identification and treatment of individuals with cCMV. It is critical that babies with cCMV have access to early hearing intervention, including audiological monitoring and treatments for SNHL, as indicated. Children with documented cCMV infection should also be referred to an infectious disease physician to discuss candidacy for antiviral therapy. Studies have shown that ganciclovir and valganciclovir can improve or stabilize hearing thresholds and potentially improve neurodevelopmental outcomes in infants with cCMV, when treatment is initiated in the first 4 weeks of life. Antiviral treatments have also been shown to improve thrombocytopenia, organ failure (most commonly spleen and/or liver), hepatitis, and pneumonitis.^{4,19}

There is currently no vaccine approved for CMV, but there are clinical trials in progress. In 1999, the Institute of Medicine (now the National Academy of Medicine) ranked the need for a cCMV vaccine as the highest level 1 need based on cost impact and quality-of-life-adjusted year saved. Many international pharmaceutical companies and academic research centers are focused on development of an effective CMV vaccine. Phase 1 and phase 2 clinical trials are underway for potential CMV vaccines.^{4,10,20}

Screening for cCMV

Due to the risk of SNHL associated with cCMV and importance of knowledge of cCMV status for follow-up diagnostic and treatment recommendations, cCMV screening has been incorporated into some hospital and statewide UNHS programs. Nationally, ~1.7% of babies (~61,500 babies in the United States) do not pass their newborn hearing screening each year.²¹ Estimates suggest that a cCMV screening costs about \$15 per infant (\$10–\$52.50 per infant).^{22,23} CMV testing is readily available and highly sensitive (sensitivity of liquid-saliva real-time polymerase chain reaction assay compared with standard rapid culture was 100% [95% CI, 95.8–100]).²⁴ CMV screening of infants who do not pass their hearing screening or present with other symptoms is covered by most private and state insurance programs. The implementation of a targeted cCMV screening program has potentially significant patient and family benefits. Knowledge of cCMV status through cCMV screening has clear benefits in management of infants and children with cCMV-related audiovestibular dysfunction. Diener et al.²⁵ found that HT-cCMV testing improves timely diagnosis of

all infants who do not pass their newborn hearing screening. Thus, this approach helps not only those diagnosed with cCMV but all infants with permanent hearing loss.

Although HT-cCMV screening improves the ability to appropriately manage infants and children with cCMV and auditory symptoms at birth, 43% of infants ultimately impacted by cCMV-related hearing loss, including those at risk for delayed onset of hearing loss, will be missed with HT-cCMV screening.²⁶ Universal cCMV screening has been proposed, and in the consensus statement on prevention, diagnosis, and therapy for cCMV, Rawlinson et al.¹⁷ stated “consideration should be given to universal neonatal cytomegalovirus screening to enable early detection of congenital cytomegalovirus-infected infants allowing early intervention for [SNHL] and developmental delay where appropriate.”

Due to concerns with universal testing and the limitation of the HT-cCMV screening, expanded targeted cCMV protocols have been introduced.²⁷ Expanded targeted cCMV testing protocol recommends CMV testing for any newborn found to meet any of the following criteria: maternal history of CMV infection, idiopathic elevated liver enzymes or bilirubin, failed hearing screen, abnormal central nervous system imaging findings suggestive of cCMV (for example, intracranial calcifications), unexplained thrombocytopenia, history of intrauterine growth restriction, small for gestational age, macrocephaly, microcephaly, intra-abdominal calcifications, unexplained hepatomegaly or splenomegaly, or petechial rash. These expanded criteria help identify many symptomatic infants who would not be identified through the HT-cCMV screening protocols.

Role of the Audiologist in cCMV

cCMV-related hearing loss is sensorineural, can be unilateral or bilateral, and is most often detectable at birth. However, SNHL presents with later onset in 10–20% of cCMV cases. Later-onset SNHL is due to inflammatory changes at the cellular level in the auditory system.^{12,13} The pathophysiology of late-onset cCMV is not well understood at this time.²⁸

The effects of untreated SNHL in children are well documented in the scientific literature. Since children with cCMV infection are at risk for late-onset or progressive SNHL, a rigorous audiological monitoring protocol is recommended for all infants diagnosed with cCMV.¹²

On the basis of the current information, the Academy recommends the following surveillance model: diagnostic evaluations every 3–6 months for the first year of life, then every 6 months until 3 years of age, and annually until 6 years of age.

The recommended monitoring protocol for cCMV-positive infants is as follows:

- Initial diagnostic audiology evaluation should take place within the first 3 months of life, even if the infant passes the newborn hearing screening.²⁹
- Hearing should be monitored using developmentally appropriate evaluations.

- If a significant change in hearing is documented, thresholds should be evaluated frequently until the hearing loss stabilizes.

This recommendation ensures that infants and children at greatest risk for delayed onset of cCMV-related hearing loss are identified as quickly as possible, and appropriate intervention is initiated to prevent developmental delays.

Infants and children with cCMV and documented SNHL should be fit expediently with amplification that is flexible enough to accommodate progression of hearing loss. Cochlear implantation may also become an option for many infants and children with cCMV. Ongoing parent–caregiver education about options for intervention is a critical part of the process.³⁰

Special considerations for managing hearing loss in infants and children with cCMV include the following:

- SNHL that initially presents as unilateral can progress to bilateral; rapid progression of SNHL is likely. Parents and caregivers of children with cCMV should be encouraged to contact their audiologist as soon as possible if any change in hearing is suspected.
- The poorer-hearing ear may worsen earlier and more precipitously than the better hearing ear.³¹
- Visual acuity is often impacted by cCMV. Parent–caregiver education should include a variety of communication options that will meet the needs of the individual child.
- Because cCMV can affect the vestibular system, as well as the auditory system, balance should be monitored with referrals for vestibular evaluation as needed. Audiologists should include screening for vestibular dysfunction (for example, monitoring movement/physical development milestones using the Centers for Disease Control and Prevention milestone checklists) at each follow-up visit. If concerns are identified, children should be referred to vestibular specialists (for example, vestibular audiologists, otolaryngologists, and physical therapists) for in-depth vestibular assessment so that appropriate management is initiated early in development.^{13,32}

As previously mentioned, individuals with cCMV are likely to have long-term neurodevelopmental disabilities including seizures and learning difficulties in addition to SNHL.^{4,11} These patients will require a multidisciplinary team for support, including, but not limited to, audiology, developmental pediatrics, infectious diseases, neurology, ophthalmology, speech language pathology, physical therapy, pediatric otolaryngology, and parent–family support. Because cCMV does not have a uniform or consistent impact, the care team should be individualized to meet each patient’s and family’s unique needs. Babies with symptomatic cCMV at birth are at a higher risk of developing more severe sequelae as a result of their infection and may need larger care teams due to medical needs.¹¹

Position Statement

The American Academy of Audiology recommends early identification of cCMV through screening to allow for appropriate early diagnosis, intervention, and monitoring for congenital, progressive, and delayed-onset hearing loss in infants with cCMV. Early identification of cCMV is a valuable component in the diagnostic evaluation of infants with SNHL. The Academy recognizes the important role audiologists serve as clinical care providers and educators and advocates for early identification and audiological management of infants with cCMV.

Disclosure

Shelley Moats serves on the Kentucky Early Hearing Detection and Intervention Advisory Board and reports stakeholder and clinical support with Bella's Bill 4 CMV. Angela Shoup serves on the Scientific Advisory Committee for the National CMV Foundation. Stacy Claycomb Stiell reports service on the Colorado Infant Hearing Advisory Committee. Jenni Chappetto, Sarah Jones, Maggie Kettler, and Wendy Steuerwald have no relevant financial or nonfinancial competing interests to declare in relation to this position statement.

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