

# Targeted Screening for Cytomegalovirus and Hearing Loss

By Karen B. Fowler, DrPH

**C**ongenital cytomegalovirus (cCMV) infection continues to be a public health problem because of its frequency (one in 200 live births) and its role in sensorineural hearing loss (SNHL) in infants and young children. About 21 percent of all permanent hearing loss at birth is due to cCMV infection; by four years of age, 25 percent of childhood hearing loss is due to cCMV infection (*New Engl J Med.* 2006;354[20]:215). Although infants with cCMV infection may have cognitive impairment, retinitis, and/or cerebral palsy following infection, SNHL is by far the most common sequelae following cCMV infection.

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Hearing loss following cCMV infection may be present at birth or occur later in the early years of life. Approximately 33 to 50 percent of SNHL due to cCMV infection occurs after the newborn period (*J Pediatr.* 1999;135:60). Late-onset hearing loss occurs throughout the first several years of life, indicating that children with cCMV infection should be evaluated for hearing function at least annually until 5 to 6 years of age, if not longer (*J Am Acad Audiol.* 2000;11:283). About 50 percent of children with SNHL following cCMV infection will have further hearing deterioration (*J Pediatr.* 1997;130:624). Another characteristic of CMV-related hearing loss is fluctuating hearing loss, which is not explained by concurrent middle ear infections. Fluctuating hearing loss may only occur in one ear, at a few frequencies within the ear, or in both ears if a child has bilateral hearing loss. About 30 to 50 percent of children with CMV-related hearing loss will have fluctuating loss.



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## AWARENESS AND ADVOCACY

Although clinicians and scientists have known for more than 50 years that cCMV infections contribute to SNHL in infants and children, CMV awareness among women is low. A recent U.S. study found that only nine percent of women and five percent of men had ever heard of CMV and knew that CMV could cause permanent hearing loss in infants and children (*JEHDI.* 2016;1[2]:39). However, parent advocate groups and organizations like the National CMV Foundation are partnering with health care providers to develop CMV education campaigns. Advocates are also lobbying and proposing CMV legislation to mandate CMV screenings for newborns. At present, nine states (Connecticut, Hawaii, Idaho, Illinois, Iowa, Oregon, Tennessee, Texas, Utah) have passed CMV legislative mandates, and six states (Maine, Michigan, Minnesota, New York, Ohio, Pennsylvania) have drafted their proposals (National CMV Foundation, 2017). Of the states that have passed CMV legislative mandates, five states (Connecticut, Illinois, Iowa, Oregon, and Utah) include CMV screening for infants who fail the newborn hearing screening (NHS).

## TARGETED SCREENING

Routine CMV screening in newborns has become feasible with the development of polymerase-chain-reaction (PCR) testing on newborn saliva for the diagnosis of congenital CMV infection (*New Engl J Med.* 2011;364:2111). Urine and/or saliva collected from an infant in the first weeks of life may be used for a definitive CMV diagnosis. Many hospitals, as well as states with CMV legislative mandates, have begun targeted CMV screening, which only tests for cCMV when a newborn fails the NHS. As part of the National Institute on Deafness and Other Communication Disorders (NIDCD)-funded CMV and Hearing Multicenter

## HEARING SCREENING

Screening (CHIMES) study, we recently examined the effectiveness of a targeted approach for identifying infants with CMV-related hearing loss where only newborns who did not pass NHS would be tested for cCMV (*Pediatr.* 2017;139[2]:e20162128).

In the CHIMES study, 99,945 infants at seven U.S. medical centers were tested for CMV, and received a NHS while in the hospital nursery. CMV-positive infants were significantly more likely to fail the NHS (7.0%) compared with CMV-negative infants (0.9%). CMV-positive infants in the neonatal intensive care nursery had the highest referral rate (20.9%). CMV-positive infants in the well-baby nursery also had a higher than average referral rate (5.5 %). Among the cCMV infants who did not pass their NHS, further diagnostic testing confirmed that 65 percent had SNHL. An additional 3.6 percent of CMV-infected infants who passed the NHS had SNHL confirmed in early infancy. These missed infants may be due to the limitations of the NHS algorithms that were unable to reliably detect milder hearing losses. Overall, the majority (57%) of CMV-related SNHL that occurred in the neonatal period was identified by targeted CMV screening. However, this approach is unable to identify the cCMV infants who are at risk of late-onset SNHL.

newborn period or SNHL at birth. All infected infants, regardless of their antiviral treatment status, should have audiological monitoring every six months until at least 3 years of age, followed by annual assessments until 6 years of age. Frequent audiological monitoring (every three months) should be considered when hearing levels are changing or until the child starts to talk. Since CMV-related hearing loss may fluctuate or progress, special attention should be given to children with hearing aids to ensure proper amplification when their hearing levels fluctuate.

Parents and health care providers should consider routine CMV testing for infants who fail the NHS. Targeted CMV screenings may not be able to identify all CMV-related hearing loss, but until universal CMV screening is implemented, this remains a valid approach to identify and treat infected infants. 

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Another advantage of targeted CMV screening is the increased identification of CMV-infected infants who can be monitored for progressive and late-onset hearing loss. Recent data from Utah, the first state to implement targeted CMV screening, show that incorporating CMV screenings into an established NHS program actually helped in improving the program's rate of audiological evaluations within 90 days—a milestone in early hearing detection and intervention (*Pediatr.* 2017;139[2]:e20160789). Targeted CMV screening is also cost-effective (*JAMA Pediatr.* 2016;170[12]:1173).

Infants who test positive for CMV should get a follow-up diagnostic laboratory confirmation by 3 weeks of age. Reliable diagnosis of cCMV can only occur within the first three weeks of life, so immediate screening after a failed NHS is practical. After an infant's permanent hearing loss is confirmed, CMV testing will no longer be able to determine the role of CMV in the hearing loss.

Infected infants with CNS and/or multi-organ involvement at birth are recommended to receive antiviral treatment within the first 30 days of life (*Lancet Infect Dis.* 2017; 17[6]:e177). Currently, there is insufficient evidence and consensus on whether to treat CMV-positive infants with transient newborn symptoms or isolated SNHL at birth. It is not recommended to treat infants identified with cCMV but do not have any clinical evidence of the disease in the