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Newborn Screening for Congenital Cytomegalovirus in Canada

Key Messages

What Is the Issue?

- Congenital cytomegalovirus (cCMV) infection is a leading cause of childhood hearing loss. It is estimated that 85% to 90% of newborns infected with cCMV will not show any symptoms at birth. Of those newborns with cCMV infection who are asymptomatic at birth, 10% to 15% will go on to develop long-term symptoms, including vision loss, hearing loss, and developmental delays.

What Did We Do?

- This brief provides a summary about newborn screening for cCMV in Canada, including whether screening is available for cCMV in each province and territory, and if so, whether screening is universal or targeted using publicly available information.

What Did We Find?

- Currently in Canada, 4 provinces (Alberta, Saskatchewan, Manitoba, Ontario) have or are implementing universal newborn screening for cCMV. Three provinces (British Columbia, New Brunswick, Nova Scotia) have province-wide targeted screening programs that offer cCMV testing to newborns who fail newborn hearing tests or who have suspected cCMV as identified by a clinician. Current clinical guidance and practice remain mixed on whether targeted or universal newborn screening is recommended, with each having a different distribution of benefits and harms.
- cCMV infections can be detected using blood, urine, or saliva tests. Most universal newborn screening programs use dried blood spot tests, which are likely to produce false-negative results; saliva tests have a lower number of false-negative results but can result in a higher number of false-positives. Some programs recommend additional testing using a different method (either saliva or urine) after an initial positive test as a validation.

What Does This Mean?

- As both universal and targeted newborn screening programs have been adopted by several jurisdictions in Canada, there is wide recognition that cCMV infection is a serious health issue and that early detection is important. Moreover, there is an opportunity to generate data and evidence about test performance and program impact over time that could support future decision-making. As evidence and new test and treatment options become available, such data will help to inform the type of newborn screening approach used for cCMV.

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Abbreviations

ACHDNC	Advisory Committee on Heritable Diseases in Newborns and Children
cCMV	congenital cytomegalovirus
CMV	cytomegalovirus
NBS	newborn screening
PCR	polymerase chain reaction
RUSP	Recommended Uniform Screening Panel

Context

This brief provides a summary about newborn screening for cCMV in Canada, including whether screening is available for cCMV in each province and territory, and if so, whether screening is universal or targeted. [Newborn screening](#) refers to testing done shortly after birth to check for serious but treatable diseases. It helps to identify certain conditions as early as possible to prevent serious health problems.

We used publicly available information identified through a targeted keyword search for publications and websites from ministries of health, regional health authorities, and newborn screening programs, supplemented with survey data gathered through CADTH's connections to provincial and territorial newborn screening programs. The data were used to inform the context surrounding cCMV infection, including available screening tools and types of newborn screening programs for cCMV that are adopted.

Further information about evidence on the clinical utility, cost-effectiveness, and clinical guidelines for universal versus targeted cCMV screening in newborns can be found in a companion report on this topic, [Newborn Screening for Congenital Cytomegalovirus](#).¹

What Is cCMV?

Cytomegalovirus (CMV) is a common herpes virus, and it is estimated that 60% to 90% of adults have been infected.² With the exception of those adults who have weakened immune systems, most people who are infected have no symptoms.³

CMV can be transferred from person to person through bodily fluids (i.e., saliva, blood, breast milk, vaginal fluids, and semen).⁴ cCMV occurs when a fetus is infected with CMV in utero by blood through the placenta; it is the most common congenital infection, affecting 1 in 200 newborns,³ and it is a reportable public health infection in 6 provinces and territories in Canada ([Appendix 1](#)).

Similar to CMV infections, 85% to 90% of newborns infected with cCMV will not show any symptoms at birth.³ Of the estimated 10% of newborns with symptoms at birth, they can present with premature birth, low birth weight, small head size, yellow skin and eyes (jaundice), enlarged and poorly functioning liver, enlarged spleen, purple skin splotches and/or rash, pneumonia, and seizures. Of those newborns with cCMV infection who are asymptomatic at birth, 10% to 15% will go on to develop long-term symptoms, including vision loss, hearing loss, and developmental delays.⁵ Permanent hearing loss, either present at birth or developing thereafter, is a common symptom of cCMV infection, as cCMV is the leading cause of sensorineural hearing loss in infants and children.⁶

Currently there are no approved vaccines or preventive therapies for cCMV; however, [phase III clinical trials are underway in Canada](#). Prevention strategies involve education and health promotion aimed at pregnant people about the risk of contagion and offering hygiene strategies for avoiding the likelihood of transmission.⁴ Therapies for newborns and infants with confirmed cCMV include using antivirals (e.g., valganciclovir and ganciclovir) from 1 month to 6 months of age.⁴

Because the symptoms of cCMV develop over time, many guidelines and clinical practices involve monitoring newborns through childhood for symptoms of cCMV. Guidelines from the Canadian Pediatric Society recommend that newborns who are diagnosed with cCMV be monitored for several years for hearing, vision, and neurologic symptoms.⁴ As an illustrative example, in British Columbia, the [care pathway](#) for a newborn with confirmed cCMV is a direct referral for an auditory brainstem response assessment, and depending on the results of the assessment, the newborn will be referred for either ongoing monitoring or early intervention.

Universal Versus Targeted Newborn Screening for Congenital Cytomegalovirus

Newborn screening programs have been implemented to identify newborns infected with cCMV. Such programs can be universal (i.e., aiming to screen all newborns born in their jurisdiction) or targeted (i.e., aiming to screen newborns who are symptomatic or deemed to be at high risk). Universal screening for cCMV in newborns is typically implemented by expanding the conditions screened for by existing newborn screening programs for inborn errors of metabolism. These programs most frequently use dried blood spot samples to identify potentially infected newborns, after which additional protocols are initiated for diagnosis (i.e., confirmatory urine or saliva testing) and early intervention, treatment, and monitoring for cCMV. Targeted screening programs are those that screen for cCMV in newborns who are symptomatic or at high risk. Targeted cCMV screening is frequently implemented as part of universal newborn hearing screening programs, through which all newborns undergo a hearing test by 1 month of age, and those newborns who fail hearing tests are tested for potential cCMV.⁷ Typically, targeted screening programs offer cCMV testing to those newborns with confirmed results from 1 or 2 hearing tests, depending on a program's algorithms. Targeted screening may miss those newborns who do not have hearing loss and are asymptomatic but develop symptoms at a later stage in life.^{4,6}

There are few jurisdictions that have implemented universal screening for cCMV. For example, in the US, [Minnesota is the first state that has implemented universal screening of all newborns for cCMV](#), while [Connecticut is planning to implement universal cCMV screening by 2025](#). Currently, 9 states (Connecticut, Florida, Iowa, Kentucky, Louisiana, New York, Texas, Utah, and Virginia) have state-wide targeted newborn screening programs, with Colorado initiating its targeted screening in March 2024.⁸

The limited number of states with universal newborn screening is likely due to cCMV not being currently recommended on the US Recommended Uniform Screening Panel (RUSP), a federal list of conditions recommended for screening by state newborn screening programs. In 2020, the Advisory Committee on Heritable Diseases in Newborns and Children (ACHDNC) [considered a nomination](#) to add cCMV to the RUSP. Based on the information provided in the nomination at the time, the committee did not proceed with an evidence review to further consider adding cCMV to the panel. In their [letter to the nominator](#), the committee noted that there were questions about the potential benefits and harms of universal newborn screening for cCMV. Given that the majority of asymptomatic newborns who are diagnosed with a cCMV infection will not

develop any further symptoms, there were questions about the potential harms of diagnosis and long-term monitoring for symptoms. Further, the benefits of early diagnosis and treatment as opposed to treating or managing symptoms was unclear. The committee requested data from a US-based pilot study to generate data for evaluating the clinical utility of universal newborn screening for cCMV.

More recently, the Institut national d'excellence en santé et en services sociaux (INESSS) in Quebec recommended [not adding universal screening for cCMV infection](#) to the blood testing platform of the Quebec newborn screening program because of the lack of evidence of its effectiveness, the absence of reliable markers to discern the severity of cases, and the risk of overdiagnosis (absence of health gains) for most of the asymptomatic children detected, and because no program that has implemented universal cCMV screening has published results yet. Similar to the ACHDNC conclusion, the INESSS recommendation pointed to limited evidence on the population benefits of universal cCMV screening and the potential harms of diagnosing large numbers of asymptomatic patients. Health system capacity considerations, which are a common criterion used by universal newborn screening programs in deciding whether to add a condition to a list,⁹ were raised, particularly as Quebec is finalizing the implementation of its universal newborn hearing screening program, which could have benefits for symptomatic newborns.¹⁰

Clinical guidelines are mixed on recommending universal versus targeted newborn screening for cCMV. A companion report, which searched for evidence-based guidelines for cCMV screening in newborns, found 2 publications that did not recommend universal screening and 1 that did recommend it.¹ Universal screening programs appear to be cost-effective when compared to targeted screening programs; for details on evidence regarding cost-effectiveness, refer to the companion report [Newborn Screening for Congenital Cytomegalovirus](#).¹ In general, clinical guidelines do not recommend universal screening for people with CMV who are pregnant.¹¹ Some guidelines recommend targeted screening for people who are pregnant and who are at high risk of CMV infection and symptoms, including immunocompromised people and people with children at home who are younger than 3 years.^{11,12}

cCMV Screening for Newborns in Canada

Both universal and targeted newborn screening programs for cCMV are currently implemented in Canada. [Table 1](#) describes the status of newborn screening for cCMV across Canada, using information from publicly available sources.

Ontario and Saskatchewan screen for cCMV through their universal dried blood spot newborn screening programs. In 2023, Alberta announced that it was adding cCMV to its universal dried blood spot newborn screening program, and the government of Manitoba announced in its 2024 budget that it would be funding universal newborn screening for cCMV.

Ontario's universal newborn screening program is integrated with its universal newborn hearing screening program. Ontario currently uses the results from the dried blood spot test to identify those newborns who have markers for permanent hearing loss including cCMV. Ontario's [province-wide protocol](#) provides that newborns who are identified with cCMV through newborn dried blood spot testing are referred directly for an

audiological assessment. If a newborn passes the assessment, depending on their clinical situation, they will be referred to either basic or intensive surveillance.

Three provinces (British Columbia, New Brunswick, Nova Scotia) have province-wide protocols for targeted screening for cCMV in newborns with suspected cCMV, as identified by a physician or who have failed a newborn hearing test. For targeted cCMV screening programs, typically these are conducted through universal newborn hearing programs that aim to screen all newborns, typically by 1 month of age. Not all provinces and territories have an established universal newborn hearing screening program.

Table 1: cCMV Screening in Newborns in Canada^a

Jurisdiction ^b	Universal newborn screening (dried blood spot)	Targeted newborn screening ^c
BC	No	CMV saliva PCR testing is offered for any newborn with suspected cCMV infection, including those who fail a newborn hearing screening test.
AB	Yes (announced in 2023 , currently being implemented)	None
SK	Yes (since 2022)	None
MB	Yes (announced in 2024 , to be implemented)	Dried blood spot screening is offered for any newborn with suspected cCMV infection, including those who fail a newborn hearing screening test.
ON	Yes (since 2019)	None
QC	No (reviewed in March 2024)	None
NB	Under consideration	Physicians and audiologists can send dried blood spot samples from infants with suspected cCMV for testing at CHEO in Ontario.
PE	Under consideration	Physicians and audiologists can send dried blood spot samples from infants with suspected cCMV for testing at CHEO in Ontario.
NS	Under consideration	Physicians and audiologists can send dried blood spot samples from infants with suspected cCMV for testing at CHEO in Ontario.
NL	No	None

AB = Alberta; BC = British Columbia; cCMV = congenital cytomegalovirus; CHEO = Children's Hospital of Eastern Ontario; MB = Manitoba; NB = New Brunswick; NBS = newborn screening; NL = Newfoundland and Labrador; NS = Nova Scotia; ON = Ontario; PE = Prince Edward Island; QC = Quebec; SK = Saskatchewan.

^aInformation identified from [CANScreen](#) and [CMV Canada](#).

^bPEI and NB participate in the [IWK Maritime Newborn Screening Program](#). Yukon, the Northwest Territories, and Nunavut are not included in this table, as they rely on NBS programs in other jurisdictions and do not have their own NBS infrastructure. Newborns in Yukon are screened through BC's program, the Northwest Territories use Alberta's program, and Nunavut uses the programs from AB, MB, and ON, depending on the region.

^cTargeted newborn screening programs are province-wide protocols that provide cCMV testing to all high-risk newborns, typically those who fail hearing tests.

Note: Not all jurisdictions [have province-wide universal newborn hearing programs](#).

Screening Tests for cCMV

Screening for cCMV is typically recommended to take place before an infant is 21 days old, because after this point in time, testing cannot differentiate between a congenital and a perinatal or postnatal CMV infection.⁶ Screening tests can use blood, saliva, or urine samples to confirm the presence of CMV or CMV antibodies. Laboratories can culture the virus in samples or use polymerase chain reaction (PCR) testing to detect the presence of the virus. Most commonly, saliva PCR tests or urine (either culture or PCR) tests are recommended as standards to diagnosis cCMV.^{4,6,10} Immunoglobulin testing for immunoglobulin M or immunoglobulin G antibodies to cCMV (using a blood sample) is another method of testing; however, these tests are not widely available, used, or recommended for cCMV screening or diagnosis in newborns.^{4,5}

While the reported performance of different methods of testing for cCMV vary,¹³ dried blood spot PCR testing is consistently reported to be less sensitive (i.e., classifying true positives as falsely negative) than either saliva or urine PCR testing.^{5,6,10} The reported performance of dried blood spot tests has led Newborn Screening Ontario to initiate a [pilot](#) (in February 2024) to determine whether dried blood spot testing or dried saliva spot testing is the most appropriate method. Saliva PCR testing is reported to have a slightly higher rate of false-positives and false-negatives than urine PCR testing, but saliva is a much easier sample to obtain.⁵ For the purposes of diagnosis, some programs recommend additional testing using a different method (either saliva or urine) after an initial positive test (whether dried blood spot, urine, or saliva).^{4,6}

Future Considerations

cCMV is a condition with active interest. Researchers are studying ways to optimize methods of testing for cCMV, including dried blood spot tests;¹⁴ improve algorithms used in targeted screening programs to capture those with cCMV beyond hearing outcomes;⁷ and understand the long-term consequences of cCMV infections, which are not well characterized. Treatment options and evidence of their effectiveness for preventing the long-term health impacts of cCMV infections are also needed,¹⁰ and potential vaccines for cCMV would lead to further changes to the newborn screening for cCMV landscape.

As both universal and targeted newborn screening programs have been adopted by several jurisdictions in Canada, there is wide recognition that cCMV infection is a serious health issue and that early detection is important. Moreover, there is an opportunity to generate data and evidence about test performance and program impact over time that could support future decision-making. As evidence and new test and treatment options become available, such data will help to inform the type of newborn screening approach for cCMV.

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Appendix 1: Public Health Reporting of cCMV in Canada

Note that this appendix has not been copy-edited.

Six jurisdictions in Canada have a protocol for notifying public health about identified cCMV infections. [Table 2](#) presents whether cCMV is a reportable disease in provinces and territories across Canada.

Table 2: cCMV as a Reportable Disease in Canada

Province	cCMV a reportable condition
Alberta	Yes
British Columbia	Yes
New Brunswick	Yes
Northwest Territories	Yes
Nunavut	Yes
Yukon	Yes
Manitoba	No
Newfoundland and Labrador	No
Nova Scotia	No
Ontario	No
Prince Edward Island	No
Quebec	No
Saskatchewan	No

cCMV = congenital cytomegalovirus.

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