

CONGENITAL CMV: A NEW LAW AND WHAT OREGON PROVIDERS NEED TO KNOW

Cytomegalovirus (CMV) infection is common among people of all ages: in the U.S., nearly 1 in 3 children become infected by age 5 years, and more than 50% of the population is infected by age 40 years.¹ Once infected, CMV stays in the body for life and can reactivate from its latent state. Most people who become infected with CMV have few symptoms, or a relatively mild illness, with fever, sore throat, and fatigue. For those who are immunocompromised, or for fetuses *in utero*, however, CMV can have serious consequences; hearing loss is the most common sequelae of congenital cytomegalovirus (cCMV) infection.

In 2017, the Oregon legislature passed HB 2754,^{*} amending the newborn hearing screening statute to include specific information for parents and providers regarding cCMV infection. The statute requires the Oregon Health Authority (OHA) to compile educational information about cCMV for providers and parents, and to recommend a newborn hearing screening schedule and referral for possible cCMV testing, if indicated.

To provide background and assist providers in navigating the legislation, this *CD Summary* reviews what is known about cCMV and hearing loss, presents details of the Oregon legislation, and provides resources for clinicians.

CONGENITAL CMV INFECTION

Cytomegalovirus is one of the most common and yet underrecognized infectious causes of birth anomalies and developmental disabilities for children in the U.S.² An estimated 1 in 200 infants are born with cCMV annually. Of these, approximately 10–15%

are determined to have symptomatic infection and show clinical signs at birth. Symptoms include petechiae, jaundice, small for gestational age, pre-term birth, microcephaly, and hepatosplenomegaly. Permanent sequelae can include microcephaly and neurodevelopmental disorders such as sensorineural hearing loss, vision loss, and intellectual impairment. Because clinical manifestations of cCMV infection can be mild and nonspecific, however, infected infants can remain undiagnosed.

TRANSMISSION

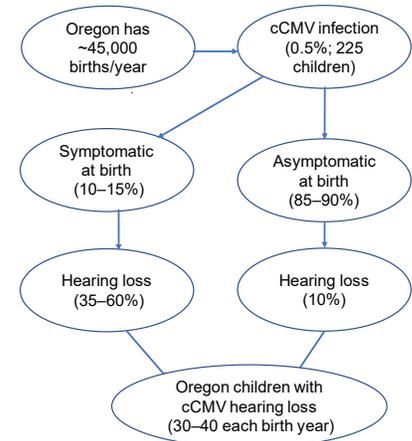
CMV is transmitted through contact with body fluids, such as saliva, urine, blood, tears, semen, and breast milk of an infected person. A woman infected with CMV can transmit the infection to her fetus during pregnancy. Risk of vertical transmission to the fetus in primary infection is approximately 30%, while risk of vertical transmission during reactivation of a latent virus (non-primary infection) is <2%.³

cCMV AND HEARING LOSS

Hearing loss is a common and largely invisible birth anomaly occurring at a rate of about 3 in every 1,000 newborns. Congenital CMV is the causative agent in 20% of cases of congenital hearing loss.³

Sensorineural hearing loss occurs when there is damage or malfunction of the cochlea and/or the auditory nerve from the inner ear to the brain. Among infants with *symptomatic* cCMV infection (10–15%), approximately 35–60% will ultimately have sensorineural hearing loss; among infants with *asymptomatic* infection, approximately 10% will develop childhood sensorineural hearing loss, nearly all within the first 6 years of life (Figure).³ Hearing loss caused by

Figure. Estimated cCMV infections in Oregon



cCMV can have delayed onset and may progress or fluctuate over time.

Hearing losses due to cCMV are significant. In systematic reviews among children with symptomatic or asymptomatic infection at birth, 76% of hearing losses were severe or profound.³ While most children with hearing loss can be expected to perform well with hearing aids, those with profound hearing loss, and some with severe hearing loss, are considered deaf. These children generally do not perform well with hearing aids and may depend on a visual language such as American Sign Language (ASL) or require a cochlear implant.

For children with hearing loss, early identification and intervention, including amplification and support for language acquisition, are crucial. Early childhood is a critical period for brain development. Late identification of hearing loss and delays in receiving supportive services put language acquisition at risk. Oregon law requires newborn hearing screening to be performed on all newborns by age one month. However, because of the potential for delayed onset, newborn hearing screening will not identify all cases of hearing loss ultimately resulting from cCMV.

* www.oregonlegislature.gov/bills_laws/lawsstatutes/2017orlaw0426.pdf

TESTING FOR CONGENITAL CMV

For symptomatic newborns in whom cCMV infection is suspected, the standard diagnostic test is polymerase chain reaction (PCR) for CMV from urine or saliva samples. If saliva is positive, it must be confirmed by urine. Both fluids pose challenges: urine can be tricky to collect by bag in an infant without stool contamination; saliva samples must be collected at least one hour after breastfeeding to prevent contamination from breastmilk. Virus isolation by culture is less sensitive and has a slower turnaround than PCR. Regardless of method, samples should be collected by 21 days of life to distinguish between congenital and postnatal infection, as well as to permit initiation of treatment by age 28 days when indicated.⁴

What about testing of asymptomatic newborns in whom cCMV is not suspected? Despite the health implications of cCMV, consensus regarding screening of asymptomatic newborns is lacking. A targeted approach would refer newborns who do not pass the newborn hearing screening for CMV testing. Currently, the American Academy of Pediatrics does not recommend targeted testing because the majority of children who later develop CMV-associated hearing loss will have normal hearing at birth.⁵ A universal approach would require every newborn be screened for CMV. This screening approach has not been endorsed for inclusion in the Recommended Uniform Screening Panel,⁶ nor have sufficient studies proven that the benefit of detecting all infected infants outweighs the burden to families of a cCMV diagnosis amid uncertainty about treatment and future effects to their child.

TREATMENT

The International Congenital Cytomegalovirus Recommendations Group recommends antiviral therapy using ganciclovir, or its oral version valganciclovir, only for congenitally infected neonates with moderate to severe symptomatic disease.² This definition does not include isolated sensorineural hearing loss. Treatment should be initiated within the first month of life and should not exceed 6 months in duration. Leukopenia, neutropenia, anemia, and thrombocytopenia are frequent adverse effects of treatment. Based on animal stud-

ies, these drugs carry box warnings for fertility impairment, fetal toxicity, mutagenesis, and carcinogenesis. Currently, evidence is lacking for the benefits of treating asymptomatic or mildly symptomatic cCMV infections, although clinical trials are underway.

PREVENTION

The best protection against acquiring CMV infection is good hygiene, including washing hands often with soap and water, especially after contacting a child's body fluids; avoiding sharing food, drinks, utensils, and toothbrushes or putting pacifiers in the mouth; and avoiding contact with saliva when kissing a child.⁷ No vaccine for CMV is currently available, although several are in development.

CONGENITAL CMV-RELATED LEGISLATION IN OREGON

Congenital CMV is not reportable in Oregon, and Oregon-specific data are not currently available. Based on national data, we estimate 225 infants in Oregon exposed to CMV *in utero* are born each year; about 10% of these being symptomatic at birth (Figure, *verso*).

In recent years, 10 states have passed legislation relating to cCMV; four states (CT, IA, NY, UT) mandate targeted testing for infants who do not pass the newborn hearing screening and nine states (CO, HI, ID, IL, IA, NY, OR, TX, UT) mandate provision of parental education about cCMV.[†] Oregon is the latest state to join the second list.

New Oregon legislation (HB 2754) enacted on January 1, 2018, creates requirements related to cCMV for specific groups of health care providers and for the OHA. **Note: the legislation does not mandate either targeted or universal cCMV testing.**

- The new requirements:
- OHA is required to compile educational information about cCMV and make it available for use by hospitals, birthing centers, health care providers, diagnostic audiologists, and the public
 - Hospitals and birthing centers that perform newborn hearing screenings are required to provide information about cCMV to parents and guardians (although to which families is not specified).
 - Diagnostic audiology facilities are required to provide information about

cCMV to parents and guardians of newborn infants diagnosed with hearing loss.

- OHA is required to provide a recommended schedule for newborn hearing screening and referral to health care providers for the purpose of determining whether testing for cCMV is indicated for a newborn child. (NB: the recommended schedule is for hearing screening, not CMV testing.)

FOR MORE INFORMATION

OHA is working with partners to develop materials for health care providers. In the meantime:

- Oregon Public Health Division — Early Hearing Detection and Intervention
www.oregon.gov/oha/PH/HEALTHYPEOPLEFAMILIES/BABIES/HEALTHSCREENING/HEARINGSCREENING/Pages/index.aspx
- CDC — Congenital CMV Infection
www.cdc.gov/cm/clinical/congenital-cmv.html
- CDC — Talking with pregnant patients about CMV: A resource for healthcare providers.
www.cdc.gov/cm/downloads/pregnant-patients-cmv.pdf

REFERENCES

1. Centers for Disease Control and Prevention. Cytomegalovirus (CMV) and congenital CMV infection. See: www.cdc.gov/cm/overview.html. Accessed 1 October 2018.
2. Rawlinson WD, Boppana SB, Fowler KB, Kimberlin DW, Lazzarotto T, Alain S, et al. Congenital Cytomegalovirus infection in pregnancy and the neonate: Consensus recommendations for prevention, diagnosis, and therapy. *Lancet Infect Dis* 2017; 17: e177–88.
3. Goderis J, De Leenheer E, Smets K, Van Hoecke H, Keymeulen A, Dhooge I. Hearing loss and congenital CMV infection: A systematic review. *Pediatrics*. 2014;134:972–82.
4. Pinninti S, Hough-Telford C, Pati S, Boppana S. Cytomegalovirus and Epstein-Barr Virus infections. *Pediatrics in Review* 2016; 37:223–32.
5. American Academy of Pediatrics. Red Book: 2015 Report of the Committee on Infectious Diseases. Kimberlin DW, ed. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015.
6. Health Resources and Services Administration. Advisory Committee on Heritable Disorders in Newborns and Children: Recommended Uniform Screening Panel. Available at www.hrsa.gov/advisory-committees/heritable-disorders/rusp/index.html. Accessed 4 August 2018.
7. Johnson J, Anderson B, Pass RF. Prevention of maternal and congenital Cytomegalovirus Infection. *Clin Obstet Gynecol* 2012; 55: 521–30. doi: 10.1097/GRF.0b013e3182510b7b www.ncbi.nlm.nih.gov/pmc/articles/PMC3347968/

† National CMV Foundation at: www.nationalcmv.org/cm-research/legislation.aspx. Accessed 1 October 2018.



Providence Portland Medical Center designates this enduring material for a maximum of .5 *AMA PRA Category 1 credit™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity. Portland Providence Medical Center is accredited by the Oregon Medical Association to sponsor continuing medical education of physicians.

You can get this document in other languages, large print, braille or a format you prefer. Contact the Public Health Division at 971-673-1222. We accept all relay calls or you can dial 711. for TTY.

