UNIVERSAL NEWBORN CCMV SCREENING POLICY BRIEF

March 2021

CANADA

POSITION

It is the position of the Canadian CMV Foundation that universal newborn cCMV screening within the first 21 days of life be offered in all provinces and territories in Canada. The existing infrastructure for universal newborn screening for other conditions as well as Early Hearing Detection and Intervention (EHDI) programs can be utilized to support timely evaluation, treatment, and follow-up for CMV-infected newborns.

BACKGROUND

Congenital Cytomegalovirus (cCMV) is the most common congenital infection and a leading cause of childhood hearing loss.[1] If cCMV is detected shortly after birth, the child's candidacy for antiviral treatment can be assessed promptly. Interventions including antiviral medications and close follow-up of hearing and early provision of support (such as hearing aids and speech/language therapy), can dramatically improve outcomes for infected infants. Presently, cCMV is not routinely screened for in most provinces, and as such most cases go undiagnosed. Because most babies are asymptomatic or have non-specific symptoms at birth, universal screening is the only way to ensure that all babies with cCMV are diagnosed in a timely matter so that they can receive the care they require.

PREVALENCE STATISTICS

- Approximately 1 in 200 Canadian infants have cCMV.
- Of those, 1 in 5 will have a permanent disability, such as hearing loss, intellectual disability or vision impairment.
- cCMV is the leading cause of non-genetic sensorineural hearing loss
- cCMV has a higher disease burden and causes more disability than all the other congenital conditions that we currently screen for at birth[2]
- Healthcare costs attributable to cCMV are $400 million per year in Canada[3]

CCMV AND HEARING LOSS

Early detection is key. Late-onset and progressive hearing loss commonly occurs in young children with cCMV during the critical period for speech language acquisition. Hearing loss in infancy will negatively impact speech and language development if not identified and managed during the first few months of life. Because late-onset hearing loss is not detected by newborn hearing screening, it typically goes unnoticed for a prolonged period. Therefore, all children with cCMV should be evaluated by an audiologist regularly until the age of 5 years to detect hearing loss as soon as possible and to appropriate intervention.[4]

Economic impact of hearing loss - Research has demonstrated the healthcare costs of one individual with hearing loss is approximately $1.2 million. This includes $280,000 in lifetime costs plus $926,000 in productivity costs. A major contributor to these costs is educational assistance. Estimates of the cost of

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[1] Ross, S. and Boppana, S. (2005). Congenital cytomegalovirus infection: Outcome and diagnosis. *Seminars in Pediatric Infectious Diseases*, 16(1), pp.44-49.

[2] Cannon, M., Griffiths, P., Aston, V. and Rawlinson, W. (2014). Universal newborn screening for congenital CMV infection: what is the evidence of potential benefit? *Reviews in Medical Virology*, 24(5), pp.291-307.

[3] Stratton, K., Durch, J. and Lawrence, R. (2000). *Vaccines for the 21st century*. Washington: National Academy Press.

[4] Fowler, K. (2013). Congenital Cytomegalovirus Infection: Audiologic Outcome. *Clinical Infectious Diseases*, pp. S182-S184.

educational assistance for severe and profound hearing loss with onset before age 6 years range from $135,000 - $290,000[5]

TREATMENT AND FOLLOW UPS

Unfortunately, most cases of cCMV are not being diagnosed. Most babies born with cCMV will be asymptomatic at birth, and approximately 15% of those cases will go on to develop late-onset hearing loss. Almost none of these cases are identified until speech and language delays are obvious. In addition, in the absence of newborn screening, studies have demonstrated that we are only diagnosing a small minority of babies with symptomatic cCMV.[6] A diagnosis of cCMV at birth would ensure proper care and follow-ups for hearing loss or other neurodevelopmental problems.

Sensorineural hearing loss due to cCMV is treatable. Research has shown that antiviral medications significantly improve hearing and cognitive outcomes in newborns that have symptoms at birth. The oral medication, valganciclovir, given twice daily for 6 months is the current standard of care for babies with symptomatic cCMV.[7] Treatment is safe and generally well tolerated. Perhaps even more important is the ability to provide early hearing aids or cochlear implants and speech/language therapy for infected children that develop hearing loss during the early childhood period that is critical for language development. Once delays have occurred, children typically do not catch up. However, if hearing loss is identified promptly through regular audiologic follow-up for children with cCMV, early intervention results in speech/language and educational outcomes that are equivalent to their hearing peers. Universal screening is the only way to ensure we catch these asymptomatic cases.

SCREENING METHODS

CMV is detectable with a simple test at birth, but screening must be done early. Testing for CMV in saliva, urine, or both, as early as possible, is needed since diagnostic tests do not distinguish congenital from postnatal cytomegalovirus infection in newborn babies older than 3 weeks of age who might have acquired the virus at birth or through breastmilk.[8]

Saliva is the gold standard. The high sensitivity (97-100%) and specificity (99.9%) of saliva PCR testing as a screening method have been validated in a large population-based cohort study and is now the accepted gold standard for screening.[9]

COST EFFECTIVENESS OF SCREENING

Screening is affordable. Although CMV tests can vary in costs, it is anticipated that a province-wide saliva CMV screen would cost less than $10 per test to administer. In addition, it is anticipated that as screening becomes more mainstream, costs will continue to decrease.[5]

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[5] Gantt, S., Dionne, F., Kozak, F., Goshen, O., Goldfarb, D., Park, A., Boppana, S. and Fowler, K. (2016). Cost-effectiveness of Universal and Targeted Newborn Screening for Congenital Cytomegalovirus Infection. *JAMA Pediatrics*, 170(12), p.1173.

[6] Vaudry, W. (2014) Congenital cytomegalovirus infection in Canada: Active surveillance for cases diagnosed by paediatricians. *Pediatric Child Health*, e1-e5.

[7] Kimberlin *et al.* (2015) Valganciclovir for Congenital Cytomegalovirus. *New England Journal of Medicine*, 372(25), pp.2462-2463.

[8] Rawlinson, W., *et al.* (2017). Congenital cytomegalovirus infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy. *The Lancet Infectious Diseases*, 17(6), pp.177-e188.

[9] Gantt, S., Bitnun, A., Renaud, C., Kakkar, F. and Vaudry, W. (2017). Diagnosis and management of infants with congenital cytomegalovirus infection. *Paediatrics & Child Health*, 22(2), pp.72-74.

Screening will lead to cost savings. With a universal screening model, symptomatic babies that are currently being missed would be diagnosed and treated, leading to improved outcomes. Among asymptomatic babies, it is estimated that there would be a 12% reduction in the costs of hearing loss owing to the earlier identification of hearing loss that results from cCMV screening and audiologic follow-up.[5] Newborn PCR-based screening programs for other diseases have already demonstrated the possibility for cost savings and the costs of high-throughput molecular diagnostics will likely continue to decrease.

In addition, establishing a universal screening program would increase community awareness. Informing pregnant women can reduce the risk of infection, and reducing cases of primary infections would, in turn, reduce the provincial health care burden.

COMMUNITY READINESS – THE PARENT PERSPECTIVE

For parents, knowing the cause for hearing loss is very important and meaningful. Receiving a timely diagnosis helps avoid the "Diagnostic Odyssey" – meaning fewer unnecessary tests, anticipatory guidance, and the comfort of putting a name to a disease.[2] When asked, 84% of parents stated they would want to know if their child has cCMV, even if they never develop problems.[10] Throughout the first year of Ontario's program, 93% of parents consented to having their newborn screened for cCMV. Simply put – parents want to know and they have the right to know.

OTHER JURISDICTIONS

Alberta	No province-wide screening measures in place
British Columbia	Targeted screening protocols in place
Manitoba	Targeted screening protocols in place
New Brunswick	No province-wide screening measures in place
Newfoundland	No province-wide screening measures in place
Nova Scotia	No province-wide screening measures in place
Ontario	Universal screening in place – as hearing loss risk factor
PEI	No province-wide screening measures in place
Quebec	No province-wide screening measures in place
Saskatchewan	No province-wide screening measures in place

CONCLUSION

Congenital CMV can cause significant morbidity and is preventable and treatable. If detected early, developmental outcomes of affected children are dramatically improved with appropriate interventions. However, without newborn screening for cCMV, the vast majority of infected children go undiagnosed resulting in missed opportunities to provide the current standard of care. Not only is CMV testing affordable, but studies have found that universal newborn CMV screening results in long-term cost savings by reducing the burden of lifelong neurodevelopmental disability. Ontario's successful universal newborn CMV screening in Canada serves as a precedent. Along with newborn CMV screening, there is a need for improved knowledge and training for healthcare providers, clinical guidelines, increased awareness and public education about the best practices for cCMV screening and care.

[10] Din, E., Brown, C., Grosse, S., Wang, C., Bialek, S., Ross, D. and Cannon, M. (2011). Attitudes Toward Newborn Screening for Cytomegalovirus Infection. PEDIATRICS, 128(6), pp.e1434-e1442.