# Perinatal Hepatitis C: Local Health Jurisdiction Public Health Investigation Protocol of Hepatitis C in Pregnant Persons and Perinatally Exposed Infants and Children

# I. What Is New?

This document makes the following updates to a 2021 protocol for local health jurisdictions (LHJs) investigating hepatitis C virus (HCV) in pregnant persons and perinatally exposed infants and children:

- Modified objectives now emphasize use of electronic laboratory reporting (ELR) data for case identification, the need to assure appropriate diagnostic testing for perinatally HCV-exposed infants and children (and their siblings if born to the same birthing parent), and the importance of treating birthing parents to cure their infections and prevent further HCV transmission.
- Incorporated 2023 U.S. Centers for Disease Control and Prevention (CDC) recommendations for testing perinatally exposed infants/children according to HCV status of their birthing parent (Table 1, page 4) and which tests should be ordered by age (Table 2, page 4).
  - Test infants exposed to HCV if the birthing parent has a reactive hepatitis C antibody test and a positive or unknown HCV RNA result, or a stand-alone HCV RNA positive test. (See Table 1 for testing recommendations if the birthing parent's test results are unknown.)
  - Test HCV-exposed infants for HCV RNA at 2-17 months of age or for HCV antibody with reflex to HCV RNA if ≥18 months of age and not yet tested.
- Updated guidance on perinatal HCV surveillance and case investigation, including on managing perinatal hepatitis C in the California Reportable Diseases Information Exchange (CalREDIE). Table 3 (page 6) summarizes actions needed in CalREDIE by infant HCV antibody and RNA test result.
- Added information on treating pregnant people with hepatitis C during pregnancy through shared decision making and on treating hepatitis C in children three years of age and older.
- Added resources with information on hepatitis C in pregnant people and in children (page 8).

# II. Background

Effective January 1, 2018, the Council of State and Territorial Epidemiologists (CSTE) created a nationally notifiable condition and public health surveillance case definition for "Hepatitis C, Perinatal," to capture HCV infections presumably transmitted from birthing parent¹ to child before, during, or immediately after birth. This California Department of Public Health (CDPH) protocol provides information for LHJs to review hepatitis C- related test results in children 2-36 months of age, apply the public health surveillance case definition, and conduct related case follow up.²

# III. Perinatal Hepatitis C Case Investigation Objectives

 Identify suspected perinatal hepatitis C cases among infants and children using electronic laboratory reporting (ELR) data and determine if a suspected case of perinatal hepatitis C meets the 2018 CSTE case definition criteria for a confirmed case of perinatal hepatitis C.

<sup>&</sup>lt;sup>1</sup> "Birthing parent" refers to the person who gave birth to the child.

<sup>&</sup>lt;sup>2</sup> Perinatal hepatitis C incidents should only be created for infants/children. For case follow up for pregnant persons with hepatitis C, please use the Local Health Department Follow Up tab in the pregnant person's chronic hepatitis C incident in CalREDIE. For more information on chronic hepatitis C case follow up, see <a href="Chronic Hepatitis C Follow Up for Priority Populations: Guidelines for Local Health Jurisdictions">CDPH, 2022</a>) (PDF) (cdph.ca.gov/Programs/CID/DCDC/Pages/STD-CalREDIE-Resources.aspx).

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- 2. Assure appropriate diagnostic testing for perinatally HCV-exposed infants and children (and their siblings if born to the same birthing parent) to identify confirmed HCV infections.
- 3. Report and classify perinatal hepatitis C cases in CalREDIE.
- 4. Assure appropriate linkage to care for children with confirmed perinatal hepatitis C infection.
- 5. Identify birthing parents of confirmed perinatal hepatitis C cases and assure they are linked to treatment (if not already treated), both to cure their infections and to prevent HCV transmission in future pregnancies.

# IV. Perinatal Hepatitis C Information

## Modes of Transmission

HCV is typically transmitted by percutaneous exposure to blood from a person with hepatitis C infection. Most new hepatitis C infections among adults in the United States are related to sharing injection drug use equipment. Less commonly, transmission also occurs through unregulated tattooing and piercing (e.g., in correctional facilities), sharing personal items with blood on them (e.g., razors) with a person with hepatitis C infection, or poor infection control in healthcare settings. <sup>3</sup> Infection via sexual contact or perinatal transmission are uncommon but possible and more likely in the presence of uncontrolled HIV coinfection. Many people with hepatitis C have no identifiable risk factors.

Transmission of HCV can occur during pregnancy or childbirth. The rate of transmission from a birthing parent with hepatitis C infection to their infant(s) is approximately 6-7 percent; 11-12 percent if the birthing parents who transmit hepatitis C to their infants also have poorly controlled HIV coinfection.<sup>4</sup> HIV viral load suppression may reduce the risk of vertical HCV transmission in pregnant persons with HIV/HCV coinfection.<sup>5</sup> Although detectable HCV RNA in a pregnant person is a known risk factor for perinatal transmission, the specific levels of HCV RNA or a specific HCV genotype are not known to be associated with additional increased risk for transmission.<sup>6</sup> However, increased HCV transmission may be associated with scenarios of membrane rupture six or more hours before delivery, the use of internal fetal monitoring (i.e., fetal scalp monitors), or following other invasive procedures (i.e., episiotomies, forceps delivery).<sup>6</sup> The risk of HCV infection is not significantly altered by the mode of delivery (i.e., vaginal or Caesarean/C-section).

There is currently no approved prophylaxis or treatment available to prevent vertical transmission of HCV infection or available data on the use of pangenotypic HCV treatment regimens during pregnancy. Per national guidelines: "Despite the lack of a recommendation, treatment can be considered during pregnancy on an individual basis after a patient-physician discussion about the potential risks and benefits. Treatment during pregnancy should be entered into the Treatment In Pregnancy for Hepatitis C Registry, an initiative supported by the U.S. Centers for Disease Control and Prevention (CDC) to record outcomes of mother (birthing parent)-infant pairs exposed to direct-acting antiviral medications

<sup>&</sup>lt;sup>3</sup> CDC. Hepatitis C Prevention and Control (cdc.gov/hepatitis-c/prevention/index.html).

<sup>&</sup>lt;sup>4</sup> U.S. Centers for Disease Control and Prevention (CDC). <u>CDC Recommendations for Hepatitis C Testing Among Perinatally Exposed</u> Infants and Children — United States, 2023. MMWR November 3, 2023;72(4);1–19.

<sup>&</sup>lt;sup>5</sup> Cabot C; et al. Mother-to-Child Transmission of Hepatitis C Virus (HCV) Among HIV/HCV-Coinfected Women. <u>J Pediatric Infect Dis Soc.</u> 2013 Jun; 2(2):126–135.

<sup>&</sup>lt;sup>6</sup> Association for the Advanced Study of Liver Diseases (AASLD)-Infectious Diseases Society of America (IDSA). Recommendations for testing, managing, and treating hepatitis C: <u>HCV in Pregnancy</u> (hcvguidelines.org/unique-populations/pregnancy).

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(DAAs) during pregnancy.

Breastfeeding/chestfeeding<sup>7</sup> does not increase HCV transmission, and currently both the American Academy of Pediatrics and the American College of Obstetricians and Gynecologists support breastfeeding/chestfeeding in HCV-infected parents. If nipples are cracked or bleeding, the breastfeeding/chestfeeding parent should stop nursing, bottle feed, and discard any milk that was pumped during the time when the nipples are cracked or bleeding and allow healing before resuming.<sup>8</sup>

HCV is not transmitted by casual contact in the absence of blood exposure. Families should not be forced to disclose a child's HCV infection status, and children should not be restricted from any routine childhood activity. Parents should be informed that universal precautions should be followed at school and in the home of children with HCV infection, such as avoiding the sharing of toothbrushes, razors, and nail clippers, and any blood spill (including dried blood) should be cleaned up using a dilution of one part household bleach to ten parts water by a person wearing gloves during the entire clean up. 10

# Clinical Symptoms<sup>11</sup>

Signs and symptoms of perinatally transmitted hepatitis C infection may range from asymptomatic to fulminant hepatitis. At least half of infants infected with hepatitis C at birth may have no symptoms, but some may still be experiencing liver damage.<sup>3</sup> If symptoms do occur among infants and children, they may include:

- Clay-colored or pale stools
- Dark urine
- Failure to gain weight
- Fever
- Loss of appetite
- Nausea and vomiting or diarrhea
- Slow growth
- Tiredness
- Yellow skin and eyes (jaundice)

## **Incubation Period**

For people who develop symptoms following exposure to HCV, the average period from exposure to symptom onset is 2-12 weeks (range: 2-26 weeks).<sup>3</sup> Information on the incubation period in infants exposed to hepatitis C at birth is limited.

# **Period of Transmission**

Persons with detectable HCV RNA remain infectious. Information on infectiousness of infants exposed to hepatitis C at birth during the first two months of age before HCV RNA testing can be conducted is limited.

<sup>&</sup>lt;sup>7</sup> The term chestfeeding is used for masculine or gender non-binary identified people feeding their baby from their chest.

<sup>&</sup>lt;sup>8</sup> University of Washington. Hepatitis C Online: Core Concepts - Counseling for Prevention of HCV Transmission. (Hepatitisc.uw.edu).

<sup>&</sup>lt;sup>9</sup> AASLD-IDSA. Recommendations for testing, managing, and treating hepatitis C: <u>HCV in children</u> (hcvguidelines.org/unique-populations/children).

<sup>&</sup>lt;sup>10</sup> University of Washington, Hepatitis C Online: <u>Household HCV Transmission</u> (hepatitisc.uw.edu/go/screening-diagnosis/counseling-prevention/core-concept/all#household-hcv-transmission)

<sup>&</sup>lt;sup>11</sup> Hepatitis C - children Information | Mount Sinai - New York

# **Testing for Perinatally Exposed Infants and Children**

Hepatitis C antibody indicates past or present infection, although children exposed to hepatitis C may retain transient hepatitis C antibody from their birthing parent until 18 months of age. Passively acquired antibodies from the birthing parent for HCV are cleared in 95% of children by 12 months of age. <sup>12</sup> HCV RNA indicates current infection and can be detected in infants as young as 2 months of age. CDC recommends HCV testing for all infants and children born to pregnant persons with current or probable HCV infection.

Table 1: CDC Recommendations for Testing Infants/Children Born to Birthing Parents with the Following Laboratory Results<sup>4,13</sup>

Birthing Parent HCV Antibody (anti-HCV) Status During Pregnancy	Birthing Parent HCV RNA (viral load) Status During Pregnancy	Test Infant or Child	
Reactive	Detected	Yes	
Reactive	Missing/unknown	Yes	
Reactive	Not detected	No	
Missing/unknown	Missing/unknown	See notes <sup>14</sup>	
Nonreactive/missing/unknown	Detected	Yes	
Nonreactive	Not detected	No	
Nonreactive	Missing/unknown	See notes <sup>15</sup>	

Table 2: HCV Tests Indicated for Perinatally Exposed Infants and Children, by Age and Test Type

Infant/Child Age	HCV Antibody (anti-HCV) Test <sup>16</sup>	HCV RNA (viral load) Test	
< 2 months <sup>17</sup>	No	No	
2-6 months <sup>18</sup>	No	Yes	
7-17 months	No	Yes <sup>19</sup>	
≥ 18 months <sup>20</sup>	Yes	Yes <sup>19</sup> (reflex testing)	

# **Natural History**

Approximately 25 to 50 percent of infants infected with hepatitis C spontaneously resolve HCV infection

<sup>&</sup>lt;sup>12</sup> Jarasvaraparn, C; et al. Updated Clinical Guidelines on the Management of Hepatitis C Infection in Children. Pathogens. 2024; (2):180. https://doi.org/10.3390/pathogens13020180.

<sup>&</sup>lt;sup>13</sup> As resources allow, review birthing parent's HCV test status to determine if an infant or child should be tested.

<sup>&</sup>lt;sup>14</sup> If birthing parent HCV test results are missing/unknown, test at delivery. If unable to test birthing parent, consider testing the child for HCV RNA at two months of age (e.g., children in foster care or infants who were safely surrendered after birth).

<sup>&</sup>lt;sup>15</sup> False negative (i.e., nonreactive) anti-HCV may occur within the first 6 months (i.e., window period) of an acute HCV infection. If a birthing parent has symptoms consistent with acute HCV infection during pregnancy or at delivery, test birthing parent for HCV RNA. If HCV RNA testing was not performed, consider testing infant/child for HCV RNA at 2 months of age.

<sup>&</sup>lt;sup>16</sup> HCV antibody testing for children under 18 months of age is <u>not recommended</u> due to transient birthing parent HCV antibody.

<sup>&</sup>lt;sup>17</sup> Reliability of detecting HCV RNA before two months of age has not been established.

<sup>&</sup>lt;sup>18</sup> Testing infants and children 2-6 months of age with a nucleic acid test (NAT) for HCV RNA (rather than waiting to test for HCV antibody with reflex to HCV RNA at 18 months) may help reduce loss to follow-up. Those with an undetectable HCV RNA do not require follow-up testing unless clinically indicated.

<sup>&</sup>lt;sup>19</sup> HCV RNA testing should be done if not already tested.

<sup>&</sup>lt;sup>20</sup> Children ≥18 months of age not previously tested should receive an HCV antibody test with reflex to NAT for HCV RNA.

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by 4 years of age without treatment (as evidenced by undetectable HCV RNA) and do not develop chronic hepatitis C infection. However, those who do not spontaneously clear the virus on their own will have HCV RNA and remain infectious unless treated and cured.

Liver disease due to chronic HCV infection generally progresses slowly in children, and cirrhosis and liver cancer occur infrequently. However, liver disease progresses over time with increasing fibrosis severity and children have a long life expectancy during which complications may develop.

# **Treatment**

Highly effective, all oral, DAAs have been approved by the U.S. Food and Drug Administration (FDA) to treat and cure hepatitis C in children, adolescents, and adults, beginning at 3 years of age and older. Treatment lasts 8-12 weeks and has minimal side effects, with cure rates >95%.

# V. <u>Perinatal Hepatitis C Case Definition</u>

# 2018 CSTE/CDC Confirmed Perinatal Hepatitis C Case Definition<sup>21</sup>:

HCV ribonucleic acid (RNA) positive test for infants between 2 to 36 months of age; **OR** HCV antigen<sup>22</sup> positive test for infants between 2 to 36 months of age or greater; **OR** HCV genotype positive test for infants between 2 to 36 months of age or greater; **AND** Is not known to have been exposed to HCV via a mechanism other than perinatal.

# VI. Perinatal Hepatitis C Case Reporting and Investigation Protocol

- 1. In CalREDIE, if there is a child ≤36 months of age with an Acute or Chronic HCV incident, change the Disease Being Reported (located in the Patient tab) to "Hepatitis C, Perinatal".
- 2. If the child is under two months of age, leave the perinatal incident open as "Suspect".
- Follow up when the child will be two months of age to ensure appropriate testing occurs as outlined in Table 2.
- 3. If the child is 2-36 months of age, confirm whether the perinatal HCV case definition is met.
- Review relevant clinical and laboratory information where available and contact the reporting provider to request follow up testing if needed. It is still common for infants and children not to receive appropriate testing (as shown in Table 2). If there are HCV antibody results done at <18 months of age or HCV RNA tests done at <2 months of age, please ensure provider is aware that appropriate testing consistent with current recommendations still needs to occur.<sup>23</sup> See **Table 3** for guidance on how to proceed based on available results.

<sup>&</sup>lt;sup>21</sup> Hepatitis C, Perinatal Infection 2018 Case Definition | CDC

<sup>&</sup>lt;sup>22</sup> When and if a test for HCV antigen(s) is FDA approved and available

<sup>&</sup>lt;sup>23</sup> LHJs can send a letter to providers referencing updated perinatal HCV testing recommendations and guidelines as soon as an initial test result is received. Waiting until 18 months of age or 36 months of age to connect infants and children to testing often results in loss to follow-up.

Table 3: HCV Test Results, Follow Up Testing Required, and Case Status in CalREDIE

Child Age	HCV Antibody (anti- HCV) Test Result	HCV RNA or Genotype Test Result	CalREDIE Resolution Status	Action Needed
2-36 months	Reactive HCV antibody only	Unknown	Suspect	Change the Resolution Status (in the Case Investigation tab) to "Suspect." Check to see if existing test results/medical records are available and then call the ordering provider for any outstanding results and to ask them to order HCV RNA testing as needed. Leave case as Suspect until you receive additional results.
2-36 months	Reactive or unknown	HCV RNA or genotype detected	Confirmed	Change Resolution Status to "Confirmed." If child subsequently tests HCV RNA negative, case should remain "Confirmed" to maintain accurate confirmed case counts over time. See protocol for patient case follow up and share recommendations with the child's and birthing parent's healthcare provider(s).
2-36 months	Reactive or unknown	HCV RNA negative only (with no previous known detected HCV RNA or genotype)	Not a Case	Change Resolution Status to "Not a Case." No clinical follow up needed. If possible, assure HCV testing for infant's siblings and birthing parent and, if positive for HCV RNA, linkages to care.

# 4. Merge subsequent HCV laboratory test results.

- Subsequent HCV laboratory test results for an existing perinatal hepatitis C case will not automatically append to that case's existing perinatal hepatitis C incident because all HCV-related ELRs coming into CalREDIE are auto-processed as suspect chronic hepatitis C. New HCV laboratory results relevant to perinatal hepatitis C cases will be entered into CalREDIE as a new suspect chronic hepatitis C disease incident. These newly created chronic hepatitis C disease incidents will need to be manually appended to the perinatal hepatitis C incident.
  - Example: A one month old child received a positive HCV antibody test result. The LHJ changed the child's chronic hepatitis C disease incident into a perinatal HCV incident and temporarily classified the child as a "Suspect" case. At six months of age, the child was tested for HCV RNA and a positive test result was submitted to CalREDIE via ELR as a new chronic HCV disease incident.
- Use CalREDIE Alerts to flag incoming chronic HCV incidents for anyone under 3 years of age.
- If new test results come in for a previously reported perinatal hepatitis C case (or one that is under investigation), change the disease incident for the newly reported test results to "Hepatitis C, Perinatal". Merge the two perinatal HCV incidents to add the new labs to the original incident. When merging, select the original incident ID, original Patient tab, original Epidemiologic Info tab, and original Contacts tab. (For more information on merging two incidents in CalREDIE, see the CalREDIE User Guide in the CalREDIE Document Repository.)

# 5. Recommended: Identify the infant's birthing parent.

- If the birthing parent has a CalREDIE ID, then link birthing parent to the perinatal hepatitis C incident in the perinatal hepatitis C incident Epi Info tab or click "Link Patient" to search for and select an existing CalREDIE profile. Click "OK" and save.
- You may create an acute or chronic HCV disease incident for the birthing parent if they have no existing disease incident in CalREDIE to either save clinical or laboratory information in CalREDIE or link the birthing parent to testing and/or treatment. **Do not** create a perinatal HCV disease incident for the birthing parent.
- If the birthing parent does not have a CalREDIE ID, then enter the birthing parent's contact information in the perinatal hepatitis C incident Contacts tab.

# 6. Recommended: Share <u>clinical management recommendations</u> with the child's and birthing parent's healthcare provider(s).

- The American Association for the Study of Liver Diseases & Infectious Diseases Society of America (AASLD-IDSA) has <u>published guidelines</u> for the clinical management and treatment of perinatal HCV infection.
- Hepatitis C DAA therapies have been FDA-approved for children > 3 years of age.
  - AASLD-IDSA guidelines recommend a confirmatory NAT for HCV RNA before initiation of DAA therapy.
  - Children with hepatitis C infection should be routinely monitored for disease progression by a regular healthcare provider who has the capacity to refer patients to a specialist, such as a pediatric hepatologist or gastroenterologist.
  - If still infected with hepatitis C at 3 years of age, children should be linked to curative hepatitis C treatment. LHJs should contact the child's pediatrician once the child is 3 years of age to recommend HCV RNA testing and inform the clinician of the child's eligibility for treatment.
  - If LHJs have capacity, they may also wish to conduct case investigation of pediatric cases of acute or chronic hepatitis C between 3 and 18 years of age to ensure appropriate testing and linkage to care.
- HCV treatment is not yet FDA approved for people who are pregnant but is being studied.
  - If treatment during pregnancy is considered on an individual basis following a
    patient-physician discussion about the potential risks and benefits, it should be
    entered into the Treatment In Pregnancy for Hepatitis C Registry, a CDC-supported
    initiative to record outcomes of mother (birthing parent)-infant pairs exposed to
    DAAs during pregnancy.
  - Birthing parents of children with perinatal HCV should be offered HCV treatment before becoming pregnant again to promote their own health and to prevent future perinatal transmission of HCV in subsequent pregnancies.
- Other recommendations may include:
  - If born to the same birthing parent, the siblings of children with perinatal HCV should be tested for HCV infection.
  - Repetitive HCV RNA testing in perinatal HCV-exposed infants prior to 18 months of age is not recommended.
  - Vaccination of birthing parent for hepatitis A and B and testing for HIV and HBV should be performed on all individuals whose status is unknown.

# 7. Recommended: Document linkage to care.

- Document status of child's linkage to care and contact information for the child's health
  care provider in the perinatal hepatitis C Epi Info tab. For reference, the perinatal
  hepatitis C case report form, which includes the information collected on the Epi Info tab,
  can be found on the <u>California Department of Public Health website</u>
  (cdph.ca.gov/Programs/PSB/Pages/CommunicableDiseaseControl.aspx).
- If the birthing parent has a chronic hepatitis C incident in CalREDIE, then record the birthing parent's linkage to care and treatment information in the birthing parent's chronic hepatitis C incident, health department follow up tab.

If it is suspected that a hepatitis C case may be healthcare-associated (i.e., needlestick injuries or lack of adherence to standard precautions), LHJs may contact the CDPH Sexually Transmitted Diseases (STD) Control Branch and the CDPH Healthcare-Associated Infections (HAI) Program. Together, they can help LHJs determine whether and how to proceed with further investigation. STD Control Branch Contact: (510) 620- 3400 (main phone line); confidential fax (916) 440-5970. HAI Contact: HAIProgram@cdph.ca.gov.

# VII. Resources

- Hepatitis C, Perinatal Infection 2018 Case Definition | CDC (ndc.services.cdc.gov/case-definitions/hepatitis-c-perinatal-infection-2018/)
- Hepatitis C Questions and Answers for Health Professionals | CDC (cdc.gov/hepatitis/hcv/hcvfaq.htm)
- CDC Recommendations for Hepatitis C Testing Among Perinatally Exposed Infants and Children
   United States, 2023 | MMWR (cdc.gov/mmwr/volumes/72/rr/rr7204a1.htm)
- HCV in Children | HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C (hcvguidelines.org/unique-populations/children)
- <u>Hepatitis C Information for Children and Teens</u> (liverfoundation.org/wp-content/uploads/2023/08/Hep-C-FOR-Kids\_Fact-Sheet.pdf)
- <u>Updated Clinical Guidelines on the Management of Hepatitis C Infection in Children,</u>
   <u>Pathogens</u> (mdpi.com/2076-0817/13/2/180)
- <u>CDPH Viral Hepatitis Clinical Guidelines</u> (cdph.ca.gov/Programs/CID/DCDC/Pages/ViralHepatitis-ClinicalGuidelines.aspx)
- <u>California Reportable Disease Information Exchange (CalREDIE) Document Repository (PDF)</u>
   (calredie.cdph.ca.gov/WebCMR/Pages/SystemAdmin/ExternalWebPage.aspx?URL=%2F
   ClientSpecificFiles%2FDocuments%2FRepository%2FRepository.html&Banner=Document%20
   Repository)
- <u>Treatment in Pregnancy for Hepatitis C (TiP-HepC) Clinical Case Registry</u> (globalhep.org/projects-research/treatment-pregnancy-hepatitis-c-tip-hepc- registry)