Committee: Infectious Disease
Title: Standardized Surveillance Case Definitions for Congenital Cytomegalovirus (cCMV) Infection and Disease

Check this box if this position statement is an update to an existing standardized surveillance case definition and include the most recent position statement number here: N/A.

Synopsis:
- This position statement creates standardized case definitions for cCMV infection and disease.
- Standardized case definitions for cCMV infection and disease are needed because multiple jurisdictions in the United States are conducting cCMV screening and surveillance activities but are using various methods and inclusion criteria for case ascertainment, reporting, and classification. As more jurisdictions pass legislation for newborn screening for cCMV, standardized case definitions for cCMV infection and disease can be used to understand the epidemiology of cCMV and compare trends across the United States.
- Case ascertainment criteria include laboratory criteria (the detection of CMV in neonatal urine, saliva, whole blood, or cerebrospinal fluid specimens, in amniotic fluid specimens, or umbilical cord or autopsy specimens), vital records criteria (infant death certificates), and healthcare records criteria (e.g., using ICD-10 diagnostic codes).
- Case classification criteria include clinical and laboratory criteria.
- Case classifications include confirmed cCMV infection, confirmed cCMV disease, and probable cCMV disease.

I. Statement of the Problem
Cytomegalovirus (CMV) infection during pregnancy can cause stillbirth, infant death, and a myriad of birth defects.1-3 In the United States (U.S.), approximately 1 in 200 babies is born with congenital CMV (cCMV) infection; one out of 5 of these babies will present with clinical signs of cCMV disease in the neonatal period and/or have long-term health conditions.4 cCMV is the most common infectious cause of developmental disabilities and non-genetic sensorineural hearing loss (SNHL) in U.S. children.5-8 Nonetheless, the burden of cCMV disease is not fully understood.9-11

Surveillance of cCMV in the U.S. is complicated by several factors. First, most newborns with cCMV infection have no clinical signs at birth and, without universal cCMV screening, are not identified.12,13 Second, neonatal clinical signs of cCMV disease are nonspecific and may be attributed to other conditions.14 Third, postnatal CMV infection is common among infants, and a reliable diagnosis of cCMV infection or disease may not be possible unless specimens are collected within the first three weeks of life.15 Finally, not all newborns with a laboratory diagnosis of cCMV infection receive a diagnostic code that would allow cases to be ascertained through a review of administrative data.16

II. Background and Justification
CMMV infection is responsible for an estimated 5-10% of cases of prelingual hearing loss among children less than 2 years of age, and an estimated 15-20% of moderate to profound bilateral SNHL among all U.S. children.7,17 A substantial proportion of cCMV-related SNHL cases occur in children with cCMV infection who do not have apparent clinical signs at birth, including those who pass the newborn hearing screen.18 Early identification and timely and appropriate intervention services are critical for improving developmental outcomes of deaf or hard-of-hearing children.19-22 Consequently, the Joint Committee on Infant Hearing recommends that all infants who test positive for cCMV receive periodic audiologic monitoring beginning no later than three months of age to allow for the provision of appropriate amplification, early intervention, and family support.23 Jurisdictional programs that monitor children with
cCMV infection or disease can assist providers and families by connecting them with resources and early intervention services. With current testing and surveillance practices, it is estimated that less than 10% of infants with cCMV infection are identified annually.24

In the U.S., cCMV infection has not yet been added by the Advisory Committee on Heritable Disorders in Newborns and Children to the Recommended Uniform Screening Panel.25 In 2013, Utah began hearing-targeted screening for infants who refer on (i.e., do not pass) their newborn hearing screening and, in 2019, expanded screening to infants at high risk of cCMV disease, such as infants presenting with select clinical, laboratory, or brain imaging findings at birth, and those with maternal history of CMV infection during pregnancy.24 In subsequent years, other states, including Connecticut, Florida, Iowa, Kentucky, Maine, New York, Pennsylvania, and Virginia, have passed legislation for hearing-targeted screening. In 2022, universal newborn cCMV screening was approved in Minnesota, and conditionally approved in New Jersey. Minnesota began screening newborns for cCMV using dried blood spot (DBS) specimens in February 2023.

While cCMV screening strategies and provider awareness may influence the likelihood of diagnosing cCMV infection or disease in infants, prevalence is also likely to vary across jurisdictions due to several factors, including maternal age and racial and ethnic composition of the population.4 Currently, routine cCMV surveillance is conducted in 10 states. However, surveillance methods vary greatly, and a standardized cCMV case definition is lacking.24

Standardized case definitions for cCMV infection and disease would allow for comparisons of infection and disease prevalence among jurisdictions with different cCMV screening strategies and provide evidence to inform national newborn screening policy. Because most infants with cCMV infection never develop sequelae, quantifying the proportion of infants with cCMV disease likely to benefit from universal newborn screening, as compared to current standards of care (testing of newborns with clinical evidence of CMV-associated findings), is of critical importance.26

Jurisdictions conducting or planning to implement cCMV surveillance with or without newborn screening may be uniquely suited to address this question. Jurisdictions may utilize data from cCMV surveillance to inform prevention efforts such as educational and awareness campaigns. Furthermore, standardized case definitions and validated methods for ascertaining cases of cCMV disease will be increasingly important to determine baseline case burden and prevalence of cCMV disease prior to licensure and routine use of CMV vaccines.27

This position statement establishes standardized cCMV case definitions for jurisdictions that wish to include cCMV infection and disease in their list of reportable conditions or conduct pilot studies or surveillance. Though this case definition is not intended for clinical use, public health officials could utilize it to provide feedback to healthcare providers and the public about the estimated burden and trends of cCMV infection and disease in their regions.

III. Statement of the Desired Actions to be Taken

CSTE recommends the following actions:

1. Implement standardized surveillance case definitions for cCMV infection and disease.

   A. Utilize standard sources (e.g., reporting*) for case ascertainment for cCMV infection and disease. Surveillance for cCMV infection and disease should use the recommended sources of data to the extent of coverage presented in Section V.

   B. Utilize standardized criteria for case ascertainment for cCMV infection and disease presented in Section VI and Table VI in Technical Supplement.

   C. Utilize standardized criteria for case classification for cCMV infection and disease presented in Section VII and Table VII in Technical Supplement.

* Reporting: process of a healthcare provider, laboratory, or other entity submitting a report (case information) of a condition under public health surveillance to local, state, or territorial public health. Note: notification is the process of a local, state, or territorial public health authority submitting a report (case information) of a condition on the Nationally Notifiable Conditions List to CDC.
IV. Goals of Surveillance

The goal of cCMV surveillance is to provide information on the burden of cCMV infection and disease in the U.S. and inform strategies to prevent cCMV-associated disability. cCMV surveillance may facilitate clinical follow-up, including connection to early intervention services for infants identified with cCMV infection and disease. Surveillance will help identify groups at higher risk of cCMV infection and disease and guide strategies to improve equity in access to services. Additionally, cCMV surveillance may provide data to inform provider and public awareness and educational activities.

V. Recommended Data Sources and Methods for Surveillance

Surveillance for cCMV infection and disease should use the following recommended sources of data and/or methodologies and the extent of coverage listed in Table V.

The most common data source for case ascertainment will be laboratory reporting. cCMV cases meeting the laboratory criteria as described in Section VI should be reported to the public health authorities within seven days of positive test result. Vital records data, birth defects registries, and diagnostic code data (see Appendix A) may be used as supplementary data sources for case finding. Universal newborn screening for cCMV, or targeted testing of high-risk populations, such as infants who refer on their newborn hearing screening, are used for identifying newborns with cCMV; follow-up testing may be required for infants who screen positive for cCMV. Laboratory testing for cCMV may be performed for diagnostic purposes when suspected by a clinician based on the presence of neonatal clinical signs, abnormal fetal ultrasound findings, or following a diagnosis of CMV infection in the gestational parent during pregnancy. Clinical information will be obtained from clinician reporting or review of medical records for case classification (see clinical requirements in Section VII).

Table V. Recommended Sources of Data, Surveillance Methods, and Extent of Coverage for Ascertainment of Cases of cCMV Infection and Disease.

<table>
<thead>
<tr>
<th>Source of Data/Methodology for Case Ascertainment</th>
<th>Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Population-Wide</td>
</tr>
<tr>
<td>Clinician reporting</td>
<td>X</td>
</tr>
<tr>
<td>Laboratory reporting</td>
<td>X</td>
</tr>
<tr>
<td>Reporting by other entities, specify:</td>
<td>X</td>
</tr>
<tr>
<td>● Hospitals, clinics, or provider offices</td>
<td></td>
</tr>
<tr>
<td>● Pharmacies</td>
<td></td>
</tr>
<tr>
<td>● Other healthcare providers (e.g., midwives, public health nurses)</td>
<td></td>
</tr>
<tr>
<td>Death certificates</td>
<td>X</td>
</tr>
<tr>
<td>Hospital discharge or outpatient records</td>
<td>X</td>
</tr>
<tr>
<td>Data from electronic medical records</td>
<td>X</td>
</tr>
<tr>
<td>Telephone or online survey</td>
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<tr>
<td>School-based survey</td>
<td></td>
</tr>
<tr>
<td>Other, specify:</td>
<td>X</td>
</tr>
<tr>
<td>● Autopsy reports</td>
<td></td>
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<tr>
<td>● Vital Records</td>
<td></td>
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<tr>
<td>● Birth Defect Registries</td>
<td></td>
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<tr>
<td>● Early Hearing Detection and Intervention (EHDI) Information Systems</td>
<td></td>
</tr>
<tr>
<td>● Early Intervention Referrals</td>
<td></td>
</tr>
</tbody>
</table>
VI. Criteria for Case Ascertainment

Case ascertainment is the process through which public health identifies potential cases of a disease or condition using data reported or provided to public health by healthcare, laboratories, and other reporting entities. This public health reporting is triggered by the case ascertainment criteria (a single criterion or a combination of criteria) included in this position statement, and each initial report sent to public health should include common data elements and disease-specific data elements. Case ascertainment criteria are not intended to be used for clinical diagnosis purposes.

A. Narrative: A description of suggested criteria for case ascertainment of a specific condition and recommended reporting procedures.

In public health jurisdictions conducting surveillance for cCMV, healthcare practitioners (including healthcare facilities and medical laboratories) should report cases of infection or disease that meet any of the laboratory, vital record, or healthcare record criteria for reporting, among children born in the jurisdiction. Case ascertainment criteria are intended to be used to identify potential cases for further investigation. Reported cases will be further reviewed for case classification.

Reporting of cCMV should be ongoing and routine.

Report to public health authorities infants or children meeting any of the following criteria:

A1. Clinical Criteria for Reporting
N/A

A2. Laboratory Criteria for Reporting
- Detection of CMV DNA by polymerase chain reaction (PCR or other nucleic acid amplification testing [NAAT]) from infant† urine, saliva, whole blood (including dried blood spot [DBS]), or cerebrospinal fluid (CSF) specimen, OR
- Detection of CMV DNA by NAAT from an amniotic fluid specimen, OR
- Isolation of CMV in viral culture from infant† urine, saliva, whole blood, or CSF specimen, OR
- Isolation of CMV in viral culture from an amniotic fluid specimen, OR
- Demonstration of CMV antigen in a biopsy from umbilical cord or autopsy specimen by immunohistochemical methods (IHC), OR
- Detection of CMV antigen by antigenemia test in infant† whole blood specimen

† Infant is defined as less than one year of age. Note: Jurisdictions to determine reporting cutoff based on capacity, e.g., 45 days, 90 days, 6 months, one year.

A3. Epidemiologic Linkage Criteria for Reporting
N/A

A4. Vital Records Criteria for Reporting
- An infant aged one year or less whose death certificate lists cCMV or CMV as an underlying cause of death or significant condition contributing to death.

A5. Healthcare Record Criteria for Reporting
- A child aged 6 years or younger whose healthcare record contains a diagnosis* of cCMV infection, OR
- An infant aged 45 days or younger whose healthcare record contains a diagnosis* of CMV disease.

* See Appendix 1 for diagnostic codes.

B. Disease-Specific Data Elements to be Included in the Initial Report

Disease-specific data elements should be included in addition to the common data elements that are to be reported for all initial individual case reports (see CSTE Position Statement 09-SI-01 “Common Core Data Elements for

- Reason test was ordered for laboratory tests, when available.
- Date of death for death certificates.

VII. Case Definition for Case Classification

This case definition for case classification is intended solely for public health surveillance purposes and does not recommend criteria for clinical diagnosis purposes. Once a public health agency has ascertained data on potential cases of a disease or condition from reporting entities, the public health agency assigns case statuses based on the case classifications included within this position statement.

A. Narrative: A description of criteria to determine how public health should classify a case of cCMV infection or disease.

CMMV infection and disease are conditions caused by in utero infection with CMV. A wide spectrum of severity exists, from clinically inapparent infection to severe disease that is clinically apparent at birth or manifests as sequelae. The following guidelines are intended to be used for the purposes of cCMV surveillance and not intended to be used as a guide to clinical management of cCMV infection or disease.

A1. Clinical Criteria

Cases should be assessed according to absence or presence of clinical evidence as defined below and the clinical data should be included in the case investigation.

In the absence of a more likely alternative etiology:

- An infant with at least one of the following clinical signs during the neonatal period:28,29
  - Hepatomegaly
  - Splenomegaly
  - Petechial rash or purpura ("blueberry muffin rash"),

  OR

- A child aged 6 years or younger with one or more of the following permanent conditions:28,29,30
  - Microcephaly (defined as head circumference measurement >2 standard deviations below the average (or <3rd percentile) for the same age and sex, notation in the medical record, or diagnostic code of microcephaly (e.g., ICD-10 code Q02),
  - Brain imaging abnormalities consistent with cCMV, such as intracranial calcifications, periventricular calcifications, leukomalacia, polymicrogyria, lissencephaly, pachygyria, schizencephaly, or ventriculomegaly
  - Sensorineural hearing loss
  - Seizures
  - Cerebral palsy
  - Chorioretinitis
  - Vision impairment, resulting from conditions consistent with cCMV, such as retinitis, retinal scarring, optic neuritis, optic atrophy, or brain damage resulting in cortical vision impairment

A2. Laboratory Criteria*

Confirmatory Laboratory Evidence†:

- Absence of a negative test (CMV DNA by NAAT or culture) on a urine specimen collected within 21 days of life, AND
- Detection of CMV DNA by NAAT from urine, whole blood (including dried blood spot [DBS]), or cerebrospinal fluid (CSF) collected from an infant within 21 days of life, OR
- Detection of CMV DNA by NAAT from amniotic fluid specimen, OR
- Isolation of CMV in viral culture from urine, whole blood, or CSF collected from an infant within 21 days of life, OR
- Isolation of CMV in viral culture from amniotic fluid specimen, OR
- Demonstration of CMV antigen in an autopsy specimen by IHC, OR
- Detection of CMV antigen by antigenemia test in whole blood collected from an infant within 21 days of life.

**Presumptive Laboratory Evidence:**
- Absence of a negative test (CMV DNA by NAAT or culture) on a urine specimen collected within 21 days of life, AND
- Detection of CMV DNA by NAAT from saliva collected from an infant within 42 days of life, OR
- Isolation of CMV in viral culture from saliva collected from an infant within 42 days of life, OR
- Detection of CMV DNA by NAAT from urine, whole blood, or CSF collected from an infant within 22–42 days of life, OR
- Isolation of CMV in viral culture from urine, whole blood, or CSF collected from an infant within 22–42 days of life.

* Note: The categorical labels used here to stratify laboratory evidence are intended to support the standardization of case classifications for public health surveillance. The categorical labels should not be used to interpret the utility or validity of any laboratory test methodology.

† Only valid in the absence of a subsequent negative test on a urine specimen that was completed for confirmatory purposes.

§ If CMV is detected in saliva, repeat testing should be performed using urine.

¶ Only valid in the absence of a prior negative test on a urine specimen collected within 21 days of life.

### A3. Epidemiologic Linkage Criteria
N/A

### A4. Case Classifications
**Confirmed:**
- cCMV infection: Meets confirmatory laboratory evidence.
- cCMV disease: Meets clinical criteria AND confirmatory laboratory evidence.

**Probable:**
- cCMV disease: Meets clinical criteria AND presumptive laboratory evidence.

**Notes:**
- Cases of confirmed cCMV infection may be reclassified as confirmed cCMV disease if clinical evidence is subsequently identified after birth or later in childhood.
- Detection of CMV DNA by NAAT or culture from saliva collected from an infant within 21 days of life is considered as presumptive laboratory evidence because false-positive results may occur. Therefore, repeat testing using urine is recommended.
- Cases with clinical evidence of cCMV disease and presumptive lab evidence are classified as probable cCMV disease. This is done to reflect the uncertainty of lab evidence. Positive results on diagnostic testing performed after 21 days of life could pick up cases of postnatal CMV infection, which is often asymptomatic in term newborns but may present with clinical signs that may also occur in cCMV disease (e.g., hepatosplenomegaly, petechiae, thrombocytopenia), particularly in very low birth weight and preterm newborns.31
- Case classifications include confirmed cCMV infection to capture newborns that will mainly be identified via newborn screening, both universal and hearing-targeted. Most infected newborns will not have clinical signs of disease, including some who do not pass the newborn hearing screening but have normal hearing upon diagnostic audiologic evaluation. Whereas the estimated cCMV prevalence is 4.5 per 1,000 live births, incidence of acquired postnatal infection is at least 3% by 4-6 weeks of life32, increasing the probability of postnatal infection in infants with any positive test result in specimens collected between 22-42 days of life. Therefore, case classifications do not include “probable” cCMV infection, which could impact jurisdictional efforts on longitudinal data collection for permanent conditions.
B. Criteria to Distinguish a New Case of cCMV infection from Reports or Notifications which Should Not be Enumerated as a New Case for Surveillance

A case should be enumerated as a new case if not previously reported.

Note: If a case was previously reported as cCMV infection but later meets criteria for cCMV disease the case would not be counted as a new case but a re-classification.

VIII. Period of Surveillance

Surveillance is expected to be ongoing.

IX. Data Sharing/Release and Print Criteria

CSTE recommends the following case statuses* be included in the ‘case’ count released outside of the public health agency:

- Confirmed
- Probable
- Suspect
- Unknown

*Which case statuses are included in case counts constitute the “print criteria.”

Jurisdictions (e.g., States and Territories) conducting surveillance under this case definition can voluntarily submit de-identified case information to CDC, if requested and in a mutually agreed upon format.

Production of national data summaries and national data re-release for non-NNCs:

- Prior to release of national data summaries CDC should follow the CDC/ATSDR Policy on Releasing & Sharing Data, issued on April 16, 2003 and referenced in 11-SI-01 and custodians of such data should consult the CDC-CSTE Intergovernmental Data Release Guidelines Working Group report (www.cste2.org/webpdfs/drgwgreport.pdf) which contains data release guidelines and procedures for CDC programs re-releasing state, local, or territorial-provided data.
- CDC programs have a responsibility, in collaboration with states, localities, and territories, to ensure that CDC program-specific data re-release procedures meet the needs of those responsible for protecting data in the states and territories.

X. Revision History

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<tr>
<th>Position Statement ID</th>
<th>Section of Document</th>
<th>Revision Description</th>
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<td>23-ID-02</td>
<td>N/A</td>
<td>This is the first standardized surveillance position statement for cCMV infection and disease.</td>
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</table>

XI. References


XII. Coordination

Subject Matter Expert (SME) Consultants:

PRIMARY SME
(1) Tatiana M. Lanzieri, MD, MPH
Medical Epidemiologist
Viral Vaccine Preventable Diseases Branch
Centers for Disease Control and Prevention
(404) 639-3031
tmlanzieri@cdc.gov

ADDITIONAL SMEs
(1) Kristen Nichols Heitman, MPH
Epidemiologist
Viral Vaccine Preventable Diseases Branch
Centers for Disease Control and Prevention
(404) 718-4670
knicholsheitman@cdc.gov
(2) Suresh B. Boppana, MD
Hugh Dillon MD Endowed Professor of Pediatrics
Heersink School of Medicine
University of Alabama at Birmingham
(205) 638-2630
sbboppana@uabmc.edu
(3) Gail J. Demmler-Harrison MD
Professor of Pediatrics
Division of Infectious Diseases
Baylor College of Medicine
(832) 824-4327
gdemmler@bcm.edu
(4) Karen B. Fowler, DrPH
Professor of Pediatrics
Heersink School of Medicine
University of Alabama at Birmingham
(205) 638-2549
karenfowler@uabmc.edu
(5) David W. Kimberlin, MD
Professor of Pediatrics
Co-Director, Division of Pediatric Infectious Diseases
The University of Alabama at Birmingham
(205) 638-2530
dkimberlin@uabmc.edu
(6) Pablo J. Sanchez, MD
Professor of Pediatrics
Nationwide Children's Hospital
The Ohio State University College of Medicine
(614) 355-6638
pablo.sanchez@nationwidechildrens.org
(7) Mark R. Schleiss, MD
American Legion and Auxiliary Heart Research Heart Research Foundation Professor of Pediatrics
University of Minnesota Medical School
(612) 626-9913
schleiss@umn.edu
(8) Kate Russell Woodworth, MD, MPH, FAAP
Medical Officer
Infant Outcomes Monitoring Research, and Prevention Branch
Centers for Disease Control and Prevention
(404) 718-1178
Vnt0@cdc.gov

Agencies for Response:
(1) Centers for Disease Control and Prevention
Mandy K. Cohen, MD, MPH
Director
1600 Clifton Road NE
Atlanta, GA 30329
(404) 639-7000
Jbc7@cdc.gov

Agencies for Information:
N/A
XIII. Author Information

Submitting and Presenting Author:
(1) Stephanie Browning McVicar, AuD, CCC-A
EHDI Programs Manager
Utah Department of Health and Human Services
195 N 1950 W
PO Box 144620
Salt Lake City, UT, 84114-4620
(801) 273-6600
smcvicar@utah.gov

Co-Authors:
(1) Active Member
Max Sidesinger, MPH
EHDI Epidemiologist/CMV Data Coordinator
Utah Department of Health and Human Services
195 N 1950 W
PO Box 144620
Salt Lake City, UT, 84114-4620
(801) 273-4125
msidesinger@utah.gov

(2) Active Member
Charla (Chas) DeBolt
Nurse Consultant Advisor for Vaccine Preventable Diseases Surveillance
Washington State Department of Health
Center for Public Health Medical & Veterinary Science
1610 NE 150th Street,
Shoreline, WA 98155
(206) 418-5500
Chas.DeBolt@DOH.WA.gov

(3) Active Member
Elizabeth Dufort, MD
Medical Epidemiologist
Minnesota Department of Health
601 N Robert Street
St. Paul, MN 55155
(651) 201-5414
elizabeth.dufort.contractor@state.mn.us

(4) Active Member
Tory Kaye, MPH
Epidemiologist
Minnesota Department of Health
601 Robert Street N
St. Paul, MN 55155
(651) 201-5515
tory.kaye@state.mn.us

(5) Active Member
Jessica Kumar, DO, MPH
Medical Director, Bureau of Immunizations
Division of Epidemiology, Center for Community Health
New York State Department of Health
ESP-Corning Tower, Room 651
Albany, NY 12237
(518) 473-4437
jessica.kumar@health.ny.gov

(6) Active Member
Nicole D. Longcore, MPH
Program Manager
New York State Department of Health
Division of Epidemiology
Empire State Plaza, Corning Tower, Room 503
Albany, NY 12237
(518) 474-2875
Nicole.Longcore@health.ny.gov

(7) Associate Member
Maryrose McInerney, PhD, CCC-A
Associate Professor
Montclair State University
1515 Broad Street
Bloomfield, NJ 07003
(973) 655-3406
mcinerneym@montclair.edu

(8) Active Member
Sondra D. Rosendahl, MS, LCGC
Newborn Screening Follow-up Supervisor
Minnesota Department of Health
601 Robert Street N
St. Paul, MN 55155
(651) 201-5922
sondra/rosendahl@state.mn.us
Table VI. Table of criteria to determine whether a case should be reported to public health authorities.

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Reporting cCMV infection or disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Criteria for Reporting</strong></td>
<td></td>
</tr>
<tr>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td><strong>Laboratory Criteria for Reporting</strong></td>
<td></td>
</tr>
<tr>
<td>Detection of CMV DNA by NAAT from infant† urine, saliva, whole blood (including DBS), or CSF specimen</td>
<td>S</td>
</tr>
<tr>
<td>Detection of CMV DNA by NAAT from amniotic fluid specimen</td>
<td>S</td>
</tr>
<tr>
<td>Isolation of CMV in viral culture from infant† urine, saliva, whole blood, or CSF specimen</td>
<td>S</td>
</tr>
<tr>
<td>Isolation of CMV in viral culture from amniotic fluid specimen</td>
<td>S</td>
</tr>
<tr>
<td>Demonstration of CMV antigen in a biopsy from umbilical cord or autopsy specimen by IHC</td>
<td>S</td>
</tr>
<tr>
<td>Detection of CMV antigen by antigenemia test in infant† whole blood specimen</td>
<td>S</td>
</tr>
<tr>
<td><strong>Epidemiologic Linkage Criteria for Reporting</strong></td>
<td></td>
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<tr>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td><strong>Vital Record Criteria for Reporting</strong></td>
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</tr>
<tr>
<td>An infant aged one year or less whose death certificate lists cCMV or CMV as an underlying cause of death or significant condition contributing to death</td>
<td>S</td>
</tr>
<tr>
<td><strong>Healthcare Record Criteria for Reporting</strong></td>
<td></td>
</tr>
<tr>
<td>A child aged 6 years or younger whose healthcare record contains a diagnosis* of cCMV infection</td>
<td>S</td>
</tr>
<tr>
<td>An infant aged 45 days or younger whose healthcare record contains a diagnosis* of CMV disease</td>
<td>S</td>
</tr>
</tbody>
</table>

Notes:
S = This criterion alone is SUFFICIENT to report a case.
† Infant is defined as less than one year of age.
*See Appendix 1 for diagnostic codes.
DBS, dried blood spot; CMV, cytomegalovirus; cCMV, congenital cytomegalovirus; CSF, cerebral spinal fluid; IHC, immunohistochemical methods; PCR, polymerase chain reaction (may also be called nucleic acid amplification test [NAAT])

Table VII.A. Classification Table: Criteria for defining a case of cCMV infection or disease.

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Case Classification</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>cCMV Infection</td>
</tr>
<tr>
<td></td>
<td>Confirmed</td>
</tr>
<tr>
<td><strong>Clinical Evidence</strong></td>
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</tr>
<tr>
<td>Hepatomegaly</td>
<td>O</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>O</td>
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<tr>
<td>Petechial rash or purpura (&quot;blueberry muffin rash&quot;)</td>
<td>O</td>
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<tr>
<td>Microcephal¥††</td>
<td></td>
</tr>
<tr>
<td>Brain imaging abnormalities*</td>
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<tr>
<td>Sensorineural hearing loss</td>
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<tr>
<td>Seizures</td>
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<tr>
<td>Cerebral palsy</td>
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<td>Chorioretinitis</td>
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<tr>
<td>Vision impairment¥</td>
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<tr>
<td>Absence of a more likely alternative etiology</td>
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<tr>
<td>Infant in neonatal period</td>
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<tr>
<td>Child aged 6 years or younger</td>
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</table>
Laboratory Evidence

<table>
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<th>Criterion</th>
<th>N</th>
<th>N</th>
<th>N</th>
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<tbody>
<tr>
<td>Absence of a negative test (CMV DNA by NAAT or culture) on a urine specimen collected within 21 days of life</td>
<td></td>
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</tr>
<tr>
<td>Detection of CMV DNA by NAAT from urine, whole blood (including DBS), or CSF collected within 21 days of life</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detection of CMV DNA by NAAT from amniotic fluid specimen</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation of CMV in viral culture from urine, whole blood, or CSF collected within 21 days of life</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation of CMV in viral culture from amniotic fluid specimen</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demonstration of CMV antigen in an autopsy specimen by IHC</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detection of CMV antigen by antigenemia test in whole blood collected within 21 days of life</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detection of CMV DNA by NAAT from saliva collected within 42 days of life§</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation of CMV in viral culture from saliva collected within 42 days of life§</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detection of CMV DNA by NAAT from urine, whole blood or CSF collected at 22–42 days of life</td>
<td>O</td>
<td>O</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation of CMV in viral culture from urine, whole blood, or CSF collected within 22–42 days of life</td>
<td>O</td>
<td>O</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Epidemiologic Linkage Evidence

| N/A |

Notes:

N = All “N” criteria in the same column are NECESSARY to classify a case.

O = At least one of these “O” (ONE OR MORE) criteria in each category (categories=clinical evidence, laboratory evidence, and epidemiologic evidence) in the same column—in conjunction with all “N” criteria in the same column—is required to classify a case.

†† Microcephaly is defined as head circumference measurement >2 standard deviations below the average (or <3rd percentile) for the same age and sex, notation in the medical record, or diagnostic code of microcephaly (e.g., ICD-10 code Q02).

* Brain imaging abnormalities consistent with cCMV, such as intracranial calcifications, periventricular calcifications, leukomalacia, polymicrogyria, lissencephaly, pachygyria, schizencephaly, ventriculomegaly.

† Vision impairments resulting from conditions consistent with cCMV, such as retinitis, retinal scarring, optic neuritis, optic atrophy, or brain damage resulting in cortical vision impairment.

§ If CMV is detected in saliva, repeat testing should be performed using urine.

DBS, dried blood spot; CMV, cytomegalovirus; cCMV, congenital cytomegalovirus; CSF, cerebral spinal fluid; IHC, immunohistochemical methods; NAAT, nucleic acid amplification test

Table VII.B. Classification Table: Criteria to distinguish a new case of cCMV infection from reports or notifications which should not be enumerated as a new case for surveillance.

<table>
<thead>
<tr>
<th>Criterion</th>
<th>cCMV Infection</th>
<th>cCMV Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>A case should be enumerated as a new case if not previously reported.</td>
<td>S</td>
<td>S</td>
</tr>
</tbody>
</table>

Council of State and Territorial Epidemiologists
Technical Supplement: 23-ID-02
Appendix 1. Diagnostic codes for case ascertainment of congenital cytomegalovirus (cCMV) infection for surveillance purposes.

### Diagnostic codes for Congenital Cytomegalovirus Infection and Cytomegalovirus Disease

<table>
<thead>
<tr>
<th>ICD-10-CM Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>P35.1</td>
<td>Congenital cytomegalovirus infection</td>
</tr>
<tr>
<td>B25.x</td>
<td>Cytomegaloviral disease</td>
</tr>
</tbody>
</table>

**Abbreviations:** ICD-10-CM, International Classification of Disease, 10th Revision

**Potential Data Sources.** Potential data sources for using ICD-10 (or future versions) diagnostic codes for ascertainment of cCMV cases for surveillance purposes include, but are not limited to, birth and death certificates, hospital inpatient, outpatient, or discharge records, and data from electronic medical records.

**Considerations:** Laboratory confirmation of cCMV should be performed on specimens collected within the first 21 days of life. If specimens are collected after 21 days, then it is challenging to distinguish congenital from postnatal infection. Researchers that have used administrative, hospital discharge, or electronic medical record data have typically used an interval of 30-90 days to ascertain potential cases of cCMV. Restricting case-finding to those infants with diagnostic codes within a certain period after birth will help to minimize the likelihood of ascertainment of postnatal CMV cases and allows for delays in conducting testing, submitting claims, or reporting results. In the absence of reporting of laboratory test results, case ascertainment using diagnostic codes may assist with cCMV surveillance and provide data to examine trends over time, although caution is recommended for interpreting findings due to several limitations outlined below.

**Limitations:** To date, the validity of diagnostic codes for cCMV surveillance has not been evaluated. Coding errors, under- or over-reporting, and inclusion of postnatal cases are possible. One study found that only 1 in 10 infants with laboratory-confirmed CMV infection within 21 days of life had a diagnostic code for cCMV. The extent to which the codes for congenital cytomegalovirus infection (ICD-10-CM code P35.1) and cytomegalovirus disease (ICD-10-CM code B25.x) are used interchangeably for cCMV disease during infancy is unknown. Unpublished analyses of administrative data using both conditions to identify cases among infants within 45 days of life indicate that 53-56% of infants have a cCMV infection code (P35.1) alone, 18-25% have a CMV disease code (B25.x) alone, and 21-28% have both codes.